## WHO Drug Information

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General Policy Topics

WHO and harmonization of pharmaceutical regulations

As an intergovernmental organization with some 190 Member States, the World Health Organization has an explicit responsibility to promote normative initiatives directed towards international harmonization of standards wherever and whenever this is appropriate within the health sector. Article 2 (u) of the WHO Constitution — with particular reference to pharmaceutical products — requires the Organization to "develop, establish and promote international standards with respect to food, biological, pharmaceutical and similar products". These standards, norms, guidelines, guiding principles and codes of good practice are prepared by the WHO Secretariat in close collaboration with Member States. The consultations, advisory meetings and WHO Expert Committee meetings which take place involve drug regulators, scientists, representatives of the pharmaceutical industry and other interested parties. Subsequently, the WHO governing bodies discuss and, if appropriate, endorse these normative recommendations with a view to implementation by Member States.

Since its very inception in 1948, WHO has been involved in several long-standing normative activities that have direct relevance to drug regulators, the pharmaceutical industry and public health worldwide, and it is now engaged in several new areas of harmonization that have immediate impact on new drug development, production and trade, and the regulatory control of pharmaceutical products.

As an example of WHO’s long-standing normative activities, the designation of International Nonproprietary Names (INNs) for Pharmaceutical Substances has been ongoing since 1953, and between 120 and 140 new INNs are currently selected and published each year. INNs identify pharmaceutical substances by unique, globally recognized names. A single internationally recognized name for an active drug substance is vital for safe prescribing and dispensing and for ease of communication among scientists and health professionals worldwide.

Work on The International Pharmacopoeia dates back to the First World Health Assembly in 1948, when WHO was requested to "set up within its Secretariat a section on the unification of pharmacopoeias." The preparation of monographs for The International Pharmacopoeia is carried out in consultation with an international panel of experts and with reference to current pharmacopoeias. Emphasis is placed on the use of methods which are accessible to modestly equipped quality control laboratories in countries with limited resources.

The aim of the WHO Certification Scheme on the quality of pharmaceutical products moving in international commerce is to provide a normative instrument and channel for the exchange of information between the competent authorities in importing and exporting countries. It provides information on the regulatory status of a product in the exporting country, the manufacturer's compliance with WHO good manufacturing practices (GMP), and approved product information in the exporting country.

More recently, harmonization activities have focused on good manufacturing practices (GMP). Revised WHO GMP Guidelines were published in 1992, and these have been complemented with guidelines on the inspection of manufacturers, validation of manufacturing processes, and GMP for investigational pharmaceutical products and biological products. As local production of pharmaceuticals and biologicals increases and spreads into the new manufacturing countries, these guidelines will become more and more relevant in underpinning the internationally recognized standards which form the basis of quality assurance.

Since its creation in 1975, the WHO Model List of Essential Drugs has been updated every two years. More recently, it has been supplemented with WHO Model Prescribing Information. The Model List provides a rational basis not only for the selection and procurement of essential drugs at national level, but also for establishing priority drug requirements within the health care system.
Guidelines for Good Clinical Practice (GCP) for trials on pharmaceutical products have also been prepared, in consultation with representatives of drug regulatory authorities, academia and the pharmaceutical industry. The purpose of the Guidelines is to set globally applicable, ethical and scientific standards for the conduct of biomedical research on human subjects.

Other areas of activity within the harmonization process are: the drafting of *Model national legislation for pharmaceuticals, Guidance to prevent antimicrobial resistance; Guidelines for the prevention of distribution and sale of counterfeit drugs;* and the *WHO model formulary for essential drugs.* Work also continues on the selection of international reference products or "comparators" for use in equivalence studies, and on *Guiding principles for regulatory approval of interchangeable multisource (generic) pharmaceutical products.*

The biologicals area is one of expansion and increasing diversity, and this is particularly reflected by the latest trends in biotechnology. This sector is evolving rapidly, not only in developed countries, but also in an increasing number of developing countries. It is important that activities within this area are supported and strengthened and that globally agreed standards are applied on a timely basis to these products. It is foreseeable that new innovative technologies and scientific breakthroughs will soon provide us with products different from anything known to us today, raising new critical issues of how to deal with safety, efficacy and quality. Such issues require internationally agreed and written physical standards, together with a global exchange of both information and experience on the development and use of biologicals.

WHO has been invited as an observer to the working groups for quality, safety and efficacy of the International Conference of Harmonisation (ICH) since its inception in 1990. WHO's presence in this forum is vital if it is to remain fully informed of progress made and to provide a communication and consultation bridge between the 17 ICH countries and the remaining non-participating WHO Member States. This point was re-emphasized by the World Health Assembly in resolution WHA45.28 in 1992 when it noted the progress made in ICH and recognized WHO's intergovernmental role within the harmonization process. The same resolution endorsed the International Conferences of Drug Regulatory Authorities (ICDRA) as an institution, and invited the pharmaceutical industry to continue to collaborate with drug regulatory authorities and with WHO, where appropriate, in order to ensure that harmonization is of benefit to all concerned.

If successful, harmonization of pharmaceutical requirements will result in substantial savings in both time and cost involved in the development and investigation of new drugs. Animal testing will be more rational and unnecessary duplication of preclinical studies will be eliminated. Harmonization will enhance regulatory assessment and approval by simplifying and unifying scientific documentation. This means that new treatments can be introduced more quickly, to the benefit of all concerned. Agreement on common core documentation and dossiers for efficacy, safety and quality will facilitate regulatory reviews and international recognition of drug approvals.

For norms and standards to be, firstly, applicable and then, effectively implemented, all partners concerned must be involved in the negotiation process as early and as fully as possible. As a member of this partnership, WHO is ready to meet the challenge of harmonization in all areas of rapidly advancing modern technology.

_Juhana E. Idänpää-Heikkilä, M.D., DMSc., Director, Division of Drug Management & Policies, World Health Organization, Geneva._
Personal Perspectives

Prevention of medication errors: vaccines

John D. Grabenstein,
Army Medical Department
University of North Carolina, USA,
& Susan M. Proulx and Michael R. Cohen,
Institute for Safe Medication Practices (ISMP)
Warminster, PA, USA.
e mail: ismpinfo@ismp.org

Vaccines are no more or less likely to be involved in medication errors than other drugs. Nevertheless, it is helpful to consider this group of medicinal products in isolation, especially in light of the consequences of immunological reactions to a medication error.

From the disciplines of engineering and aerospace research, medication error experts have borrowed the term "failure mode and effects" and have created an analysis system (FMEA). This technique recognizes the inevitability of human error and encourages the development of systems to anticipate, prevent and recover from human error. The goal of FMEA is to identify mistakes that could happen before they happen, and determine whether the consequences of such errors are tolerable or intolerable. When FMEA indicates that an error would be intolerable, "safety layers" are added to the procedures involved. The more layers or error traps that are added, the safer the system — albeit cumbersome — and the less likely it will be for the patient to suffer injury (1). By planning ahead, health professionals can strengthen their error-detection system and minimize the potential for error, or at least its consequences. The following is a summary and discussion of some reports of errors involving vaccines, as well as anecdotal reports known to the authors (2). By agreement with the United States Pharmacopeia, the Institute for Safe Medication Practices (ISMP) is notified of all voluntary reports submitted by practitioners to the USP's Medication Errors Reporting Programme. The ISMP also reviews medication error reports submitted to the US Food & Drug Administration MedWatch programme.

