

# WHO Drug Information

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## Contents

### Herbal Medicines

Herbal medicinal products in the European Union	115
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### Current Topics

Miltefosine registered for visceral leishmaniasis in India	119
Tetanus vaccine pre-filled injection device	119
Nonoxinol 9 ineffective in preventing HIV infection	120
New formula oral rehydration salts	121
International AIDS Society recommendations for antiretroviral treatment: adult HIV infection	122

### Good Clinical Practices

Development of Chinese good clinical practices (GCP)	125
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### Safety Information

Statins: rhabdomyolysis and myopathy	130
Tamoxifen and risks of thromboembolic events	132
Oral contraceptives and risk of cervical cancer	132
HIV-associated lipodystrophy syndrome overview	132

### Regulatory Action

Alosetron hydrochloride: restricted marketing	135
Baclofen: abrupt discontinuation dangerous	135
Irinotecan: prescribing changes	135
Sodium oxybate/GHB approved for cataplexy	136
Rofecoxib: new indication and label changes	136

### Essential Medicines

New procedures for updating the Model List of Essential Medicines	138
Core Model List	139
Complementary Model List	151

### Recent Publications and Sources of Information

Genomics and world health	155
Legal status of traditional and complementary medicine	155
Kinetoplastid research source launched	155
Endocrine disrupting chemicals	156

### Proposed International Nonproprietary Names: List 87

157

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# Herbal Medicines

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## Herbal medicinal products in the European Union

European pharmaceutical law classifies herbal products as "regular" medicinal products if they claim to treat or prevent illness or if they are to be administered with a view to restoring, correcting or modifying physiological functions (1). Several decisions of the European Court of Justice confirm this status. There are examples where a herbal preparation, such as peppermint tea, could be either food or medicine, depending on the claim made for the product. In other cases, such as for senna extract, a product has to be declared a medicine (notwithstanding the labelled claim) by virtue of its pharmacological action: in this case that of a laxative stimulant. The characteristics of herbal medicinal products make regulatory assessment difficult and present a challenge to health agencies and national authorities.

For centuries, herbal medicinal products have been part of cultural heritage. This may be one reason why herbal medicinal products continue to be widely used in Germany. In a recent study, more than 70% of the German population declared that they used natural medicines, and for most of them herbal medicinal products were the first choice in the treatment of minor diseases or disorders (2). With 39% of the total European market, the German market holds the biggest share by value, followed by France (29%), Italy (7%), Poland (6%) and the United Kingdom (6%). It is important to stress that in Germany and some other European Union countries, herbal medicines are fully integrated into conventional therapies, especially by general practitioners. The share in the prescribed herbal medicines market is 73% in France, 43% in the United Kingdom and 38% in Germany. Herbal medicinal products are found among the top 200 of the 2000 most prescribed medicines that were reimbursed by state-supported health insurances in the year 2000 (3). As an example, a product com-

posed of *Saccharomyces* yeast used for the symptomatic treatment of diarrhoea holds rank 51 with 1.5 million prescriptions, whereas the most popular brand antidiarrhoeal, loperamide, is placed at 145 with 851 000 prescriptions. By value, the most important herbals are ginkgo leaves, hypericum, ivy (*Hedera helix*), mistletoe, hawthorn, saw palmetto and horse chestnut.

These data show that herbal medicines are rightly classified as medicinal products because they are used as such. Another reason involves the risks that may be associated with these products. Some herbal medicines may present risks even when properly used. Such risks are mostly mild and can be avoided by appropriate labelling. However, in some cases, the withdrawal of products from the market has been necessary because serious reactions were identified.

An increasing problem is the potential interaction of herbal medicinal products with conventional medicines: the most prominent example here is hypericum. Such risks have to be carefully assessed, balanced against potential benefits and clearly labelled for consumers and health professionals in order to protect public health. Such an approach can be enforced if herbal medicines are subject to pharmaceutical legislation.

An additional aspect that makes herbal products a very special group is the particular character of the quality requirements. Herbal products are, even if they contain only one herb, very complex biological mixtures and in most cases it will not be possible to identify a certain chemical constituent responsible for the efficacy of the product in question. Consistent production parameters and process validation become increasingly important to achieve reproducible efficacy. Because of this complexity, strict quality control is a prerequisite for safety. There are plenty of examples where insufficient quality control has led to toxic effects, such as by contamination with heavy metals or adulteration with toxic plants.

Since many herbal products rely on traditional use, only very few new clinical studies are available. Industry is not motivated to perform such studies, because the results cannot be patented and protec-

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*Lecture presented at the 26th International Conference on Internal Medicine, Kyoto May 25-30, 2002, by Konstantin Keller, Federal Institute for Drugs and Medical Devices, Bonn, Germany, and Chair of the EMEA / CPMP Herbal Medicinal Products Working Party.*

tion of intellectual property is practically absent. Clinical trials with herbal medicinal products pose specific difficulties. For essential oils, blinded studies are not feasible because of their strong smell and taste. Recent studies with hypericum in major depression demonstrate that in studies with an active comparator, sertraline in the case of hypericum, the comparator was unblinded due to side effects (6). This makes the interpretation of results very difficult. Finally, anyone who has been involved in the design of clinical trials will agree that trials that are particularly important for herbal medicines (i.e. symptomatic treatment of minor conditions in an over-the-counter (OTC) environment) are most difficult to plan and perform.

### Regulatory action

These specific challenges were acknowledged at the Eighth International Conference of Drug Regulatory Authorities (ICDRA), in Bahrain in 1996. WHO Member States were encouraged to establish groups of experts for herbal medicines in their own countries and regions and to update national legislation in order to allow registration of herbal medicinal products. This was reconfirmed at the Ninth ICDRA in Berlin in 1999.

In 1996, the European Parliament requested facilitated systems for marketing of herbal medicinal products; and in 1997 a specific Herbal Medicinal Products Working Party was created at the European Medicines Evaluation Agency (EMA). A permanent working group is now composed of delegates from all member countries of the European Union, experts and observers from future new member countries, the European Commission, European Parliament and European Pharmacopoeia.

The main focus of the group is to facilitate mutual recognition of marketing authorizations within the European Union by preparing guidance for documentation and assessment of quality, safety and efficacy of herbal medicines. In addition to these tasks, the group may give advice on pharmacovigilance action and on future legislation. All documents prepared by the group are available from <http://www.emea.eu.int>. The work of the group is complemented by the European Pharmacopoeia that has established two working parties to prepare general and specific monographs on herbal drugs. These monographs are fully integrated into the official European Pharmacopoeia.

### Quality assurance

Quality assurance and control of herbal medicinal products has to start at a very early stage, i.e. at collection or agricultural production of a medicinal herb. A specific guideline addressing this aspect was published recently. Two other documents defining criteria on how to test quality and how to set appropriate specifications are available as well. One important part of both guidelines is the glossary that explains how the term "herbal medicinal product" is defined in the European Union. It should be understood that isolated constituents such as digoxin, taxol, or menthol are not classified as herbal drug preparations.

### Safety and efficacy

The most controversial topic relates to assessment of the safety and efficacy of herbal medicines. The European Union facilitates the registration of well-established and traditional herbal medicinal products by permitting different types of applications for marketing authorization.

Herbal medicines may be authorized on the basis of new pre-clinical tests and new clinical trials. This type of full dossier application is mandatory for any new product, including herbals. The same type of dossier is required if a completely new indication is requested for a product that has already been marketed for a different use. However, if the product has "well-established medicinal use with recognized efficacy and an acceptable level of safety" an applicant may substitute new tests and trials by reference to bibliographic data.

The concept is based on the idea that long-term use in humans will probably have resulted in sufficient and even more reliable experience than animal experiments could ever provide. Factors that have to be taken into account are the time and extent of use, the amount and quality of bibliographic information and the consistency of that information. A minimum time frame of ten years of medicinal use within the EU is requested.

The European Herbal Medicinal Products Working Party has clarified the extent of pre-clinical data that are required for a bibliographic application for a herbal medicinal product: new studies should concentrate on effects that are difficult — or even impossible — to detect clinically. This includes data on mutagenicity / genotoxicity, toxicity on reproduction and carcinogenicity. If sufficient experience in

humans can be extracted from the literature, tests such as single dose toxicity, repeated dose toxicity, immunotoxicity and local tolerance are not required. Due to the complex composition of herbal medicinal products, pharmacokinetic studies are not required unless there are safety concerns.

A specific guideline addresses the assessment of efficacy. The strategy is to follow the concept of evidence-based medicine and to require evidence that will relate to the type of claim, e.g. treatment of symptoms, cure or prophylaxis of disease, etc. and seriousness of diseases. For the treatment of symptoms in minor disorders, a lower level of evidence will be acceptable if experience with a particular herbal medicinal product is well documented and plausible on the basis of pharmacological data. However, such an approach can only be accepted if the product does not present any risk to the consumer / patient. For more serious conditions, or if the product may present any direct risk, a higher level of evidence must be provided and the therapeutic alternatives have to be carefully considered.

This concept is in line with WHO guidelines (5) published in 2001, and similar approaches in other countries, such as Australia. On the basis of this concept, agreement has been reached for a number of herbal drugs, and core data have been published. These core data give a summary of the herbal product characteristics, including indications, contra-indications, side effects, warnings, etc. An example would be isphagula husks, where different levels of evidence support three different indications.

Despite the fact that these two types of marketing authorization will be appropriate for a great number of herbal medicinal products, especially those covered by monographs published by the WHO (6) or the European Scientific Cooperative on Phytopharmaceuticals, ESCOP, (7) it is evident that there will be traditional herbal medicinal products that do not dispose of sufficient bibliographic evidence. As an example, the hop plant has been used as a mild sedative for centuries but experimental or clinical data are virtually absent. The question was raised whether such products should be classified as food or whether a third level should be introduced under pharmaceutical law.

The European Union has decided to introduce a new category of traditional medicines into pharma-

ceutical legislation and a proposed Directive is about to be discussed by the European Parliament (8). The benefit of this regulation will be that traditional medicines are classified, labelled and controlled as medicines. This will include strict quality control, compliance with good manufacturing practice (GMP), control of safety, and application of all rules and regulations related to pharmacovigilance.

Herbal medicinal products that have been used for at least 30 years, with a minimum of 15 years in the European Union, will be eligible for registration as a traditional medicinal product. In respect of quality-related data, such registration will be identical to full marketing authorization. The applicant has to submit bibliographic evidence that the product is safe. For the documentation of efficacy, the applicant must produce expert evidence of the traditional use that makes the claim of efficacy plausible — even though scientific evidence is not available. A new committee will be set up to publish European lists of traditional herbal substances and monographs on traditional and well-established herbal medicinal products. These lists and monographs will serve as the basis of any marketing authorization within the EU unless new evidence is submitted.

This threefold requirement for more complete evidence for new products and for treatment options in serious diseases, lesser evidence for minor claims, and allowing a “traditionally used” label for really traditional herbal medicinal products, will guarantee protection of consumers from fraudulent and unsafe herbal medicines while allowing access to well-founded and safe treatment options.

In summary, the European experience is that herbal medicines are rightly classified as medicinal products because they are used in the same way as any other medicine, they may have risks that must be identified, assessed and labelled as with any other medicine; they have clear pharmacological effects and need, probably more than many chemically defined pure substances, strict quality control and adherence to GMP.

To do this, specific experience and expertise is needed coupled with fair assessment of long-term experience; while marketing authorization procedures have to be adapted to this special group of medicines.

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**References**

1. Directive 2001/83/EC of the European Parliament and of the Council of 6 November 2001. Community Code relating to Medicinal Products for Human Use. *Official Journal*, Number L 311, 28 November 2001. <http://pharmacos.eudra.org>
2. Institut für Demoskopie Allensbach: *Naturheilmittel* (2002) [www.ifd-allensbach.de](http://www.ifd-allensbach.de)
3. Schwabe, U., Paffrath, D. *Arzneiverordnungsreport* 2001, Springer-Verlag, Berlin, 2001.
4. Hypericum Depression Trial Study Group. *Journal of the American Medical Association*, **287**: 1807–1814 (2002).
5. World Health Organization. *General Guidelines for Methodologies on research and evaluation of traditional medicine*. WHO/EDM/TRM/2001.1 (2001)
6. World Health Organization. *WHO monographs on selected medicinal plants*, Volume I (1999)
7. <http://www.phytotherapy.org>
8. Commission of the European Communities. Proposal for a directive of the European Parliament and of the Council amending the Directive 2001/83/EC as regards traditional herbal medicinal products, January 17, 2002. <http://pharmacos.eudra.org>

# Current Topics

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## Miltefosine registered for visceral leishmaniasis in India

Scientists have developed a new treatment for visceral leishmaniasis — a disease also known as "black fever" and "kala azar". The new drug, miltefosine (Impavido®) could potentially save most of the 60 000 people who die from the disease every year. Miltefosine is likely to cost less and is much easier to deliver than all current therapies. In clinical trials, it cured 95% of treated patients.

Miltefosine is the first oral drug against leishmaniasis. It moved from the laboratory bench through to registration in 6 years (most medicines take twice as long) thanks to collaboration between the Government of India, the drug's manufacturer, German biopharmaceutical company Zentaris, and TDR (Tropical Diseases Research), a programme co-sponsored by UNDP, the World Bank, and WHO. Miltefosine has now been approved for use in India, which has 50% of the global burden of visceral leishmaniasis. With this drug, the Government of India hopes to reach its goal of eliminating leishmaniasis by 2010.

Leishmaniasis is a parasitic disease transmitted through the bite of the sandfly. The disease is found in 88 countries. While the 350 million people living in these areas are the most vulnerable, others at risk are travellers, vacationers, missionaries, development workers and soldiers. The regions where leishmaniasis is endemic have expanded significantly since 1993. Mass population movements are fuelling the growing epidemic. Major outbreaks in Brazil, for example, were triggered by large migrations of rural populations to the suburbs of the country's largest cities. An outbreak in Sudan killed 100 000 in an area with a population of less than 1 million. More recently, co-infections of leishmaniasis and HIV are becoming more common. The interaction of the two diseases makes each more destructive, accelerating the onset of AIDS and shortening the life of HIV-infected people.

Until now, all treatments for the disease have had substantial drawbacks. Some are toxic and can cause permanent damage such as diabetes. Up to 60% of cases in India are now resistant to the first-

line drug. Other drugs trigger dangerous reactions that can be lethal in about 9% of patients. Some treatments require injections while others need to be provided intravenously over a period of 15 to 30 days in hospital. And all are so expensive that the people infected are unable to afford them.

Asta Medica originally developed miltefosine to fight breast cancer, but TDR scientists discovered that it also had an effect on the leishmaniasis parasite. No drug is without some side effects. The drug can induce vomiting, but this is not strong and usually limited to a few days. Due to a potential danger to the foetus, care must be taken when administering the drug to women of child-bearing age. Studies are under way in India to assess how well the drug performs in a real life situations and its potential long term impact on the control of leishmaniasis.

Researchers hope the future will yield better methods of diagnosing visceral leishmaniasis. In many tropical settings, the high fever brought on by the disease is easily confused with malaria. An easy to use test would greatly facilitate visceral leishmaniasis control. Trials, supported by TDR, of such diagnostic kits are now under way in Ethiopia, Kenya and Sudan.

**Reference:** *Weekly Epidemiological Record*, 77: 210–212 (2002) and <http://www.who.int/tdr>

## Tetanus vaccine pre-filled injection device

UNICEF has announced concentrated efforts to deliver a vaccine against maternal and neonatal tetanus in an effort to potentially save the lives of thousands of women and their newborn children. The first campaign, begun in Mali, is being enhanced by the introduction of a pre-filled injection device that will make it easier to immunize women in remote areas. The new device is a single dose, pre-filled syringe with tetanus toxoid that can be administered by lay people.

Maternal and neonatal tetanus can be eliminated globally through immunization and hygienic birth practices. But it has often been difficult to reach

women and children in remote communities since the traditional vaccine can only be administered by trained health workers. As a result, last year alone, tetanus claimed the lives of 200 000 newborns and 30 000 women in 57 developing countries.

Since lay people can use the new device, traditional birth attendants, teachers and community workers are being trained to support health workers in immunizing women in communities without access to clinics or health centres.

The pre-filled device has additional advantages:

- It is a single-use needle and syringe, reducing the possibility of transmission of blood-borne diseases such as HIV and hepatitis.
- It has a very small needle, about an inch long, making it easier to dispel fears of needles and vaccinations.

UnijectT® is manufactured by Becton, Dickinson and Company and Bio Farma produces the vaccine and fills the syringe. The two companies have jointly donated 9 million units to UNICEF over the next three years for use in the collaborative effort to eliminate maternal and neonatal tetanus.

The global campaign to eliminate maternal and neonatal tetanus is being spearheaded by Ministries of Health, UNICEF, WHO, UNFPA, PATH, BASICS, Save the Children (US) and other partners. The Maternal and Neonatal Tetanus Elimination Initiative has received major donations from the Government of Japan, the US Fund for UNICEF, the UK National Committee for UNICEF, Ronald McDonald House Charities, The Bill and Melinda Gates Foundation, and Becton Dickinson.

### **About maternal and neonatal tetanus**

Neonatal tetanus is a deadly disease, common in poor countries, mostly affecting populations with little or no access to basic health care services and education. The disease, which was eliminated in the industrialized world as far back as the 1950s, is still a major killer of infants in the developing world, responsible for no less than 200 000 infant deaths every year and accounting for 14% of all neonatal deaths.

Up to 70% of all babies that develop the disease die in their first month of life. Tetanus occurs as a result of unhygienic birth practices, leading to contamination of the umbilical cord with tetanus

spores when it is being cut or dressed after delivery. The disease usually presents itself on the third day after birth, causing the baby to stop feeding due to stiffness of the jaw muscles. The baby then goes into painful convulsions, coma and eventually dies.

Maternal tetanus is also caused by contamination from tetanus spores through puncture wounds, and is linked to unsafe and unclean deliveries. Maternal tetanus is responsible for at least five per cent of all maternal deaths, and accounts for up to 30 000 deaths each year.

Unlike smallpox and polio, complete eradication of tetanus is not possible as the tetanus spores can survive outside the human body, in dirt and in the stools of infected people and animals. The disease can be transmitted without any human contact. Over the 2-year period since the Initiative began (in 1999/2000) the partnership has been able to prevent 15 000 additional newborn deaths.

**Reference:** UNICEF Press Centre, 26 July 2002 <http://www.unicef.org/newsline/02pr46mali.htm>

## **Nonoxinol 9 ineffective in preventing HIV infection**

Spermicides containing nonoxynol-9 do not protect against HIV infection and, according to a WHO report, may even increase the risk of HIV infection in women using these products frequently (1). The report also advises women at high risk of HIV infection against using nonoxinol 9 spermicides for contraception.

The report contains the recommendations of a meeting of experts convened by WHO's Department of Reproductive Health and Research and the CONRAD Program based in the Eastern Virginia Medical School, USA. The experts also concluded that spermicides containing nonoxinol 9 do not protect against two other common sexually transmitted infections — cervical gonorrhoea and chlamydia.

Nonoxinol 9 is present in most spermicides on the market today. It has been used over the past half-century in a wide range of spermicidal products — vaginal gels, creams, foams, suppositories, sponges, and films, used alone or with other contraceptive devices, such the diaphragm. While it had been hoped that these products might reduce the



risk of sexually transmitted infections, including HIV infection, they have primarily been used as methods of contraception. Estimated numbers of women of reproductive age using spermicides vary from country to country, from less than 1 % in Asia to nearly 17% in some Latin American countries.

In the 1970s and 1980s, laboratory tests showed that nonoxinol 9 could inactivate the organisms that cause gonorrhoea, chlamydial infections, and other sexually transmitted infections, as well as HIV. These findings fuelled hopes that it could be used not only for contraceptive but also for microbicidal purposes. Clinical trials conducted to date do not support these hopes.

On the contrary, two studies mentioned in the report point to an increased risk of sexually transmitted infections, including HIV infection, in women using nonoxinol 9 products. A possible reason, suggested by the findings of other studies, is that nonoxinol 9 can disrupt the epithelium, or wall, of the vagina, thereby potentially facilitating invasion by an infective organism. The frequency of this epithelial disruption seems to depend on the intensity of use of the product — from 18% of women using the product every other day to 53% using it four times a day.

Regarding the use of spermicides for contraception, the report concluded that, when used alone, nonoxinol is only moderately effective for pregnancy prevention but better than no contraceptive method at all. Nonoxinol 9 is sometimes added to male condoms as a lubricant. The experts found no evidence that nonoxinol 9-lubricated condoms provided any more protection against pregnancy or sexually transmitted infections than condoms lubricated with silicone and nonoxinol 9 may cause adverse effects.

**Reference:** WHO/CONRAD Technical Consultation on Nonoxinol 9 Summary Report of the Meeting held on 9–10 October 2001. <http://www.who.int/reproductive-health/rtis/index.htm>

## New formula oral rehydration salts

A new formula for oral rehydration salts (ORS), has been released by the World Health Organization. The new formula ORS, a sodium and glucose solution, is widely used to treat children with acute diarrhoea. Since WHO adopted ORS in 1978 as its primary tool to fight diarrhoea, the mortality rate for children suffering from acute diarrhoea has fallen from 5 million to 1.3 million deaths annually.

The new improved formula is the result of extensive research sponsored by WHO's Department of Child and Adolescent Health and Development and supported by the United States Agency for International Development (USAID). The latest study was conducted in five developing countries among children from one month to two years old with acute diarrhoea and dehydration.

The study's findings suggest that using the low-sodium, low-glucose ORS formulation reduces the need for intravenous fluids by 33 percent. The effect of this reduction could result in fewer children requiring hospitalization, fewer secondary infections, a diminished need to handle blood with its potentially dangerous consequences, and lower health care costs.

### Reduced osmolarity

For more than 25 years, WHO and UNICEF have recommended a single formulation of glucose-based oral rehydration salts to prevent or treat dehydration from diarrhoea irrespective of the cause or age group affected. This product, which provides a solution containing 90 mEq/l of sodium with a total osmolarity of 311 mOsm/l, has proven effective and without apparent adverse effects in worldwide use. It has contributed substantially to the dramatic global reduction in mortality from diarrhoeal disease during the period.

For the past 20 years, numerous studies have been undertaken to develop an "improved" ORS. The goal was a product that would be at least as safe and effective as standard ORS for preventing or treating dehydration from all types of diarrhoea but which, in addition, would reduce stool output or have other important clinical benefits. One approach has consisted in reducing the osmolarity of ORS solution to avoid possible adverse effects of hypertonicity on net fluid absorption. This was done by reducing the solution's glucose and salt (NaCl) concentrations.

Studies to evaluate this approach were reviewed at a consultative technical meeting held in New York (USA) in July 2001, and technical recommendations were made to WHO and UNICEF on the efficacy and safety of reduced osmolarity ORS in children with acute non-cholera diarrhoea, and in adults and children with cholera.

These studies showed that the efficacy of ORS solution for treatment of children with acute non-cholera diarrhoea is improved by reducing its

Reduced osmolarity ORS	grams/litre	Reduced osmolarity ORS	mmol/litre
Sodium chloride	2.6	Sodium	75
Glucose, anhydrous	13.5	Chloride	65
Potassium chloride	1.5	Glucose, anhydrous	75
Trisodium citrate dihydrate	2.9	Potassium	20
		Citrate	10
		<b>Total Osmolarity</b>	<b>245</b>

sodium concentration to 75 mEq/l, its glucose concentration to 75 mmol/l, and its total osmolarity to 245 mOsm/l. The need for unscheduled supplemental IV therapy in children given this solution was reduced by 33%. In a combined analysis of this study and studies with other reduced osmolarity ORS solutions (osmolarity 210-268 mOsm/l, sodium 50-75 mEq/l) stool output was also reduced by about 20% and the incidence of vomiting by about 30%. The 245 mOsm/l solution also appeared to be as safe and at least as effective as standard ORS for use in children with cholera.

The reduced osmolarity ORS containing 75 mEq/l sodium, 75 mmol/l glucose (total osmolarity of 245 mOsm/l) is as effective as standard ORS in adults with cholera. However, it is associated with an increased incidence of transient, asymptomatic hyponatraemia. This reduced osmolarity ORS may be used in place of standard ORS for treating adults with cholera, but careful monitoring is advised to better assess the risk, if any, of symptomatic hyponatraemia.

Because of the improved effectiveness of reduced osmolarity ORS solution, especially for children with acute, non-cholera diarrhoea, WHO and UNICEF now recommend that countries use and manufacture the following formulation in place of the previously recommended ORS solution with a total osmolarity of 311 mOsm/l.

Although this single ORS formulation is recommended, WHO and UNICEF have previously published criteria, which remain unchanged, for acceptable ORS formulations. These criteria are listed below; they specify the desired characteristics of the solution after it has been prepared according to the instructions on the packet:

**The total substance concentration** (including that contributed by glucose) should be within the range of **200-310 mmol/l**.

#### The individual substance concentration:

**Glucose** should at least equal that of sodium but **should not exceed 111 mmol/l**

**Sodium** should be within the range of **60-90 mEq/l**

**Potassium** should be within the range of **15-25 mEq/l**

**Citrate** should be within the range of **8-12 mmol/l**

**Chloride** should be within the range of **50-80 mEq/l**

### International AIDS Society recommendations for antiretroviral treatment: adult HIV infection

Because of increased awareness of the activity and toxicity of current drugs, the threshold for initiation of therapy has shifted to a later time in the course of HIV disease. However, the optimal time to initiate therapy remains imprecisely defined. Availability of new drugs has broadened options for therapy initiation and management of treatment failure. The present updated recommendations written by the International AIDS Society, USA panel, are intended to guide practising physicians in the care of HIV infection and AIDS.

Progress in antiretroviral therapy has resulted in achievements as well as new challenges. The partial restoration of CD4 and CD8 T cell number and function during suppression of HIV replication with potent antiretroviral therapy has resulted in dramatic reductions in morbidity, mortality, and health care utilization. However, the toxicity of many current regimens, suboptimal activity and tolerability, and the emergence of drug resistance all point to the need for effective treatment strategies.

The emerging threshold for initiating therapy is the result of recognition of limitations of currently available agents and is not necessarily a reflection of a major change in understanding of disease pathogenesis, nor an indication that more aggressive treatment approaches should not be pursued.

### When to initiate antiretroviral therapy

Highly active antiretroviral therapy (HAART) is usually effective in reducing plasma HIV RNA levels (viral load) in antiretroviral-naïve patients, accompanied by a gradual increase in CD4 cell counts. Because currently available antiretroviral regimens will not eradicate HIV, the goal of therapy is to durably inhibit viral replication so that the patient can attain and maintain an effective immune response to most potential microbial pathogens.

Recent cohort data have provided support for the CD4 cell count being the major determinant of initiating therapy. It is clear that antiretroviral therapy should not be delayed until the patient is at high risk for serious opportunistic diseases.

The CD4 cell level above 200/ $\mu$ L at which to initiate therapy remains unclear and the following considerations support use of a CD4 cell count threshold higher than 200/ $\mu$ L.

- Some serious illnesses, especially active tuberculosis and bacteraemic pneumonia, may occur when the CD4 cell count is above 200/ $\mu$ L (16).
- The immune reconstitution syndrome and its associated morbidity may be observed in some patients starting antiretroviral therapy at low CD4 cell counts.
- Some laboratory markers show lower rates of favourable responses when antiretroviral therapy is delayed until the 200 cells/ $\mu$ L threshold is reached.
- Finally, the genetic complexity of HIV in persons increases with time, and this may facilitate escape from host immune defences.

In persons with CD4 cell counts above 350/ $\mu$ L, risk of 3-year clinical progression is low. For persons who have already initiated therapy at higher CD4 cell count thresholds and have had durable HIV RNA suppression and no adverse effects over periods of months to years, it is not clear whether it is safe to discontinue therapy.

Physicians and patients must thoroughly weigh risks and benefits of starting antiretroviral therapy for CD4 cell counts in the 200/ $\mu$ L to 350/ $\mu$ L range and above, and make individualized informed decisions. The strength of the recommendation should depend on the immunologic status, as well as the patient's understanding of and commitment to an often complex regimen.

Therapy continues to be recommended in all patients with symptomatic established HIV infection. Immediate treatment, but not prophylaxis, of a serious opportunistic infection in patients with advanced HIV disease may take precedence over starting antiretroviral therapy. If potential for adverse drug-drug interactions exists, it is wise to choose drugs with minimal or no interactions, or to delay antiretroviral treatment for a few weeks until drugs causing the interactions can be discontinued.

### Choice of initial therapy

No drug combination can be defined as the optimal initial regimen in all patients. Therapy should thus be individualized using a number of criteria, including efficacy and durability of antiretroviral activity, tolerability and adverse effects, convenience of the regimen, drug-drug interactions, and potential salvageability of initial regimen. Many patients will ultimately experience at least one treatment failure.

There are currently no data on preferred sequencing of NRTIs. Stavudine and didanosine in combination should be avoided or used with caution in pregnant women because of increased risks of lactic acidosis.

There are generally three types of initial combination regimens that should be considered:

- a protease inhibitor (with or without low-dose ritonavir) with two nucleoside reverse transcriptase inhibitors (NRTIs);
- a non-nucleoside reverse transcriptase inhibitor (NNRTI) with two NRTIs; or
- three NRTIs.

Other regimen combinations include a protease inhibitor (with or without low-dose ritonavir) with an NNRTI plus one or two NRTIs, which should be reserved for special circumstances; and a protease inhibitor (with low-dose ritonavir) with an NNRTI.

### **Adherence: assessment and reinforcement**

Incomplete adherence to one or more prescribed medications is a key cause of virological failure of antiretroviral regimens. Factors that limit full adherence are complex and incompletely defined but may include high pill number and large pill size, medication schedule and dietary restrictions, toxic adverse effects, and ineffective education and support of patients regarding adherence. Progress in developing new drug formulations and fixed-dose combinations that can simplify regimens is encouraging.

Effective communication between patient and provider is essential both before and after treatment has begun. Some health care centres may use non-physicians (pharmacists, nurses, peer educators, and others) to effectively assess and support adherence, but the physician should also be actively involved. Once treatment has begun, weekly contact may be appropriate until the patient has established a consistent daily routine of medication use and has passed the time that any short-term adverse effects would be expected. Reinforcing the need for adherence at every health care provider contact is important.

### **Changing drugs or therapy**

In the absence of virological or immunologic failure, a regimen may pose problems with adherence, intolerance, or cumulative (long-term) toxic effects. As long as the antiviral activity of the overall regimen is maintained, exchanging individual components of the regimen is acceptable.

### **Treatment failure**

The definition of "treatment failure" (a term that subsumes virological, immunologic, or clinical failure) depends on the clinical setting and mirrors the objective of ongoing therapy at a given time in the patient's treatment course.

In the case of the first or second regimen, when virus is wild type or harbours few resistance mutations, maintaining an undetectable viral load is an achievable goal of therapy; in this setting, treatment failure is best defined as inability to achieve a viral load below assay detection limits (<50 copies/mL) or as any sustained return of the viral load to above the target value (>400 copies/mL). With increasing rounds of treatment failure, the level and spectrum of virus resistance may increase, and it may be-

come more difficult to construct an active combination. In patients for whom several regimens have failed, the virus may become multiply resistant, with fewer than three active drugs being available, and the objective of achieving stable undetectable viral load with conventional regimens may be unrealistic. Problems with toxicity may further restrict the number of available drugs.

Treatment failure occurs within the first year of therapy in a substantial proportion of treatment-naïve patients. Thus, failure should be anticipated as part of the long-term strategy of antiretroviral treatment.

### **Adjuvant therapy to antiretroviral drugs**

The concept of manipulating the immune response for host benefit has received increased emphasis. Approaches include attempts to augment or dampen the immune response generally, and attempts designed to stimulate relevant HIV-specific immune effector responses. At this point, however, sufficient clinical data do not exist to recommend these approaches beyond the setting of a clinical trial.

### **Summary**

The future of antiretroviral therapy rests with the development of new drugs that will result in simpler, more effective, and less toxic regimens along with development of an improved understanding of innate immune system responses and novel approaches to exploit these responses. Several new agents are currently in development, derived from current drug classes and new drug classes, including entry inhibitors and integrase inhibitors. Potential advantages of these drugs include once-daily dosing, smaller pill size, lower incidence of adverse effects, new viral targets, and activity against virus that is resistant to other drugs in the respective classes.

The benefits of current and future agents will continue to be felt by HIV-infected persons in the developed world. Extending these benefits to those living with HIV in the developing world is a challenge that needs to be met.

**Reference:** Yeni, P.G., Hammer, S.M., Carpenter, C.J. et al. Antiretroviral treatment for adult HIV infection in 2002. *Journal of the American Medical Association*, **288**: 222–235 (2002).

# Good Clinical Practices

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## Development of Chinese good clinical practices (GCP)

*Sang Guo-wei*  
*State Drug Administration*  
*Beijing, China*

The State Drug Administration (SDA) was established in August 1998 to enhance government administration of drug regulation and took over responsibility for regulating pharmaceutical products and medical devices from the Ministry of Public Health. Through new regulations, the SDA is making efforts to upgrade pharmaceutical regulations and strengthen their implementation to meet international standards and thereby ensure the safety and efficacy of medicines. In line with China's adherence to the World Trade Organization (WTO), the SDA will continue to improve pharmaceutical product legislation and will implement the "rule of law" in the pharmaceutical sector, including regulations covering clinical trial performance and protection of trial subjects, through good clinical practices (GCP).

On 28 February 2001, the newly revised Drug Administration Law of the People's Republic of China was approved by the National People's Congress and entered into force on 1 December, 2001. Detailed Rules of Drug Administration Law are about to be promulgated. The main objectives of the new regulations and law are:

1. To ensure protection of rights, safety and welfare of human subjects.
2. To conform with international, generally recognized principles on clinical trials, ethical standards and scientific principles.
3. To ensure that clinical trials of all drugs, including biotechnology products and traditional medicines (in whatever phase, including human bioavailability or bioequivalence studies) are performed according to Chinese GCP.
4. To ensure that the clinical trial process is standardized and the results scientific and credible.

5. To emphasize the importance of ethics committees and informed consent to ensuring the protection of trial subjects.

## Drug Administration Law

The new law addresses implementation of clinical trials in China. This law has been enacted to:

- strengthen drug administration;
- ensure drug quality and safety; and
- protect people's health and their legitimate rights and interests in the use of drugs.

All institutions and individuals engaged in research, production, distribution, use, or administration of drugs in the People's Republic of China shall abide by this law. The drug regulatory authority, the SDA, is responsible for drug administration nationwide. Practical, effective and new drug administrative procedures covering research and development of new drugs are included in the new law.

Before approval for conducting a clinical trial can be obtained, a dossier for new drug research and development should be submitted to the SDA specifying:

- the manufacturing process;
- quality specifications;
- results of pharmacological and toxicological studies;
- related data and samples.

Finally, this new law clearly indicates that the clinical research institution shall implement GCP. Therefore, Chinese GCP has become an important part of law which can be legally enforced.

## Major regulations on new drug clinical evaluation

China has made significant progress in recent years to improve its medicinal product regulatory and evaluation procedures. Within the structure of

**Table 1. Regulations concernig new drug evaluation and management in China*****Key elements related to GCP and protection of trial subjects  
in the New Drug Approval provisions***

1. The sponsor and clinical research institution shall comply with the requirements of "good clinical practice" (GCP) stipulated by the State Drug Administration when a clinical study for a new drug is carried out.
2. When submitting the application for a clinical trial, the sponsor should select the principal clinical research institution and the research sites from the clinical research bases designated by the SDA (except for Phase IV clinical trials). The selection should be approved by the SDA. If an additional research site is needed or the clinical study will be performed in hospitals other than clinical research bases for a particular reason, additional applications should be submitted for approval.
3. The designated clinical research institutions should be aware of the properties, action, efficacy and safety of the test drug. The institution should subscribe to the clinical trial protocol with the sponsor in accordance with the requirements of GCP and conduct the trial strictly in line with the protocol.
4. The sponsor should appoint a qualified person to monitor the clinical trial so as to ensure implementation of the protocol in compliance with the requirements of GCP. Drug administration bodies at provincial level are responsible for the supervision and inspection of the clinical study as requested by the SDA.
5. In case of the occurrence of serious adverse events during the clinical study, the research sites must immediately take all necessary measures to protect the subject from risk, and report the events to the local drug administration at provincial level and the SDA within 24 hours.

the SDA, two major departments deal with drug registration and drug safety and inspection. They are jointly responsible for the evaluation and inspection of conducting clinical trials and inspecting new drugs. Since April 1999, certain provisions have been introduced by SDA to replace and update regulations established in 1985. Table 1 above gives details of major regulations on new drug clinical evaluation and their interaction.

**Development of Chinese GCP**

In order to guarantee the safe and proper use of new drugs, and to participate in international competition and cooperate in the field of medical and pharmaceutical science, technology and trade, the drug regulatory department and scientists in China are fully aware that Chinese regulations and laws regarding the development of a new drug must be in line with international standards. SDA concluded that the existing regulations were inappropriate for the change from a planned to a market economy, in particular after China's entry into the WTO. Since 1992, China recognizes GCP as the international ethical and scientific standard for designing, con-

ducting, recording, and reporting clinical trials that involve the participation of human subjects.

The *International Guidelines for Biomedical Research Involving Human Subjects*, prepared by the Council of International Organization for Medical Sciences (CIOMS) indicates how ethical principles set forth in the *Declaration of Helsinki* can be effectively applied, particularly in developing countries, with consideration of their socioeconomic circumstances, laws, regulations, executive and administrative arrangements.

Table 2 on page 127 summarizes activities undertaken in the preparation and development of Chinese GCP guidelines. These were adopted by the SDA on 23 July 1999 and entered into force from 1 September 1999

**Ethical principles and trial subject protection**

Chinese GCP contains 13 chapters and includes 66 articles. The *Declaration of Helsinki* is included as an appendix. Fundamental articles relating to ethics and protection of trial subjects are as follows:

**Table 2. Development of GCP in China**

1986–1992	Information/data collection
1993	Translation into Chinese of Code of Federal Regulations and FDA guidelines; WHO GCP; GCP from EC, Australia, Canada, France, Japan, Nordic countries, and Republic of Korea
1994	Preparation meeting and workshop on GCP
1995	Establishing a 5 member draft group for Chinese GCP
1996	Training course on GCP; A computer-based clinical research training and reference system was introduced into China
1998	Chinese GCP was promulgated by Ministry of Public Health
1999	Chinese GCP was revised and promulgated by SDA, and entered into effect
2000	GCP training and teaching material published by SDA
2001	Translation into Chinese of ICH GCP and revised Declaration of Helsinki
2002	SDA commences re-revision of Chinese GCP
1999–2001	Training and implementation on GCP by SDA's Training Centre

**Table 3. Designation and Development of Drug Clinical Research Bases in China**

Year	Number of bases	Disciplines	Designator
1990	46	30	MOPH
1998	113	70	MOPH
2000	132	66	SDA

- All research involving human subjects shall be conducted in accordance with the ethical principles contained in the *Declaration of Helsinki*, namely justice, respect for persons, beneficence (maximize benefits and minimize harms and wrongs) and non-maleficence (do no harm) (Article 4).
- Prior to planning a clinical trial in humans, specific aims, problems to be solved, anticipated efficacy and possible risks must be considered thoroughly. Anticipated benefits should prevail over possible risks. The chosen clinical trial solutions must conform to scientific and ethical standards (Article 5).
- An ethics Committee should be established within the medical institution where the clinical trial is to be conducted to ensure the protection of the rights and welfare of human subjects taking part in the trial and to provide public reassurance (Article 9).
- Prior to a clinical trial, the protocol must be approved by the Ethics Committee before implementation. During the trial, any subsequent protocol amendment must be approved by the Ethics Committee before its implementation. All serious adverse events occurring during the trial must be reported to the Ethics Committee (Article 10).
- In order to protect the rights and welfare of trial subjects, the Ethics Committee should review the protocol strictly (Article 12).
- Investigators, or their appointed representatives, should provide trial subjects with detailed information relating to the clinical trial (Article 14).
- Informed consent is obtained after a sufficient and comprehensive explanation of the trial (Article 15).

8. The contents of a trial protocol should include the following (Article 17):

- Purpose and objectives of the trial, including the known potential risks and benefits to human subjects.
- Criteria for inclusion and exclusion of trial subjects and process of recruitment, methods of allocation of subjects, withdrawal criteria.

9. The investigator is required to conduct the clinical trial in an institution with sound medical facilities, laboratory equipment and staff. The institution should have all necessary emergency facilities to ensure safety of trial subjects (Article 21).

10. The investigator is responsible for medical decision-making in relation to the trial, and to ensure adequate medical treatment to be provided to the subject whenever any adverse event occurs (Article 24).

11. The investigator is obliged to take necessary measures to ensure the safety of subjects, and such measures should be documented. In case of serious adverse events, the investigator must take appropriate measures to protect subjects, and report to the drug regulatory authorities, the sponsor and the Ethics Committee immediately (Article 25).

12. As soon as a serious adverse event occurs, the sponsor must discuss this with the investigator(s), take necessary measures to safeguard trial subjects, report in a timely manner to drug regulatory authorities, and notify the other investigators involved in the same trial (Article 39).

13. The sponsor should provide insurance and treatment compensation to trial subjects to cover trial-related injuries or death, and provide indemnity (legal and financial coverage) for the investigator, except for claims resulting from medical malpractice (Article 42).

### **Requirements for foreign agencies conducting clinical studies in China (Interim)**

1. A foreign agency can conduct a clinical study in China only after the SDA approves the application filed by the Chinese agent.

2. Foreign products intended to be studied within a clinical study in China must be registered abroad or have entered into Phase II clinical trials for drugs and Phase III for vaccines.

3. The application form for a *Clinical Trial of a Foreign Drug in China* should be completed and submitted with the relevant dossiers for approval.

4. The protocol of the clinical study must be formulated and implemented according to Chinese GCP.

5. If, at any time, the drug demonstrates serious or unexpected adverse reactions in any other countries, it must be reported in a timely way to the SDA according to regulations.

Globalization tends to ignore individual needs, especially those of developing countries. When clinical trials are planned in China, it is the ethical duty of investigators and pharmaceutical companies to consider the specific needs and benefits of the Chinese people. The newly Revised *Declaration of Helsinki* (5th Amendment at the 52 General Assembly, Edinburgh, October 2000) should be followed.

### **Shortcomings in GCP management**

The following problems have been encountered during the application of GCP within China.

1. There is a wide range in the practice and implementation of clinical trials, of considerable variety, (although most leading investigators follow GCP and ICH).

2. In some cases, clinical trials have started without approval by SDA and an ethics committee. This practice also involved foreign vaccine trials.

3. Not all institutions have an ethics committee. In others, the ethics committee may not have the required membership, or correctly follow meeting schedules and record-keeping.

4. Use of a written informed consent containing inadequate information. The explanation given is that doctors worry that if all potential adverse effects are listed in the informed consent form, the subject will not wish to enrol.

6. Conduct of the clinical trial may not follow strictly the protocol.



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7. The protocol may be changed or modified without informing the ethics committee and drug regulatory authority.

8. Domestic sponsors are less aware of the *Declaration of Helsinki* and GCP principles.

### **Conclusion**

1. Basic requirements for conducting a clinical trial of medical products in China should meet internationally-recognized principles on ethics issues and protection of subject's rights, welfare and safety.

2. All clinical trials conducted in China should be performed according to the Drug Administration Law, Chinese GCP and related regulations.

3. Familiarity with and implementation of the principles of the Declaration of Helsinki, WHO or ICH GCP will enable data from clinical trials conducted in China to be accepted internationally.

4. It is important for investigators, sponsors and regulatory authorities to join in efforts to improve the current status of implementation of GCP in China thereby protecting subject's rights, welfare and safety.

5. Special guidelines for biotechnology products and vaccine clinical trials should be formulated on the basis of their specific characteristics. More attention should be paid to the safety of vaccines and recombinant products in relation to ethical considerations.

6. A general training programme for medical doctors, manufacturers and the public on the ethical principles and protection of subjects in drug clinical trial is strongly recommended in China in order to comply with international standards.

# Safety Information

## Statins: rhabdomyolysis and myopathy

Statins belong to a class of cholesterol-lowering agents that inhibit the liver enzyme 3-hydroxy-3-methylglutaryl-coenzyme A (HMG-CoA) reductase. The use of HMG-CoA reductase inhibitors has been associated with severe myopathy, including rhabdomyolysis (1–6).

The statins approved for sale in Canada include atorvastatin (Lipitor®), cerivastatin (Baycol®), fluvastatin (Lescol®), lovastatin (Mevacor®, Apo-Lovastatin®, Gen-Lovastatin®), pravastatin

(Pravachol®, Apo-Pravastatin®, Bio Pravastatin®, Lin-Pravastatin®) and simvastatin (Zocor®). In August 2001, Bayer voluntarily suspended the marketing and distribution of Baycol® in Canada (7, 8). The continued scrutiny of postmarketing reports of rhabdomyolysis, including related deaths, has revealed an increased reporting rate of rhabdomyolysis with Baycol compared to other statins, especially when gemfibrozil is prescribed concurrently (7).

The Canadian Adverse Drug Reaction Monitoring Program (CADRMP) has received reports of rhabdomyolysis or myopathy with all statins approved for sale in Canada (Table 1). In severe cases,

**Table 1. Rhabdomyolysis, myopathy and increased CPK reactions associated with statins as reported to the CADRMP from date marketed in Canada to 24 August 2001\***

Reaction <sup>†</sup>	Drug and year marketed in Canada: no. of reports					
	Atorvastatin 1997	Cerivastatin 1998	Fluvastatin 1994	Lovastatin 1988	Pravastatin 1990	Simvastatin 1990
Rhabdomyolysis	10	54	–	12	3	7
Myopathy <sup>‡</sup>	32	8	5	24	17	34
CPK increased with myopathy <sup>‡</sup>	16	11	1	6	4	6
CPK increased without myopathy <sup>‡</sup>	5	6	–	4	6	5
Total no. of reports received	231	121	43	182	123	170

CPK = creatine phosphokinase, CADRMP = Canadian Adverse Drug Reaction Monitoring Program.

\* These data cannot be used to determine the incidence of adverse drug reactions because neither patient exposure nor the amount of time the drug was on the market has been taken into consideration.

<sup>†</sup>Each report may contain more than one of these reactions; however, reports were only included in the most significant category.

<sup>‡</sup> Myopathy may include muscle symptoms such as myositis, myalgia, muscle ache, muscle weakness, muscle cramp, muscle discomfort.

rhabdomyolysis can result in kidney failure (8). The statin cases of rhabdomyolysis outlined in Table 1 with which acute renal failure was also reported were: atorvastatin (2 cases), cerivastatin (15), lovastatin (5), pravastatin (1) and simvastatin (2). The reports of rhabdomyolysis with a fatal outcome were: atorvastatin (1), cerivastatin (2) and lovastatin (1).

Various factors may increase the risk of myopathy and rhabdomyolysis with statins. Rhabdomyolysis can occur with all statins when used alone and particularly when combined with other drugs or chemicals that are themselves myotoxic or that elevate the concentrations of the statin to the toxic range (9). Evidence suggests that myopathy is dose-dependent, (9) and it is usually recommended that statin therapy be initiated at lower therapeutic doses (1–6). Combined use with niacin in lipid-lowering doses, with fibric acid derivatives such as bezafibrate, fenofibrate and gemfibrozil, (1–6) or with drugs or foods that inhibit the cytochrome P450 (CYP450) system, particularly CYP3A4, (including but not limited to cyclosporins, macrolide antibiotics, antidepressants such as nefazodone, azole antifungals and grapefruit juice) can potentially increase the toxicity of statins (1,3,5,6,9)

Atorvastatin, cerivastatin, lovastatin and simvastatin are metabolized mainly by CYP3A4 (10). Lovastatin and simvastatin may particularly be affected by the inhibition of first-pass metabolism, which could result in 10- to 20-fold elevations (oral availability increasing from 5% to 100%) in steady-state concentrations with a marked potential for drug toxicity (9). Pravastatin is not metabolized by CYP3A4 to a clinically significant extent (2). Fluvastatin is metabolized mainly by CYP2C9 (4, 10) and would have a different spectrum of interactions than would statins metabolized by CYP3A4 (9). Further information concerning drug interactions may be obtained from the product monograph of each statin (1–6). In addition, caution should be exercised when using statins in patients with impaired renal function (1–6).

The product monograph of each statin has no clear recommendation for biochemical monitoring of muscle effect (creatinine phosphokinase [CPK] measurement). In the absence of symptoms, there is no evidence to suggest that routine monitoring of plasma CPK activity is of benefit (10). However, further investigation is required to provide more definitive monitoring guidelines. It was suggested in a recent review article (10) that it is important to

measure the baseline CPK level at least once before starting statin therapy.

Patients taking a statin or a fibrate should be made aware of rhabdomyolysis as a potential side effect. They should be advised to report promptly any signs of muscle problems (i.e., unexplained muscle weakness, tenderness or pain, either occurring at rest or exacerbated by exercise) and dark urine, particularly if these symptoms are accompanied by malaise or fever.

*Duc Vu, Mano Murty, and Marielle McMorran,  
Bureau of Licensed Product Assessment,  
Canada*

## References

1. Mevacor, lovastatin tablets [product monograph]. Kirkland (QC): Merck Sharp & Dohme Canada. 10 September (1998).
2. Pravachol, pravastatin sodium tablets [product monograph]. Montréal (QC): Bristol-Myers Squibb Canada. 22 February (2000).
3. Zocor, simvastatin tablets [product monograph]. Kirkland (QC): Merck Frosst Canada. 23 August 1999).
4. Lescol, fluvastatin sodium capsules [product monograph]. Dorval (QC): Novartis Pharmaceuticals Canada. 14 February (2001).
5. Lipitor, atorvastatin calcium tablets [product monograph]. Kirkland (QC): Pfizer Canada. 31 May (2001).
6. Baycol, cerivastatin sodium tablets [product monograph]. Etobicoke (ON): Bayer. 27 December (2000).
7. Market withdrawal of Baycol (cerivastatin) [Dear Healthcare Professional letter]. Toronto (ON): Bayer; August 8 2001. [http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/advisory/industry/baycol\\_cerivastatin\\_e.html](http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/advisory/industry/baycol_cerivastatin_e.html).
8. Voluntary withdrawal of Baycol [public advisory]. Ottawa (ON): Health Canada; August 10 2001. [http://www.hc-sc.gc.ca/english/protection/warnings/2001/2001\\_89e.htm](http://www.hc-sc.gc.ca/english/protection/warnings/2001/2001_89e.htm).
9. Herman RJ. Drug interactions and the statins. *Canadian Medical Association Journal*, **161**(10):1281–1286 (1999).
10. Baker, S.K., Tarnopolsky, M.A. Statin myopathies: pathophysiologic and clinical perspectives [review]. *Clinical Investigative Medicine*, **24**(5):258–271 (2001).

## Tamoxifen and risks of thromboembolic events

Tamoxifen is already a widely used hormonal treatment in women following treatment for early and advanced breast cancer. Now, in addition to its use as a treatment in cancer, preliminary results from the International Breast Cancer Intervention Study (IBIS) provide evidence for the use of tamoxifen to prevent breast cancer in healthy women at high risk. The results so far show that the incidence of breast cancer has been reduced by one-third in women at high risk, compared to women taking placebo. However, the study also indicated that tamoxifen can increase the risk of thromboembolism, particularly during and immediately after major surgery or periods of immobility. The Department of Health in the United Kingdom has communicated the following information.

1. The benefits for women being treated for breast cancer with tamoxifen outweigh the risks. It is important that women taking the drug as a treatment continue to do so.
2. There is evidence of some increase in risk from thromboembolism with tamoxifen especially during and immediately after major surgery or periods of immobility. Patients should be made aware of the symptoms of venous thromboembolism and if they have any sudden onset of breathlessness they should consult their doctor immediately.
2. The IBIS study gives evidence of the preventative action of tamoxifen in breast cancer. However this is not a use of tamoxifen that has yet been approved except in the context of clinical trials.

**Reference:** Urgent Communication from Chief Medical Officer, 27 March 2002. <http://www.mca.gov.uk>

## Oral contraceptives and risk of cervical cancer

The Department of Health in the United Kingdom has issued an urgent communication informing health professionals of a recent study which, although not conclusive, strengthens the evidence that oral contraceptives may contribute to the development of cervical cancer in women with high risk type human papilloma (HPV) (1) .

The study reports an association between increasing risk of cervical cancer and duration of use of oral contraceptives (threefold increase in risk following 5–9 years of oral contraceptive use versus a fourfold increase after 10 or more years) in women with HPV. HPV is a sexually transmitted infection. There are more than 80 HPV viruses, but only a few are associated with an increased risk of cervical cancer. On current evidence it is difficult to state whether it is the use of oral contraceptives, sexual activity, the type of HPV or the duration of HPV infection which is /are the main precipitating factor(s) for cervical cancer.

Furthermore, the original studies were carried out in women from developing countries with no adequate cervical screening programme. While cervical screening is not perfect, between 80% and 90% of cervical abnormalities can be detected and treated in women who attend regular screening programmes. The communication therefore advises that all sexually active women, especially those on long-term oral contraceptives, be encouraged to have regular cervical smears. The benefits of using OCs outweigh the risks in the vast majority of women who use them.

### References

1. Urgent Communication from Chief Medical Officer, 27 March 2002. <http://www.mca.gov.uk>
2. *Lancet*, **359**: 1085–1101 (2002).

## HIV-associated lipodystrophy syndrome overview

HIV-associated lipodystrophy syndrome (LDS) is a disorder in HIV-infected patients receiving highly active antiretroviral therapy (1–3). It presents as a range of *clinical* (morphologic) and *metabolic* changes. The following clinical changes have been described: body fat redistribution such as visceral adiposity (fat gain within the abdomen, breasts, over the dorsocervical spine and other lipomata) and peripheral lipoatrophy (fat loss in the face, limbs, buttocks). The metabolic changes have included hypertriglyceridemia, hypercholesterolemia, insulin resistance, type 2 diabetes mellitus, impaired glucose tolerance and lactic acidemia (1, 2, 4). The term “lipodystrophy” has been used to describe fat loss, fat redistribution and, on a broader level, both clinical and metabolic features of HIV-associated LDS (2).

The pathogenesis of LDS is unknown (1). However, it has been associated with combination antiretroviral therapy including protease inhibitors and nucleoside reverse transcriptase inhibitors, the latter having been linked to mitochondrial toxicity (1–3). As well, it has been suggested that LDS features are the result of chronic HIV infection, chronic immunodeficiency or recovery from immune dysfunction (5).

No validated case definition of LDS has yet been formulated. However, a working case definition has been described as having at least one *clinical* feature and at least one *metabolic* abnormality, and no AIDS-defining event or other severe clinical illness or use of anabolic steroids, glucocorticoids or immune modulators within 3 months of assessment (4).

The CADRMP database was searched for LDS-related ADRs up to 31 August 2001. The search

focused on metabolic and nutritional disorders and endocrine disorders associated with antiretroviral drugs containing abacavir, amprenavir, delavirdine, didanosine, efavirenz, indinavir, lamivudine, lopinavir, nelfinavir, nevirapine, ritonavir, saquinavir (base and mesylate), stavudine or zalcitabine. A total of 119 ADR reports were found, of which only 4 met the LDS working case definition (Table 1). In addition to the cases described in Table 1, other reports found in the database denoted potential LDS: lipodystrophy (3 cases) and fat disorder (13 cases). These additional cases did not clearly report the presence of combined clinical and metabolic features, possibly because of the available scientific knowledge at that time.

Retrospective studies have reported a prevalence of LDS of 17%–84% among HIV-infected cohorts receiving highly active antiretroviral therapy (6). It is clear that LDS is highly underreported to Health Canada. Reports of ADRs are an important source

**Table 1. Cases of potential lipodystrophy syndrome\* associated with antiretroviral drugs reported to the CADRMP (up to 31 August 2001)**

Reported clinical reactions†	Reported metabolic reactions†	Concomitant drugs	Duration of treatment	Suspect drug reported	
				PI	NRTI
Lipodystrophy	Diabetes mellitus	lamivudine, nadolol, Plevacid®, Zolof®	NA	–	stavudine
Fat disorder	Hyperglycaemia	lamivudine, stavudine	26 wks	indinavir	–
Fat disorder	Hyperglycaemia, hypertriglyceridaemia	nelfinavir	NA	saquinavir	–
Lipodystrophy, enlarged abdomen	Hypertriglyceridaemia	azithromycin, lamivudine, saquinavir, stavudine	Continuing	ritonavir	–

*CADRMP = Canadian Adverse Drug Reaction Monitoring Program, PI = protease inhibitor, NRTI = nucleoside reverse transcriptase inhibitor, NA = not available.*

*\* Met working case definition: at least one clinical feature and at least one metabolic abnormality, and no AIDS-defining event or other severe clinical illness or use of anabolic steroids, glucocorticoids or immune modulators within 3 months of assessment.*

*† Based on the "preferred term" of the World Health Organization Adverse Reaction Dictionary (WHOART).*

of potential new and undocumented signals. To this end, a pilot project under way within the Therapeutic Products Directorate is promoting increased reporting to Health Canada of ADRs in HIV-infected patients (7). Its purpose is to develop alternative methods and formats for clinicians and patients to report ADRs. One such method proposed for testing in the pilot project is the electronic entry of ADR data as part of the everyday practice of clinicians.

*Susanne Reid, Bureau of Licensed Product Assessment, Canada*

### References

1. Carr, A., Cooper, D.A. Adverse effects of antiretroviral therapy. *Lancet*, **356**: 1423–1430 (2000).
2. Qaqish, R.B., Fisher, E., Rublein, J., Wohl, D.A. HIV-associated lipodystrophy syndrome. *Pharmacotherapy*, **20**(1): 13–22 (2000).
3. Brinkman, K., Smeitink, J.A., Romijn, J.A., Reiss, P. Mitochondrial toxicity induced by nucleoside-analogue reverse transcriptase inhibitors is a key factor in the pathogenesis of antiretroviral-therapy-related lipodystrophy. *Lancet*, **354**: 1112–1115 (1999).
4. Carr, A., Samaras, K., Thorisdottir, A. et al. Diagnosis, prediction, and natural course of HIV-1 protease-inhibitor-associated lipodystrophy, hyperlipidaemia, and diabetes mellitus: a cohort study. *Lancet*, **353**: 2093–2099 (1999).
5. Miller, J., Carr, A., Smith, D. et al. Lipodystrophy following antiretroviral therapy of primary HIV infection. *AIDS*, **14**: 2406–2407 (2000).
6. Mauss, S. HIV-associated lipodystrophy syndrome. *AIDS*, **14**(Suppl 3):S197–S207 (2000).
7. Enhanced postmarketing surveillance of HIV/AIDS drug therapies — pilot project. Phase 1: Proof of concept summary & evaluation report. Ottawa: Therapeutic Products Directorate, Health Canada, in partnership with the University of Ottawa, Health Services; 2000. [http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/hiv/hiv-aids\\_1\\_e.pdf](http://www.hc-sc.gc.ca/hpb-dgps/therapeut/zfiles/english/hiv/hiv-aids_1_e.pdf).

*\*Spontaneous monitoring systems are useful in detecting signals of relatively rare, serious and unexpected adverse drug reactions. A signal is defined as "reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously. Usually, more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information". All signals must be validated before any regulatory decision can be made.*

# Regulatory Action

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## **Alosetron hydrochloride: restricted marketing**

**United States of America** — The Food and Drug Administration (FDA) has approved a supplemental new drug application (sNDA) that permits marketing of alosetron hydrochloride (Lotronex®) with restrictions. The manufacturer of the drug will be implementing a risk management and prescribing programme for physicians who wish to prescribe alosetron. The drug's indication has been narrowed to treatment of women with severe, diarrhoea-predominant irritable bowel syndrome (IBS) who have failed to respond to conventional IBS therapy. Limiting the use of alosetron to this severely affected population is intended to maximize the benefit to risk ratio.

Serious and unpredictable gastrointestinal adverse events, including some that resulted in death, have been reported in association with alosetron use. Less than 5% of IBS is considered severe, and only a fraction of severe cases are diarrhoea-predominant IBS. Severe IBS is a chronic condition (in this case, generally lasting more than six months) with symptoms that disable or significantly curtail the daily activities of patients.

The risk management programme is designed to help ensure that patients and physicians are fully informed of the risks and benefits and that only appropriate patients are prescribed the drug. Action follows a recommendation by FDA's Gastrointestinal Drugs Advisory Committee and the Drug Safety and Risk Management Subcommittee of the Advisory Committee for Pharmaceutical Science.

FDA first approved alosetron in February 2000. The manufacturer voluntarily withdrew alosetron hydrochloride from the market in November 2000.

**Reference:** <http://www.fda.gov/cder/drug/infopage/lotronex/lotronex.htm>.

## **Baclofen: abrupt discontinuation dangerous**

**United states of America** — The prescribing information for baclofen injection (Lioresal® Intrathecal) has been updated to include a warning about

rare cases of withdrawal that can lead to life threatening sequelae and/or death in patients who abruptly discontinue therapy.

Baclofen injection is indicated for use in the management of severe spasticity of cerebral and spinal origin. A warning has been added to the prescribing information as follows.