A standard approach to classifying errors is to create categories such as: wrong patient, wrong drug, wrong dose. However, this method does little to pinpoint where improvements in the delivery system can be made.

Instead, we suggest classifying errors according to severity (3). This helps concentrate quality-improvement efforts where risks are greatest. It will also help identify where:

• the system failed to catch the error, and how this affected the patient;

• the system worked and stopped the error before it affected the patient; and

• the system identified an uncorrected risk, which can be defined as "someone will be harmed if a change is not made".

Next, the component of the system that failed must be categorized (4). A single incident can involve multiple failures of a system. The following illustrative examples serve to show how this works. Most are actual cases; others are accidents that could happen.

1. Paediatric-strength diphtheria-tetanus toxoids (DT) have been confused with adult-strength tetanus-diphtheria toxoids (Td) because of the similarity in label wording and print-type styles and because official titles of the products are so similar. This error can be averted through clearer labelling.

2. An obsolete colloquial term for rubella in the United States is German measles. The wrong vaccine has been given when health workers confuse vaccines against measles and German measles. Alternative terms for the two are no better: rubeola and rubella. In this case, use of the words measles and rubella should be encouraged and use of the other terms should be actively discouraged. This can be achieved through training and the cooperation of industry and regulatory authorities.

3. Several sound-alike or look-alike names involve vaccines: varicella and vaccinia; hepatitis A and hepatitis B; Haemophilus influenzae type B (HiB)
4. Abbreviations are another major source of error (5, 6). DTP is commonly understood in English to refer to diphtheria-tetanus-pertussis vaccine. But it has also been used in the United States as shorthand for a sedative cocktail of Demerol (meperidine, pethidine), Thorazine (chlorpromazine) and Phenergan (promethazine). Several cases have occurred where a child was vaccinated rather than receiving the sedative mixture. No doubt analogous situations exist in other countries.

5. What does the abbreviation MR mean? Some people will guess measles-rubella vaccine, while others will assume mumps-rubella vaccine. There is no single correct answer and the listener or reader can infer a different product than the one intended. It is the speaker’s or writer’s responsibility to be clear.

6. Reliance on brand names is helpful only if all workers fully understand the ingredients involved. Suffixes attached to a brand name are a special source of confusion. An error occurred when Imovax ID for pre-exposure rabies immunization was inadvertently substituted for Imovax for pre- and post-exposure treatment. The error was caught after an exposed patient received pre-exposure vaccine for two of the five post-exposure doses. Luckily, the patient suffered no ill effects.

7. Other sources of miscommunication involve bad handwriting. Many errors have occurred when a health worker misunderstood a written order. Using abbreviations such as "u" for units can lead to fatal overdoses when mistaken for a zero or the figure four. The word "units" should never be abbreviated. Trailing zeros after a decimal point have led to ten-fold overdoses when the decimal point is overlooked. To prevent this error always use 4 mg – not 4.0 mg. On the other hand, use a zero preceding a decimal point for amounts less than one. Write, for example 0.2 ml and not .2 ml. The US Pharmacopeia insists on this within the USA.

8. Not having enough information about the patient is another factor in vaccine mishaps. For example, failure can occur when charts or computerized patient profiles are not marked adequately; when patients or parents are not queried about reactions after a previous dose; or when clinicians do not use the proper diagnostic process to identify true adverse events after immunization.

A question frequently arises concerning intramuscular injections that are inadvertently administered subcutaneously. Subcutaneous injections, in general are absorbed more slowly than the equivalent volume injected intramuscularly. This has resulted in reduced antibody titres in some cases (7).

Perhaps the most frequently reported errors involving vaccines concern improper dose measurements. The main culprit within the USA may be hepatitis B vaccine, where a wide variety of doses are recommended, depending on the patient’s age and the brand of the vaccine. If health care institutions change from one brand to the other, or from paediatric to adult formulations, vaccine administrators need to be alerted to the change in dose volumes. When this error occurred recently at a hospital, some 1400 newborns were left vulnerable to hepatitis B over a 2-year period. After changing brands, the pre-printed order forms that listed the old volume of hepatitis B vaccine were not updated with the correct volume for the new brand. To address the error, the hospital pharmacy involved switched to dispensing pre-filled single-dose syringes and expanded its educational programmes (8).

The complexity of products and schedules for HiB vaccines presents more opportunities for error. Workers are often accustomed to vaccines being available from only one manufacturer or, occasionally, prophylactically equivalent vaccines being available from a short-list of manufacturers with comparable instructions for use. Several non-equivalent protein-conjugated HiB vaccines present an entirely different situation — one disease with many unique vaccines used on several distinct schedules: Act HIB (SmithKline & Connaught), HibTITER (Wyeth-Lederle), PedvaxHIB (Merck) and ProHIBiT (Connaught).

If adult-strength tetanus-diphtheria toxoids (Td) are prescribed, but DTP is delivered, the error is in the drug distribution system. Was there no Td on hand, and was DTP erroneously provided? Or were both products in the refrigerator, but placed in the wrong locations? Or did the person who took the DTP out of the proper bin in the refrigerator not understand the distinction between the two products? Whatever the answer, the way to prevent future errors of this sort lies in correct purchasing and drug storage methods, and in education.

In another case, health workers reached into a refrigerator and somehow pulled out the neuro-
muscular blocker pancuronium bromide instead of influenza vaccine. This error was repeated for five or six patients before it was discovered. Fortunately, in this case no harm came to the patients at the 0.5 ml dose but it was found that similarly coloured labels were at the root of the mix-up.

This phenomenon is called "confirmation bias" and happens when practitioners rely too often on familiar evidence — the colour and shape of the vials for instance — while missing the drug names on the containers. Health workers easily confuse look-alike packaging and one way to reduce error potential of this type is to repeat the name of the drug to yourself and then read the container label.

Another report describes the case of two people reporting to a clinic. One was to be vaccinated against hepatitis B and the other with Td. Instead, both people received a dose of hepatitis B vaccine. A cause for the error was not found, but it is easy to speculate that it could have been caused by a telephone call or a visitor distracting the nurse. Alternatively, the mistake may have resulted from a lapse in attention, stress, or miscommunication. Personnel turnover or other forms of inadequate staffing can place health workers in a situation where they are insufficiently prepared.

Mumps skin test antigen (MSTA) and mumps vaccine have been confused over the years, in both directions. MSTA has been administered in a futile attempt to immunize and mumps vaccine has been given in a fruitless effort to assess cell-mediated immunity. In many cases, these errors result from rapid staff turnover that places inadequately trained personnel in decision-taking positions. This particular error is abetted by related system failures involving nomenclature and distribution.

Any quality improvement system needs a means of evaluating errors and averting future ones. One of the most effective methods of safety evaluation is often overlooked: that is, to discuss reports of errors from elsewhere.

Professional groups, including the Institute for Safe Medication Practices in the USA, publish accounts of errors in journals and newsletters to alert health workers to the problems. Efforts are also under way by the FIP (Fédération internationale pharmaceutique) and ISMP to stimulate such programmes worldwide. Risk-management should be on the agenda for discussion wherever this is a relevant issue. To receive ISMP's biweekly safety alerts and error reduction tips, send your e-mail address to ismpinfo@ismp.org.

Among the greatest risks are the silent errors which go unrecognized. Not only can they do harm to individual patients, but they can be repeated again and again (10). Hospitals and health institutions need open systems where preventing future errors takes precedence over blaming or punishing employees. Talented, creative employees must have an opportunity to communicate their ideas on error prevention. People are much more likely to share ideas if they feel that action will be taken to address the problems.

While computers can speed delivery of medications to patients and provide a basis for information retrieval and storage, they can also contribute to errors. A hospital's computer system is only as good as the people who use it. Orders entered into the computer must be double-checked against the original order before filling.

Because so many vaccines are identified by their abbreviations, the potential for error using computer mnemonics for their names is great. So-called "short codes" can be interpreted in many different ways.

We all expect vaccines to perform minor miracles in just one or a few doses. If a decade or more of protection results from these doses, vulnerability to a preventable infection as a result of vaccine failure may persist for a long term, and may even prove fatal.

According to studies, at least one error occurs for every patient hospitalized (10). Professionals should therefore take the following precautions:

- Be involved in the selection of vaccines used at your practice site.
- Consider the potential for product mix-ups when storing vaccines and other injectables.
- Keep reference information which is up-to-date for each vaccine and educate health workers on proper use.
- Double-check your work. Ask others to do the same.
• Use single-dose injections wherever possible. The added cost is far outweighed by the increased safety to the patient.

• Counsel the patient on the medication being used. Educated patients notice errors.

• Recognize that children are more vulnerable to the effects of errors because of pharmacokinetic and dose-related factors.

• Consider using pre-printed forms, but revise them periodically, as required.

Professionals are requested to compile data on errors to educate health workers and prevent subsequent repetition. By informing others, the chance of error recurrence can be eliminated.

References


Combined oral contraceptives and stroke

The risk of venous thromboembolism associated with low-dose combined oral contraceptives (OCs) containing the progestogens desogestrel and gestodene has been under review by drug regulatory authorities in the last year as a result of findings from the WHO Collaborative Study of Cardiovascular Disease and Steroid Hormone Contraception (1). The WHO study (2, 3) and other studies reported an approximate doubling of the risk of venous thromboembolic events among users of these so-called third-generation OCs compared with similar low-dose OCs containing, for example, levonorgestrel. Many drug regulatory agencies, including now New Zealand (4), have revised their prescription recommendations for low-dose OCs containing desogestrel or gestodene. WHO continues to publish findings from the large multicentre, hospital-based case-control study carried out in 21 centres in 17 countries in Africa, Asia, Europe and Latin America. The most recent publications report findings on ischaemic and haemorrhagic stroke, and overall risk of stroke associated with use of modern oral contraceptives (5, 6).

Ischaemic stroke

The association between ischaemic stroke and use of OCs was examined in 697 cases and 1962 age-matched hospital controls in Africa, Asia, Europe and Latin America. Overall, the estimated relative risk of ischaemic stroke for current use of OCs was 2.99 (95% CI 1.65–5.40) in Europe, and 2.93 (2.15–4.00) in developing countries. The risk estimates were lower in younger women and those who did not have hypertension, and less than 2 in women who did not have hypertension and who reported that their blood pressure had been checked before the current episode of OC use. In women with a history of hypertension, the relative risk was 10.7 in Europe and 14.5 in developing countries. In Europe, OCs containing 50 µg or more of ethinylestradiol were associated with higher risk estimates than OCs containing 30–35 µg or less ethinylestradiol. In developing countries, there was no significant difference between the overall estimates of risk associated with use of higher-dose and low-dose OCs. This differential effect of estrogen dose of OCs was interpreted to be due to the different prevalence of cardiovascular risk factors in users of higher-dose and low dose OCs in the two groups of countries. No significant increase of the risk estimates was observed with increasing duration of OC use among current users, and the risks were not significantly increased after cessation of use of OCs.

Haemorrhagic stroke

The WHO study included 1068 cases of haemorrhagic stroke and 2910 age-matched controls. In women of less than 35 years of age currently using OCs, the relative risk estimate of haemorrhagic stroke was not elevated in either group of countries, while in women aged 35 years or more, the risk estimates were 2.17 and 2.46 in Europe and developing countries, respectively. In women with a history of hypertension, the OC-associated risk estimates were substantially elevated (ten to fifteen-fold), and in both groups of countries the risks were elevated to about three in women using OCs who also smoked. The dose of estrogen and dose or type of progestogen were not found to modify the risk estimates, which were not significantly increased among women who had previously used OCs.

Overall risk of stroke

The evaluation of risk of ischaemic and haemorrhagic stroke separately is of scientific and clinical importance since the two diseases have different etiology, clinical course and prognosis. However, for women choosing a contraceptive method, and medical staff giving counselling and advice, the overall risk of stroke associated with use of OCs appears to be a more relevant consideration. In the WHO study, the overall risk of stroke for low-dose and higher-dose OCs was respectively 1.41 and 2.71 in Europe, and 1.86 and 1.92 in the developing countries.

The incidence of stroke in women of reproductive age is low. From data from the Oxford Centre in the United Kingdom which participated in the study, the overall incidence rate of stroke in women aged 20–44 years not using OCs was estimated to be 4.8 per 100 000 women-years; for women using low-dose OCs the estimate was 6.7, and for higher-dose OCs it was 12.9 per 100 000 women-years. Thus the excess risk associated with use of OCs...
can be estimated to be 2 per 100 000 women-years of low-dose OCs and 8 for higher-dose OCs.

Results similar to those from the WHO study were also recently reported from a population-based case-control study in the United States which used data from the California Kaiser Permanente Medical Care Programme (5). The overall incidence of stroke in women of reproductive age (15–44 years) was estimated at 11.3 per 100 000 women-years in this population. On the basis of data from 295 women with stroke and their controls, the adjusted relative risk estimate for ischaemic stroke in women using low-dose OCs was 1.18 and for haemorrhagic stroke it was 1.14. For women who used OCs and smoked, the risk estimate for haemorrhagic stroke was 3.64. In the USA study, there were few women with hypertension who were current users of OCs and only a small proportion of women aged 35 years or older were using OCs.

The results indicate that women with cardiovascular risk factors such as smoking or hypertension, particularly if they are in the later half of the reproductive age-span, will have some increased risk of stroke if they choose to use OCs. However, use of low-dose OCs by carefully screened healthy women is associated with, at most, a small excess risk of stroke.