Abrupt discontinuation of intrathecal baclofen, regardless of the cause, has resulted in sequelae that include high fever, altered mental status, exaggerated rebound spasticity, and muscle rigidity, that in rare cases has advanced to rhabdomyolysis, multiple organ-system failure and death.

Prevention of abrupt discontinuation of intrathecal baclofen requires careful attention to proper programming and monitoring of the infusion system, refill scheduling and procedures, and pump alarms. Special attention should be given to patients at apparent risk (e.g. spinal cord injuries at T-6 or above, communication difficulties, history of withdrawal symptoms from oral or intrathecal baclofen).

In the first 9 years of post-marketing experience, 27 cases of withdrawal temporally related to the cessation of baclofen therapy were reported; six patients died.

**Reference:** Novartis Pharmaceuticals Corporation letter posted on the FDA's MedWatch program at <http://www.fda.gov/medwatch>

## **Irinotecan: prescribing changes**

**United States of America** — Changes in the prescribing information for irinotecan (Camptosar®), indicated as a component of therapy for first-line treatment of metastatic colorectal cancer in combination with 5-fluorouracil (5-FU) and leucovorin (LV) and for treatment of metastatic colorectal cancer that has recurred or progressed following initial 5-FU based treatment.

The following labelling changes arose following recommendations made at a meeting of the Food and Drug Administration's Oncologic Drugs Advisory Committee.

- Both the bolus and the infusional regimens of CAMPTOSAR plus 5-FU/LV® remain approved for the first-line treatment of patients with meta-static colorectal cancer.
- The starting dose and schedule for both regimens remain unchanged.

The prescribing information has been revised to identify patients at higher risk of severe toxicity, to clarify dose modification guidelines, and to augment the information about management of treatment-related toxicities.

**Reference:** Pharmacia Oncology Web site <http://www.pharmaciaoncology.com>

## Sodium oxybate/GHB approved for cataplexy

**United States of America** — The Food and Drug Administration has approved sodium oxybate or gamma hydroxybutyrate (also known as GHB) (Xyrem®) for treatment of patients with narcolepsy who experience episodes of cataplexy, a condition characterized by weak or paralysed muscles. Because of safety concerns associated with the use of the drug, distribution will be highly restricted.

In the early 1990s, GHB was marketed as a dietary supplement with claims for enhancing athletic performance, sexual activity and for inducing sleep. It was also abused as a recreational drug and is well-known for use in date rape. As a result of a number of serious adverse events, including death, FDA intervened to prohibit marketing of GHB.

Sodium oxybate has been designated as a Schedule III Controlled Substance for medical use, meaning it cannot be sold, distributed, or provided to anyone other than for its prescribed use. Illicit use will be subject to penalties under Schedule I, the most restrictive schedule of the Controlled Substances Act.

Narcolepsy affects about 120 000 people in the United States. This rare condition causes an irresistible tendency to fall asleep even in unlikely circumstances such as in the middle of a conversation or at a meal. Cataplexy, a symptom of this condition, is a sudden loss of muscular control and weakness usually triggered by emotions such as amusement, anger or excitement, and is estimated

to affect about 20 000 to 50 000 individuals. The effects of cataplexy range from dropping of the jaw and slumping of the head, to buckling of the legs and even collapse of the whole body. These effects can last for a few seconds or up to many minutes.

Side effects associated with sodium oxybate include confusion, depression, nausea, vomiting, dizziness, headache, bedwetting, and sleepwalking. Abuse could also lead to dependence, i.e. craving for the medicine, and severe withdrawal symptoms. A medication guide further advises patients about proper use, administration and disposal of the drug.

**Reference:** <http://www.fda.gov/medwatch>

## Rofecoxib: new indication and label changes

**United States of America** — The Food and Drug Administration has approved new labelling text and precautions for rofecoxib based on the results of the Vioxx Gastrointestinal Outcomes Research (VIGOR) study.

The VIGOR study, a prospective, randomized, double-blind, one year study, evaluated approximately 4000 patients on rofecoxib 50 mg a day (twice the highest approved dose for chronic use) and approximately 4000 patients on the standard dose of naproxen, 1000 mg a day, a nonsteroidal anti-inflammatory drug (NSAID). Patients who were under treatment with low dose aspirin for heart attack prevention were excluded from the study.

The study demonstrated that rofecoxib was associated with a lower incidence of serious upper gastrointestinal (GI) adverse events of major bleeding, perforation and obstruction compared to naproxen. The reduction in risk was over 50 percent in cumulative rates for rofecoxib (.52%) compared to naproxen (1.22%).

An additional finding in the study, however, was that there was a higher cumulative rate of serious cardiovascular thromboembolic adverse events (such as heart attacks, angina pectoris, and peripheral vascular events) in the rofecoxib group (1.8%) compared to the naproxen group (0.6%). Data from two smaller studies comparing placebo and rofecoxib 25 mg daily did not show a difference in the rate of serious cardiovascular thromboembolic adverse events. The relationship of the cardiovas-



cular findings in the VIGOR study to use of rofecoxib is not known.

After carefully reviewing the results of the VIGOR Study, FDA agreed with the Arthritis Advisory Committee recommendations of February 8, 2001 that the label for Vioxx® should include gastrointestinal and cardiovascular information. The committee advised that the NSAID-class warning regarding GI adverse events should be modified, but not removed, from the VIOXX® label. This warning advises patients and their doctors about the risks of GI ulcers, bleeding, and perforation.

The committee also advised that the CV findings should be included in the Vioxx® label to provide doctors and patients with the available data on the potential risks and benefits compared to naproxen. The new labelling information approved by FDA will advise doctors to use caution in prescribing rofecoxib for patients with ischemic heart disease and notes that rofecoxib 50 mg is not recommended for chronic use.

In addition, the geriatric section of the label will reinforce information in the existing standard warning section of all NSAIDs indicating that the elderly are at higher risk of serious GI and renal events such as GI bleeding and acute renal failure.

The Food and Drug Administration has approved a supplemental application for the use of rofecoxib (Vioxx®) for rheumatoid arthritis in addition to the previously approved indications for osteoarthritis and pain. The new label also provides information from studies of patients with rheumatoid arthritis at the chronic dose of 25 mg rofecoxib compared to naproxen.

#### References

1. *FDA Talk Paper*, T02-18, 11 April 2002
2. Letter from Merck & Co. Inc. dated April 2002 <http://www.fda.gov>

# Essential Medicines

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## New procedures for updating the Model List of Essential Medicines

At its previous meeting in 1999, the Expert Committee on Selection and Use of Essential Drugs proposed that methods for updating and disseminating the Model List of Essential Drugs be revised with regard to (i) advances in the science of evidence-based decision-making; (ii) the increasing link between essential medicines and guidelines for clinical health care; and (iii) the high cost of many new and effective medicines. The Expert Committee concluded that current procedures do not define the range of conditions covered with adequate specificity, nor are the reasons for inclusion recorded with sufficient clarity.

In May 2001, an information document containing a proposed timetable for developing revised procedures to update the Model List was presented to the WHO Executive Board and all Member States were invited to comment on a discussion paper "Updating and disseminating the WHO Model List of Essential Drugs: the way forward". Comment was also requested from WHO collaborating centres, members of expert advisory panels, organizations of the United Nations system, nongovernmental organizations, professional associations, national essential medicines programmes, universities, representatives of the pharmaceutical industry, and patients' organizations.

### Key features of the new procedure

As a result of the consultation process, a new procedure for updating and disseminating the Model List has been developed. Major features include:

1. Use of the term "essential medicines" as an alternative to "essential drugs" with immediate effect, reflecting the common use of the term "medicines" to describe pharmaceutical preparations used in clinical health care practice.
2. A more systematic approach to encouraging and handling applications for medicines to be included in or deleted from the Model List.
3. A more transparent process for selecting medicines to be included in the list, including systematic analysis of medicines proposed for use in the care of different health conditions (comparing efficacy, safety and, where possible and appropriate, cost-effectiveness).
4. Opportunities for interested parties to comment on both an application and the draft recommendations of the Expert Committee.
5. The full involvement of different WHO departments in the application and selection process, linking the process to clinical guidelines disseminated by WHO.
6. Development of a new WHO essential medicines library which facilitates access to information about medicines on the Model List.
7. Steps to ensure that the Expert Committee operates with full scientific independence as it makes its final recommendations (in line with current practice for decisions on regulatory approval, procurement, and reimbursement within Member States).

At the WHO Executive Board in January 2002 the new procedures were presented in a Report by the Secretariat (1). The Board noted the report and its Annex with the new procedures and the Department of Essential Drugs and Medicines Policy was requested to organize the next meeting of the Expert Committee according to the new procedures while recognizing that due to the relatively short time these could not all be implemented immediately.

### References

1. Annex to Document EB109/8 (WHO, 2002), also reproduced on the WHO/Medicines website as "Procedures to update and disseminate the WHO Model List of Essential Medicines". <http://www.who.int/medicines>
2. Guidelines for Scaling Up Antiretroviral Therapy. <http://www.who.int/medicines>
3. 2002 WHO Model List of Essential Drugs. <http://www.who.int/medicines>

# WHO Model List of Essential Medicines

## Core list (revised in April 2002)

### 1: Anaesthetics

#### 1.1 GENERAL ANAESTHETICS AND OXYGEN

ether, anaesthetic (1c) (2)	inhalation
halothane (2)	inhalation
ketamine (2)	injection, 50 mg (as hydrochloride)/ml in 10-ml vial
nitrous oxide (2)	inhalation
oxygen	inhalation (medicinal gas)
<sup>a</sup> thiopental (2)	powder for injection, 0.5 g, 1.0 g (sodium salt) in ampoule

#### 1.2 LOCAL ANAESTHETICS

<sup>a</sup> bupivacaine (2, 9)	injection, 0.25%, 0.5% (hydrochloride) in vial injection for spinal anaesthesia, 0.5% (hydrochloride) in 4-ml ampoule to be mixed with 7.5% glucose solution
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<sup>a</sup> lidocaine	injection, 1%, 2% (hydrochloride) in vial injection for spinal anaesthesia, 5% (hydrochloride) in 2-ml ampoule to be mixed with 7.5% glucose solution topical forms, 2–4% (hydrochloride)
<sup>a</sup> lidocaine + epinephrine (adrenaline)	injection, 1%, 2% (hydrochloride) + epinephrine 1:200 000 in vial dental cartridge, 2% (hydrochloride) + epinephrine 1:80 000

#### 1.3 PREOPERATIVE MEDICATION & SEDATION FOR SHORT-TERM PROCEDURES

atropine	injection, 1 mg (sulfate) in 1-ml ampoule
chloral hydrate	syrup, 200 mg/5 ml
<sup>a</sup> diazepam (1b)	injection, 5 mg/ml in 2-ml ampoule tablet, 5 mg

### Explanatory Notes

The core list presents a list of minimum medicine needs for a basic health care system, listing the most efficacious, safe and cost-effective medicines for priority conditions. Priority conditions are selected on the basis of current and estimated future public health relevance, and potential for safe and cost-effective treatment.

When the strength of a drug is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as". Many drugs included in the list are preceded by a box <sup>a</sup> to indicate that they represent an example of a therapeutic group and that various drugs could serve as alternatives. It is imperative that this is understood when drugs are selected at national level, since choice is then influenced by the comparative cost and availability of equivalent products. Examples of acceptable substitutions include:

- Hydrochlorothiazide: any other thiazide-type diuretic currently in broad clinical use.
- Hydralazine: any other peripheral vasodilator having an antihypertensive effect.
- Senna: any stimulant laxative (either synthetic or of plant origin).

Numbers in parentheses following drug names indicate:

- (1) Drugs subject to international control under: (a) the Single Convention on Narcotic Drugs (1961); (b) the Convention on Psychotropic Substances (1971); or (c) the United Nations Convention against Illicit Traffic in Narcotic Drugs and Psychotropic Substances (1988).
- (2) Specific expertise, diagnostic precision, individualization of dosage or special equipment required for proper use.
- (3) Greater potency or efficacy.
- (4) In renal insufficiency, contraindicated or dosage adjustments necessary.
- (5) To improve compliance.
- (6) Special pharmacokinetic properties.
- (7) Adverse effects diminish benefit/risk ratio.
- (8) Limited indications or narrow spectrum of activity.
- (9) For epidural anaesthesia.
- (10) Sustained-release preparations are available. A proposal to include such a product in a national list of essential drugs should be supported by adequate documentation.
- (11) Monitoring of therapeutic concentrations in plasma can improve safety and efficacy.

Drugs are listed in alphabetical order.

°morphine (1a)	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule
°promethazine	elixir or syrup, 5 mg (hydrochloride)/5 ml

## 2: Analgesics, Antipyretics, Nonsteroidal Anti-Inflammatory Medicines (NSAIMs), Medicines Used to Treat Gout and Disease-Modifying Agents used in Rheumatic Disorders (DMARDs)

### 2.1 NON-OPIOID ANALGESICS & NON-STEROIDAL ANTI-INFLAMMATORY MEDICINES (NSAIMs)

acetylsalicylic acid	tablet, 100–500 mg suppository, 50–150 mg
°ibuprofen	tablet, 200 mg, 400 mg
paracetamol	tablet, 100–500 mg suppository, 100 mg syrup, 125 mg/5 ml

### 2.2 OPIOID ANALGESICS

°codeine (1a)	tablet, 30 mg (phosphate)
°morphine (1a)	injection, 10 mg (sulfate or hydrochloride) in 1-ml ampoule oral solution, 10 mg (hydrochloride or sulfate)/5 ml tablet, 10 mg (sulfate)

### 2.3 MEDICINES USED TO TREAT GOUT

allopurinol (4)	tablet, 100 mg
colchicine (7)	tablet, 500 micrograms

### 2.4 DISEASE-MODIFYING AGENTS USED IN RHEUMATIC DISORDERS

azathioprine (2)	tablet, 50 mg
chloroquine (2)	tablet, 100 mg, 150 mg (as phosphate or sulfate)
cyclophosphamide (2)	tablet, 25 mg
methotrexate (2)	tablet, 2.5 mg (as sodium salt)
penicillamine (2)	capsule or tablet, 250 mg
sulfasalazine (2)	tablet, 500 mg

## 3: Antiallergics and Medicines Used in Anaphylaxis

°chlorphenamine	tablet, 4 mg (hydrogen maleate) injection, 10 mg (hydrogen maleate) in 1-ml ampoule
°dexamethasone	tablet, 500 micrograms, 4 mg injection, 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule
epinephrine (adrenaline)	injection, 1 mg (as hydrochloride or hydrogen tartrate) in 1-ml ampoule
hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
°prednisolone	tablet, 5 mg

## 4: Antidotes and Other Substances Used in Poisoning

### 4.1 NON-SPECIFIC

°charcoal, activated	powder
ipecacuanha	syrup, containing 0.14% ipecacuanha alkaloids calculated as emetine

### 4.2 SPECIFIC

acetylcysteine	injection, 200 mg/ml in 10-ml ampoule
atropine	injection, 1 mg (sulfate) in 1-ml ampoule
calcium gluconate (2, 8)	injection, 100 mg/ml in 10-ml ampoule
deferoxamine	powder for injection, 500 mg (mesilate) in vial
dimercaprol (2)	injection in oil, 50 mg/ml in 2-ml ampoule
°DL-methionine	tablet, 250 mg
methylthioninium chloride (methylene blue)	injection, 10 mg/ml in 10-ml ampoule
naloxone	injection, 400 micrograms (hydrochloride) in 1-ml ampoule
penicillamine (2)	capsule or tablet, 250 mg
potassium ferric hexacyano-ferrate(II) ·2H <sub>2</sub> O (Prussian blue)	powder for oral administration
sodium calcium edetate (2)	injection, 200 mg/ml in 5-ml ampoule

sodium nitrite	injection, 30 mg/ml in 10-ml ampoule
sodium thiosulfate	injection, 250 mg/ml in 50-ml ampoule

## 5: Anticonvulsants/Antiepileptics

carbamazepine (10, 11)	scored tablet, 100 mg, 200 mg
<sup>a</sup> diazepam (1b)	injection, 5 mg/ml in 2-ml ampoule (intravenous or rectal)
ethosuximide	capsule, 250 mg syrup, 250 mg/5 ml
magnesium sulfate	injection, 500 mg/ml in 2-ml ampoule 500 mg/ml in 10-ml ampoule
phenobarbital (1b, 11)	tablet, 15–100 mg elixir, 15 mg/5 ml
phenytoin (7, 11)	capsule or tablet, 25 mg, 50 mg, 100 mg (sodium salt) injection, 50 mg (sodium salt)/ml in 5-ml vial
valproic acid (7, 11)	enteric coated tablet, 200 mg, 500 mg (sodium salt)

## 6: Anti-infective Medicines

### 6.1 ANTHELMINTHICS

#### 6.1.1 INTESTINAL ANTHELMINTHICS

albendazole	chewable tablet, 400 mg
levamisole	tablet, 50 mg, 150 mg (as hydrochloride)
<sup>a</sup> mebendazole	chewable tablet, 100 mg, 500 mg
niclosamide	chewable tablet, 500 mg
praziquantel	tablet, 150 mg, 600 mg
pyrantel	chewable tablet, 250 mg (as embonate) oral suspension, 50 mg (as embonate)/ml

#### 6.1.2 ANTIFILARIALS

diethylcarbamazine	tablet, 50 mg, 100 mg (dihydrogen citrate)
ivermectin	scored tablet, 3 mg, 6 mg

#### 6.1.3 ANTISCHISTOSOMALS AND OTHER ANTITREMATODE MEDICINES

praziquantel	tablet, 600 mg
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triclabendazole	tablet, 250 mg
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## 6.2 ANTIBACTERIALS

### 6.2.1 BETA LACTAM MEDICINES

<sup>a</sup> amoxicillin	capsule or tablet, 250 mg, 500 mg (anhydrous) powder for oral suspension, 125 mg (anhydrous)/5 ml
ampicillin	powder for injection, 500 mg, 1 g (as sodium salt) in vial
benzathine benzylpenicillin	powder for injection, 1.44 g benzylpenicillin (= 2.4 million IU) in 5-ml vial
benzylpenicillin	powder for injection, 600 mg (= 1 million IU), 3 g (= 5 million IU) (sodium or potassium salt) in vial
<sup>a</sup> cloxacillin	capsule, 500 mg, 1 g (as sodium salt) powder for oral solution, 125 mg (as sodium salt)/5 ml powder for injection, 500 mg (as sodium salt) in vial
phenoxymethylpenicillin	tablet, 250 mg (as potassium salt) powder for oral suspension, 250 mg (as potassium salt)/5 ml
procaine benzylpenicillin	powder for injection, 1 g (= 1 million IU), 3 g (= 3 million IU) in vial

### 6.2.2 OTHER ANTIBACTERIALS

<sup>a</sup> chloramphenicol (7)	capsule, 250 mg oral suspension, 150 mg (as palmitate)/5 ml powder for injection, 1 g (sodium succinate) in vial
<sup>a</sup> ciprofloxacin	tablet, 250 mg (as hydrochloride)
<sup>a</sup> doxycycline (5, 6)	capsule or tablet, 100 mg (hydrochloride)
<sup>a</sup> erythromycin	capsule or tablet, 250 mg (as stearate or ethyl succinate) powder for oral suspension, 125 mg (as stearate or ethyl succinate) powder for injection, 500 mg (as lactobionate) in vial
<sup>a</sup> gentamicin (2, 4, 7, 11)	injection, 10 mg, 40 mg (as sulfate)/ml in 2-ml vial

° metronidazole	tablet, 200–500 mg injection, 500 mg in 100-ml vial suppository, 500 mg, 1 g oral suspension, 200 mg (as benzoate)/5 ml
nalidixic acid (8)	tablet, 250 mg, 500 mg
nitrofurantoin (4, 8)	tablet, 100 mg
spectinomycin (8)	powder for injection, 2 g (as hydrochloride) in vial
° sulfadiazine (4)	tablet, 500 mg injection, 250 mg (sodium salt) in 4-ml ampoule
° sulfamethoxazole + trimethoprim (4)	tablet, 100 mg + 20 mg, 400 mg + 80 mg oral suspension, 200 mg + 40 mg/5 ml injection, 80 mg + 16 mg/ml in 5-ml and 10-ml ampoule
trimethoprim (8)	tablet, 100 mg, 200 mg injection, 20 mg/ml in 5-ml ampoule

### 6.2.3 ANTILEPROSY MEDICINES

clofazimine	capsule, 50 mg, 100 mg
dapsone	tablet, 25 mg, 50 mg, 100 mg
rifampicin	capsule or tablet, 150 mg, 300 mg

### 6.2.4 ANTITUBERCULOSIS MEDICINES

ethambutol (4)	tablet, 100–400 mg (hydrochloride)
isoniazid	tablet, 100–300 mg
isoniazid + ethambutol (5)	tablet, 150 mg + 400 mg
pyrazinamide	tablet, 400 mg
rifampicin	capsule or tablet, 150 mg, 300 mg
rifampicin + isoniazid (5)	tablet, 60 mg + 30 mg, 150 mg + 75 mg, 300 mg + 150 mg tablet, 60 mg + 60 mg (for intermittent use 3 times weekly) tablet, 150 mg + 150 mg (for intermittent use 3 times weekly)
rifampicin + isoniazid + pyrazinamide (5)	tablet, 60 mg + 30 mg + 150 mg, 150 mg + 75 mg + 400 mg tablet, 150 mg + 150 mg + 500 mg (for intermittent use 3 times weekly)

rifampicin + isoniazid + pyrazinamide + ethambutol	tablet, 150 mg + 75 mg + 400 mg + 275 mg
streptomycin (4)	powder for injection, 1 g (as sulfate) in vial

### 6.3 ANTIFUNGAL MEDICINES

amphotericin B (4)	powder for injection, 50 mg in vial
° fluconazole	capsule, 50 mg injection, 2 mg/ml in vial oral suspension, 50 mg/5-ml
griseofulvin (7)	capsule or tablet, 125 mg, 250 mg
nystatin	tablet, 100 000, 500 000 IU lozenge, 100 000 IU pessary, 100 000 IU

### 6.4 ANTIVIRAL MEDICINES

#### 6.4.1 ANTIHERPES MEDICINES

aciclovir (8)	tablet, 200 mg powder for injection, 250 mg (as sodium salt) in vial
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#### 6.4.2 ANTIRETROVIRALS

*Antiretrovirals do not cure HIV infection, they only temporarily suppress viral replication and improve symptoms. They have various adverse effects and patients receiving this therapy require careful monitoring by adequately trained health professionals. For these reasons, continuous rigorous promotion of measures to prevent new infections is essential and the need for this has not been diminished in any way by the addition of antiretrovirals to the Model List. Adequate resources and trained health professionals are a prerequisite for the introduction of this class of drugs. Effective therapy requires commencement of three or four antiretrovirals simultaneously, and alternative regimens are necessary to meet specific requirements at start-up, to substitute for first-line regimens in the case of toxicity, or to replace failing regimens. The Committee strongly recommends the use of three- or four-combinations as specifically recommended in the WHO treatment guidelines. The use of fixed dose preparations for these combinations is also recommended, with assured pharmaceutical quality and interchangeability with the single products as approved by the relevant drug regulatory authority.*

#### 6.4.2.1 NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS\*

abacavir (ABC)	tablet, 300 mg (as sulfate) oral solution, 100 mg (as sulfate)/5 ml
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\* Refer to WHO Model Formulary 2002 for full details of dosage form and use (<http://www.who.int/medicines/organization/par/formulary>)

didanosine (ddl)	(chewable) tablet, 25 mg, 50 mg, 100 mg, 150 mg, 200 mg capsule, 125 mg, 200 mg, 250 mg, 400 mg powder for oral solution, 100 mg, 167 mg, 250 mg (sachet)
lamivudine (3TC)	tablet, 150 mg, oral solution, 50 mg/5 ml
stavudine (d4T)	capsule, 15 mg, 20 mg 30 mg, 40 mg powder for oral solution, 5 mg/5 ml
zidovudine (ZDV or AZT)	tablet, 300 mg capsule, 100 mg, 250 mg oral solution or syrup, 50 mg/5 ml solution for infusion, 10 mg/ml in 20-ml vial

#### 6.4.2.2 NON-NUCLEOSIDE REVERSE TRANSCRIPTASE INHIBITORS\*

efavirenz (EFV or EFZ)	capsule, 50 mg, 100 mg, 200 mg oral solution, 150 mg/5ml
nevirapine (NVP)	tablet, 200 mg oral suspension, 50 mg/5 ml

#### 6.4.2.3 PROTEASE INHIBITORS\*

*Selection of two or three protease inhibitors from the Model List will need to be determined by each country after consideration of local treatment guidelines and experience, as well as the comparative costs of available products. Ritonavir is recommended for use in combination with indinavir, lopinavir and saquinavir as a booster, and not as a therapy in its own right.*

indinavir (IDV)	capsule, 100 mg, 200 mg, 333 mg, 400 mg (as sulfate)
ritonavir (RTV/r)	capsule, 100 mg oral solution, 400 mg/5 ml
lopinavir (LPV/r) + ritonavir	capsule, 133.3 mg + 33.3 mg oral solution, 400 mg/5 ml + 100 mg/5 ml
nelfinavir (NFV)	tablet, 250 mg (as mesilate) powder, 50 mg (as mesilate)/g
saquinavir (SQV)	capsule, 200 mg

### 6.5 ANTIPROTOZOAL MEDICINES

#### 6.5.1 ANTIAMOEBIAC AND ANTIGIARDIASIS MEDICINES

▫ diloxanide	tablet, 500 mg (furoate)
▫ metronidazole	tablet, 200–500 mg injection, 500 mg in 100-ml vial oral suspension, 200 mg (as benzoate)/5 ml

#### 6.5.2 ANTILEISHMANIASIS MEDICINES

▫ meglumine antimoniate	injection, 30%, equivalent to approx. 8.1% antimony, in 5-ml ampoule
pentamidine (5)	powder for injection, 200 mg, 300 mg (isetionate) in vial

#### 6.5.3 ANTIMALARIAL MEDICINES

##### 6.5.3.1 FOR CURATIVE TREATMENT

artemether + lumefantrine	tablet, 20 mg + 120 mg
▫ chloroquine	tablet, 100 mg, 150 mg (as phosphate or sulfate) syrup, 50 mg (as phosphate or sulfate)/5 ml injection, 40 mg (as hydrochloride, phosphate or sulfate)/ml in 5-ml ampoule
primaquine	tablet, 7.5 mg, 15 mg (as diphosphate)
▫ quinine	tablet, 300 mg (as bisulfate or sulfate) injection, 300 mg (as dihydrochloride)/ml in 2-ml ampoule

##### 6.5.3.2 FOR PROPHYLAXIS

chloroquine	tablet, 150 mg (as phosphate or sulfate) syrup, 50 mg (as phosphate or sulfate)/5 ml
doxycycline	capsule or tablet, 100 mg (hydrochloride)
mefloquine	tablet, 250 mg (as hydrochloride)
proguanil ( <i>for use only in combination with chloroquine</i> )	tablet, 100 mg (hydrochloride)

\* Refer to WHO Model Formulary 2002 for full details of dosage form and use (<http://www.who.int/medicines/organization/par/formulary>)

### 6.5.4 ANTIPNEUMOCYSTOSIS AND ANTITOXOPLASMOSIS MEDICINES

pentamidine (2)	tablet, 200 mg, 300 mg
pyrimethamine	tablet, 25 mg
sulfamethoxazole + trimethoprim	injection, 80 mg + 16 mg/ml in 5-ml ampoule, 80 mg + 16 mg/ml in 10-ml ampoule

### 6.5.5 ANTITRYPANOSOMAL MEDICINES

#### 6.5.5.1 AFRICAN TRYPANOSOMIASIS

melarsoprol (2)	injection, 3.6% solution
pentamidine (2)	powder for injection, 200 mg, 300 mg (isetionate) in vial
suramin sodium	powder for injection, 1 g in vial

#### 6.5.5.2 AMERICAN TRYPANOSOMIASIS

benznidazole (7)	tablet, 100 mg
nifurtimox (2, 8)	tablet, 30 mg, 120 mg, 250 mg

### 6.6 INSECT REPELLENTS

diethyltoluamide	topical solution, 50%, 75%
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## 7: Antimigraine Medicines

### 7.1 FOR TREATMENT OF ACUTE ATTACK

acetylsalicylic acid	tablet, 300–500 mg
ergotamine (1c) (7)	tablet, 1 mg (tartrate)
paracetamol	tablet, 300–500 mg

### 7.2 FOR PROPHYLAXIS

<sup>a</sup> propranolol	tablet, 20 mg, 40 mg (hydrochloride)
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## 8: Antineoplastic and Immunosuppressive Medicines, and Medicines Used in Palliative Care

### 8.1 IMMUNOSUPPRESSIVE MEDICINES

Please see complementary list.

### 8.2 CYTOTOXIC MEDICINES

Please see complementary list.

### 8.3 HORMONES AND ANTIHORMONES

Please see complementary list.

### 8.4 DRUGS USED IN PALLIATIVE CARE

The WHO Expert Committee on the Selection and Use of Essential Medicines recommended that all the drugs mentioned in the WHO publication *Cancer Pain Relief: with a Guide to Opioid Availability, Second edition*, be considered essential. The drugs are included in the relevant sections of the Model List according to their therapeutic use, e.g. analgesics.

## 9: Antiparkinsonism Medicines

<sup>a</sup> biperiden	tablet, 2 mg (hydrochloride) injection, 5 mg (lactate) in 1-ml ampoule
levodopa + <sup>a</sup> carbidopa (5, 6)	tablet, 100 mg + 10 mg, 250 mg + 25 mg

## 10: Medicines affecting the Blood

### 10.1 ANTIANAEMIA MEDICINES

ferrous salt	tablet, equivalent to 60 mg iron oral solution, equivalent to 25 mg iron (as sulfate)/ml
ferrous salt + folic acid ( <i>nutritional supplement for use during pregnancy</i> )	tablet, equivalent to 60 mg iron + 400 microgram folic acid

folic acid (2)	tablet, 1 mg, 5 mg injection, 1 mg (as sodium salt) in 1-ml ampoule
hydroxocobalamin (2)	injection, 1 mg in 1-ml ampoule

### 10.2 MEDICINES AFFECTING COAGULATION

desmopressin (8)	injection, 4 micrograms (acetate)/ml in 1-ml ampoule nasal spray, 10 micrograms (acetate)/metered dose
heparin sodium	injection, 1000 IU/ml, 5000 IU/ml, 20 000 IU/ml in 1-ml ampoule
phytomenadione	injection, 10 mg/ml in 5-ml ampoule tablet, 10 mg
protamine sulfate	injection, 10 mg/ml in 5-ml ampoule
<sup>a</sup> warfarin (2, 6)	tablet, 1 mg, 2 mg and 5 mg (sodium salt)



## 11: Blood Products and Plasma Substitutes

### 11.1 PLASMA SUBSTITUTES

°dextran 70	injectable solution, 6%
°polygeline	injectable solution, 3.5%

### 11.2 PLASMA FRACTIONS FOR SPECIFIC USE

All plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components, and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2.

## 12: Cardiovascular Medicines

### 12.1 ANTIANGINAL MEDICINES

°atenolol	tablet, 50 mg, 100 mg
glyceryl trinitrate	tablet (sublingual), 500 micrograms
°isosorbide dinitrate	tablet (sublingual), 5 mg
°verapamil (10)	tablet, 40 mg, 80 mg (hydrochloride)

### 12.2 ANTIARRHYTHMIC MEDICINES

°atenolol	tablet, 50 mg, 100 mg
digoxin (4, 11)	tablet, 62.5 micrograms, 250 micrograms oral solution, 50 micrograms/ml injection, 250 micrograms/ml in 2-ml ampoule
lidocaine	injection, 20 mg (hydrochloride)/ml in 5-ml ampoule
verapamil (8, 10)	tablet, 40 mg, 80 mg (hydrochloride) injection, 2.5 mg (hydrochloride)/ml in 2-ml ampoule

### 12.3 ANTIHYPERTENSIVE MEDICINES

°atenolol	tablet, 50 mg, 100 mg
°captopril	scored tablet, 25 mg
°hydralazine	tablet, 25 mg, 50 mg (hydrochloride) powder for injection, 20 mg (hydrochloride) in ampoule
°hydrochlorothiazide	scored tablet, 25 mg

methyl dopa (7)	tablet, 250 mg
°nifedipine (10)	sustained-release formulations tablet, 10 mg
°reserpine	tablet, 100 micrograms, 250 micrograms injection, 1 mg in 1-ml ampoule

### 12.4 MEDICINES USED IN HEART FAILURE

°captopril	scored tablet, 25 mg
digoxin (4, 11)	tablet, 62.5 micrograms, 250 micrograms oral solution, 50 micrograms/ml injection, 250 micrograms/ml in 2-ml ampoule
dopamine	injection, 40 mg (hydrochloride) in 5-ml vial

°hydrochlorothiazide	tablet, 25 mg, 50 mg
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### 12.5 ANTITHROMBOTIC MEDICINES

acetylsalicylic acid	tablet, 100 mg
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### 12.6 LIPID-LOWERING AGENTS

The WHO Expert Committee on Selection and Use of Essential Medicines recognizes the value of lipid-lowering drugs in treating patients with hyperlipidaemia. HMG CoA reductase inhibitors, often referred to as "statins", are a family of potent and effective lipid-lowering drugs with a good tolerability profile. Several of these drugs have been shown to reduce the incidence of fatal and non-fatal myocardial infarction, stroke and mortality (all causes), as well as the need for coronary by-pass surgery. All remain very costly but may be cost-effective for secondary prevention of cardiovascular disease as well as for primary prevention in some very high-risk patients. Since no single drug has been shown to be significantly more effective or less expensive than others in the group, none is included in the Model List; the choice of drug for use in patients at highest risk should be decided at national level.

## 13: Dermatological Medicines (topical)

### 13.1 ANTIFUNGAL MEDICINES

benzoic acid + salicylic acid	ointment or cream, 6% + 3%
°miconazole	ointment or cream, 2% (nitrate)
sodium thiosulfate	solution, 15%

**13.2 ANTI-INFECTIVE MEDICINES**

°methylrosanilinium chloride (gentian violet)	aqueous solution, 0.5% tincture, 0.5%
neomycin sulfate + °bacitracin (7)	ointment, 5 mg neomycin sulfate + 500 IU bacitracin zinc/g
potassium permanganate	aqueous solution, 1:10 000
silver sulfadiazine	cream, 1%, in 500-g container

**13.3 ANTI-INFLAMMATORY AND ANTI-PRURITIC MEDICINES**

°betamethasone (3)	ointment or cream, 0.1% (as valerate)
°calamine lotion	lotion
°hydrocortisone	ointment or cream, 1% (acetate)

**13.4 ASTRINGENT MEDICINES**

aluminium diacetate	solution, 13% for dilution
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**13.5 MEDICINES AFFECTING SKIN DIFFERENTIATION AND PROLIFERATION**

benzoyl peroxide	lotion or cream, 5%
coal tar	solution, 5%
dithranol	ointment, 0.1–2%
fluorouracil	ointment, 5%
°podophyllum resin (7)	solution, 10–25%
salicylic acid	solution 5%
urea	ointment or cream, 10%

**13.6 SCABICIDES AND PEDICULICIDES**

°benzyl benzoate	lotion, 25%
permethrin	cream, 5% lotion, 1%

**13.7 ULTRAVIOLET-BLOCKING AGENTS**

*Please see complementary list*

**14: Diagnostic Agents****14.1 OPHTHALMIC MEDICINES**

fluorescein	eye drops, 1% (sodium salt)
°tropicamide	eye drops, 0.5%

**14.2 RADIOCONTRAST MEDIA**

°amidotrizoate	injection, 140–420 mg iodine (as sodium or meglumine salt)/ml in 20-ml ampoule
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barium sulfate	aqueous suspension
°iohexol	injection, 140–350 mg iodine/ml in 5-ml, 10-ml and 20-ml ampoule
°iopanoic acid	tablet, 500 mg
°propylidone ( <i>For administration only into the bronchial tree.</i> )	oily suspension, 500–600 mg/ml in 20-ml ampoule

**15: Disinfectants and Antiseptics****15.1 ANTISEPTICS**

°chlorhexidine	solution, 5% (digluconate) for dilution
°ethanol	solution, 70% (denatured)
°polyvidone iodine	solution, 10%

**15.2 DISINFECTANTS**

°chlorine base compound	powder (0.1% available chlorine) for solution
°chloroxylenol	solution, 4.8%
glutaral	solution, 2%

**16: Diuretics**

°amiloride (4, 7, 8)	tablet, 5 mg (hydrochloride)
°furosemide	tablet, 40 mg injection, 10 mg/ml in 2-ml ampoule
°hydrochlorothiazide	tablet, 25 mg, 50 mg
spironolactone (8)	tablet, 25 mg

**17: Gastrointestinal Medicines****17.1 ANTACIDS AND OTHER ANTI-ULCER MEDICINES**

aluminium hydroxide	tablet, 500 mg oral suspension, 320 mg/5 ml
°cimetidine	tablet, 200 mg injection, 200 mg in 2-ml ampoule
magnesium hydroxide	oral suspension, equivalent to 550 mg magnesium oxide/10 ml

**17.2 ANTIEMETIC MEDICINES**

metoclopramide	tablet, 10 mg (hydrochloride)
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	injection, 5 mg (hydrochloride)/ml in 2-ml ampoule
°promethazine	tablet, 10 mg, 25 mg (hydrochloride) elixir or syrup, 5 mg (hydrochloride)/5 ml injection, 25 mg (hydrochloride)/ml in 2-ml ampoule

### 17.3 ANTIHAEMORRHOIDAL MEDICINES

°local anaesthetic, astringent and anti-inflammatory drug	ointment or suppository
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### 17.4 ANTI-INFLAMMATORY MEDICINES

hydrocortisone	suppository, 25 mg (acetate) °retention enema
°sulfasalazine (2)	tablet, 500 mg suppository, 500 mg retention enema

### 17.5 ANTISPASMODIC MEDICINES

°atropine	tablet, 1 mg (sulfate) injection, 1 mg (sulfate) in 1-ml ampoule
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### 17.6 LAXATIVES

°senna	tablet, 7.5 mg (sennosides) (or traditional dosage forms)
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### 17.7 MEDICINES USED IN DIARRHOEA

#### 17.7.1 ORAL REHYDRATION

oral rehydration salts (for glucose– electrolyte solution)	powder, 27.9 g/l
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*Components to reconstitute  
one litre of glucose electrolyte  
solution* g/l

sodium chloride	3.5
trisodium citrate dihydrate*	2.9
potassium chloride	1.5
glucose	20.0

\*Trisodium citrate dihydrate may be replaced by sodium bicarbonate (sodium hydrogen carbonate).

#### 17.7.2 ANTIDIARRHOEAL (SYMPTOMATIC) MEDICINES

°codeine (1a)	tablet, 30 mg (phosphate)
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## 18: Hormones, other Endocrine Medicines and Contraceptives

### 18.1 ADRENAL HORMONES AND SYNTHETIC SUBSTITUTES

°dexamethasone	tablet, 500 micrograms, 4 mg injection, 4 mg dexamethasone phosphate (as disodium salt) in 1-ml ampoule
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hydrocortisone	powder for injection, 100 mg (as sodium succinate) in vial
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°prednisolone	tablet, 1 mg, 5 mg
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### 18.2 ANDROGENS

### 18.3 CONTRACEPTIVES

#### 18.3.1 HORMONAL CONTRACEPTIVES

°ethinylestradiol + °levonorgestrel	tablet, 30 micrograms + 150 micrograms,
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°ethinylestradiol + °levonorgestrel	tablet, 50 micrograms + 250 micrograms (pack of four)
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°ethinylestradiol + °norethisterone	tablet, 35 micrograms + 1.0 mg
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levonorgestrel	tablet, 0.75 mg (pack of two)
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#### 18.3.2 INTRAUTERINE DEVICES

copper-containing device

#### 18.3.3 BARRIER METHODS

condoms with or without spermicide (nonoxinol<sup>+</sup>)

diaphragms with spermicide (nonoxinol<sup>+</sup>)

### 18.4 ESTROGENS

°ethinylestradiol	tablet, 10 micrograms, 50 micrograms
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### 18.5 INSULINS AND OTHER ANTIDIABETIC AGENTS

°glibenclamide	tablet, 2.5 mg, 5 mg
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insulin injection (soluble)	injection, 40 IU/ml in 10-ml vial, 100 IU/ml in 10-ml vial
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intermediate-acting insulin	injection, 40 IU/ml in 10-ml vial, 100 IU/ml in 10-ml vial (as compound insulin zinc suspension or isophane insulin)
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+ See also page 120 for further information.

metformin                      tablet, 500 mg (hydrochloride)

### 18.6 OVULATION INDUCERS

<sup>m</sup>clomifene (2, 8)                      tablet, 50 mg (citrate)

### 18.7 PROGESTOGENS

norethisterone                      tablet, 5 mg

### 18.8 THYROID HORMONES AND ANTITHYROID DRUGS

levothyroxine                      tablet, 50 micrograms,  
100 micrograms  
(sodium salt)

potassium iodide                      tablet, 60 mg

<sup>m</sup>propylthiouracil                      tablet, 50 mg

## 19: Immunologicals

### 19.1 DIAGNOSTIC AGENTS

All tuberculins should comply with the WHO Requirements for Tuberculins (Revised 1985). WHO Expert Committee on Biological Standardization Thirty-sixth report (WHO Technical Report Series, No. 745, 1987, Annex 1).

tuberculin,    injection  
purified protein derivative (PPD)

### 19.2 SERA AND IMMUNOGLOBULINS

*All plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components and Plasma Derivatives (Revised 1992). WHO Expert Committee on Biological Standardization Forty-third report (WHO Technical Report Series, No. 840, 1994, Annex 2).*

anti-D immunoglobulin                      injection, 250 micrograms in  
(human)    single-dose vial

<sup>m</sup>antitetanus immunoglobulin                      injection, 500 IU  
(human)    in vial

antivenom serum    injection

diphtheria antitoxin    injection, 10 000 IU,  
20 000 IU in vial

immunoglobulin,    injection (intramuscular)  
human normal (2)

immunoglobulin,    injection (intravenous)  
human normal (2, 8)

<sup>m</sup>rabies immunoglobulin    injection, 150 IU/ml

### 19.3 VACCINES

*All vaccines should comply with the WHO Requirements for Biological Substances.*

### 19.3.1 FOR UNIVERSAL IMMUNIZATION

BCG vaccine

diphtheria vaccine

hepatitis B vaccine

measles vaccine

pertussis vaccine

poliomyelitis vaccine

tetanus vaccine

### 19.3.2 FOR SPECIFIC GROUPS OF INDIVIDUALS

influenza vaccine

meningococcal meningitis vaccine

mumps vaccine

rabies vaccine (inactivated: prepared in cell culture)

rubella vaccine

typhoid vaccine

yellow fever vaccine

## 20: Muscle Relaxants (peripherally acting) and Cholinesterase Inhibitors

<sup>m</sup>alcuronium chloride (2)    injection, 5 mg/ml  
in 2-ml ampoule

<sup>m</sup>neostigmine    tablet, 15 mg (bromide)  
injection, 500 micrograms, 2.5 mg  
(metilsulfate) in 1-ml ampoule

pyridostigmine (2, 8)    tablet, 60 mg (bromide)  
injection, 1 mg  
in 1-ml ampoule

suxamethonium (2)    injection, 50 mg (chloride)/ml  
in 2-ml ampoule  
powder for injection

## 21: Ophthalmological Preparations

### 21.1 ANTI-INFECTIVE AGENTS

<sup>m</sup>gentamicin    solution (eye drops), 0.3%  
(sulfate)

<sup>m</sup>idoxuridine    solution (eye drops), 0.1%  
eye ointment, 0.2%

silver nitrate    solution (eye drops), 1%

<sup>m</sup>tetracycline    eye ointment, 1% (hydrochloride)

**21.2 ANTI-INFLAMMATORY AGENTS**

°prednisolone solution (eye drops), 0.5%  
(sodium phosphate)

**21.3 LOCAL ANAESTHETICS**

°tetracaine solution (eye drops), 0.5%  
(hydrochloride)

**21.4 MIOTICS AND ANTIGLAUCOMA DRUGS**

acetazolamide tablet, 250 mg

°pilocarpine solution (eye drops), 2%, 4%  
(hydrochloride or nitrate)

°timolol solution (eye drops), 0.25%, 0.5%  
(as maleate)

**21.5 MYDRIATICS**

atropine solution (eye drops),  
0.1%, 0.5%, 1% (sulfate)

**22: Oxytocics and Antioxytocics****22.1 OXYTOCICS**

ergometrine tablet, 200 micrograms  
(hydrogen maleate)  
injection, 200 micrograms  
(hydrogen maleate)  
in 1-ml ampoule

oxytocin injection, 10 IU in 1-ml ampoule

**22.2 ANTIOXYTOCICS**

°salbutamol (2) tablet, 4 mg (as sulfate)  
injection, 50 micrograms  
(as sulfate)/ml  
in 5-ml ampoule

**23: Peritoneal Dialysis Solution**

intra-peritoneal dialysis solution parenteral solution  
(of appropriate composition)

**24: Psychotherapeutic Medicines****24.1 MEDICINES USED IN PSYCHOTIC DISORDERS**

°chlorpromazine tablet, 100 mg (hydrochloride)  
syrup, 25 mg  
(hydrochloride)/5 ml  
injection, 25 mg  
(hydrochloride)/ml in 2-ml ampoule

°fluphenazine (5) injection, 25 mg  
(decanoate or enantate)  
in 1-ml ampoule

°haloperidol tablet, 2 mg, 5 mg  
injection, 5 mg in  
1-ml ampoule

**24.2 MEDICINES USED IN MOOD DISORDERS****24.2.1 MEDICINES USED IN DEPRESSIVE DISORDERS**

°amitriptyline tablet, 25 mg (hydrochloride)

**24.2.2 MEDICINES USED IN BIPOLAR DISORDERS**

carbamazepine (10, 11) scored tablet, 100 mg, 200 mg

lithium carbonate (2, 4) capsule or tablet, 300 mg

valproic acid (7, 11) enteric coated tablet,  
200 mg, 500 mg (sodium salt)

**24.3 MEDICINES USED IN GENERALIZED ANXIETY AND SLEEP DISORDERS**

°diazepam (1b) scored tablet, 2 mg, 5 mg

**24.4 MEDICINES USED IN OBSESSIVE COMPULSIVE DISORDERS AND PANIC ATTACKS**

clomipramine capsules, 10 mg, 25 mg  
(hydrochloride)

**25: Medicines Acting on the Respiratory Tract****25.1 ANTI-ASTHMATIC MEDICINES**

°aminophylline (2) injection, 25 mg/ml  
in 10-ml ampoule

°beclometasone inhalation (aerosol), 50 micrograms,  
250 micrograms,  
(dipropionate) per dose

°epinephrine (adrenaline) injection, 1 mg  
(as hydrochloride or hydrogen  
tartrate) in 1-ml ampoule

ipratropium bromide inhalation (aerosol),  
20 micrograms/metered dose

°salbutamol tablet, 2 mg, 4 mg (as sulfate)  
inhalation (aerosol), 100 micrograms  
(as sulfate) per dose  
syrup, 2 mg (as sulfate)/5 ml

injection, 50 micrograms (as sulfate)/ml in 5-ml ampoule	(equivalent to Na <sup>+</sup> 1000 mmol/l, HCO <sub>3</sub> <sup>-</sup> 1000 mmol/l)
respiratory solution for use in nebulizers, 5 mg (as sulfate)/ml	<sup>a</sup> sodium lactate, compound solution injectable solution

theophylline (10, 11) tablet, 100 mg, 200 mg, 300 mg

## 25.2 ANTITUSSIVES

<sup>a</sup>dextromethorphan oral solution,  
3.5 mg (bromide)/5 ml

## 26: Solutions correcting Water, Electrolyte and Acid-base Disturbances

### 26.1 ORAL

oral rehydration salts (for glucose–  
electrolyte solution) for composition  
see section 17.7.1

potassium chloride powder for solution

### 26.2 PARENTERAL

glucose injectable solution,  
5% isotonic, 10% isotonic,  
50% hypertonic

glucose with injectable solution, 4%  
sodium chloride glucose, 0.18% sodium chloride  
(equivalent to Na<sup>+</sup> 30 mmol/l  
Cl<sup>-</sup> 30 mmol/l)

potassium chloride (2) 11.2% solution in  
20-ml ampoule, (equivalent to  
K<sup>+</sup> 1.5 mmol/ml, Cl<sup>-</sup> 1.5 mmol/ml)

sodium chloride injectable solution, 0.9%  
isotonic (equivalent to Na<sup>+</sup> 154  
mmol/l, Cl<sup>-</sup> 154 mmol/l)

sodium hydrogen injectable solution, 1.4%  
carbonate isotonic (equivalent to Na<sup>+</sup> 167  
mmol/l, HCO<sub>3</sub><sup>-</sup> 167 mmol/l)

solution, 8.4% in 10-ml ampoule

## 26.3 MISCELLANEOUS

water for injection 2-ml, 5-ml, 10-ml ampoules

## 27: Vitamins and Minerals

ascorbic acid tablet, 50 mg

<sup>a</sup>ergocalciferol capsule or tablet, 1.25 mg  
(50 000 IU)  
oral solution,  
250 micrograms/ml (10 000 IU/ml)

iodine (8) iodized oil, 1 ml (480 mg iodine),  
0.5 ml (240 mg iodine) in  
ampoule (oral or injectable)  
solution, 0.57 ml, (308 mg iodine)  
in dispenser bottle  
capsule, 200 mg

<sup>a</sup>nicotinamide tablet, 50 mg

pyridoxine tablet, 25 mg (hydrochloride)

<sup>a</sup>retinol sugar-coated tablet, 10 000 IU  
(as palmitate) (5.5 mg)  
capsule, 200 000 IU (as  
palmitate) (110 mg)

oral oily solution,  
100 000 IU/ml in multidose  
dispenser (as palmitate)

water-miscible injection,  
100 000 IU (as palmitate)  
(55 mg) in 2-ml ampoule

riboflavin tablet, 5 mg

<sup>a</sup>sodium fluoride in any appropriate formulation

thiamine tablet, 50 mg (hydrochloride)

The following additions to the WHO Model List (both core and complementary lists) have been approved by the WHO Expert Committee on the Selection and Use of Essential Medicines. The report of the meeting will be published in the WHO Technical Report Series.

abacavir, didanosine, lamivudine, stavudine, efavirenz, indinavir, ritonavir, lopinavir, nelfinavir, saquinavir, artemether + lumefantrine, amikacin, *p*-aminosalicylic acid, capreomycin, cycloserine, ethionamide, kanamycin, levofloxacin, ofloxacin.

# WHO Model List of Essential Medicines: Complementary List

## 1: Anaesthetics

### 1.2 LOCAL ANAESTHETICS

ephedrine (C) injection, 30 mg  
(For use in spinal anaesthesia (hydrochloride)/ml in  
during delivery to prevent hypotension) 1-ml ampoule

## 2: Analgesics, Antipyretics, Nonsteroidal Anti-Inflammatory Medicines (NSAIDs), Medicines Used to Treat Gout and Disease- Modifying Agents used in Rheumatic Disorders (DMARDs)

### 2.2 OPIOID ANALGESICS

°pethidine (A) (1a, 4) injection, 50 mg  
(hydrochloride) in 1-ml ampoule  
tablet, 50 mg, 100 mg (hydrochloride)

## 5: Anticonvulsants/Antiepileptics

°clonazepam (B) (1b) scored tablet, 500 micrograms

## 6: Anti-infective Medicines

### 6.1 ANTHELMINTHICS

#### 6.1.2 ANTIFILARIALS

suramin sodium (B) (2, 7) powder for injection,  
1 g in vial

#### 6.1.3 ANTISCHISTOSOMALS AND OTHER ANTITREMATODE MEDICINES

oxamniquine (C) (8) capsule, 250 mg  
syrup, 250 mg/5 ml

### 6.2 ANTIBACTERIALS

#### 6.2.1 BETA LACTAM MEDICINES

##### *Restricted indications*

°amoxicillin + tablet, 500 mg + 125 mg  
°clavulanic acid (D)

## Explanatory Notes

The **complementary list** presents essential medicines for priority diseases which are efficacious, safe and cost-effective but not necessarily affordable, or for which specialised health care facilities or services may be needed.

When the strength of a drug is specified in terms of a selected salt or ester, this is mentioned in brackets; when it refers to the active moiety, the name of the salt or ester in brackets is preceded by the word "as". Many drugs included in the list are preceded by a box (☐) to indicate that they represent an example of a therapeutic group and that various drugs could serve as alternatives. It is imperative that this is understood when drugs are selected at national level, since choice is then influenced by the comparative cost and availability of equivalent products. Examples of acceptable substitutions include:

- ☐ Hydrochlorothiazide: any other thiazide-type diuretic currently in broad clinical use.
- ☐ Hydralazine: any other peripheral vasodilator having an antihypertensive effect.
- ☐ Senna: any stimulant laxative (either synthetic or of plant origin).

Numbers in parentheses following drug names indicate:  
(1) Drugs subject to international control under: (a) the Single Convention on Narcotic Drugs (1961); (b) the Convention on Psychotropic Substances (1971); or (c) the United Nations Convention against Illicit Traffic in Narcotic

Drugs and Psychotropic Substances (1988).

(2) Specific expertise, diagnostic precision, individualization of dosage or special equipment required for proper use.

(3) Greater potency or efficacy.

(4) In renal insufficiency, contraindicated or dosage adjustments necessary.

(5) To improve compliance.

(6) Special pharmacokinetic properties.

(7) Adverse effects diminish benefit/risk ratio.

(8) Limited indications or narrow spectrum of activity.

(9) For epidural anaesthesia.

(10) Sustained-release preparations are available. A proposal to include such a product in a national list of essential drugs should be supported by adequate documentation.

(11) Monitoring of therapeutic concentrations in plasma can improve safety and efficacy.

Letters in parentheses following the drug names indicate the reasons for the inclusion:

(A) When drugs in the main list cannot be made available.

(B) When drugs in the main list are known to be ineffective or inappropriate for a given individual.

(C) For use in rare disorders or in exceptional circumstances.

(D) Reserve antimicrobials to be used only when there is significant resistance to other drugs on the list.

Drugs are listed in alphabetical order

ceftazidime (D)	powder for injection, 250 mg (as pentahydrate) in vial
<sup>a</sup> ceftriaxone (D)	powder for injection, 250 mg (as sodium salt) in vial
imipenem + cilastatin (D)	powder for injection, 250 mg (as monohydrate) + 250 mg, (as sodium salt) 500 mg (as monohydrate) + 500 mg (as sodium salt) in vial

### 6.2.2 OTHER ANTIBACTERIALS

chloramphenicol (C)	oily suspension for injection, 0.5 g (as sodium succinate)/ml in 2-ml ampoule
clindamycin (B) (8)	capsule 150 mg,  injection, 150 mg (as phosphate)/ml

#### *Restricted indication*

vancomycin (D)	powder for injection 250 mg (as hydrochloride) in vial
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### 6.2.4 ANTITUBERCULOSIS MEDICINES

thioacetazone + isoniazid (A) (5, 7)	tablet, 50 mg + 100 mg, 150 mg + 300 mg
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*Reserve second-line medicines for the treatment of multidrug-resistant tuberculosis (MDR-TB) should be used in specialized centres adhering to WHO standards for TB control.*

amikacin (D)	powder for injection. 1000 mg in vial
<i>p</i> -aminosalicylic acid (D)	tablet 500 mg  granules, 4 g in sachet
capreomycin (D)	powder for injection, 1000 mg in vial
ciprofloxacin (D)	tablet, 250 mg, 500 mg
<sup>a</sup> cycloserine (D)	capsule or tablet, 250 mg
<sup>a</sup> ethionamide (D)	tablet, 125 mg, 250 mg
kanamycin (D)	powder for injection, 1000 mg in vial
levofloxacin (D)	tablet, 250 mg, 500 mg
ofloxacin (D)	tablet, 200 mg 400 mg

### 6.3 ANTIFUNGAL MEDICINES

flucytosine (B) (4, 8)	capsule, 250 mg  infusion, 2.5 g in 250 ml
potassium iodide (A)	saturated solution

## 6.5 ANTIPROTOZOAL MEDICINES

### 6.5.2 ANTILEISHMANIASIS MEDICINES

amphotericin B (B) (4)	powder for injection, 50 mg in vial
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### 6.5.3 ANTIMALARIAL MEDICINES

#### 6.5.3.1 FOR CURATIVE TREATMENT

<sup>a</sup> doxycycline (B) ( <i>for use only in combination with quinine</i> )	capsule or tablet, 100 mg (hydrochloride)
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mefloquine (B)	tablet, 250 mg (as hydrochloride)
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<sup>a</sup> sulfadoxine + pyrimethamine (B)	tablet, 500 mg + 25 mg
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#### *Restricted indications*

artemether (D)	injection, 80 mg/ml in 1-ml ampoule
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artesunate (D)	tablet, 50 mg
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### 6.5.5 ANTITRYPANOSOMAL MEDICINES

eflornithine (C)	injection, 200 mg (hydro- chloride)/ml in 100-ml bottles
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## 8: Antineoplastic and Immunosuppressive Medicines and Medicines Used in Palliative Care

### 8.1 IMMUNOSUPPRESSIVE MEDICINES

*Adequate resources and specialist oversight are a prerequisite for the introduction of this class of drugs.*

<sup>a</sup> azathioprine (2)	tablet, 50 mg  powder for injection, 100 mg (as sodium salt) in vial
<sup>a</sup> ciclosporin (2) ( <i>for organ transplantation</i> )	capsule, 25 mg  concentrate for injection, 50 mg/ml in 1-ml ampoule

### 8.2 CYTOTOXIC MEDICINES

*Adequate resources and specialist oversight are a prerequisite for the introduction of this class of drugs.*

asparaginase (2)	powder for injection, 10 000 IU in vial
bleomycin (2)	powder for injection, 15 mg (as sulfate) in vial
calcium folinate (2)	tablet, 15 mg  injection, 3 mg/ml in 10-ml ampoule
chlorambucil (2)	tablet, 2 mg
chlormethine (2)	powder for injection, 10 mg (hydrochloride) in vial



cisplatin (2)	powder for injection, 10 mg, 50 mg in vial
cyclophosphamide (2)	tablet, 25 mg powder for injection, 500 mg in vial
cytarabine (2)	powder for injection, 100 mg in vial
dacarbazine (2)	powder for injection, 100 mg in vial
dactinomycin (2)	powder for injection 500 µg in vial
daunorubicin (2)	powder for injection, 50 mg (as hydrochloride) in vial
°doxorubicin (2)	powder for injection, 10 mg, 50 mg (hydrochloride) in vial
etoposide (2)	capsule, 100 mg injection, 20 mg/ml in 5-ml ampoule
fluorouracil (2)	injection, 50 mg/ml in 5-ml ampoule
levamisole (2)	tablet, 50 mg (as hydrochloride)
mercaptopurine (2)	tablet, 50 mg
methotrexate (2)	tablet, 2.5 mg (as sodium salt) powder for injection, 50 mg (as sodium salt) in vial
procarbazine	capsule, 50 mg (as hydrochloride)
vinblastine (2)	powder for injection, 10 mg (sulfate) in vial
vincristine (2)	powder for injection, 1 mg, 5 mg (sulfate) in vial

### 8.3 HORMONES AND ANTIHORMONES

°prednisolone	tablet, 5 mg powder for injection, 20 mg, 25 mg (as sodium phosphate or sodium succinate) in vial
tamoxifen	tablet, 10 mg, 20 mg (as citrate)

### 8.4 MEDICINES USED IN PALLIATIVE CARE

The WHO Expert Committee on Selection and Use of Essential Medicines recommended that all the drugs mentioned in the WHO publication *Cancer Pain Relief: with a Guide to Opioid Availability, 2nd edition*, be considered essential. The drugs are included in the relevant sections of the model list according to their therapeutic use, e.g. analgesics.

## 10: Medicines affecting the Blood

### 10.1 ANTIANAEMIA DRUGS

°iron dextran (B) (5)	injection, equivalent to 50 mg iron/ ml in 2-ml ampoule
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## 11: Blood Products and Plasma Substitutes

### 11.2 PLASMA FRACTIONS FOR SPECIFIC USE

All plasma fractions should comply with the WHO Requirements for the Collection, Processing and Quality Control of Blood, Blood Components, and Plasma Derivatives (Revised 1992). WHO Technical Report Series, No. 840, 1994, Annex 2.