References

Azithromycin: a new opportunity for control of trachoma

Trachoma is still the leading cause of preventable blindness globally, despite several decades of control efforts. Progress in the medical treatment of trachoma has been slow, and in the absence of socioeconomic improvements in the communities concerned, the disease tends to remain an important cause of visual loss. Currently, it is estimated that there are some 146 million cases of active trachoma, with an additional 5.9 million blind or severely visually disabled persons (1).

Trachoma is caused by Chlamydia trachomatis, a microorganism that exists as different variants; some of these are responsible for eye disease in the form of trachoma, whereas other strains lead to venereal disease and related complications.

Trachoma is typically a disease of the poorest-of-the-poors, with foci of blinding disease in underserved rural communities or urban slums. Trachoma was endemic in many European countries well into this century, but it disappeared as a result of improved standards of living and hygiene, mainly before the era of antibiotics. Today, trachoma is found in underprivileged communities where there is little hope of rapid economic development, which makes the need for medical intervention imperative, to break the trend of increasing poverty due to blindness, with its socioeconomic consequences.

The treatment of trachoma can be either preventive/suppressive or curative. The latter is more difficult, because of the extensive treatment schedules needed. These are therefore usually reserved for severe, potentially blinding, cases. Based on a series of field studies in the 1950s and 1960s, the treatment recommended by WHO has long been topical application of 1% tetracycline eye ointment (2). This regimen can either be applied twice daily for six weeks, or as an intermittent treatment twice daily for five consecu-five days each month for at least six consecutive months per year. However, this treatment can only be considered as suppressive. It reduces the intensity of inflammation in the conjunctiva, and breaks the vicious circle of bacterial conjunctivitis and trachoma reinfection — which often occurs as seasonal epidemics. This topical suppressive
against antibiotics carries the hope of particular efficacy an azalide derived from the macrolide class of through in terms of possible control. Azithromycin, potent against trachoma may represent a break-through with tetracycline eye ointment (3). It is in this perspective that a new antibiotic which is treatment with tetracycline eye ointment (3). As a rule, systemic antibiotics have therefore only been used in cases of severe inflammatory trachoma, not responding to the ordinary topical treatment with tetracycline eye ointment (3). Curative single-patient treatment has been administered in the form of sulfonamides or antibiotics since the 1950s. However, large-scale treatment with sulfonamides was abandoned after a few years because of the difficulty of dealing with serious side-effects such as Stevens-Johnson syndrome. The antibiotics commonly used have included tetracycline or, recently, doxycycline, and erythromycin. Whichever antibiotic is chosen, it must be administered for a minimum of 15 days. This again leads to a problem of compliance and the ensuing operational difficulties in large-scale treatment schemes. Furthermore, the use of systemic tetracycline with its potential teratogenic and bone-growth inhibitory effects, makes its use in women of child-bearing age and children difficult. As a rule, systemic antibiotics have therefore only been used in cases of severe inflammatory trachoma, not responding to the ordinary topical treatment with tetracycline eye ointment (3).

It is in this perspective that a new antibiotic which is potent against trachoma may represent a break-through in terms of possible control. Azithromycin, an azalide derived from the macrolide class of antibiotics carries the hope of particular efficacy against Chlamydia trachomatis. Azithromycin is active against a wide variety of Gram-positive and Gram-negative bacteria by the inhibition of bacteria protein synthesis. Furthermore, azithromycin has particular pharmacokinetic properties; it is rapidly and widely distributed throughout the body, and it shows markedly high concentrations in tissue as compared to plasma. Thus, the drug is heavily tissue-bound, with up to 150 times higher levels in some tissues in relation to plasma concentrations (4). This, together with its relatively slow elimination and a tissue depletion half-life of 2 to 4 days, makes azithromycin an ideal drug for treatment of several infectious disorders. In the case of trachoma, the high tissue affinity is of great importance in reducing the conjunctival infection with follicle formation: a particular feature of azithromycin is that it rapidly penetrates the phagocyte cells. Its outstanding effect on Chlamydia trachomatisis also documented in the effective application of a single 1g dose for treatment of urethritis caused by this organism (5).

So far, azithromycin has been used against trachoma in a few field trials, with very promising results (6, 7). Research is still needed to determine the optimal application of azithromycin against trachoma; it seems clear, though, that this drug carries the potential for large-scale treatment schemes based on an annual, or possibly six-monthly, dose which appears to reduce inflammatory trachoma to non-blinding intensity. The target groups for such treatment would be children, from the age of 2–3 years, and to some extent women.

The use of azithromycin in field programmes will require careful planning particularly with regard to contraindications, post-treatment surveillance, and monitoring of both the results and possible antibiotic resistance. For individual cases of trachoma, azithromycin is at present clearly the drug of choice, but use in large-scale public health programmes will require urgent and careful consideration, not least in assuring that the drug is both accessible and affordable to those most in need.

Dr B. Thylefors, Programme for Prevention of Blindness and Deafness, WHO

References


Alendronic acid-induced oesophageal ulcers

United States of America — Alendronic acid is the first non-hormonal therapy to be approved in a number of countries for the treatment of osteoporosis in postmenopausal women; it is also indicated for the treatment of Paget disease.

Since introduction of the product onto the market, the manufacturer has received a number of case reports of oesophagitis and oesophageal ulceration where patients have presented with retrosternal pain, and difficulty or pain in swallowing.

As a result, the manufacturer has circulated a letter to doctors and other health professionals stating that oesophageal reactions have been reported that are of a greater severity than those observed during controlled clinical trials. The manufacturer has duly revised the package labelling and patient insert to emphasize that reactions such as oesophageal erosion, ulceration or oesophagitis may be avoided or reduced by carefully following the instructions for use as set out in the new recommendations.

Each tablet should be swallowed with a full glass of plain water immediately on rising in the morning and at least 30 minutes before the first food, beverage or medication of the day. Patients should be instructed not to lie down for at least 30 minutes after taking the tablet, and not to take the drug at bedtime or before rising for the day.


Oral contraceptives containing desogestrel or gestodene: updated position statement

European Union — The Committee for Proprietary Medicinal Products (CPMP) held a meeting in April 1996 to discuss further the risks of thromboembolism associated with combined oral contraceptives containing desogestrel or gestodene. In addition to the previous statement published in October 1995 (1) the following position statement has now been issued by the CPMP.

Venous thromboembolism is a serious but rare risk associated with the use of oral contraceptives. Because this complication is rare it is difficult to study, and estimates of its incidence are not precise.

All studies hitherto presented to the CPMP indicate that the risk for venous thromboembolism is higher in users of desogestrel or gestodene-containing oral contraceptives than in users of levonorgestrel-containing oral contraceptives. The impact of biases and confounders on the difference still cannot be fully evaluated.

Data from studies of haemostatic factors indicate differences between levonorgestrel-containing oral contraceptives (so-called second generation) and desogestrel or gestodene-containing oral contraceptives (so-called third generation), but these are of unknown clinical relevance as yet.