°factor VIII concentrate (C) (2, 8)	dried
°factor IX complex (coagulation factors II, VII, IX, X) concentrate (C) (2, 8)	dried

## 12: Cardiovascular Medicines

### 12.2 ANTIARRHYTHMIC MEDICINES

epinephrine (adrenaline) (C)	injection, 1 mg (as hydrochloride)/ml in ampoule
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isoprenaline (C)	injection, 20 micrograms (hydrochloride)/ml
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°procainamide (B)	injection, 100 mg (hydrochloride)/ml in 10-ml ampoule
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°quinidine (A) (7)	tablet, 200 mg (sulfate)
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### 12.3 ANTIHYPERTENSIVE MEDICINES

°prazosin (B)	tablet, 500 micrograms, 1 mg
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°sodium nitroprusside (C) (2, 8)	powder for infusion, 50 mg in ampoule
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### 12.5 ANTITHROMBOTIC MEDICINES

streptokinase (C)	powder for injection, 100 000 IU, 750 000 IU in vial
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## 13: Dermatological Medicines (topical)

### 13.1 ANTIFUNGAL MEDICINES

selenium sulfide (C)	detergent-based suspension, 2%
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**13.7 ULTRAVIOLET-BLOCKING AGENTS**

topical sun protection agent with activity against ultraviolet A and ultraviolet B (C) cream, lotion or gel

**14: Diagnostic Agents****14.2 RADIOCONTRAST MEDIA**

⌘ meglumine iotroxate (C) solution, 5 – 8 g iodine in 100–250 ml

**16: Diuretics**

⌘ mannitol (C) injectable solution, 10%, 20%

**18: Hormones, other Endocrine Medicines and Contraceptives****18.1 ADRENAL HORMONES AND SYNTHETIC SUBSTITUTES**

fludrocortisone (C) tablet, 100 micrograms (acetate)

**18.2 ANDROGENS**

testosterone (C) (2) injection, 200 mg (enantate) in 1-ml ampoule

**18.3 CONTRACEPTIVES****18.3.1 HORMONAL CONTRACEPTIVES**

levonorgestrel tablet, 30 micrograms

medroxyprogesterone acetate (B) (7, 8) depot injection, 150 mg in 1-ml vial

norethisterone enantate (B) (7, 8) oily solution, 200 mg/ml in 1-ml ampoule

**18.7 PROGESTOGENS**

medroxyprogesterone acetate (B) tablet, 5 mg

**20: Muscle Relaxants (peripherally acting) and Cholinesterase Inhibitors**

vecuronium bromide (C) powder for injection, 10 mg in vial

**21: Ophthalmological Preparations****21.5 MYDRIATICS**

epinephrine (A) solution (eye drops), 2% (as hydrochloride)

**25: Medicines acting on the Respiratory Tract****25.1 ANTI-ASTHMATIC MEDICINES**

⌘ cromoglicic acid (B) inhalation (aerosol), 20 mg (sodium salt) per dose

**27: Vitamins and Minerals**

calcium gluconate (C) (2, 8) injection, 100 mg/ml in 10-ml ampoule

# Recent Publications and Sources of Information

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## Genomics and world health

The report of the Advisory Committee on Health Research "Genomics and World Health" concludes that information generated by genomics will, in the long term have major benefits for the prevention, diagnosis and management of many diseases which have been difficult or impossible to control. However, if public education in genomics is not achieved, it will be impossible for society to enter into informed debate on the ethical issues involved and there is a danger that those who administer health services will be unable to distinguish between hyperbole and reality in a new and rapidly expanding research field.

Societies need to be better prepared for the era of genomics. Genomics research is complex and an understanding of its medical potential and the ethical issues involved requires a basic understanding of the principles of genetics. The report warns that the planned development of large-scale genetic data bases offers a series of hazards and ethical issues which have not been previously encountered. There is still considerable controversy about the desirability of establishing data bases of this type and there are many ambiguities regarding access and control. Another ethical problem deals with the decisions families may make regarding children as a result of DNA research.

This publication serves as a state-of-the-art guide to this field of science.

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*Genomics and World Health is available from: Distribution and Sales, World Health Organization, 1211 Geneva 27, Switzerland. ISBN 92 4 154554 2 Price: US\$ 31.50 publications@who.int*

## Legal status of traditional and complementary medicine

National policies are the basis for defining the role of traditional and complementary/alternative medicine in national health care programmes ensuring that the necessary regulatory and legal mechanisms are created for promoting and maintaining

good practice: assuring authenticity, safety and efficacy of traditional and complementary therapies: and providing equitable access to health care resources and information about those resources.

National recognition and regulation of traditional and complementary medicine varies considerably from one country to another. The present worldwide review of the legal status of traditional and complementary medicine covers data from 123 countries and is intended to facilitate the development of legal frameworks and sharing of experience between countries. This information will be beneficial to policy makers, researchers, universities, the public, insurance companies and the pharmaceutical industry.

*Legal status of traditional and complementary/alternative medicine. WHO/EDM/TRM/2001.2. Available from Essential Drugs and Medicines Policy, World Health Organization, 1211 Geneva 27, Switzerland.*

## Kinetoplastid research source launched

*Kinetoplastid Biology and Disease* (KBD) is an electronic publication which aims to strengthen ties between research and clinical/field applications, increasing dialogue between bench scientists, theoreticians and planners, and the professionals in the field. KBD accepts basic science, epidemiologic, public health, clinical, veterinary and agricultural papers on trypanosomiasis, leishmaniasis and related disease which meet the criteria of peer review.

The advent of KBD enables the free dissemination of scientific information about kinetoplastid diseases and their control. This is critical, since most scientific journals are not free and even the ones with cheaper subscription rates may not be accessible to researchers, clinicians, and field researchers in the poorest and affected developing countries. Moreover, the journal will serve as a focus in which the whole kinetoplastid community can participate: to educate, notify and debate about progress and direction. We hope our new journal will serve as a vehicle to promote pragmatic research and as a

practical first step in tackling some of the communication difficulties that face those concerned with the eradication of these diseases.

KBD is created as peer-review journal, freely available to anyone in the world with a networked computer. KBD is published by BiomedCentral ([www.biomedcentral.com](http://www.biomedcentral.com)), and has a world class editorial board (<http://www.kinetoplastids.com/edboard/>). It will be indexed by most of the major scientific indexing services such as PubMed. Articles will be available in html and .pdf formats. KBD is supported by the Vice-Presidencia de Desenvolvimento Institucional, Informacao e Comunicacao" and the "Instituto Oswaldo Cruz" of the Oswaldo Cruz Foundation. The journal is recipient of a Soros Foundation award for promoting open publishing.

In its first issue, *Kinetoplastid Biology and Disease* presents:

- Combating Kinetoplastid diseases, <http://www.kinetoplastids.com/content/pdf/1475-9292-1-6.pdf>
- Salivaria or Stercoraria? The Trypanosoma rangeli dilemma, <http://www.kinetoplastids.com/content/pdf/1475-9292-1-5.pdf>
- What can we hope to gain for trypanosomiasis control from molecular studies on tsetse biology? <http://www.kinetoplastids.com/content/1/1/4>
- From the cell biology to the development of new chemotherapeutic approaches against trypanosomatids: dreams and reality. <http://www.kinetoplastids.com/content/pdf/1475-9292-1-3.pdf>
- PCR identification of Trypanosoma lewisi, a common parasite of laboratory rats, <http://www.kinetoplastids.com/content/1/1/2>
- Molecular determinants and regulation of Leishmania virulence, <http://www.kinetoplastids.com/content/1/1/1>

Papers and feedback may be sent to [kbd@trypanosome.com](mailto:kbd@trypanosome.com)

*Kinetoplastid Biology and Disease* is available from: <http://www.kinetoplastids.com>

## Endocrine disrupting chemicals

Are chemicals that have the potential to interfere with the normal functioning of the endocrine system threatening future generations of humans and certain wildlife species? An IPCS report concludes that further research and information is needed on endocrine disrupting chemicals or EDCs.

The report, entitled *Global Assessment of the State-of-the-Science of Endocrine Disruptors*, is the result of a global comprehensive review of the publicly available scientific literature on EDCs organized by the International Programme on Chemical Safety (IPCS). The IPCS is sponsored by the World Health Organization (WHO), the United Nations Environment Programme (UNEP) and the International Labour Organization.

The report states that there is sufficient evidence that adverse effects have occurred as a result of exposure to EDCs in some wildlife species. Therefore, because of continuing concerns and scientific uncertainties, studies on the potential effects posed by these chemicals should remain a high global priority requiring coordinated and strengthened international research strategies. There is, in particular, an urgent need for studies in vulnerable populations, and especially in infants and children, since exposure during critical developmental periods may have irreversible effects.

This assessment was requested in 1997 by the Intergovernmental Forum on Chemical Safety, the 1997 Declaration of the Environment Leaders of the Eight on Children's Environmental Health, and endorsed by the 50<sup>th</sup> World Health Assembly in 1997. The assessment is unique in providing a global perspective on the endocrine disruptor issue, and in providing a framework by which strength-of-the-evidence analysis can be performed to determine whether there is a causal association between an adverse biological effect and exposure to an endocrine disrupting chemical.

*Global Assessment of the State-of-the-Science of Endocrine Disruptors* is available at [http://www.who.int/pcs/pcs\\_new.html](http://www.who.int/pcs/pcs_new.html). Printed copies of the report are available from: [prout@niehs.nih.gov](mailto:prout@niehs.nih.gov)

# International Nonproprietary Names for Pharmaceutical Substances (INN)

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Notice is hereby given that, in accordance with article 3 of the Procedure for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances, the names given in the list on the following pages are under consideration by the World Health Organization as Proposed International Nonproprietary Names. The inclusion of a name in the lists of Proposed International Nonproprietary Names does not imply any recommendation of the use of the substance in medicine or pharmacy.

Lists of Proposed (1–85) and Recommended (1–45) International Nonproprietary Names can be found in *Cumulative List No. 10, 2002* (available in CD-ROM only). The statements indicating action and use are based largely on information supplied by the manufacturer. This information is merely meant to provide an indication of the potential use of new substances at the time they are accorded Proposed International Nonproprietary Names. WHO is not in a position either to uphold these statements or to comment on the efficacy of the action claimed. Because of their provisional nature, these descriptors will neither be revised nor included in the Cumulative Lists of INNs.

## Dénominations communes internationales des Substances pharmaceutiques (DCI)

Il est notifié que, conformément aux dispositions de l'article 3 de la Procédure à suivre en vue du choix de Dénominations communes internationales recommandées pour les Substances pharmaceutiques les dénominations ci-dessous sont mises à l'étude par l'Organisation mondiale de la Santé en tant que dénominations communes internationales proposées. L'inclusion d'une dénomination dans les listes de DCI proposées n'implique aucune recommandation en vue de l'utilisation de la substance correspondante en médecine ou en pharmacie.

On trouvera d'autres listes de Dénominations communes internationales proposées (1–85) et recommandées (1–45) dans la *Liste récapitulative No. 10, 2002* (disponible sur CD-ROM seulement). Les mentions indiquant les propriétés et les indications des substances sont fondées sur les renseignements communiqués par le fabricant. Elles ne visent qu'à donner une idée de l'utilisation potentielle des nouvelles substances au moment où elles sont l'objet de propositions de DCI. L'OMS n'est pas en mesure de confirmer ces déclarations ni de faire de commentaires sur l'efficacité du mode d'action ainsi décrit. En raison de leur caractère provisoire, ces informations ne figureront pas dans les listes récapitulatives de DCI.

## Denominaciones Comunes Internacionales para las Sustancias Farmacéuticas (DCI)

De conformidad con lo que dispone el párrafo 3 del "Procedimiento de Selección de Denominaciones Comunes Internacionales Recomendadas para las Sustancias Farmacéuticas", se comunica por el presente anuncio que las denominaciones detalladas en las páginas siguientes están sometidas a estudio por la Organización Mundial de La Salud como Denominaciones Comunes Internacionales Propuestas. La inclusión de una denominación en las listas de las DCI Propuestas no supone recomendación alguna en favor del empleo de la sustancia respectiva en medicina o en farmacia.

Las listas de Denominaciones Comunes Internacionales Propuestas (1–85) y Recomendadas (1–45) se encuentran reunidas en *Cumulative List No. 10, 2002* (disponible sólo en CD-ROM). Las indicaciones sobre acción y uso que aparecen se basan principalmente en la información facilitada por los fabricantes. Esta información tiene por objeto dar una idea únicamente de las posibilidades de aplicación de las nuevas sustancias a las que se asigna una DCI Propuesta. La OMS no está facultada para respaldar esas indicaciones ni para formular comentarios sobre la eficacia de la acción que se atribuye al producto. Debido a su carácter provisional, esos datos descriptivos no deben incluirse en las listas recapitulativas de DCI.

## Proposed International Nonproprietary Names: List 87

Comments on, or formal objections to, the proposed names may be forwarded by any person to the INN Programme of the World Health Organization within four months of the date of their publication in *WHO Drug Information*, i.e., for **List 87 Proposed INN not later than 28 February 2003**.

## Dénominations communes internationales proposées: Liste 87

Des observations ou des objections formelles à l'égard des dénominations proposées peuvent être adressées par toute personne au Programme des Dénominations communes internationales de l'Organisation mondiale de la Santé dans un délai de quatre mois à compter de la date de leur publication dans *WHO Drug Information*, c'est à dire pour la **Liste 87 de DCI Proposées le 28 février 2003 au plus tard**.

## Denominaciones Comunes Internacionales Propuestas: Lista 87

Cualquier persona puede dirigir observaciones u objeciones respecto de las denominaciones propuestas, al Programa de Denominaciones Comunes Internacionales de la Organización Mundial de la Salud, en un plazo de cuatro meses, contados desde la fecha de su publicación en *WHO Drug Information*, es decir, para la **Lista 87 de DCI Propuestas el 28 de febrero de 2003 a más tardar**.

<i>Proposed INN (Latin, English, French, Spanish)</i>	<i>Chemical name or description: Action and use: Molecular formula Chemical Abstracts Service (CAS) registry number: Graphic formula</i>
<i>DCI Proposée</i>	<i>Nom chimique ou description: Propriétés et indications: Formule brute Numéro dans le registre du CAS: Formule développée</i>
<i>DCI Propuesta</i>	<i>Nombre químico o descripción: Acción y uso: Fórmula empírica Número de registro del CAS: Fórmula desarrollada</i>

### albaconazolom

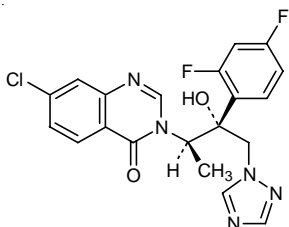
albaconazole 7-chloro-3-[(1*R*,2*R*)-2-(2,4-difluorophenyl)-2-hydroxy-1-methyl-3-(1*H*-1,2,4-triazol-1-yl)propyl]quinazolin-4(3*H*)-one  
*antifungal*

albaconazole 7-chloro-3-[(1*R*,2*R*)-2-(2,4-difluorophényl)-2-hydroxy-1-méthyl-3-(1*H*-1,2,4-triazol-1-yl)propyl]quinazolin-4(3*H*)-one  
*antifongique*

albaconazol 7-cloro-3-[(1*R*,2*R*)-2-(2,4-difluorofenil)-2-hidroxil-1-metil-3-(1*H*-1,2,4-triazol-1-il)propil]quinazolin-4(3*H*)-ona  
*antifúngico*



187949-02-6



**alvimopanum**

alvimopan

[[[(2*S*)-2-[[[(3*R*,4*R*)-4-(3-hydroxyphenyl)-3,4-dimethylpiperidin-1-yl]methyl]-3-phenylpropanoyl]amino]acetic acid  
*μ*-opioid receptor antagonist

alvimopan

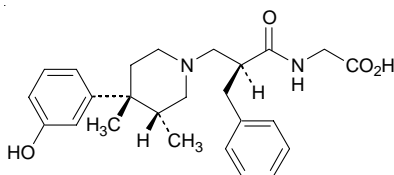
acide [[[(2*S*)-2-[[[(3*R*,4*R*)-4-(3-hydroxyphényl)-3,4-diméthylpipéridin-1-yl]méthyl]-3-phénylpropanoyl]amino]acétique  
*antagoniste des récepteurs μ aux opiacés*

alvimopán

ácido [[[(2*S*)-3-fenil-2-[[[(3*R*,4*R*)-4-(3-hidroxifenil)-3,4-dimetilpiperidin-1-il]metil]propanoil]amino]acético  
*antagonista del receptor μ de opiáceos*

C<sub>25</sub>H<sub>32</sub>N<sub>2</sub>O<sub>4</sub>

156053-89-3

**apaziquonum**

apaziquone

5-(aziridin-1-yl)-3-(hydroxymethyl)-2-[(1*E*)-3-hydroxyprop-1-enyl]-1-methyl-1*H*-indole-4,7-dione  
*antineoplastic*

apaziquone

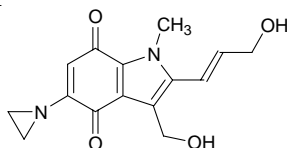
5-(aziridin-1-yl)-3-(hydroxyméthyl)-2-[(1*E*)-3-hydroxyprop-1-ényl]-1-méthyl-1*H*-indole-4,7-dione  
*antinéoplasique*

apazicuona

5-(aziridin-1-il)-3-(hidroximetil)-2-[(1*E*)-3-hidroxiprop-1-enil]-1-metil-1*H*-indol-4,7-diona  
*antineoplásico*

C<sub>15</sub>H<sub>16</sub>N<sub>2</sub>O<sub>4</sub>

114560-48-4



**apolizumabum**

apolizumab immunoglobulin G1, anti-(human histocompatibility antigen HLA-DR) (human-mouse monoclonal Hu1D10  $\gamma$ 1-chain), disulfide with human-mouse monoclonal Hu1D10 light chain, dimer  
*immunomodulator*

apolizumab immunoglobuline G1, anti-(antigène d'histocompatibilité HLA-DR humain) (chaîne  $\gamma$ 1 de l'anticorps monoclonal de souris Hu1D10 humanisé), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris Hu1D10 humanisé  
*immunomodulateur*

apolizumab inmunoglobulina G1, anti-(antígeno de histocompatibilidad HLA-DR humano) (cadena  $\gamma$ 1 del anticuerpo monoclonal humanizado de ratón Hu1D10), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal humanizado de ratón Hu1D10  
*inmunomodulador*

267227-08-7

**asenapinum**

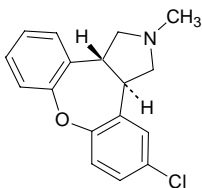
asenapine (3a*RS*,12b*RS*)-5-chloro-2-methyl-2,3,3a,12b-tetrahydro-1*H*-dibenzo[2,3:6,7]oxepino[4,5-*c*]pyrrole  
*psychostimulant*

asénapine (3a*RS*,12b*RS*)-5-chloro-2-méthyl-2,3,3a,12b-tétrahydro-1*H*-dibenzo[2,3:6,7]oxépino[4,5-*c*]pyrrole  
*psychostimulant*

asenapina (3a*RS*,12b*RS*)-5-cloro-2-metil-2,3,3a,12b-tetrahidro-1*H*-dibenzo[2,3:6,7]oxepino[4,5-*c*]pirrol  
*psicoestimulante*

C<sub>17</sub>H<sub>16</sub>ClNO

85650-56-2



and enantiomer  
et énantiomère  
y enantiómero

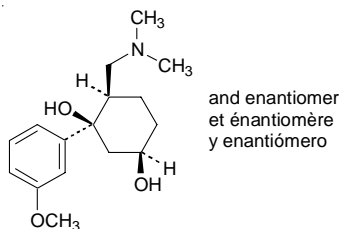


**axomadolum**

axomadol (1*RS*,3*RS*,6*RS*)-6-[(dimethylamino)méthyl]-1-(3-méthoxyphényl)cyclohexane-1,3-diol  
*analgesic*

axomadol (1*RS*,3*RS*,6*RS*)-6-[(diméthylamino)méthyl]-1-(3-méthoxyphényl)cyclohexane-1,3-diol  
*analgésique*

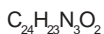
axomadol (1*RS*,3*RS*,6*RS*)-6-[(dimetilamino)metil]-1-(3-metoxifenil)ciclohexano-1,3-diol  
*analgésico*

**bifeprunoxum**

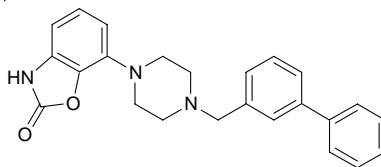
bifeprunox 7-[4-(biphenyl-3-ylmethyl)piperazin-1-yl]benzoxazol-2(3*H*)-one  
*antipsychotic*

biféprunox 7-[4-(biphényl-3-ylméthyl)pipérazin-1-yl]benzoxazol-2(3*H*)-one  
*psychotrope*

bifeprunox 7-[4-(bifenil-3-ilmetil)piperazin-1-il]benzoxazol-2(3*H*)-ona  
*antipsicótico*



350992-10-8



**canertinibum**

canertinib

*N*-[4-[(3-chloro-4-fluorophenyl)amino]-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl]prop-2-enamide  
*antineoplastique*

canertinib

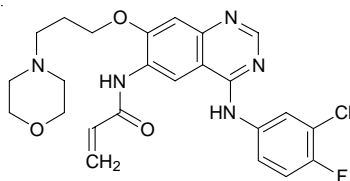
*N*-[4-[(3-chloro-4-fluorophényl)amino]-7-[3-(morpholin-4-yl)propoxy]quinazolin-6-yl]prop-2-énamide  
*antineoplasique*

canertinib

*N*-[4-[(3-cloro-4-fluorofenil)amino]-7-[3-(morfolin-4-il)propoxi]quinazolin-6-il]prop-2-enamida  
*antineoplásico*

C<sub>24</sub>H<sub>25</sub>ClFN<sub>5</sub>O<sub>3</sub>

267243-28-7

**cefovecinum**

cefovecin

(6*R*,7*R*)-7-[[*(2Z)*-(2-aminothiazol-4-yl)(methoxyimino)acetyl]amino]-8-oxo-3-[(2*S*)-tetrahydrofuran-2-yl]-5-thia-1-azabicyclo[4.2.0]oct-2-ene-2-carboxylic acid  
*antibacteriel (veterinary drug)*

céfovécine

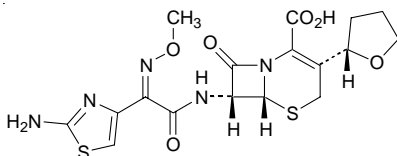
acide (6*R*,7*R*)-7-[[*(2Z)*-(2-aminothiazol-4-yl)(méthoxyimino)acétyl]amino]-8-oxo-3-[(2*S*)-tétrahydrofuran-2-yl]-5-thia-1-azabicyclo[4.2.0]oct-2-ène-2-carboxylique  
*antibactérien (médicament vétérinaire)*

cefovecina

ácido (6*R*,7*R*)-7-[[*(2Z)*-(2-aminothiazol-4-il)(metoxiimino)acetil]amino]-8-oxo-3-[(2*S*)-tetrahydrofuran-2-il]-5-tia-1-azabicyclo[4.2.0]oct-2-eno-2-carboxílico  
*antibacteriano (medicamento veterinario)*

C<sub>17</sub>H<sub>19</sub>N<sub>5</sub>O<sub>6</sub>S<sub>2</sub>

234096-34-5



**cethromycinum**

cethromycin

(3a*S*,4*R*,7*R*,9*R*,10*R*,11*R*,13*R*,15*R*,15a*R*)-4-ethyl-3a,7,9,11,13,15-hexamethyl-11-[[[3-(quinolin-3-yl)prop-2-enyl]oxy]-10-[[3,4,6-trideoxy-3-(dimethylamino)-β-*D*-xylo-hexopyranosyl]oxy]octahydro-2*H*-oxacyclotetradecino[4,3-*d*]oxazole-2,6,8,14(1*H*,7*H*,9*H*)-tetrone  
*antibacterial*

céthromycine

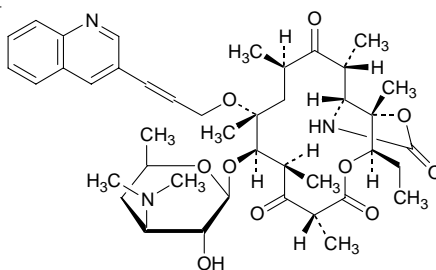
(3a*S*,4*R*,7*R*,9*R*,10*R*,11*R*,13*R*,15*R*,15a*R*)-4-éthyl-3a,7,9,11,13,15-hexaméthyl-11-[[[3-(quinoléin-3-yl)prop-2-ényl]oxy]-10-[[3,4,6-tridésoxy-3-(diméthylamino)-β-*D*-xylo-hexopyranosyl]oxy]octahydro-2*H*-oxacyclotétradécino[4,3-*d*]oxazole-2,6,8,14(1*H*,7*H*,9*H*)-tétrone  
*antibactérien*

cetromicina

(3a*S*,4*R*,7*R*,9*R*,10*R*,11*R*,13*R*,15*R*,15a*R*)-4-etil-3a,7,9,11,13,15-hexametil-11-[[[3-(quinolein-3-il)prop-2-enil]oxi]-10-[[3,4,6-tridesoxi-3-(dimetilamino)-β-*D*-xilo-hexopiranosil]oxi]octahidro-2*H*-oxaciclote-tradecino[4,3-*d*]oxazol-2,6,8,14(1*H*,7*H*,9*H*)-tetrone  
*antibacteriano*

C<sub>42</sub>H<sub>59</sub>N<sub>3</sub>O<sub>10</sub>

205110-48-1

**dabigatranum etexilatum**

dabigatran etexilate

ethyl 3-[[[2-[[[4-[[[(hexyloxy)carbonyl]amino]iminomethyl]phenyl]amino]methyl]-1-methyl-1*H*-benzimidazol-5-yl]carbonyl](pyridin-2-yl)amino]propanoate  
*antithrombotic*

dabigatran étexilate

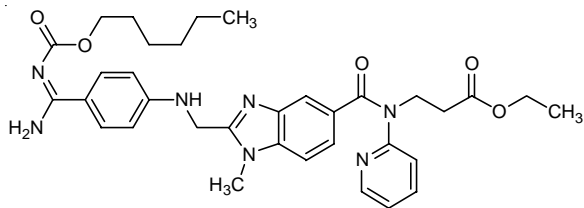
3-[[[2-[[[4-[[[(hexyloxy)carbonyl]amino]iminométhyl]phényl]amino]méthyl]-1-méthyl-1*H*-benzimidazol-5-yl]carbonyl](pyridin-2-yl)amino]propanoate d'éthyle  
*antithrombotique*

dabigatrán etexilato

3-[[[2-[[[4-[[[(hexiloxi)carbonil]amino]iminometil]fenil]amino]metil]-1-metil-1*H*-bencimidazol-5-il]carbonil](piridin-2-il)amino]propanoato de etilo  
*antitrombótico*

$C_{34}H_{41}N_7O_5$ 

211915-06-9

**deluceminum**

delucemine

3,3-bis(3-fluorophenyl)-*N*-methylpropan-1-amine  
*NMDA receptor antagonist*

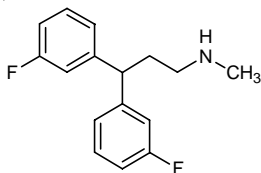
délucémine

3,3-bis(3-fluorophényl)-*N*-méthylpropan-1-amine  
*antagoniste des récepteurs du NMDA*

delucemina

3,3-bis(3-fluorofenil)-*N*-metilpropan-1-amina  
*antagonista de los receptores del NMDA* $C_{16}H_{17}F_2N$ 

186495-49-8

**ecromeximabum**

ecromeximab

immunoglobulin G1, anti-(GD3 ganglioside) (human-mouse monoclonal KM871  $\gamma$ 1-chain), disulfide with human-mouse monoclonal KM871  $\kappa$ -chain, dimer  
*immunomodulator*

écromeximab

immunoglobuline G1, anti-(ganglioside GD3) (chaîne  $\gamma$ 1 de l'anticorps monoclonal chimérique homme-souris KM871), dimère du disulfure avec la chaîne  $\kappa$  de l'anticorps monoclonal chimérique homme-souris KM871  
*immunomodulateur*

ecromeximab

immunoglobulina G1, anti-(gangliósido GD3) (cadena  $\gamma$ 1 del anticuerpo monoclonal quimérico hombre-ratón KM871), dímero del disulfuro con la cadena  $\kappa$  del anticuerpo monoclonal quimérico hombre-ratón KM871  
*immunomodulador*

292819-64-8

**eculizumabum**

eculizumab	immunoglobulin, anti-(human complement C5 $\alpha$ -chain) (human-mouse monoclonal 5G1.1 heavy chain), disulfide with human-mouse monoclonal 5G1.1 light chain, dimer <i>immunomodulator</i>
éculizumab	immunoglobuline, anti-(chaîne $\alpha$ du complément C5 humain) (chaîne lourde de l'anticorps monoclonal de souris 5G1.1 humanisé), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris 5G1.1 humanisé <i>immunomodulateur</i>
eculizumab	immunoglobulina, anti-(cadena $\alpha$ del complemento C5 humano) (cadena pesada del anticuerpo monoclonal humanizado de ratón 5G1.1), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal humanizado de ratón 5G1.1 <i>immunomodulador</i>

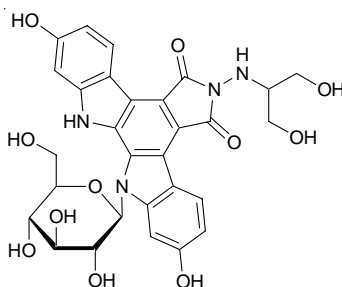
219685-50-4

**edotecarinum**

edotecarin	12- $\beta$ -D-glucopyranosyl-2,10-dihydroxy-6-[[2-hydroxy-1-(hydroxymethyl)ethyl]amino]-12,13-dihydro-6H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7-dione <i>antineoplastic</i>
édotécarine	12- $\beta$ -D-glucopyranosyl-2,10-dihydroxy-6-[[2-hydroxy-1-(hydroxyméthyl)éthyl]amino]-12,13-dihydro-6H-indolo[2,3-a]pyrrolo[3,4-c]carbazole-5,7-dione <i>antineoplasique</i>
edotecarina	12- $\beta$ -D-glucopiranosil-2,10-dihidroxi-6-[[2-hidroxi-1-(hidroximetil)etil]amino]-12,13-dihidro-6H-indolo[2,3-a]pirrolo[3,4-c]carbazol-5,7-diona <i>antineoplásico</i>

 $C_{29}H_{28}N_4O_{11}$ 

174402-32-5



**eglumegadum**

eglumegad

(1*S*,2*S*,5*R*,6*S*)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylic acid  
*psychostimulant*

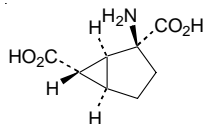
églumégad

acide (1*S*,2*S*,5*R*,6*S*)-2-aminobicyclo[3.1.0]hexane-2,6-dicarboxylique  
*psychostimulant*

eglumegad

ácido (1*S*,2*S*,5*R*,6*S*)-2-aminobiciclo[3.1.0]hexano-2,6-dicarboxílico  
*psicoestimulante* $C_8H_{11}NO_4$ 

176199-48-7

**elzasonanum**

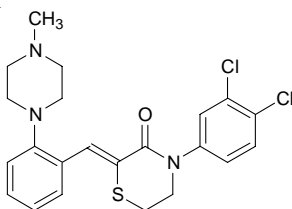
elzasonan

(2*Z*)-4-(3,4-dichlorophenyl)-2-[2-(4-methylpiperazin-1-yl)benzylidene]thiomorpholin-3-one  
*antidepressant*

elzasonan

(2*Z*)-4-(3,4-dichlorophényl)-2-[2-(4-méthylpipérazin-1-yl)benzylidène]thiomorpholin-3-one  
*antidépresseur*

elzasonán

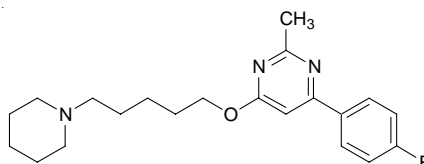
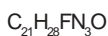
(2*Z*)-4-(3,4-diclorofenil)-2-[2-(4-metilpiperazin-1-il)benzilideno]tiomorfolin-3-ona  
*antidepresivo* $C_{22}H_{23}Cl_2N_3OS$ 

**enecadinum**

enecadin 4-(4-fluorophenyl)-2-methyl-6-[[5-(piperidin-1-yl)pentyl]oxy]pyrimidine  
*sodium/calcium channel blocker*

énécadine 4-(4-fluorophényl)-2-méthyl-6-[[5-(pipéridin-1-yl)pentyl]oxy]pyrimidine  
*antagoniste des canaux sodiques/calciques*

enecadina 4-(4-fluorofenil)-2-metil-6-[[5-(piperidin-1-il)pentil]oxi]pirimidina  
*bloqueante de los canales del sodio y del calcio*

**ertiprotafibum**

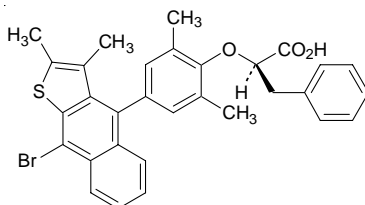
ertiprotafib (2R)-2-[4-(9-bromo-2,3-dimethylnaphtho[2,3-b]thiophen-4-yl)-2,6-dimethylphenoxy]-3-phenylpropanoic acid  
*antidiabetic*

ertiprotafib acide (2R)-2-[4-(9-bromo-2,3-diméthylnaphto[2,3-b]thiophén-4-yl)-2,6-diméthylphénoxy]-3-phénylpropanoïque  
*antidiabétique*

ertiprotafib ácido (2R)-2-[4-(9-bromo-2,3-dimetilnafto[2,3-b]tiefen-4-il)-2,6-dimetilfenoxi]-3-fenilpropanoico  
*antidiabético*



251303-04-5



**eszopiclonum**

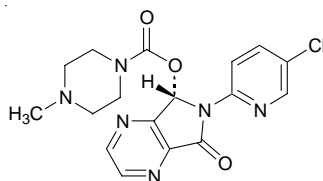
eszopiclone (5S)-6-(5-chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazin-5-yl-4-methylpiperazine-1-carboxylate  
*sedative, hypnotic*

eszopiclone 4-méthylpiperazine-1-carboxylate de (5S)-6-(5-chloropyridin-2-yl)-7-oxo-6,7-dihydro-5H-pyrrolo[3,4-b]pyrazin-5-yle  
*sédatif, hypnotique*

eszopiclona 4-metilpiperazina-1-carboxilato de (5S)-6-(5-cloropiridin-2-il)-7-oxo-6,7-dihidro-5H-pirrolo[3,4-b]pirazin-5-ilo  
*sedante, hipnótico*

 $C_{17}H_{17}ClN_6O_3$ 

138729-47-2

**fandosentanum**

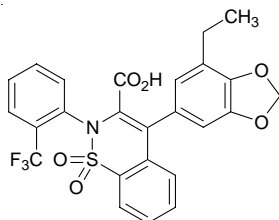
fandosentan 4-(7-ethyl-1,3-benzodioxol-5-yl)-2-[2-(trifluoromethyl)phenyl]-2H-1,2-benzothiazine-3-carboxylic acid 1,1-dioxide  
*endothelin receptor antagonist*

fandosentan 1,1-dioxyde de l'acide 4-(7-éthyl-1,3-benzodioxol-5-yl)-2-[2-(trifluorométhyl)phényl]-2H-1,2-benzothiazine-3-carboxylique  
*antagoniste du récepteur de l'endothéline*

fandosentán 1,1-dióxido del ácido 4-(7-etil-1,3-benzodioxol-5-il)-2-[2-(trifluorometil)fenil]-2H-1,2-benzotiazina-3-carboxílico  
*antagonista del receptor de endotelina*

 $C_{25}H_{18}F_3NO_6S$ 

221241-63-0





**fontolizumabum**

- fontolizumab immunoglobulin G1, anti-(human interferon  $\gamma$ ) (human-mouse monoclonal HuZAF  $\gamma$ 1-chain), disulfide with human-mouse monoclonal HuZAF light chain, dimer  
*immunomodulator*
- fontolizumab immunoglobuline G1, anti-(interféron  $\gamma$  humain) (chaîne  $\gamma$ 1 de l'anticorps monoclonal de souris HuZAF humanisé), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris HuZAF humanisé  
*immunomodulateur*
- fontolizumab inmunoglobulina G1, anti-(interferón  $\gamma$  humano) (cadena  $\gamma$ 1 del anticuerpo monoclonal humanizado de ratón HuZAF), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal humanizado de ratón HuZAF  
*inmunomodulador*

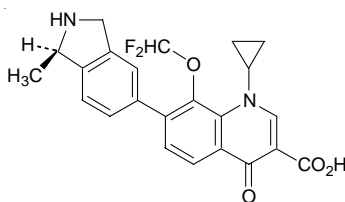
326859-36-3

**garenoxacinum**

- garenoxacin 1-cyclopropyl-8-(difluoromethoxy)-7-[(1*R*)-1-methyl-2,3-dihydro-1*H*-isoindol-5-yl]-4-oxo-1,4-dihydroquinoline-3-carboxylic acid  
*antibacterial*
- garénoxacine acide 1-cyclopropyl-8-(difluorométhoxy)-7-[(1*R*)-1-méthyl-2,3-dihydro-1*H*-isoindol-5-yl]-4-oxo-1,4-dihydroquinoléine-3-carboxylique  
*antibactérien*
- garenoxacina ácido 1-ciclopropil-8-(difluorometoxi)-7-[(1*R*)-1-metil-2,3-dihidro-1*H*-isoindol-5-il]-4-oxo-1,4-dihidroquinolina-3-carboxílico  
*antibacteriano*

 $C_{23}H_{20}F_2N_2O_4$ 

194804-75-6



**idusulfasum**

idusulfase  $\alpha$ -L-iduronate sulfate sulfatase  
*enzyme*

idusulfase sulfatase du sulfate de  $\alpha$ -L-iduronate  
*enzyme*

idusulfasa sulfatasa del sulfato de  $\alpha$ -L-iduronato  
*enzima*

$C_{2689}H_{4057}N_{699}O_{792}S_1$  50936-59-9  
(*subunit protein moiety reduced*)

SETQANSTTD	ALNVLLIIVD	DLRPSLGCYG	DKLVRSPNID
QLASHSLLFQ	NAFAQQAVCA	PSRVSFLTGR	RPDTTRLYDF
NSYWRVHAGN	FSTIPQYFKE	NGYVTMSVGK	VFHPGISSNH
TDDSPYSWSF	PPYHPSSEKY	ENTKTCRGPD	GELHANLLCP
VDVLDVPEGT	LPDKQSTEQA	IQLLEKMKTS	ASPFFLAVGY
HKPHIPFRYP	KEFQKLYPLE	NITLAPDPEV	PDGLPPVAYN
PWMDIRQRED	VQALNISVPY	GPIPVDQFQK	IRQSYFASVS
YLDTQVGRLL	SALDDLQLAN	STIIAFTSDH	GWALGEHGEW
AKYSNFDVAT	HVPLIFYVPG	RTASLPEAGE	KLFPYLDPFD
SASQLMEPGR	QSMDLVELVS	LFPTLAGLAG	LQVPPRCVPV
SFHVELCREG	KNLLKHFRFR	DLEEDPYLPG	NPRELIAYSQ
YRPSDIPQW	NSDKPSLKDI	KIMGYSIRTI	DYRYTVWVGF
NPDEFLANFS	DIHAGELYFV	DSDPLQDHNM	YNDSQGGDLF
QLLMP			

**indiplonum**

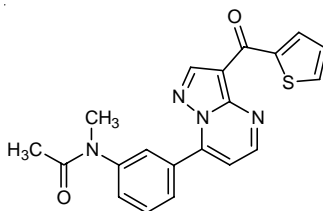
indiplon *N*-methyl-*N*-[3-[3-(thiophen-2-ylcarbonyl)pyrazolo[1,5-*a*]pyrimidin-7-yl]phenyl]acetamide  
*sedative, hypnotic*

indiplon *N*-méthyl-*N*-[3-[3-(thiophén-2-ylcarbonyl)pyrazolo[1,5-*a*]pyrimidin-7-yl]phényl]acétamide  
*sédatif, hypnotique*

indiplón *N*-metil-*N*-[3-[3-(tiiofen-2-ilcarbonil)pirazolo[1,5-*a*]pirimidin-7-il]fenil]acetamida  
*sedante, hipnótico*

C<sub>20</sub>H<sub>16</sub>N<sub>4</sub>O<sub>2</sub>S

325715-02-4

**inecalcitolum**

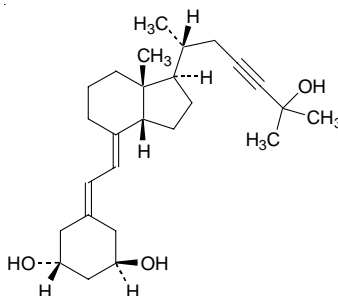
inecalcitol (7*E*)-19-nor-9,10-seco-14β-cholesta-5,7-dien-23-yne-1α,3β,25-triol  
*vitamin D analogue*

inécalcitol (7*E*)-19-nor-9,10-séco-14β-cholesta-5,7-dién-23-yne-1α,3β,25-triol  
*analogue de la vitamine D*

inecalcitol (7*E*)-19-nor-9,10-seco-14β-colesta-5,7-dien-23-ino-1α,3β,25-triol  
*análogo de la vitamina D*

C<sub>26</sub>H<sub>40</sub>O<sub>3</sub>

163217-09-2

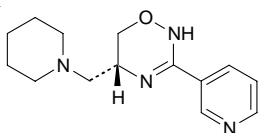


**iroxanadinum**

iroxanadine	(-)-5-(piperidin-1-ylmethyl)-3-(pyridin-3-yl)-5,6-dihydro-2H-1,2,4-oxadiazine <i>cardiac stimulant</i>
iroxanadine	(-)-5-(pipéridin-1-ylméthyl)-3-(pyridin-3-yl)-5,6-dihydro-2H-1,2,4-oxadiazine <i>cardiotonique</i>
iroxanadina	(-)-5-(piperidin-1-ilmetil)-3-(piridin-3-il)-5,6-dihidro-2H-1,2,4-oxadiazina <i>cardiotónico</i>



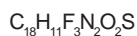
276690-58-5



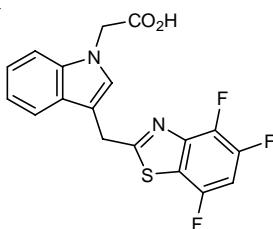
or enantiomer  
ou énantiomère  
o enantiómero

**lidorestatum**

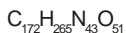
lidorestat	[3-[(4,5,7-trifluorobenzothiazol-2-yl)methyl]-1H-indol-1-yl]acetic acid <i>aldose reductase inhibitor</i>
lidorestat	acide [3-[(4,5,7-trifluorobenzothiazol-2-yl)méthyl]-1H-indol-1-yl]acétique <i>inhibiteur de l'aldose réductase</i>
lidorestat	ácido [3-[(4,5,7-trifluorobenzotiazol-2-il)metil]-1H-indol-1-il]acético <i>inhibidor de la reductasa de aldosas</i>



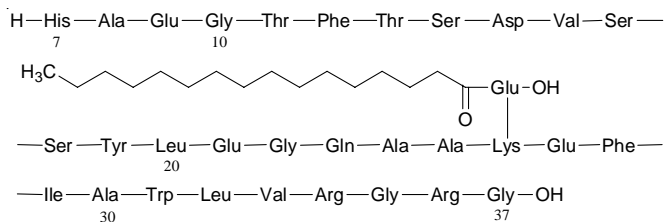
245116-90-9

**liraglutidum**

liraglutide	N <sup>26</sup> -(hexadecanoyl-γ-glutamyle)-[34-arginine]GLP-1-(7-37)-peptide <i>antidiabetic</i>
liraglutide	N <sup>26</sup> -(hexadécanoyl-γ-glutamyle)-[34-arginine]GLP-1-(7-37)-peptide <i>antidiabétique</i>
liraglutida	N <sup>26</sup> -(hexadecanoil-γ-glutamilo)-[34-arginina]GLP-1-(7-37)-péptido <i>antidiabético</i>



204656-20-2

**Iubazodonum**

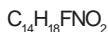
Iubazodone

(2S)-2-[[[(7-fluoro-2,3-dihydro-1H-inden-4-yl)oxy]methyl]morpholine  
*antidepressant*

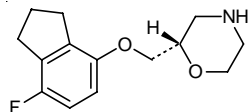
Iubazodone

(2S)-2-[[[(7-fluoro-2,3-dihydro-1H-indén-4-yl)oxy]méthyl]morpholine  
*antidépresseur*

Iubazodona

(2S)-2-[[[(7-fluoro-2,3-dihidro-1H-inden-4-il)oxi]metil]morfolina  
*antidepresivo*

161178-07-0

**Iubiprostonum**

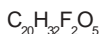
Iubiprostone

(-)-7-[(2R,4aR,5R,7aR)-2-(1,1-difluoropentyl)-2-hydroxy-  
 6-oxooctahydrocyclopenta[b]pyran-5-yl]heptanoic acid  
*prostaglandin*

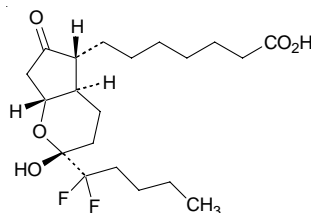
Iubiprostone

(-)-acide 7-[(2R,4aR,5R,7aR)-2-(1,1-difluoropentyl)-2-hydroxy-  
 6-oxooctahydrocyclopenta[b]pyran-5-yl]heptanoïque  
*prostaglandine*

Iubiprostona

(-)-ácido 7-[(2R,4aR,5R,7aR)-2-(1,1-difluoropentil)-2-hidroxí-  
 6-oxooctahidrociclopenta[b]piran-5-il]heptanoico  
*prostaglandina*

136790-76-6

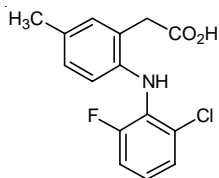


**lumiracoxibum**

lumiracoxib	[2-[(2-chloro-6-fluorophenyl)amino]-5-methylphenyl]acetic acid <i>cyclooxygenase-2 inhibitor</i>
lumiracoxib	acide [2-[(2-chloro-6-fluorophényl)amino]-5-méthylphényl]acétique <i>anti-inflammatoire</i>
lumiracoxib	ácido [2-[(2-cloro-6-fluorofenil)amino]-5-metilfenil]acético <i>inhibidor de la ciclooxigenasa-2</i>

C<sub>15</sub>H<sub>13</sub>ClFNO<sub>2</sub>

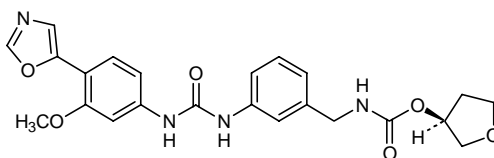
220991-20-8

**merimepodibum**

merimepodib	(3S)-tetrahydrofuran-3-yl [3-[[[3-methoxy-4-(oxazol-5-yl)phenyl]carbamoyl]amino]benzyl]carbamate <i>immunosuppressant</i>
mérimépodib	[3-[[[3-méthoxy-4-(oxazol-5-yl)phényl]carbamoil]amino]benzil]carbamate de (3S)-tétrahydrofuran-3-yle <i>immunosuppresseur</i>
merimepodib	[3-[[[3-metoxi-4-(oxazol-5-il)fenil]carbamoil]amino]benzil]carbamato de (3S)-tetrahidrofuran-3-ilo <i>inmunosupresor</i>

C<sub>23</sub>H<sub>24</sub>N<sub>4</sub>O<sub>6</sub>

198821-22-6



**mozavaptanum**

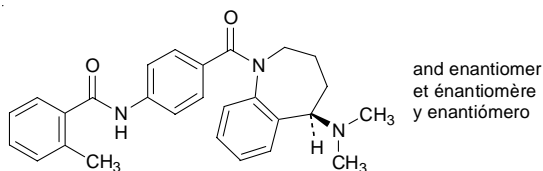
mozavaptan *N*-[4-[[[(5*RS*)-5-(dimethylamino)-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-yl]carbonyl]phenyl]-2-methylbenzamide  
*vasopressin V<sub>2</sub> receptor antagonist*

mozavaptan *N*-[4-[[[(5*RS*)-5-(diméthylamino)-2,3,4,5-tétrahydro-1*H*-1-benzazépin-1-yl]carbonyl]phényl]-2-méthylbenzamide  
*antagoniste du récepteur V<sub>2</sub> de la vasopressine*

mozavaptán *N*-[4-[[[(5*RS*)-5-(dimetilamino)-2,3,4,5-tetrahydro-1*H*-1-benzazepin-1-il]carbonil]fenil]-2-metilbenzamida  
*antagonista del receptor V<sub>2</sub> de la vasopresina*

C<sub>27</sub>H<sub>29</sub>N<sub>3</sub>O<sub>2</sub>

137975-06-5

**nalfurafinum**

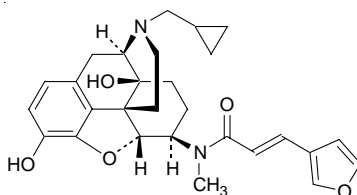
nalfurafine (*E*)-*N*-[17-(cyclopropylmethyl)-4,5α-epoxy-3,14-dihydroxymorphinan-6β-yl]-3-(furan-3-yl)-*N*-methylprop-2-enamide  
*κ-opioid receptor antagonist*

nalfurafine (*E*)-*N*-[17-(cyclopropylméthyl)-4,5α-époxy-3,14-dihydroxymorphinan-6β-yl]-3-(furan-3-yl)-*N*-méthylprop-2-énamide  
*antagoniste des récepteurs κ aux opiacés*

nalfurafina (*E*)-*N*-[17-(ciclopropilmetil)-4,5α-epoxi-3,14-dihidroxiomorfinan-6β-il]-3-(furan-3-il)-*N*-metilprop-2-enamida  
*antagonista del receptor κ de opiáceos*

C<sub>28</sub>H<sub>32</sub>N<sub>2</sub>O<sub>5</sub>

152657-84-6



**naminidilum**

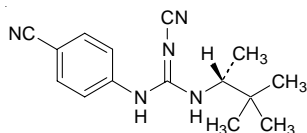
naminidil *N*-cyano-*N'*-(4-cyanophenyl)-*N''*-[(1*R*)-1,2,2-trimethylpropyl]guanidine  
*potassium channel opener*

naminidil *N*-cyano-*N'*-(4-cyanophényl)-*N''*-[(1*R*)-1,2,2-triméthylpropyl]guanidine  
*potentialisateur de l'ouverture des canaux potassiques*

naminidil *N*-ciano-*N'*-(4-cianofenil)-*N''*-[(1*R*)-1,2,2-trimetilpropil]guanidina  
*estimulante de la apertura de los canales de potasio*

C<sub>15</sub>H<sub>19</sub>N<sub>5</sub>

220641-11-2

**nemifitidum**

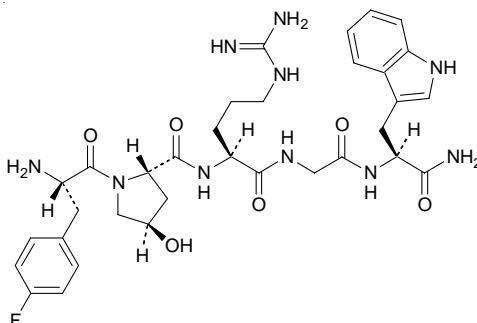
nemifitide 4-fluoro-L-phenylalanyl-*trans*-4-hydroxy-L-prolyl-L-arginylglycyl-L-tryptophanamide  
*antidepressant*

némifitide (4-fluoro-L-phénylalanil)-(trans-4-hydroxy-L-prolyl)-L-arginyl-glycyl-L-tryptophanamide  
*antidépresseur*

nemifitida (4-fluoro-L-fenilalanil)-(trans-4-hidroxi-L-proliil)-L-arginilglicil-L-triptofanamida  
*antidepresivo*

C<sub>33</sub>H<sub>43</sub>FN<sub>10</sub>O<sub>6</sub>

173240-15-8





**nortopixantrone**

nortopixantrone

2-[2-[(2-hydroxyethyl)amino]ethyl]-  
5-[[2-(methylamino)ethyl]amino]indazolo[4,3-*gh*]isoquinolin-6(2*H*)-one  
*antineoplastic*

nortopixantrone

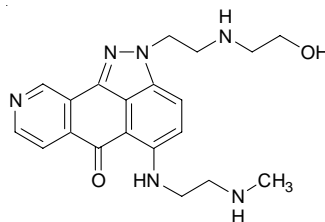
2-[2-[(2-hydroxyéthyl)amino]éthyl]-  
5-[[2-(méthylamino)éthyl]amino]indazolo[4,3-*gh*]isoquinoléin-6(2*H*)-one  
*antineoplasique*

nortopixantrona

2-[2-[(2-hidroxietyl)amino]etil]-  
5-[[2-(metilamino)etil]amino]indazolo[4,3-*gh*]isoquinolin-6(2*H*)-ona  
*antineoplásico*

C<sub>20</sub>H<sub>24</sub>N<sub>6</sub>O<sub>2</sub>

156090-17-4

**oblimersenum**

oblimersen

*P*-thiothymidyl-(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-*P*-thiothymidyl-(  
(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-  
2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-*P*-thioadenyl-(3'→5')-2'-deoxy-  
*P*-thioguanyl-(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-  
*P*-thioguanyl-(3'→5')-*P*-thiothymidyl-(3'→5')-2'-deoxy-*P*-thioguanyl-(  
(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-*P*-thioguanyl-(3'→5')-  
2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-*P*-thiocytidyl-(3'→5')-2'-deoxy-  
*P*-thioadenyl-(3'→5')-thymidine  
*antineoplastic*

oblimersen

*P*-thiothymidyl-(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-*P*-thiothymidyl-(  
(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-  
2'-désoxy-*P*-thiocytidyl-(3'→5')-2'-désoxy-*P*-thioadényl-(3'→5')-  
2'-désoxy-*P*-thioguanyl-(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-  
2'-désoxy-*P*-thioguanyl-(3'→5')-*P*-thiothymidyl-(3'→5')-2'-désoxy-  
*P*-thioguanyl-(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-2'-désoxy-  
*P*-thioguanyl-(3'→5')-2'-désoxy-*P*-thiocytidyl-(3'→5')-2'-désoxy-  
*P*-thiocytidyl-(3'→5')-2'-désoxy-*P*-thioadényl-(3'→5')-thymidine  
*antineoplasique*

oblimerseno

*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-*P*-tiotimidilil-(3'→5')-  
2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-  
*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(  
(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-  
*P*-tiotimidilil-(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-  
(3'→5')-2'-desoxi-*P*-tioguanilil-(3'→5')-2'-desoxi-*P*-tiocitidilil-(3'→5')-  
2'-desoxi-*P*-tiocitidilil-(3'→5')-2'-desoxi-*P*-tioadenilil-(3'→5')-timidina  
*antineoplásico*

C<sub>172</sub>H<sub>221</sub>N<sub>62</sub>O<sub>91</sub>P<sub>17</sub>S<sub>17</sub>

190977-41-4

**ortataxelum**

ortataxel

(3a*S*,4*R*,5*E*,7*R*,8a*S*,9*S*,10a*R*,12a*S*,12b*R*,13*S*,13a*S*)-7,12a-bis(acetyloxy)-13-(benzoyloxy)-9-hydroxy-5,8a,14,14-tetramethyl-2,8-dioxo-3a,4,7,8,8a,9,10,10a,12,12a,12b,13-dodecahydro-6,13a-methano-13a*H*-oxeto[2'',3''':5',6']benzo[1',2':4,5]cyclodeca[1,2-*d*]-1,3-dioxol-4-yl (2*R*,3*S*)-3-[[[(1,1-diméthylethoxy)carbonyl]amino]-2-hydroxy-5-méthylhexanoate  
*antineoplastic*

ortataxel

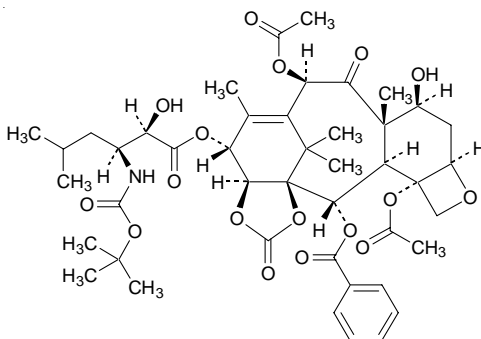
(2*R*,3*S*)-3-[[[(1,1-diméthylethoxy)carbonyl]amino]-2-hydroxy-5-méthylhexanoate de (3a*S*,4*R*,5*E*,7*R*,8a*S*,9*S*,10a*R*,12a*S*,12b*R*,13*S*,13a*S*)-7,12a-bis(acétyloxy)-13-(benzoyloxy)-9-hydroxy-5,8a,14,14-tétraméthyl-2,8-dioxo-3a,4,7,8,8a,9,10,10a,12,12a,12b,13-dodécahydro-6,13a-méthano-13a*H*-oxéto[2'',3''':5',6']benzo[1',2':4,5]cyclodéca[1,2-*d*]-1,3-dioxol-4-yle  
*antineoplasique*

ortataxel

(2*R*,3*S*)-3-[[[(1,1-dimétiletoxi)carbonil]amino]-2-hidroxi-5-metilhexanoato de (3a*S*,4*R*,5*E*,7*R*,8a*S*,9*S*,10a*R*,12a*S*,12b*R*,13*S*,13a*S*)-7,12a-bis(acetiloxi)-13-(benzoiloxi)-9-hidroxi-5,8a,14,14-tetrametil-2,8-dioxo-3a,4,7,8,8a,9,10,10a,12,12a,12b,13-dodecahidro-6,13a-metano-13a*H*-oxeto[2'',3''':5',6']benzo[1',2':4,5]ciclodéca[1,2-*d*]-1,3-dioxol-4-ilo  
*antineoplásico*

C<sub>44</sub>H<sub>57</sub>NO<sub>17</sub>

186348-23-2

**osemozotanum**

osemozotan

3-(1,3-benzodioxol-5-yloxy)-*N*-[[[(2*S*)-2,3-dihydro-1,4-benzodioxin-2-yl]méthyl]propan-1-amine  
*serotonin receptor agonist*

osémozotan

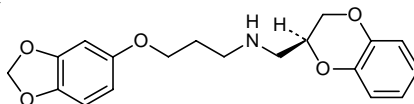
3-(1,3-benzodioxol-5-yloxy)-*N*-[[[(2*S*)-2,3-dihydro-1,4-benzodioxin-2-yl]méthyl]propan-1-amine  
*agoniste de récepteurs de la sérotonine*

osemozotán

3-(1,3-benzodioxol-5-iloxi)-*N*-[[[(2*S*)-2,3-dihidro-1,4-benzodioxin-2-il]metil]propan-1-amina  
*agonista de los receptores de la serotonina*

$C_{19}H_{21}NO_5$ 

137275-81-1

**palindorum**

palindore

(2S)-2-[(benzylamino)methyl]-2,3,7,9-tetrahydro-8H-1,4-dioxino[2,3-e]indol-8-one  
*antipsychotic*

palindore

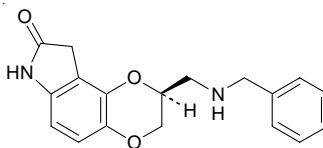
(2S)-2-[(benzylamino)méthyl]-2,3,7,9-tétrahydro-8H-1,4-dioxino[2,3-e]indol-8-one  
*psychotrope*

palindor

(2S)-2-[(bencilamino)metil]-2,3,7,9-tetrahydro-8H-1,4-dioxino[2,3-e]indol-8-ona  
*antipsicótico*

 $C_{18}H_{18}N_2O_3$ 

189681-70-7

**pascolizumabum**

pascolizumab

immunoglobulin G1, anti-(human interleukin 4) (human-mouse monoclonal SB-240683  $\gamma$ 1-chain), disulfide with human-mouse monoclonal SB-240683  $\kappa$ -chain, dimer  
*immunomodulator*

pascolizumab

immunoglobuline G1, anti-(interleukine 4 humaine) (chaîne  $\gamma$ 1 de l'anticorps monoclonal de souris SB-240683 humanisé), dimère du disulfure avec la chaîne  $\kappa$  de l'anticorps monoclonal de souris SB-240683 humanisé  
*immunomodulateur*

pascolizumab

inmunoglobulina G1, anti-(interleukina 4 humana) (cadena  $\gamma$ 1 del anticuerpo monoclonal humanizado de ratón SB-240683), dímero del disulfuro con la cadena  $\kappa$  del anticuerpo monoclonal humanizado de ratón SB-240683  
*inmunomodulador*

331243-22-2

**pegaptanibum**

pegaptanib

5'-ester of (2'-deoxy-2'-fluoro)C-Gm-Gm-A-A-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)C-Am-Gm-(2'-deoxy-2'-fluoro)U-Gm-Am-Am-(2'-deoxy-2'-fluoro)U-Gm-(2'-deoxy-2'-fluoro)C-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)U-Am-(2'-deoxy-2'-fluoro)U-Am-(2'-deoxy-2'-fluoro)C-Am-(2'-deoxy-2'-fluoro)U-(2'-deoxy-2'-fluoro)C-(2'-deoxy-2'-fluoro)C-Gm-(3'→3')-dT with  $\alpha, \alpha'$ -[[[(1S)-1-[[5-(phosphonoxy)pentyl]carbamoyl]pentane-1,5-diyl]bis(iminocarbonyl)]bis[ $\omega$ -methoxypoly(oxyethane-1,2-diyl)]]