The requested pooled analyses of acute myocardial infarction have not yet been performed and currently available data do not allow a conclusion that desogestrel or gestodene-containing oral contraceptives have an advantage over levonorgestrel-containing oral contraceptives in this respect.

There is no evidence that from a public health point of view the other major benefits or risks (e.g. reliability of contraception) are different from desogestrel or gestodene-containing oral contraceptives. For the individual there may, however, be benefits in quality of life.

Factors other than the "generation" of pill used, such as heredity and immobilization, also have an important role for the occurrence of venous thromboembolic events.

To further evaluate to what extent biases and confounding factors have contributed to the difference in risk of venous thromboembolic events in users of desogestrel or gestodene-containing oral contraceptives and levonorgestrel-containing oral contraceptives respectively, and to clarify whether there are differences in effect on myocardial infarction rates, the CPMP will request further analysis of the data presented, and carefully keep the ongoing studies under review.
The previous message to doctors/users is still relevant and in addition doctors/users are reminded of the following:

- Discontinuation of oral contraceptives should be seriously considered in situations that are associated with an increased risk of venous thromboembolic events, such as immobilization, major trauma or major surgery.

- Due to the vague symptomatology of many venous thromboembolic events, discontinuation of oral contraceptives should be considered in cases of suspected thrombosis in patients on oral contraceptives, while diagnostic interventions are being pursued.

- In cases of an uncertain diagnosis of venous thromboembolic events, alternative contraceptive strategies should be discussed with the patient, since the event may represent a first signal of oral contraceptive-associated thrombophilia.

Source: Position statement of the CPMP on oral contraceptives containing desogestrel or gestodene. CPMP/374/96, EMEA, 17 April 1996.

Temazepam now a controlled drug

United Kingdom — The Secretary of State for Health has announced that temazepam, a short-acting benzodiazepine, is to be transferred from schedule 4 of the Misuse of Drugs Regulations 1985 to schedule 3, which will mean tighter controls on its availability. These measures are being taken in an attempt to prevent misuse (1). It is also announced that gel-filled capsules of the drug will no longer be prescribed on the National Health Service.

Liquid-filled temazepam capsules have been widely abused on the illicit drugs market, the liquid gel lending itself to intravenous administration. This formulation was replaced in the United Kingdom by tablets and capsules containing semi-solid gel, which it was considered difficult to inject. In spite of this there has still been evidence of abuse (2).

The rescheduling means that:

- Simple possession of the drug without authority will be an offence;

- Import and export of the drug are required to be licensed;

- Temazepam will become subject to a set of safe custody requirements, and the drug will be kept in locked controlled-drug cabinets;

- Additional documentation will be required when a person other than a doctor supplies the drug, and will require persons who are not already authorized to possess, supply or produce schedule 3 drugs to obtain an appropriate written authority;

- Supply on prescription will be more carefully undertaken; and

- Containers in which the drug is supplied will be suitably marked.

Existing requirements which apply to schedule 4 drugs, such as keeping of records of the quantities produced, imported and exported, will remain in effect.

References


HIV protease inhibitors and spontaneous bleeding

France — The Medicines Agency has reported 9 cases of haematoma in haemophiliac patients with AIDS who are being treated with the HIV protease inhibitors indinavir, ritonavir and saquinavir. An inquiry is in progress (1). It should be noted that factor VIII infusion in these patients has had to be increased since the beginning of treatment.

United States of America & Canada — The FDA has learned of 15 case reports of spontaneous bleeding episodes in HIV-positive patients with haemophilia receiving protease inhibitors in Europe. Of these cases, 11 have involved haematomas and 5 haemarthroses. None involved serious injury or death. The majority of patients, who are on multiple drug therapy, have continued taking the HIV protease inhibitors despite the bleeding event. No events have been reported within the United States. To date, there is no conclusive evidence to establish that this class of drugs is the cause of spontaneous bleeding episodes. However, the FDA
will continue to keep close watch on the situation since the three products in question have been given marketing approval under the FDA's accelerated approval mechanism for treatment of life-threatening illness.

The FDA and manufacturers of the products in question recommend that health-care providers monitor haemophiliac patients for spontaneous bleeding episodes whenever any protease inhibitors are used as part of HIV treatment. However, patients with haemophilia and HIV infection who are currently on protease inhibitor therapy should not discontinue treatment, but consult with their health care providers if they have any concerns (2).

The Canadian Health Protection Branch is also closely monitoring the situation and, in addition to the above-mentioned cases, has received a report of one Canadian patient affected by spontaneous bleeding. HPB states that all of the reports involved patients with haemophilia and advanced HIV infection who were receiving multiple drug treatment. Clinical studies using HIV protease inhibitors have not so far reported an increased incidence of either bleeding or coagulation abnormalities in patients with or without haemophilia (3).

References

2. Letter to US health-care providers from the Department of Health & Human Services, sent on 17 July 1996.
3. Notice to health care providers in Canada sent by the Health Protection Branch on 18 July 1996.

Terbinafine: surprising number of reports

Australia — Terbinafine is a new antifungal drug with activity against infections due to dermatophytes and *Candida albicans*. The product was first marketed in Australia in late 1993, and since that time the Adverse Drug Reactions Advisory Committee (ADRAC) has received 168 reports documenting a total of 323 suspected adverse reactions. ADRAC is concerned by the number and nature of these reports, considering that the drug is often used for minor conditions and for a prolonged period.

There are two prominent groups of adverse reactions. Those involving the gastrointestinal tract, which include taste perversion or loss, and those involving the skin, suggestive of hypersensitivity or photosensitivity. So far, ADRAC has received 2 reports describing suspected neutropenia and one case of agranulocytosis. Finally, there are 11 reports of adverse hepatic reactions.

While all the above reactions are mentioned in the product information, careful prescribing and close monitoring must be encouraged.


Withdrawal of topical products containing gentamicin

Malaysia — In view of the fact that long-term use of topical antibiotics can lead to development of hypersensitivity and widespread use can lead to a risk of emergence of resistant strains, the Drug Control Authority has withdrawn marketing of topical cream or ointment products containing gentamicin. Out of 28 products available for topical use in Malaysia, 16 contained gentamicin as the sole active substance, while the other 12 preparations were combinations of gentamicin with a corticosteroid.


Emergency contraceptives recommended for over-the-counter (OTC) use?

New Zealand — The Medicines Classification Committee (MCC) has recommended that emergency contraceptive tablets be sold by pharmacists over-the-counter. These will be supplied in a special pack which contains instructions approved by the Ministry of Health. Meanwhile, the recommendation cannot be implemented until approval has been given by the Cabinet to amend the Medicines Regulations.

Source: *New Zealand Prescriber*. Update No. 12, July 1996.
Conjugated estrogens and generic pharmaceuticals

United States of America — Natural conjugated estrogens excreted by pregnant mares are used for estrogen replacement to treat symptoms of the menopause and allied disorders such as postmenopausal osteoporosis, atrophic vaginitis, kraurosis vulvae and atrophic urethritis. Discussion is now centred on which active hormonal ingredient contributes to the effectiveness and safety of the brand product, Premarin®, Wyeth Ayerst, and which of these components should be included in the generic version of the product.

Two estrogen ingredients — estrone sulfate and equilin sulfate — have been regarded as Premarin’s main active substances. Despite the company’s petition, the contribution made to the product’s safety and effectiveness by the remaining estrogens (which include estrogen-8, 9-dehydroestrone sulfate – delta-8-DHES) has been questioned by generic companies. The US Food and Drug Administration has prepared a document entitled Preliminary analysis of scientific data on the composition of conjugated estrogens, and has included this as part of the public docket for the petition. A Federal Register notice providing an opportunity for public comment on this preliminary analysis will soon be published.


Chlormezanone withdrawn following skin reactions

France — In agreement with the French Medicines Agency, the manufacturers of chlormezanone-containing products (Trancopal®, Trancogesic®, Sanofi Winthrop and Alinam®, Therabel Lucien Pharma) have decided to stop marketing the product and recall batches immediately (1). The decision was based on findings of a recently published multicountry case-control study on the risk of Stevens-Johnson syndrome and toxic epidermal necrolysis (2). Based on these developments, Sanofi Winthrop has decided to withdraw the drug worldwide (3).

Chlormezanone is a mild tranquillizer with muscle-relaxant properties and a sedative effect which has been available since the 1960s in a single formulation, and later in combination with either analgesics or nonsteroidal anti-inflammatory drugs.

It is generally used as adjunctive therapy for the treatment of lumbago, torticollis or pain caused by minor injuries.

Results of the study show that the incidence of Stevens-Johnson syndrome is estimated at 1 to 6 cases per million person-years and toxic epidermal necrolysis at 0.4 to 1.2 cases per million person-years. Although these conditions are rather infrequent, they may kill or severely disable previously healthy people and they are frequently associated with drug use. When skin detachment is very extensive, prognosis is poor, with death rates of 30 to 40 per cent. Documentation of a causal relationship with medication requires widespread population studies because of the low frequency of disorders. This explains the fact that drugs may have been used for many years before such data on adverse reactions become available. The present study began in 1989 and included about 120 million people in France, Germany, Italy and Portugal.

The continued reporting and monitoring of adverse drug reactions has once again proven crucial in the benefit/risk assessment of treatment. Whenever safer alternative drugs or therapy become available, older therapies are subject to reassessment. The present withdrawal should thus be appreciated as a sign of improvement and appropriateness of available treatment.

References

Marketing authorization of fixed combination medicinal products

European Union— The Committee for Proprietary Medicinal Products (CPMP) has approved guidelines for submission of an application for marketing authorization of fixed-dose combination medicinal products. The guidance comes into effect for European Union countries in October 1996.

Pharmaceutical companies submitting an application are now required to justify the particular
combination of active substances proposed. Fixed-combination products will only be considered acceptable if the proposed combination is based on valid therapeutic principles.

For any individual fixed combination, it is necessary to assess the potential advantages in a clinical setting against possible disadvantages in order to determine whether the product meets the requirements of efficacy and safety.

Potential advantages of fixed combinations should include one of the following:

(a) An improvement of the benefit/risk assessment due to:

1. Addition or potentiation of therapeutic activities of their substances, which results in:

   • a level of efficacy similar to the one achievable by each active substance used alone at higher doses than in combination, but associated with a better safety profile; or
   • a level of efficacy above the one achievable by a single substance with an acceptable safety profile.

2. The counteracting by one substance of an adverse reaction produced by another.

(b) A simplification of therapy which improves patient compliance. (When it is the only claim, it would be restricted to a particular situation such as non-prescription products).

Disadvantages of fixed combinations include:

• the fact that even a combination which meets the needs of the average patient is unlikely to be ideally adjusted for the needs of each individual patient; and

• the addition of the different adverse reactions specific to each substance.

The guideline points out that fixed combinations, in principle, may not be considered rational if the duration of action of the substances differ significantly. This may not apply where it can be shown that the combination is clinically valid despite differences in this respect, i.e. if one substance is intended to enhance absorption of the other or where the substances are intended to exert their effects successively.

Each substance of the fixed combination must have a justified action. The inclusion of a substance to counteract an adverse reaction of another substance may be considered justified, but only if the adverse reaction is a serious or commonly occurring one. However, the inclusion of a substance intended to produce unpleasant adverse effects as a means of preventing abuse is undesirable. It is considered that substances having a critical dosage range or a narrow therapeutic index are inappropriate for inclusion in fixed combinations.

The guideline goes on to discuss indications, drug interactions and dosage levels of each of the substances, and the need for pharmacodynamic and pharmacokinetic studies, and clinical trials to prove efficacy and safety of fixed combinations. It also points out that safety studies in animals should be conducted, but may not be required if all the substances concerned have been extensively used in humans in identical or very similar combinations and if their safe long-term use has been well documented.

International Nonproprietary Names for Pharmaceutical Substances (INN)

Recommended International Nonproprietary Names (Rec. INN):
List 36
Notice is hereby given that, in accordance with paragraph 7 of the Procedure for the Selection of Recommended International Nonproprietary Names for Pharmaceutical Substances [Off. Rec. Wld Health Org., 1955, 60, 3 (Resolution EB15.R7); 1969, 173, 10 (Resolution EB43.R9)], the following names are selected as Recommended International Nonproprietary Names. The inclusion of a name in the lists of Recommended International Nonproprietary Names does not imply any recommendation of the use of the substance in medicine or pharmacy.

Lists of Proposed (1–73) and Recommended (1–35) International Nonproprietary Names can be found in Cumulative List No. 9, 1996.

Dénominations communes internationales des Substances pharmaceutiques (DCI)

Dénominations communes internationales recommandées (DCI Rec):
Liste 36
Il est notifié que, conformément aux dispositions du paragraphe 7 de la Procédure à suivre en vue du choix de Dénominations communes internationales recommandées pour les Substances pharmaceutiques [Actes off. Org. mond. Santé, 1955, 60, 3 (résolution EB15.R7); 1969, 173, 10 (résolution EB43.R9)] 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 (1–73) et recommandées (1–35) dans la Liste récapitulative No. 9, 1996.

Denominaciones Comunes Internacionales para las Sustancias Farmacéuticas (DCI)

Denominaciones Comunes Internacionales Recomendadas (DCI Rec.):
Lista 36
De conformidad con lo que dispone el párrafo 7 del Procedimiento de Selección de Denominaciones Comunes Internacionales Recomendadas para las Sustancias Farmacéuticas [Act. Of. Mund. Salud, 1955, 60, 3 (Resolución EB15.R7); 1969, 173, 10 (Resolución EB43.R9)], se comunica por el presente anuncio que las denominaciones que a continuación se expresan han sido seleccionadas como Denominaciones Comunes Internacionales Recomendadas. La inclusión de una denominación en las listas de Denominaciones Comunes Recomendadas no supone recomendación alguna en favor del empleo de la sustancia respectiva en medicina o en farmacia.