*angiogenesis inhibitor*

pégaptanib

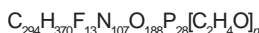
(2'-désoxy-2'-fluoro)C-Gm-Gm-A-A-(2'-désoxy-2'-fluoro)U-(2'-désoxy-2'-fluoro)C-Am-Gm-(2'-désoxy-2'-fluoro)U-Gm-Am-Am-(2'-désoxy-2'-fluoro)U-Gm-(2'-désoxy-2'-fluoro)C-(2'-désoxy-2'-fluoro)U-(2'-désoxy-2'-fluoro)U-Am-(2'-désoxy-2'-fluoro)U-Am-(2'-désoxy-2'-fluoro)C-Am-(2'-désoxy-2'-fluoro)U-(2'-désoxy-2'-fluoro)C-(2'-désoxy-2'-fluoro)C-Gm-(3'→3')-dT 5'-estérifié par  $\alpha, \alpha'$ -[[[(1S)-1-[[5-phosphonoxy)pentyl]=carbamoyl]pentane-1,5-diyl]bis(iminocarbonyl)]bis[ $\omega$ -méthoxypoly(oxyéthane-1,2-diyl)]]

*inhibiteur de l'angiogénèse*

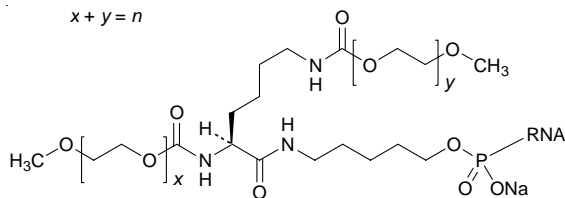
pegaptanib

(2'-desoxi-2'-fluoro)C-Gm-Gm-A-A-(2'-desoxi-2'-fluoro)U-(2'-desoxi-2'-fluoro)C-Am-Gm-(2'-desoxi-2'-fluoro)U-Gm-Am-Am-(2'-desoxi-2'-fluoro)U-Gm-(2'-desoxi-2'-fluoro)C-(2'-desoxi-2'-fluoro)U-(2'-desoxi-2'-fluoro)U-Am-(2'-desoxi-2'-fluoro)U-Am-(2'-desoxi-2'-fluoro)C-Am-(2'-desoxi-2'-fluoro)U-(2'-desoxi-2'-fluoro)C-(2'-desoxi-2'-fluoro)C-Gm-(3'→3')-dT 5'-esterificado con  $\alpha, \alpha'$ -[[[(1S)-1-[[5-(fosfonooxi)pentil]=carbamoil]pentano-1,5-diil]bis(iminocarbonil)]bis[ $\omega$ -metoxipoli(oxietano-1,2-diilo)]]

*inhibidor de la angiogénesis*



$$x + y = n$$

**pegsunerceptum**

pegsunercept

pegylated L-methionyl-1-105-human tumor necrosis factor receptor p55  
*antihyperlipidaemic*

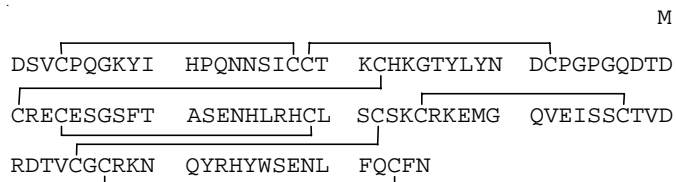
pegsunercept

L-méthionyl-1-105-récepteur p55 du facteur de nécrose tumorale humain,  
pegylé  
*antihyperlipidémiant*

pegsunercept

L-metionil-1-105-receptor p55 del factor de necrosis tumoral humano,  
pegilado  
*antihiperlipémico*

$C_{502}H_{758}N_{154}O_{165}S_{16}$  (protein portion) 330988-75-5

**perflubrodecum**

perflubrodec

1-bromohénicosafluorodecane  
*oxygen carrier*

perflubrodec

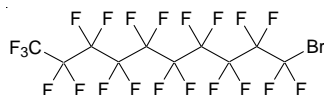
1-bromohénicosafluorodécane  
*porteur d'oxygène*

perflubrodec

1-bromohénicosafluorodecano  
*portador de oxígeno*

$C_{10}BrF_{21}$

307-43-7

**picoplatinum**

picoplatin

(*SP*-4-3)-amminedichloro(2-methylpyridine)platinum  
*antineoplastica*

picoplatine

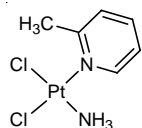
(*SP*-4-3)-amminedichloro(2-méthylpyridine)platine  
*antineoplasique*

picoplatino

(*SP*-4-3)-aminodicloro(2-metilpiridina)platino  
*antineoplásico*

$C_6H_{10}Cl_2N_2Pt$

181630-15-9



**plevitrexedum**

plevitrexed

(2*S*)-2-[[4-[[[(2,7-dimethyl-4-oxo-1,4-dihydroquinazolin-6-yl)methyl](prop-2-ynyl)amino]-2-fluorobenzoyl]amino]-4-(1*H*-tetrazol-5-yl)butanoic acid  
*antineoplastic*

plévitrexed

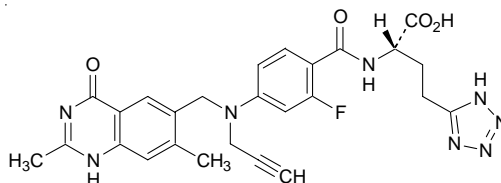
acide (2*S*)-2-[[4-[[[(2,7-diméthyl-4-oxo-1,4-dihydroquinazolin-6-yl)méthyl](prop-2-ynyl)amino]-2-fluorobenzoyl]amino]-4-(1*H*-tétraazol-5-yl)butanoïque  
*antinéoplasique*

plevitrexed

ácido (2*S*)-2-[[4-[[[(2,7-dimetil-4-oxo-1,4-dihidroquinazolin-6-il)metil](prop-2-inil)amino]-2-fluorobenzoi]amino]-4-(1*H*-tetrazol-5-il)butanoico  
*antineoplásico*

C<sub>26</sub>H<sub>25</sub>FN<sub>6</sub>O<sub>4</sub>

153537-73-6

**pumosetragum**

pumosetrag

*N*-[(3*R*)-1-azabicyclo[2.2.2]oct-3-yl]-7-oxo-4,7-dihydrothieno[3,2-*b*]pyridine-6-carboxamide  
*laxative*

pumosétrag

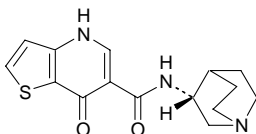
*N*-[(3*R*)-1-azabicyclo[2.2.2]oct-3-yl]-7-oxo-4,7-dihydrothiéno[3,2-*b*]pyridine-6-carboxamide  
*laxatif*

pumosetrag

*N*-[(3*R*)-1-azabicyclo[2.2.2]oct-3-il]-7-oxo-4,7-dihidrotieno[3,2-*b*]piridina-6-carboxamida  
*laxante*

C<sub>15</sub>H<sub>17</sub>N<sub>3</sub>O<sub>2</sub>S

153062-94-3



**siplizumabum**

siplizumab	immunoglobulin G1, anti-(human CD2 (antigen)) (human-rat monoclonal MEDI-507 $\gamma$ 1-chain), disulfide with human-rat monoclonal MEDI-507 light chain, dimer <i>immunomodulator</i>
siplizumab	immunoglobuline G1, anti-(antigène humain CD2) (chaîne $\gamma$ 1 de l'anticorps monoclonal de rat MEDI-507 humanisé), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de rat MEDI-507 humanisé <i>immunomodulateur</i>
siplizumab	inmunoglobulina G1, anti-(antígeno humano CD2) (cadena $\gamma$ 1 del anticuerpo monoclonal de rata humanizado MEDI-507), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal de rata humanizado MEDI-507 <i>inmunomodulador</i>

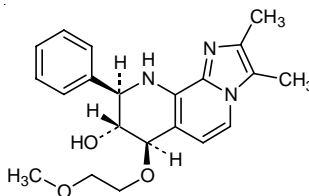
288392-69-8

**soraprazanum**

soraprazan	(7 <i>R</i> ,8 <i>R</i> ,9 <i>R</i> )-7-(2-methoxyethoxy)-2,3-dimethyl-9-phenyl-7,8,9,10-tetrahydroimidazo[1,2- <i>h</i> ][1,7]naphthyridin-8-ol <i>acid pump antagonist</i>
soraprazan	(7 <i>R</i> ,8 <i>R</i> ,9 <i>R</i> )-7-(2-méthoxyéthoxy)-2,3-diméthyl-9-phényl-7,8,9,10-tétrahydroimidazo[1,2- <i>h</i> ][1,7]naphtyridin-8-ol <i>antagoniste de la pompe à proton</i>
soraprazán	(7 <i>R</i> ,8 <i>R</i> ,9 <i>R</i> )-9-fenil-2,3-dimetil-7-(2-metoxietoxi)-7,8,9,10-tetrahydroimidazo[1,2- <i>h</i> ][1,7]naftiridin-8-ol <i>antagonista de la bomba de ácido</i>

C<sub>21</sub>H<sub>25</sub>N<sub>3</sub>O<sub>3</sub>

261944-46-1



**tacapenemum**

tacapenem

(+)-(4*R*,5*S*,6*S*)-6-[(1*R*)-1-hydroxyethyl]-4-methyl-7-oxo-3-[[[(3*R*)-5-oxopyrrolidin-3-yl]sulfanyl]-1-azabicyclo[3.2.0]hept-2-ene-2-carboxylic acid  
*antibiotic*

tacapénem

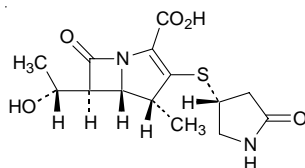
(+)-acide (4*R*,5*S*,6*S*)-6-[(1*R*)-1-hydroxyéthyl]-4-méthyl-7-oxo-3-[[[(3*R*)-5-oxopyrrolidin-3-yl]sulfanyl]-1-azabicyclo[3.2.0]hept-2-ène-2-carboxylique  
*antibiotique*

tacapenem

(+)-ácido (4*R*,5*S*,6*S*)-6-[(1*R*)-1-hidroxietil]-4-metil-7-oxo-3-[[[(3*R*)-5-oxopirrolidin-3-il]sulfanil]-1-azabicyclo[3.2.0]hept-2-eno-2-carboxílico  
*antibiótico*

C<sub>14</sub>H<sub>18</sub>N<sub>2</sub>O<sub>5</sub>S

193811-33-5

**tapentadolum**

tapentadol

3-[(1*R*,2*R*)-3-(dimethylamino)-1-ethyl-2-methylpropyl]phenol  
*analgesic*

tapentadol

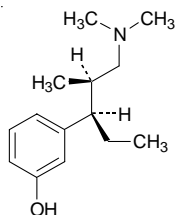
3-[(1*R*,2*R*)-3-(diméthylamino)-1-éthyl-2-méthylpropyl]phénol  
*analgésique*

tapentadol

3-[(1*R*,2*R*)-3-(dimetilamino)-1-etil-2-metilpropil]fenol  
*analgésico*

C<sub>14</sub>H<sub>23</sub>NO

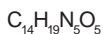
175591-09-0



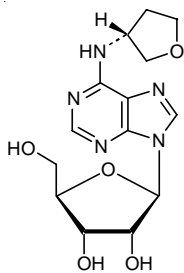


**tecadenosonum**

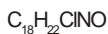
tecadenoson	9-β-D-ribofuranosyl- <i>N</i> -[(3 <i>R</i> )-tetrahydrofuran-3-yl]-9 <i>H</i> -purin-6-amine <i>adenosine receptor A agoniste</i>
técadénoson	9-β-D-ribofuranosyl- <i>N</i> -[(3 <i>R</i> )-tétrahydrofuran-3-yl]-9 <i>H</i> -purin-6-amine <i>agoniste des récepteurs de l'adénosine</i>
tecadenosón	9-β-D-ribofuranosil- <i>N</i> -[(3 <i>R</i> )-tetrahidrofuran-3-il]-9 <i>H</i> -purin-6-amina <i>agonista del receptor A de la adenosina</i>



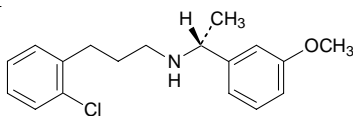
204512-90-3

**tecalcetum**

tecalcet	3-(2-chlorophenyl)- <i>N</i> -[(1 <i>R</i> )-1-(3-methoxyphenyl)ethyl]propan-1-amine <i>calcimimetic</i>
técalcet	3-(2-chlorophényl)- <i>N</i> -[(1 <i>R</i> )-1-(3-méthoxyphényl)éthyl]propan-1-amine <i>antihyperparathyroïdisme</i>
tecalcet	3-(2-clorofenil)- <i>N</i> -[(1 <i>R</i> )-1-(3-metoxifenil)etil]propan-1-amina <i>calciomimético</i>



148717-54-8



**teneliximabum**

teneliximab immunoglobulin G1, anti-(human CD40 (antigen)) (human-mouse monoclonal chi220  $\gamma$ 1-chain), disulfide with human-mouse monoclonal chi220 light chain, dimer  
*immunomodulator*

ténéliximab immunoglobuline G1, anti-(antigène CD40 humain) (chaîne  $\gamma$ 1 de l'anticorps monoclonal chimérique homme souris chi220), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal chimérique homme souris chi220  
*immunomodulateur*

teneliximab inmunoglobulina G1, anti-(antígeno CD40 humano) (cadena  $\gamma$ 1 del anticuerpo monoclonal quimérico hombre ratón chi220), dímero del disulfuro con la cadena ligera del anticuerpo monoclonal quimérico hombre ratón chi220  
*inmunomodulador*

299423-37-3

**topixantronum**

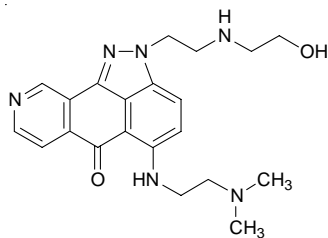
topixantrone 5-[[2-(dimethylamino)ethyl]amino]-2-[2-[(2-hydroxyethyl)amino]ethyl]indazolo[4,3-*gh*]isoquinolin-6(2*H*)-one  
*antineoplastic*

topixantrone 5-[[2-(diméthylamino)éthyl]amino]-2-[2-[(2-hydroxyéthyl)amino]éthyl]indazolo[4,3-*gh*]isoquinoléin-6(2*H*)-one  
*antinéoplasique*

topixantrona 5-[[2-(dimetilamino)etil]amino]-2-[2-[(2-hidroxietil)amino]etil]indazolo[4,3-*gh*]isoquinolin-6(2*H*)-ona  
*antineoplásico*

 $C_{21}H_{26}N_6O_2$ 

156090-18-5



**toralizumabum**

- toralizumab immunoglobulin G1, anti-(human CD40 ligand) (human-mouse monoclonal IDEC-131  $\gamma$ 1-chain), disulfide with human-mouse monoclonal IDEC-131  $\kappa$ -chain, dimer  
*immunomodulator*
- toralizumab immunoglobuline G1, anti-(ligand CD40 humain) (chaîne  $\gamma$ 1 de l'anticorps monoclonal de souris IDEC-131 humanisé), dimère du disulfure avec la chaîne  $\kappa$  de l'anticorps monoclonal de souris IDEC-131 humanisé  
*immunomodulateur*
- toralizumab inmunoglobulina G1, anti-(ligando CD40 humano) (cadena  $\gamma$ 1 del anticuerpo monoclonal humanizado de ratón IDEC-131), dímero del disulfuro con la cadena  $\kappa$  del anticuerpo monoclonal humanizado de ratón IDEC-131  
*inmunomodulador*

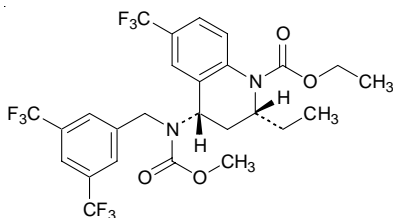
252662-47-8

**torcetrapium**

- torcetrapium ethyl (2*R*,4*S*)-4-[[3,5-bis(trifluoromethyl)benzyl](methoxycarbonyl)amino]-2-ethyl-6-(trifluoromethyl)-3,4-dihydroquinoline-1(2*H*)-carboxylate  
*antihyperlipidaemic*
- torcétrapium (2*R*,4*S*)-4-[[3,5-bis(trifluorométhyl)benzyl](méthoxycarbonyl)amino]-2-éthyl-6-(trifluorométhyl)-3,4-dihydroquinoléine-1(2*H*)-carboxylate d'éthyle  
*antihyperlipémiant*
- torcetrapium (2*R*,4*S*)-4-[[3,5-bis(trifluorometil)bencil](metoxicarbonil)amino]-2-etil-6-(trifluorometil)-3,4-dihidroquinolina-1(2*H*)-carboxilato de etilo  
*antihiperlipémico*

C<sub>26</sub>H<sub>25</sub>F<sub>9</sub>N<sub>2</sub>O<sub>4</sub>

262352-17-0



**torcitabinum**

torcitabine

4-amino-1-(2-deoxy-β-L-*erythro*-pentofuranosyl)pyrimidin-2(1*H*)-one  
*antiviral*

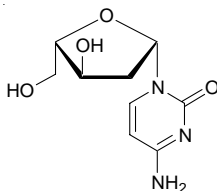
torcitabine

4-amino-1-(2-désoxy-β-L-*érythro*-pentofuranosyl)pyrimidin-2(1*H*)-one  
*antiviral*

torcitabina

4-amino-1-(2-desoxi-β-L-*eritro*-pentofuranosil)pirimidin-2(1*H*)-ona  
*antiviral* $C_9H_{13}N_3O_4$ 

40093-94-5

**trabectedinum**

trabectedin

(1'*R*,6*R*,6*aR*,7*R*,13*S*,14*S*,16*R*)-6',8,14-trihydroxy-7',9-dimethoxy-4,10,23-trimethyl-19-oxo-3',4',6,7,12,13,14,16-octahydrospiro[6,16-(epithiopropanooxymethano)-7,13-imino-6*aH*-1,3-dioxolo[7,8]isoquino[3,2-*b*][3]benzocine-20,1'(2'*H*)-isoquinolin]-5-yl acetate  
*antineoplastic*

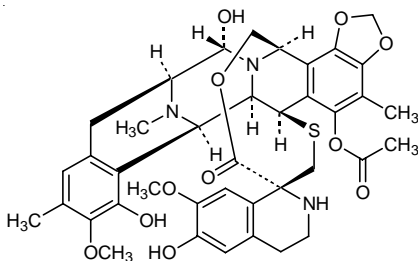
trabectédine

acétate de (1'*R*,6*R*,6*aR*,7*R*,13*S*,14*S*,16*R*)-6',8,14-trihydroxy-7',9-diméthoxy-4,10,23-triméthyl-19-oxo-3',4',6,7,12,13,14,16-octahydrospiro[6,16-(épithiopropanooxyméthano)-7,13-imino-6*aH*-1,3-dioxolo[7,8]isoquino[3,2-*b*][3]benzocine-20,1'(2'*H*)-isoquinoléin]-5-yle  
*antinéoplasique*

trabectedina

acetato de (1'*R*,6*R*,6*aR*,7*R*,13*S*,14*S*,16*R*)-6',8,14-trihidroxi-7',9-dimetoxi-4,10,23-trimetil-19-oxo-3',4',6,7,12,13,14,16-octahidrospiro[6,16-(epitiopropanooximetano)-7,13-imino-6*aH*-1,3-dioxolo[7,8]isoquino[3,2-*b*][3]benzocina-20,1'(2'*H*)-isoquinolin]-5-ilo  
*antineoplásico* $C_{39}H_{43}N_3O_{11}S$ 

114899-77-3



**treprostinilum**

treprostinil

[[[(1*R*,2*R*,3*aS*,9*aS*)-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-2,3,3*a*,4,9,9*a*-hexahydro-1*H*-cyclopenta[*b*]naphthalen-5-yl]oxy]acetic acid  
*vasodilator, prostacyclin*

tréprostinil

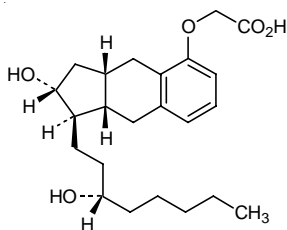
acide [[[(1*R*,2*R*,3*aS*,9*aS*)-2-hydroxy-1-[(3*S*)-3-hydroxyoctyl]-2,3,3*a*,4,9,9*a*-hexahydro-1*H*-cyclopenta[*b*]naphthalén-5-yl]oxy]acétique  
*prostacycline*

treprostinilo

ácido [[[(1*R*,2*R*,3*aS*,9*aS*)-2-hidroxi-1-[(3*S*)-3-hidroxiocetil]-2,3,3*a*,4,9,9*a*-hexahidro-1*H*-ciclopenta[*b*]naftalen-5-il]oxi]acético  
*vasodilatador, prostaciclina*

C<sub>23</sub>H<sub>34</sub>O<sub>5</sub>

81846-19-7

**triplatinum tetranitras**

triplatin tetranitrate

*trans*-[bis[*trans*-diamminechloroplatinium(μ-hexane-1,6-diamine)]]diammineplatinum tetranitrate  
*antineoplastic*

tétranitrate de triplatine

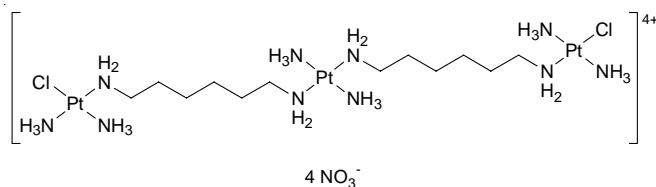
tétranitrate de *trans*-[bis[*trans*-diamminechloroplatine(μ-hexane-1,6-diamine)]]diammineplatine  
*antineoplasique*

tetranitrato de triplatino

tetranitrato de *trans*-[bis[*trans*-diaminacloroplatino(μ-hexano-1,6-diamina)]]diaminaplato  
*antineoplásico*

C<sub>12</sub>H<sub>50</sub>Cl<sub>2</sub>N<sub>14</sub>O<sub>12</sub>Pt<sub>3</sub>

172903-00-3



**tulathromycinum**

tulathromycin

Mixture of two compounds (in equilibrium in solution):

tulathromycinum A

(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]- $\alpha$ -L-ribo-hexopyranosyl)oxy]-2-ethyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexamethyl-11-[[3,4,6-trideoxy-3-(dimethylamino)- $\beta$ -D-xyl-o-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadecan-15-one

tulathromycinum B

(2R,3R,6R,8R,9R,10S,11S,12R)-11-[(2,6-dideoxy-3-C-methyl-3-O-methyl-4-C-[(propylamino)methyl]- $\alpha$ -L-ribo-hexopyranosyl)oxy]-2-[(1R,2R)-1,2-dihydroxy-1-methylbutyl]-8-hydroxy-3,6,8,10,12-pentamethyl-9-[[3,4,6-trideoxy-3-(dimethylamino)- $\beta$ -D-xyl-o-hexopyranosyl]oxy]-1-oxa-4-azacyclotridecan-13-one  
antibacterial (veterinary drug)

tulathromycine

Mélange de deux composés (en équilibre en solution):

tulathromycinum A

(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-didésoxy-3-C-méthyl-3-O-méthyl-4-C-[(propylamino)méthyl]- $\alpha$ -L-ribo-hexopyranosyl)oxy]-2-éthyl-3,4,10-trihydroxy-3,5,8,10,12,14-hexaméthyl-11-[[3,4,6-tridésoxy-3-(diméthylamino)- $\beta$ -D-xyl-o-hexopyranosyl]oxy]-1-oxa-6-azacyclopentadécan-15-one

tulathromycinum B

(2R,3R,6R,8R,9R,10S,11S,12R)-11-[(2,6-didésoxy-3-C-méthyl-3-O-méthyl-4-C-[(propylamino)méthyl]- $\alpha$ -L-ribo-hexopyranosyl)oxy]-2-[(1R,2R)-1,2-dihydroxy-1-méthylbutyl]-8-hydroxy-3,6,8,10,12-pentaméthyl-9-[[3,4,6-tridésoxy-3-(diméthylamino)- $\beta$ -D-xyl-o-hexopyranosyl]oxy]-1-oxa-4-azacyclotridécane-13-one  
antibactérien (médicament vétérinaire)

tulatromicina

Mezcla de dos componentes (en equilibrio en solución):

tulathromycinum A

(2R,3S,4R,5R,8R,10R,11R,12S,13S,14R)-13-[(2,6-didesoxi-3-C-metil-3-O-metil-4-C-[(propilamino)metil]- $\alpha$ -L-ribo-hexopiranosil)oxi]-2-etil-3,4,10-trihidroxi-3,5,8,10,12,14-hexametil-11-[[3,4,6-tridesoxi-3-(dimetilamino)- $\beta$ -D-xilo-hexopiranosil]oxi]-1-oxa-6-azaciclopentadecan-15-ona

tulathromycinum B

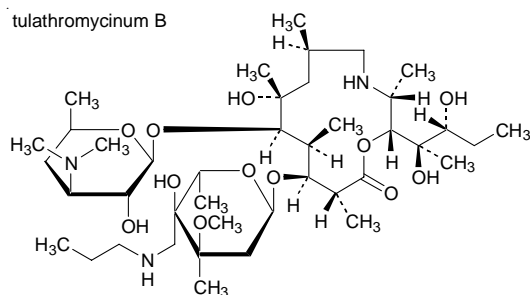
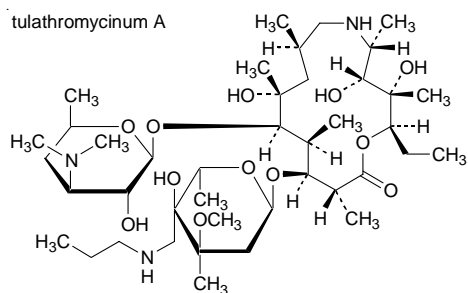
(2R,3R,6R,8R,9R,10S,11S,12R)-11-[(2,6-didesoxi-3-C-metil-3-O-metil-4-C-[(propilamino)metil]- $\alpha$ -L-ribo-hexopiranosil)oxi]-2-[(1R,2R)-1,2-dihidroxi-1-metilbutil]-8-hidroxi-3,6,8,10,12-pentametil-9-[[3,4,6-tridesoxi-3-(dimetilamino)- $\beta$ -D-xilo-hexopiranosil]oxi]-1-oxa-4-azaciclotridecan-13-ona  
antibacteriano (medicamento veterinario)

C<sub>41</sub>H<sub>79</sub>N<sub>3</sub>O<sub>12</sub> tulathromycinum A

217500-96-4 tulathromycinum A

C<sub>41</sub>H<sub>79</sub>N<sub>3</sub>O<sub>12</sub> tulathromycinum B

280755-12-6 tulathromycinum B

**vapaliximabum**

vapaliximab

immunoglobulin G2, anti-(human vascular adhesion protein VAP-1) (human-mouse monoclonal 2D10  $\gamma$ 2-chain), disulfide with human-mouse monoclonal 2D10  $\kappa$ -chain, dimer  
*immunomodulator*

vapaliximab

immunoglobuline G2, anti-(protéine d'adhésion vasculaire humaine VAP-1) (chaîne  $\gamma$ 2 de l'anticorps monoclonal chimérique homme-souris 2D10), dimère du disulfure avec la chaîne  $\kappa$  de l'anticorps monoclonal chimérique homme-souris 2D10  
*immunomodulateur*

vapaliximab

immunoglobulina G2, anti-(proteína de adhesión vascular humana VAP-1) (cadena  $\gamma$ 2 del anticuerpo monoclonal quimérico hombre-ratón 2D10), dímero del disulfuro con la cadena  $\kappa$  del anticuerpo monoclonal quimérico hombre-ratón 2D10  
*inmunomodulador*

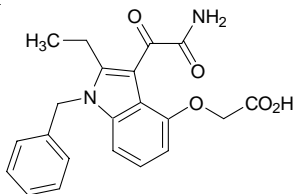
336801-86-6

**varespladibum**

varespladib	[[3-(aminooxoacetyl)-1-benzyl-2-ethyl-1 <i>H</i> -indol-4-yl]oxy]acetic acid <i>secretory phospholipase A<sub>2</sub> inhibitor</i>
varespladib	acide [[3-(aminooxoacétyl)-1-benzyl-2-éthyl-1 <i>H</i> -indol-4-yl]oxy]acétique <i>inhibiteur de sécrétion de phospholipase A<sub>2</sub></i>
varespladib	ácido [[3-(aminooxoacetil)-1-bencil-2-etil-1 <i>H</i> -indol-4-il]oxi]acético <i>inhibidor de la fosfolipasa A<sub>2</sub> segregada</i>

 $C_{21}H_{20}N_2O_5$ 

172732-68-2





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**AMENDMENTS TO PREVIOUS LISTS  
MODIFICATIONS APPORTÉES AUX LISTES ANTÉRIEURES  
MODIFICACIONES A LAS LISTAS ANTERIORES**

**Proposed International Nonproprietary Names (Prop. INN): List 82**

**Dénominations communes internationales proposées (DCI Prop.): Liste 82**

**Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Lista 82**

*(WHO Drug Information, Vol. 13, No. 4, 1999)*

p. 289 *delete/supprimer/suprimase insert/insérer/insértese*

**tebipenemum**

tebipenem

tébipénem

tebipenem

**tebipenem pivoxilum**

tebipenem pivoxil

tébipénem pivoxil

tebipenem pivoxilo

**Proposed International Nonproprietary Names (Prop. INN): List 84**

**Dénominations communes internationales proposées (DCI Prop.): Liste 84**

**Denominaciones Comunes Internacionales Propuestas (DCI Prop.): Lista 84**

*(WHO Drug Information, Vol. 14, No. 4, 2000)*

p. 265 *delete/supprimer/suprimase insert/insérer/insértese*

pittrakinraum

pittrakinrum

p. 266 reglitazarum

reglitazar

*sustituyase la descripción por la siguiente:*

*(4RS)-4-[4-[2-fenil-5-metiloxazol-4-il)etoxi]bencil]isoxazolidina-3,5-diona*

p. 267 rivoglitazonum

rivoglitazona

*sustituyase la descripción por la siguiente:*

*(5RS)-5-[4-[(1-metil-6-metoxi-1H-bencimidazol-2-il)metoxi]bencil]tiazolidina-2,4-diona*

p. 272 tipifarnibum

tipifarnib

*sustituyase la descripción por la siguiente:*

*(+)-6-[(R)-amino(4-clorofenil)(1-metil-1H-imidazol-5-il)metil]-4-(3-clorofenil)-1-metilquinolin-2(1H)-ona*

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## Annex 1

### PROCEDURE FOR THE SELECTION OF RECOMMENDED INTERNATIONAL NONPROPRIETARY NAMES FOR PHARMACEUTICAL SUBSTANCES\*

The following procedure shall be followed by the World Health Organization in the selection of recommended international nonproprietary names for pharmaceutical substances, in accordance with the World Health Assembly resolution WHA3.11:

1. Proposals for recommended international nonproprietary names shall be submitted to the World Health Organization on the form provided therefor.