Las listas de Denominaciones Comunes Internacionales Propuestas (1–73) y Recomendadas (1–35) se encuentran reunidas en Cumulative List No. 9, 1996
<table>
<thead>
<tr>
<th>Recommended INN</th>
<th>Chemical name or description and Molecular formula</th>
<th>DCI</th>
<th>DCI</th>
<th>Spanish</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Latin, English, French, Spanish)</td>
<td>Nom chimique ou description et Formule brute</td>
<td>Nombre químico o descripción y Fórmula empírica</td>
<td>Recomendada</td>
<td>DCI</td>
</tr>
<tr>
<td><strong>abirateronum</strong></td>
<td>17-(3-pyridyl)androsta-5,16-dien-3β-ol</td>
<td>abiraterone</td>
<td>abiraterona</td>
<td>abraterona</td>
</tr>
<tr>
<td><strong>abitesartanum</strong></td>
<td>17-{3-pyridyl}androsta-5,16-dien-3β-ol</td>
<td>abitesartan</td>
<td>abitiesartan</td>
<td>abitésartan</td>
</tr>
<tr>
<td><strong>acidum ranelicum</strong></td>
<td>5-[bis(carboxymethyl)amino]-2-carboxy-4-cyano-3-thiophenacetic acid</td>
<td>acide ranelique</td>
<td>acido ranelico</td>
<td>acide ranélique</td>
</tr>
<tr>
<td><strong>almurtidum</strong></td>
<td>2-acetamido-3-O-[[[(1S)-1-[[[1R]-1-carbamoyl-3-carboxypropyl]carbamoyl][ethyl]carbamoyl]methyl]-2-désoxy-β-D-glucopyranose</td>
<td>almurtide</td>
<td>almutrida</td>
<td>almurtide</td>
</tr>
<tr>
<td><strong>amelometasonum</strong></td>
<td>(+)-9-fluoro-11β,17-dihydroxy-21-methoxy-16β-methylpregna-1,4-diene-3,20-dione 17-proponate</td>
<td>amelometasone</td>
<td>amélometasone</td>
<td>amérométasone</td>
</tr>
<tr>
<td></td>
<td>17-proponato de (+)-9-fluoro-11β,17-dihidroxi-21-metoxi-16β-metilpregna-1,4-dien-3,20-dione</td>
<td>amelometasona</td>
<td>amelometasona</td>
<td>amelometasona</td>
</tr>
</tbody>
</table>
apafluranum
apaflurane
apaflurane
apaflurano
1,1,1,2,3,3,3-heptafluoropropane

arcitumomab
arcitumomab
immunoglobulin G 1 (mouse monoclonal IMMU-4 Fab' fragment γ-chain anti-human antigen CEA), disulfide with mouse monoclonal IMMU-4 light chain

arcitumomab
immunoglobuline G 1 (chaîne γ du fragment Fab' de l'anticorps monoclonal de souris IMMU-4 anti-antigène CEA humain), disulfure avec la chaîne légère de l'anticorps monoclonal de souris IMMU-4

arcitumomab
immunoglobulina G 1 (cadena γ del fragmento Fab' del anticuerpo monoclonal de ratón IMMU-4 anti-antigeno CEA humano) disulfuro con la cadena ligera del anticuerpo monoclonal de ratón IMMU-4

asimadolinum
asimadoline
$N\{\{(\alpha S)-\alpha-[\{(3S)-3-hydroxy-1-pyrrolidinyl]methyl\}benzyl\}-N-methyl-2,2-diphenylacetamide$

asimadoline
$N\{\{(1S)-2-[\{(3S)-3-hydroxy-1-pyrrolidin-1-yl\}]-1-phenyléthyl\}]-N-méthyl-2,2-diphéénylacétamid$

asimadolina
$N\{\{(\alpha S)-\alpha-[\{(3S)-3-hidroxi-1-pirrolídinil\}metil\}bencil\}-N-metil-2,2-difenilacetamida$

avorelinum
avorelin

avorelin

avorelina

azalanstatum
azalanstat
$1\{[[2S,4S]-4-[[p-aminophényl]thio]méthyl]]-2-(p-chlorophénényl)-1,3-dioxolan-2-yl]méthyl\}imidazole$

azalanstat
$1\{[[2S,4S]-4-[[4-aminophényl]sulfanyl]méthyl]-2-(4-chlorophényl)éthyl\}-1,3-dioxolan-2-yl]méthyl\}1H-imidazole$

azalanstat
$1\{[[2S,4S]-4-[[p-aminofenil]bio]metil\}-2-(p-clorofenetil]-1,3-dioxolan-2-il]metil\}imidazoi$

becaplerminum
becaplermin
recombinant human platelet-derived growth factor B

bécaplermine
facteur de croissance B d'origine plaquettaire humain obtenu par génie génétique