2. Such proposals shall be submitted by the Director-General of the World Health Organization to the members of the Expert Advisory Panel on the International Pharmacopoeia and Pharmaceutical Preparations designated for this purpose, for consideration in accordance with the "General principles for guidance in devising International Nonproprietary Names", appended to this procedure. The name used by the person discovering or first developing and marketing a pharmaceutical substance shall be accepted, unless there are compelling reasons to the contrary.

3. Subsequent to the examination provided for in article 2, the Director-General of the World Health Organization shall give notice that a proposed international nonproprietary name is being considered.

A. Such notice shall be given by publication in the *Chronicle of the World Health Organization*<sup>1</sup> and by letter to Member States and to national pharmacopoeia commissions or other bodies designated by Member States.

(i) Notice may also be sent to specific persons known to be concerned with a name under consideration.

B. Such notice shall:

(i) set forth the name under consideration;

(ii) identify the person who submitted a proposal for naming the substance, if so requested by such person;

(iii) identify the substance for which a name is being considered;

(iv) set forth the time within which comments and objections will be received and the person and place to whom they should be directed;

(v) state the authority under which the World Health Organization is acting and refer to these rules of procedure.

C. In forwarding the notice, the Director-General of the World Health Organization shall request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the proposed name during the period it is under consideration by the World Health Organization.

4. Comments on the proposed name may be forwarded by any person to the World Health Organization within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization*.<sup>1</sup>

5. A formal objection to a proposed name may be filed by any interested person within four months of the date of publication, under article 3, of the name in the *Chronicle of the World Health Organization*.<sup>1</sup>

A. Such objection shall:

(i) identify the person objecting;

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\* Text adopted by the Executive Board of WHO in resolution EB15.R7 (*Off. Rec. Wld Health Org.*, 1955, 60, 3) and amended by the Board in resolution EB43.R9 (*Off. Rec. Wld Hlth Org.*, 1969, 173, 10).

<sup>1</sup> The title of this publication was changed to *WHO Chronicle* in January 1959. From 1987 onwards lists of INNs are published in *WHO Drug Information*.

(ii) state his interest in the name;

(iii) set forth the reasons for his objection to the name proposed.

6. Where there is a formal objection under article 5, the World Health Organization may either reconsider the proposed name or use its good offices to attempt to obtain withdrawal of the objection. Without prejudice to the consideration by the World Health Organization of a substitute name or names, a name shall not be selected by the World Health Organization as a recommended international nonproprietary name while there exists a formal objection thereto filed under article 5 which has not been withdrawn.

7. Where no objection has been filed under article 5, or all objections previously filed have been withdrawn, the Director-General of the World Health Organization shall give notice in accordance with subsection A of article 3 that the name has been selected by the World Health Organization as a recommended international nonproprietary name.

8. In forwarding a recommended international nonproprietary name to Member States under article 7, the Director-General of the World Health Organization shall:

A. request that it be recognized as the nonproprietary name for the substance; and

B. request that Member States take such steps as are necessary to prevent the acquisition of proprietary rights in the name, including prohibiting registration of the name as a trade-mark or trade-name.

## Annex 2

### GENERAL PRINCIPLES FOR GUIDANCE IN DEVISING INTERNATIONAL NONPROPRIETARY NAMES FOR PHARMACEUTICAL SUBSTANCES\*

1. International Nonproprietary Names (INN) should be distinctive in sound and spelling. They should not be inconveniently long and should not be liable to confusion with names in common use.

2. The INN for a substance belonging to a group of pharmacologically related substances should, where appropriate, show this relationship. Names that are likely to convey to a patient an anatomical, physiological, pathological or therapeutic suggestion should be avoided.

*These primary principles are to be implemented by using the following secondary principles:*

3. In devising the INN of the first substance in a new pharmacological group, consideration should be given to the possibility of devising suitable INN for related substances, belonging to the new group.

4. In devising INN for acids, one-word names are preferred; their salts should be named without modifying the acid name, e.g. "oxacillin" and "oxacillin sodium", "ibufenac" and "ibufenac sodium".

5. INN for substances which are used as salts should in general apply to the active base or the active acid. Names for different salts or esters of the same active substance should differ only in respect of the name of the inactive acid or the inactive base.

For quaternary ammonium substances, the cation and anion should be named appropriately as separate components of a quaternary substance and not in the amine-salt style.

6. The use of an isolated letter or number should be avoided; hyphenated construction is also undesirable.

\* In its twentieth report (WHO Technical Report Series, No. 581, 1975), the WHO Expert Committee on Nonproprietary Names for Pharmaceutical Substances reviewed the general principles for devising, and the procedures for selecting, international nonproprietary names (INN) in the light of developments in pharmaceutical compounds in recent years. The most significant change has been the extension to the naming of synthetic chemical substances of the practice previously used for substances originating in or derived from natural products. This practice involves employing a characteristic "stem" indicative of a common property of the members of a group. The reasons for, and the implications of, the change are fully discussed.

7. To facilitate the translation and pronunciation of INN, “f” should be used instead of “ph”, “t” instead of “th”, “e” instead of “ae” or “oe”, and “i” instead of “y”; the use of the letters “h” and “k” should be avoided.

8. Provided that the names suggested are in accordance with these principles, names proposed by the person discovering or first developing and marketing a pharmaceutical preparation, or names already officially in use in any country, should receive preferential consideration.

9. Group relationship in INN (see Guiding Principle 2) should if possible be shown by using a common stem. The following list contains examples of stems for groups of substances, particularly for new groups. There are many other stems in active use.<sup>1</sup> Where a stem is shown without any hyphens it may be used anywhere in the name.

<i>Latin</i>	<i>English</i>	
-acum	-ac	anti-inflammatory agents of the ibufenac group
-actidum	-actide	synthetic polypeptides with a corticotropin-like action
-adolum	-adol )	analgetics
-adol-	-adol- )	
-astum	-ast	antiasthmatic, anti-allergic substances not acting primarily as antihistaminics
-astinum	-astine	antihistaminics
-azepamum	-azepam	diazepam derivatives
-bactamum	-bactam	β-lactamase inhibitors
bol	bol	steroids, anabolic
-buzonum	-buzone	anti-inflammatory analgesics, phenylbutazone derivatives
-cain-	-cain-	antifibrilliant substances with local anaesthetic activity
-cainum	-caine	local anaesthetics
cef-	cef-	antibiotics, cephalosporanic acid derivatives
-cillinum	-cillin	antibiotics, derivatives of 6-aminopenicillanic acid
-conazolium	-conazole	systemic antifungal agents, miconazole derivatives
cort	cort	corticosteroids, except prednisolone derivatives
-dipinum	-dipine	calcium channel blockers, nifedipine derivatives
-fibratum	-fibrate	clofibrate derivatives
gest	gest	steroids, progestogens
gli-	gli-	sulfonamide hypoglycaemics
io-	io-	iodine-containing contrast media
-ium	-ium	quaternary ammonium compounds
-metacinum	-metacin	anti-inflammatory substances, indometacin derivatives
-mycinum	-mycin	antibiotics, produced by <i>Streptomyces</i> strains
-nidazolium	-nidazole	antiprotozoal substances, metronidazole derivatives
-ololum	-olol	β-adrenoreceptor antagonists
-oxacinum	-oxacin	antibacterial agents, nalidixic acid derivatives
-pridum	-pride	sulpiride derivatives
-pril(at)um	pril(at)	angiotensin-converting enzyme inhibitors
-profenum	-profen	anti-inflammatory substances, ibuprofen derivatives
prost	prost	prostaglandins
-relinum	-relin	hypophyseal hormone release-stimulating peptides
-terolum	-terol	bronchodilators, phenethylamine derivatives
-tidinum	-tidine	histamine H <sub>2</sub> -receptor antagonists
-trexatum	-trexate	folic acid antagonists
-verinum	-verine	spasmolytics with a papaverine-like action
vin-	vin- )	vinca alkaloids
-vin-	-vin- )	

<sup>1</sup> A more extensive listing of stems is contained in the working document WHO/EDM/QSM 99.6 which is regularly updated and can be requested from the INN Programme, WHO, Geneva.

## Annexe 1

### PROCEDURE A SUIVRE EN VUE DU CHOIX DE DENOMINATIONS COMMUNES INTERNATIONALES RECOMMANDEES POUR LES SUBSTANCES PHARMACEUTIQUES\*

L'Organisation mondiale de la Santé observe la procédure exposée ci-dessous pour l'attribution de dénominations communes internationales recommandées pour les substances pharmaceutiques, conformément à la résolution WHA3.11 de l'Assemblée mondiale de la Santé:

1. Les propositions de dénominations communes internationales recommandées sont soumises à l'Organisation mondiale de la Santé sur la formule prévue à cet effet.

2. Ces propositions sont soumises par le Directeur général de l'Organisation mondiale de la Santé aux experts désignés à cette fin parmi les personnalités inscrites au Tableau d'experts de la Pharmacopée internationale et des Préparations pharmaceutiques; elles sont examinées par les experts conformément aux "Directives générales pour la formation des dénominations communes internationales", reproduites ci-après. La dénomination acceptée est la dénomination employée par la personne qui découvre ou qui, la première, fabrique et lance sur le marché une substance pharmaceutique, à moins que des raisons majeures n'obligent à s'écarter de cette règle.

3. Après l'examen prévu à l'article 2, le Directeur général de l'Organisation mondiale de la Santé notifie qu'un projet de dénomination commune internationale est à l'étude.

A. Cette notification est faite par une insertion dans la *Chronique de l'Organisation mondiale de la Santé*<sup>1</sup> et par l'envoi d'une lettre aux Etats Membres et aux commissions nationales de pharmacopée ou autres organismes désignés par les Etats Membres.

(i) Notification peut également être faite à toute personne portant à la dénomination mise à l'étude un intérêt notoire.

B. Cette notification contient les indications suivantes:

(i) dénomination mise à l'étude;

(ii) nom de l'auteur de la proposition tendant à attribuer une dénomination à la substance, si cette personne le demande;

(iii) définition de la substance dont la dénomination est mise à l'étude;

(iv) délai pendant lequel seront reçues les observations et les objections à l'égard de cette dénomination; nom et adresse de la personne habilitée à recevoir ces observations et objections;

(v) mention des pouvoirs en vertu desquels agit l'Organisation mondiale de la Santé et référence au présent règlement.

C. En envoyant cette notification, le Directeur général de l'Organisation mondiale de la Santé demande aux Etats Membres de prendre les mesures nécessaires pour prévenir l'acquisition de droits de propriété sur la dénomination proposée pendant la période au cours de laquelle cette dénomination est mise à l'étude par l'Organisation mondiale de la Santé.

4. Des observations sur la dénomination proposée peuvent être adressées à l'Organisation mondiale de la Santé par toute personne, dans les quatre mois qui suivent la date de publication de la dénomination dans la *Chronique de l'Organisation mondiale de la Santé*<sup>1</sup> (voir l'article 3).

\* Le texte reproduit ici a été adopté par le Conseil exécutif dans la résolution EB15.R7 (*Actes off. Org. mond. Santé*, 1955, **60**, 3) qui l'a ultérieurement amendé par la résolution EB43.R9 (*Actes off. Org. mond. Santé*, 1969, **173**, 10).

<sup>1</sup> Depuis janvier 1959, cette publication porte le titre de *Chronique OMS*. A partir de 1987, les listes des DCIs sont publiées dans les *Informations pharmaceutiques OMS*.

5. Toute personne intéressée peut formuler une objection formelle contre la dénomination proposée dans les quatre mois qui suivent la date de publication de la dénomination dans la *Chronique de l'Organisation mondiale de la Santé*<sup>1</sup> (voir l'article 3).

A. Cette objection doit s'accompagner des indications suivantes:

- i) nom de l'auteur de l'objection;
- ii) intérêt qu'il porte à la dénomination en cause;
- iii) raisons motivant l'objection contre la dénomination proposée.

6. Lorsqu'une objection formelle est formulée en vertu de l'article 5, l'Organisation mondiale de la Santé peut soit soumettre la dénomination proposée à un nouvel examen, soit intervenir pour tenter d'obtenir le retrait de l'objection. Sans préjudice de l'examen par elle d'une ou de plusieurs appellations de remplacement, l'Organisation mondiale de la Santé n'adopte pas d'appellation comme dénomination commune internationale recommandée tant qu'une objection formelle présentée conformément à l'article 5 n'est pas levée.

7. Lorsqu'il n'est formulé aucune objection en vertu de l'article 5 ou que toutes les objections présentées ont été levées, le Directeur général de l'Organisation mondiale de la Santé fait une notification conformément aux dispositions de la sous-section A de l'article 3, en indiquant que la dénomination a été choisie par l'Organisation mondiale de la Santé en tant que dénomination commune internationale recommandée.

8. En communiquant aux Etats Membres, conformément à l'article 7, une dénomination commune internationale recommandée, le Directeur général de l'Organisation mondiale de la Santé:

A. demande que cette dénomination soit reconnue comme dénomination commune de la substance considérée, et

B. demande aux Etats Membres de prendre les mesures nécessaires pour prévenir l'acquisition de droits de propriété sur cette dénomination, notamment en interdisant le dépôt de cette dénomination comme marque ou appellation commerciale.

## Annexe 2

### DIRECTIVES GENERALES POUR LA FORMATION DE DENOMINATIONS COMMUNES INTERNATIONALES APPLICABLES AUX SUBSTANCES PHARMACEUTIQUES\*

1. Les dénominations communes internationales (DCI) devront se distinguer les unes des autres par leur consonance et leur orthographe. Elles ne devront pas être d'une longueur excessive, ni prêter à confusion avec des appellations déjà couramment employées.

2. La DCI de chaque substance devra, si possible, indiquer sa parenté pharmacologique. Les dénominations susceptibles d'évoquer pour les malades des considérations anatomiques, physiologiques, pathologiques ou thérapeutiques devront être évitées dans la mesure du possible.

*Outre ces deux principes fondamentaux, on respectera les principes secondaires suivants:*

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\* Dans son vingtième rapport (Série de Rapports techniques de l'OMS, No. 581, 1975), le Comité OMS d'experts des Dénominations communes pour les Substances pharmaceutiques a examiné les directives générales pour la formation des dénominations communes internationales et la procédure à suivre en vue de leur choix, compte tenu de l'évolution du secteur pharmaceutique au cours des dernières années. La modification la plus importante a été l'extension aux substances de synthèse de la pratique normalement suivie pour désigner les substances tirées ou dérivées de produits naturels. Cette pratique consiste à employer des syllabes communes ou groupes de syllabes communes (segments clés) qui sont caractéristiques et indiquent une propriété commune aux membres du groupe des substances pour lequel ces segments clés ont été retenus. Les raisons et les conséquences de cette modification ont fait l'objet de discussions approfondies.

3. Lorsqu'on formera la DCI de la première substance d'un nouveau groupe pharmacologique, on tiendra compte de la possibilité de former ultérieurement d'autres DCI appropriées pour les substances apparentées du même groupe.

4. Pour former des DCI des acides, on utilisera de préférence un seul mot. Leurs sels devront être désignés par un terme qui ne modifie pas le nom de l'acide d'origine: par exemple "oxacilline" et "oxacilline sodique", "ibufénac" et "ibufénac sodique".

5. Les DCI pour les substances utilisées sous forme de sels devront en général s'appliquer à la base active (ou à l'acide actif). Les dénominations pour différents sels ou esters d'une même substance active ne différeront que par le nom de l'acide inactif (ou de la base inactive).

En ce qui concerne les substances à base d'ammonium quaternaire, la dénomination s'appliquera de façon appropriée au cation et à l'anion en tant qu'éléments distincts d'une substance quaternaire. On évitera de choisir une désignation évoquant un sel aminé.

6. On évitera d'ajouter une lettre ou un chiffre isolé; en outre, on renoncera de préférence au trait d'union.

7. Pour simplifier la traduction et la prononciation des DCI, la lettre "f" sera utilisée à la place de "ph", "t" à la place de "th", "e" à la place de "ae" ou "oe" et "i" à la place de "y"; l'usage des lettres "h" et "k" sera aussi évité.

8. On retiendra de préférence, pour autant qu'elles respectent les principes énoncés ici, les dénominations proposées par les personnes qui ont découvert ou qui, les premières, ont fabriqué et lancé sur le marché les préparations pharmaceutiques considérées, ou les dénominations déjà officiellement adoptées par un pays.

9. La parenté entre substances d'un même groupe (voir Directive générale 2) sera si possible indiquée dans les DCI par l'emploi de segments clés communs. La liste ci-après contient des exemples de segments clés pour des groupes de substances, surtout pour des groupes récents. Il y a beaucoup d'autres segments clés en utilisation active.<sup>1</sup> Les segments clés indiqués sans trait d'union pourront être insérés n'importe où dans une dénomination.

<i>Latin</i>	<i>Français</i>	
-acum	-ac	substances anti-inflammatoires du groupe de l'ibufénac
-actidum	-actide	polypeptides synthétiques agissant comme la corticotropine
-adolum	-adol )	analgésiques
-adol-	-adol- )	
-astum	-ast	antiasthmatiques, antiallergiques n'agissant pas principalement en tant qu'antihistaminiques
-astinum	-astine	antihistaminiques
-azepamum	-azépam	substances du groupe du diazépam
-bactamum	-bactame	inhibiteurs de $\beta$ -lactamases
bol	bol	stéroïdes anabolisants
-buzonum	-buzone	analgésiques anti-inflammatoires du groupe de la phénylbutazone
-cain-	-caïn-	substances antifibrillantes à action anesthésique locale
-cainum	-caïne	anesthésiques locaux
cef-	céf-	antibiotiques, dérivés de l'acide céphalosporanique
-cillinum	-cilline	antibiotiques, dérivés de l'acide 6-aminopénicillanique
-conazolium	-conazole	agents antifongiques systémiques du groupe du miconazole
cort	cort	corticostéroïdes, autres que les dérivés de la prednisolone
-dipinum	-dipine	inhibiteurs du calcium du groupe de la nifédipine
-fibratum	-fibrate	substances du groupe du clofibrate
gest	gest	stéroïdes progestogènes
gli-	gli-	sulfamides hypoglycémiantes
io-	io-	produits de contraste iodés
-ium	-ium	ammoniums quaternaires
-metacinum	-métacine	substances anti-inflammatoires du groupe de l'indométacine

<sup>1</sup> Une liste plus complète de segments clés est contenue dans le document de travail WHO/EDM/QSM 99.6 qui est régulièrement mis à jour et qui peut être demandé auprès du Programme des DCI, OMS, Genève.

<i>Latin</i>	<i>Français</i>	
-mycinum	-mycine	antibióticos producidos por cepas de <i>Streptomyces</i>
-nidazololum	-nidazole	substancias antiprotozoarias del grupo del metronidazol
ololum	-olol	antagonistas de receptores $\beta$ -adrenérgicos
-oxacinum	-oxacine	substancias antibacterianas del grupo de l'acido nalidixico
-pridum	-pride	substancias del grupo del sulpirido
-profenum	-profène	substancias anti-inflamatorias del grupo de l'ibuprofène
-pril(at)um	-pril(ate)	inhibidores de l'enzima de conversión de l'angiotensina
prost	prost	prostaglandinas
-relinum	-réline	peptidos estimulando la liberación de hormonas hipofisarias
-terolum	-térol	broncodilatadores, derivados de la fenétilamina
-tidinum	-tidine	antagonistas de receptores $H_2$ de l'histamina
-trexatum	-trexate	antagonistas de l'acido folico
-verinum	-vérine	spasmolíticos actuando como la papaverina
vin-	vin- )	alcaloides del tipo vinca
-vin-	-vin- )	

## Anexo 1

### PROCEDIMIENTO DE SELECCION DE DENOMINACIONES COMUNES INTERNACIONALES RECOMENDADAS PARA LAS SUSTANCIAS FARMACEUTICAS\*

La Organización Mundial de la Salud seguirá el procedimiento que se expone a continuación para la selección de denominaciones comunes internacionales recomendadas para las sustancias farmacéuticas, de conformidad con lo dispuesto en la resolución WHA3.11 de la Asamblea Mundial de la Salud:

1. Las propuestas de denominaciones comunes internacionales recomendadas se presentarán a la Organización Mundial de la Salud en los formularios que se proporcionen a estos efectos.

2. Estas propuestas serán sometidas por el Director General de la Organización Mundial de la Salud a los Miembros del Cuadro de Expertos de la Farmacopea Internacional y las Preparaciones Farmacéuticas encargados de su estudio, para que las examinen de conformidad con los "Principios Generales de Orientación para formar Denominaciones Comunes Internacionales para Sustancias Farmacéuticas", anexos a este Procedimiento. A menos que haya poderosas razones en contra, la denominación aceptada será la empleada por la persona que haya descubierto, fabricado o puesto a la venta por primera vez una sustancia farmacéutica.

3. Una vez terminado el estudio a que se refiere el artículo 2, el Director General de la Organización Mundial de la Salud notificará que está en estudio un proyecto de denominación internacional.

A. Esta notificación se hará mediante una publicación en la *Crónica de la Organización Mundial de la Salud*<sup>1</sup> y el envío de una carta a los Estados Miembros y a las comisiones nacionales de las farmacopeas u otros organismos designados por los Estados Miembros.

(i) La notificación puede enviarse también a las personas que tengan un interés especial en una denominación objeto de estudio.

\* El texto corregido que aquí se reproduce fue adoptado por el Consejo Ejecutivo en la resolución EB15.R7 (*Act. of. Org. mund. Salud*, 1955, **60**, 3) y enmendado por el Consejo en la resolución EB43.R9 (*Act. of. Org. mund. Salud*, 1969, **173**, 10).

<sup>1</sup> Denominada *Crónica de la OMS* desde enero de 1959. A partir de 1987, las listas de DCI se publican en *Información Farmacéutica OMS*.



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B. En estas notificaciones se incluyen los siguientes datos:

- (i) denominación sometida a estudio;
- (ii) nombre de la persona que ha presentado la propuesta de denominación de la sustancia si lo pide esta persona;
- (iii) definición de la sustancia cuya denominación está en estudio;
- (iv) plazo fijado para recibir observaciones y objeciones, así como nombre y dirección de la persona a quien deban dirigirse, y
- (v) mención de los poderes conferidos para el caso a la Organización Mundial de la Salud y referencia al presente procedimiento.

C. Al enviar esta notificación, el Director General de la Organización Mundial de la Salud solicitará de los Estados Miembros la adopción de todas las medidas necesarias para impedir la adquisición de derechos de propiedad sobre la denominación propuesta, durante el periodo en que la Organización Mundial de la Salud tenga en estudio esta denominación.

4. Toda persona puede formular a la Organización Mundial de la Salud observaciones sobre la denominación propuesta, dentro de los cuatro meses siguientes a su publicación en la *Crónica de la Organización Mundial de la Salud*, conforme a lo dispuesto en el artículo 3.

5. Toda persona interesada puede presentar una objeción formal contra la denominación propuesta, dentro de los cuatro meses siguientes a su publicación en la *Crónica de la Organización Mundial de la Salud*, conforme a lo dispuesto en el artículo 3.

A. Esta objeción deberá acompañarse de los siguientes datos:

- i) nombre de la persona que formula la objeción;
- ii) causas que motivan su interés por la denominación, y
- iii) causas que motivan su objeción a la denominación propuesta.

6. Cuando se haya presentado una objeción formal en la forma prevista en el artículo 5, la Organización Mundial de la Salud puede someter a nuevo estudio la denominación propuesta, o bien utilizar sus buenos oficios para lograr que se retire la objeción. Sin perjuicio de que la Organización Mundial de la Salud estudie una o varias denominaciones en sustitución de la primitiva, ninguna denominación podrá ser seleccionada por la Organización Mundial de la Salud como denominación común internacional recomendada en tanto que exista una objeción formal, presentada como previene el artículo 5, que no haya sido retirada.

7. Cuando no se haya formulado ninguna objeción en la forma prevista en el artículo 5, o cuando todas las objeciones presentadas hayan sido retiradas, el Director de la Organización Mundial de la Salud notificará, conforme a lo dispuesto en el párrafo A del artículo 3, que la denominación ha sido seleccionada por la Organización Mundial de la Salud como denominación común internacional recomendada.

8. Al comunicar a los Estados Miembros una denominación común internacional conforme a lo previsto en el artículo 7, el Director General de la Organización Mundial de la Salud:

A. solicitará que esta denominación sea reconocida como denominación común para la sustancia de que se trate, y

B. solicitará de los Estados Miembros la adopción de todas las medidas necesarias para impedir la adquisición de derechos de propiedad sobre la denominación, incluso la prohibición de registrarla como marca de fábrica o como nombre comercial.

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## Anexo 2

### PRINCIPIOS GENERALES DE ORIENTACION PARA FORMAR DENOMINACIONES COMUNES INTERNACIONALES PARA SUSTANCIAS FARMACEUTICAS\*

1. Las Denominaciones Comunes Internacionales (DCI) deberán diferenciarse tanto fonética como ortográficamente. No deberán ser incómodamente largas, ni dar lugar a confusión con denominaciones de uso común.

2. La DCI de una sustancia que pertenezca a un grupo de sustancias farmacológicamente emparentadas deberá mostrar apropiadamente este parentesco. Deberán evitarse los nombres que puedan inducir fácilmente en el paciente sugerencias anatómicas, fisiológicas, patológicas o terapéuticas.

*Estos principios primarios deberán ser tenidos en cuenta al aplicar los siguientes principios secundarios:*

3. Al idear la DCI de la primera sustancia de un nuevo grupo farmacológico, deberá tenerse en cuenta la posibilidad de formar DCI convenientes para las sustancias emparentadas que vengan a incrementar el nuevo grupo.

4. Al idear DCI para ácidos, se preferirán las de una sola palabra; sus sales deberán denominarse sin modificar el nombre de ácido; p. ej., "oxacilina" y "oxacilina sódica", "ibufenaco" e "ibufenaco sódico".

5. Las DCI para las sustancias que se usan en forma de sal, deberán en general aplicarse a la base activa o, respectivamente, al ácido activo. Las denominaciones para diferentes sales o ésteres de la misma sustancia activa solamente deberán diferir en el nombre de ácido o de la base inactivos.

En los compuestos de amonio cuaternario, el catión y el anión deberán denominarse adecuadamente por separado, como componentes independientes de una sustancia cuaternaria y no como sales de una amina.

6. Deberá evitarse el empleo de una letra o un número aislados; también es indeseable el empleo de guiones.

7. Para facilitar la traducción y la pronunciación se emplearán de preferencia las letras "f" en lugar de "ph", "t" en lugar de "th", "e" en lugar de "ae" u "oe" e "i" en lugar de "y"; se deberá evitar el empleo de las letras "h" y "k".

8. Siempre que las denominaciones que se sugieran estén de acuerdo con estos principios, recibirán una consideración preferente las denominaciones propuestas por la persona que haya descubierto la sustancia, o la que primeramente fabrique o ponga a la venta la sustancia farmacéutica, así como las denominaciones oficialmente adoptadas en cualquier país.

9. En las DCI, la relación de grupo o parentesco (véanse los Principios Generales de Orientación, apartado 2) se indicará en lo posible utilizando una partícula común. En la lista siguiente se dan algunos ejemplos de estas partículas en relación con diversos grupos de sustancias, en particular los de nuevo cuño. Hay otras muchas partículas comunes en uso.<sup>1</sup> Cuando la partícula no lleva ningún guión, cabe utilizarla en cualquier parte de la denominación.

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\* En su 20º informe (OMS, Serie de Informes Técnicos, No. 581, 1975) el Comité de Expertos de la OMS en Denominaciones Comunes para Sustancias Farmacéuticas examina los principios generales de orientación para formar denominaciones comunes internacionales (DCI) y el procedimiento de selección de las mismas, teniendo en cuenta las novedades registradas en los últimos años en materia de preparaciones farmacéuticas. Entre las modificaciones, la más importante ha sido la extensión a las sustancias químicas sintéticas de la práctica reservada anteriormente para designar sustancias originarias o derivadas de productos naturales. Esta práctica consiste en emplear una partícula característica que indique una propiedad común a los miembros de un determinado grupo de sustancias. En el informe se examinan a fondo las razones de esta modificación y sus consecuencias.

<sup>1</sup> El documento de trabajo WHO/EDM/QSM 99.6, que se pone al día regularmente, contiene una lista más extensa de partículas comunes. Las personas que deseen recibirlo deberán solicitar su envío al Programa DCI, OMS, Ginebra (Suiza).

<i>Latin</i>	<i>Español</i>	
-acum	-aco	antiinflamatorios del grupo del ibufenaco
-actidum	-actida	polipéptidos sintéticos de acción semejante a la corticotropina
-adolom	-adol }	analgésicos
-adol-	-adol- }	
-astum	-ast	antiasmáticos y antialérgicos que no actúan principalmente como antihistamínicos
-astinum	-astina	antihistamínicos
-azepamum	-azepam	sustancias del grupo del diazepam
-bactamum	-bactam	inhibidores de $\beta$ -lactamasas
bol	bol	esteroides anabólicos
-buzonum	-buzona	analgésicos antiinflamatorios del grupo de la fenilbutazona
-cain-	-cain-	antifibrilantes con actividad anestésica local
-cainum	-caina	anestésicos locales
cef-	cef-	antibióticos derivados del ácido cefalosporánico
-cillinum	-cilina	antibióticos derivados del ácido 6-aminopenicilánico
-conazolom	-conazol	antifúngicos sistémicos del grupo del miconazol
cort	cort	corticosteroides, excepto los del grupo de la prednisolona
-dipinum	-dipino	antagonistas del calcio del grupo del nifedipino
-fibratum	-fibrato	sustancias del grupo del clofibrato
gest	gest	esteroides progestágenos
gli-	gli-	sulfonamidas hipoglucemiantes
io-	io-	medios de contraste que contienen yodo
-ium	-io	compuestos de amonio cuaternario
-metacinum	-metacina	antiinflamatorios del grupo de la indometacina
-mycinum	-micina	antibióticos, producidos por cepas de <i>Streptomyces</i>
-nidazolom	-nidazol	antiprotozoarios del grupo del metronidazol
-ololum	-olol	bloqueadores $\beta$ -adrenérgicos
-oxacinum	-oxacino	antibacterianos del grupo del ácido nalidíxico
-pridum	-prida	sustancias del grupo de la sulpirida
-pril(at)um	-pril(at)	inhibidores de la enzima transformadora de la angiotensina
-profenum	-profeno	antiinflamatorios del grupo del ibuprofeno
prost	prost	prostaglandinas
-relinum	-relina	péptidos estimulantes de la liberación de hormonas hipofisarias
-terolum	-terol	broncodilatadores derivados de la fenetilamina
-tidinum	-tidina	antagonistas del receptor H <sub>2</sub> de la histamina
-trexatum	-trexato	antagonistas del ácido fólico
-verinum	-verina	espasmolíticos de acción semejante a la de la papaverina
vin-	vin- }	alcaloides de la vinca
-vin-	-vin- }	