becaplermina
factor B de crecimiento derivado de plaquetas (humano recombinante)
<table>
<thead>
<tr>
<th><strong>'bisnafidum</strong>**'</th>
<th>$N,N'-[\text{ethylenebis}[\text{mimo}[(R)-1-\text{methylene}]]][\text{bis}[3\text{-nitronaphthalimide}]]$</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>'bisnafide'</strong></td>
<td>$2,2'-[\text{éthylènebis}[\text{mimo}[(R)-1-\text{méthyléthylène}]]][\text{bis}[5\text{-nitro-2H-benzo}][\text{de}]=isoquinoxoène-1,3-\text{dione}]]$</td>
</tr>
<tr>
<td><strong>'bisnafida'</strong></td>
<td>$N,N'-[\text{étilenbis}[\text{mimo}[(R)-1-\text{metiletlen}]]][\text{bis}[3\text{-nitronafthalimida}]]$</td>
</tr>
<tr>
<td><strong>'cariporidum'</strong></td>
<td>$N-(\text{diaminométhylène})-4\text{-isopropyl}-3-(\text{méthylsulfonil})\text{benzamide}$</td>
</tr>
<tr>
<td><strong>'cariporide'</strong></td>
<td>$N-(\text{diaminométhylène})-4-(1\text{-méthyléthyl})-3-(\text{méthylsulfonil})\text{benzamide}$</td>
</tr>
<tr>
<td><strong>'cariporida'</strong></td>
<td>$N-(\text{diaminometilen})-4\text{-isopropil}-3-(\text{méthil sulfonil})\text{benzamida}$</td>
</tr>
<tr>
<td><strong>'cellacefatum'</strong></td>
<td>a mixed acetate and hydrogen phthalate ester of cellulose (about 50% of the hydroxyl groups are acetylated and about 25% are esterified with one of the carboxy groups of phthalic acid)</td>
</tr>
<tr>
<td><strong>'cellacefate'</strong></td>
<td>mélange partiel d'esters acétique et phthalique de cellulose (50% environ des groupes hydroxy sont acétylés et 25% sont estérifiés par l'un des groupes carboxy de l'acide phthalique)</td>
</tr>
<tr>
<td><strong>'cellacefato'</strong></td>
<td>mezcla de acetato y biftalato de celulosa en la que alrededor del 50% de los hidroxilos están acetilados y alrededor del 25% están esterificados por uno de los carboxilos del ácido ftálico</td>
</tr>
<tr>
<td><strong>'cerivastatinum'</strong></td>
<td>$(3R,5S,6E)-7-[4\text{-}(p\text{-fluorophenyl)}-2,6\text{-disopropyl}-5\text{-}(\text{méthoxyméthyl})\text{-3-pyridyl}]-3,5\text{-dihydroxy-6-heptenoic acid}$</td>
</tr>
<tr>
<td><strong>'cerivastatin'</strong></td>
<td>acide $(6E)-(3R,5S)-7-[4\text{-}(4\text{-fluorophényl})-5\text{-}(\text{méthoxyméthyl})\text{-2,6-bis(1\text{-méthyléthyl})-3-pyridyl}]-3,5\text{-dihydroxyhept-6-énoique}$</td>
</tr>
<tr>
<td><strong>'cerivastatina'</strong></td>
<td>ácido $(3R,5S,6E)-7-[4\text{-}(p\text{-fluorofenil})-2,6\text{-disopropil}-5\text{-}(\text{metoximetil})\text{-3-piridil}]-3,5\text{-dihidroxi-6-heptenoico}$</td>
</tr>
<tr>
<td><strong>'ciaftalan zincum'</strong></td>
<td>$(SP\text{-}4\text{-}1\text{-}[\text{phthalocyaninato}(2\text{-})\text{-}\text{N}^{29}, \text{N}^{30}, \text{N}^{31}, \text{N}^{32}]\text{zinc}$</td>
</tr>
<tr>
<td><strong>'ciaftalan zinc'</strong></td>
<td>$(SP\text{-}4\text{-}1\text{-}[29\text{H},31\text{H}\text{-phthalocyaninato}(2\text{-})\text{-}\text{N}^{29}, \text{N}^{30}, \text{N}^{31}, \text{N}^{32}]\text{zinc}$</td>
</tr>
<tr>
<td><strong>'ciaftálán zinc'</strong></td>
<td>$(SP\text{-}4\text{-}1\text{-}[\text{ftalocianinato}(2\text{-})\text{-}\text{N}^{29}, \text{N}^{30}, \text{N}^{31}, \text{N}^{32}]\text{zinc}$</td>
</tr>
<tr>
<td><strong>'cisatracurii besilas'</strong></td>
<td>$(1R,2R)-2\text{-}[2\text{-carboxyéthyl}]-1,2,3,4\text{-tétrahydro-6,7\text{-diméthoxy-2-méthyl-1-\text{veratrylisouquinolinoïd benzénesulfonate, pentaméthylène ester}}$</td>
</tr>
<tr>
<td><strong>'cisatracurium besilate'</strong></td>
<td>dibenzenésulfonate de $2,2\text{-}[\text{pantan-1,5-diybis(oxycarboxyléthylène)}]=\text{bis}[(1R,2R)-1\text{-}[3,4\text{-diméthoxybenzyl}]-6,7\text{-diméthoxy-2-méthyl-1,2,3,4\text{-tétrahydroisouquinolinion}]$</td>
</tr>
<tr>
<td><strong>'bésilate de cisatracurium'</strong></td>
<td>benzenesulfonate de $[1R\text{-}(\alpha,\alpha\text{(}1'R,2'R\text{)})]-2,2\text{-}[1,5\text{-pentanodiibis[oxi(3-oxo-3,1\text{-propanodiibis[oxi(3-4\text{-diméthoxybenzyl}]-6,7\text{-diméthoxy-2-méthyl-1,2,3,4\text{-tétrahydroisouquinolinion})]$</td>
</tr>
<tr>
<td><strong>'besilato de cisatracurio'</strong></td>
<td>$C_{65}H_{80}N_{2}O_{18}S_{2}$</td>
</tr>
</tbody>
</table>
**colestilanum**
*colestilan*  
2-methylimidazole polymer with 1-chloro-2,3-epoxypropane
*colestilan*  
copolymère de 2-méthylimidazole et de 1-chloro-2,3-époxypropane
*colestilan*  
polímero de 2-metilimidazol con 1-cloro-2,3-epoxipropano
(C₄H₆N₂C₂H₅ClO)ₙ

**dabelotinum**
*dabelotine*  
(±)-1,2,3,4-tetrahydro-1-methyl-8-{[2-morpholino(3H)methoxy]quinoline
(±)-1-méthyl-8-[2RS-morpholino-2-yl]méthoxy]-1,2,3,4-tétrahydroquinoléine
(±)-1,2,3,4-tetrahidro-1-metil-8-(2-morfolina metoxi)quinolina
C₁₅H₂₂N₂O₂

**danaparoidum natricum**
*danaparoid sodium*  
mixture of:  
mucopolysaccharides derived from hog intestinal mucosa consisting of sodium salts of heparan sulfate (major component), dermatan sulfate, and chondroitin sulfate
*danaparoide sodique*  
mélange de:
mucopolysaccharides extraits de la muqueuse intestinale de porc, constitue par les sels de sodium du sulfate dhéparan (principal composant), du sulfate de dermatane et du sulfate de chondrotine
*danaparoide sódico*  
mezcla de:
mucopolisacaridos de mucosa intestinal de cerdo consistentes en sales sodicas de heparan sulfato (componente principal), dermatan sulfato y condroitin sulfato)

**dapitantum**
*dapitant*  
(3aS,4S,7aS)-hexahydro-2-{[(αS)-o-methoxyhydratropyl]-4-(o-methoxyphenyl)-7,7-diphenyl-4-isoindolinol
(3aS,4S,7aS)-4-hydroxy-4-(2-méthoxyphényl)-2-{[(2S)-2-(2-méthoxyphenyle)=propanoyl]-7,7-diphényloctahydro-1H-isouindole
(3aS,4S,7aS)-hexahidro-2-[(αS)-o-metoxihidratropoil]-4-(o-metoxifenil)-7 7-difenil-4-isouindolinol
C₃₇H₃₉N₄O₄

**darsidominum**
*darsidomine*  
3-(cis-2,6-dimethylpiperidino)sydnone imine
*darsidomine*  
3-(cis-2,6-diméthylpipérídino)sydnone imine
*darsidomina*  
3-(cis-2,6-dimetilpipericino)sidnona imina
C₉H₁₅N₄O
delequaminum

delequamine

\[
(8aR,12aS,13aS)-5,8,8a,9,10,11,12,12a,13,13a-decahydro-3-methoxy-12-(methylsulfonfyl)-6H-isoquinoline[2,1-g][1,6]naphthyridine
\]

deletquamine

\[
(8aR,12aS,13aS)-3-methoxy-12-(methylsulfonfyl)-5,8,8a,9,10,11,12,12a,13,13a-decahydro-6H-isoquinoline[2,1-g][1,6]naphthyridine
\]

delecuamina

\[
(8aR,12aS,13aS)-5,8,8a,9,10,11,12,12a,13,13a-decahydro-3-methoxy-12-(methylsulfonfyl)-6H-isoquinoline[2,1-g][1,6]naphthyridine
\]

C_{18}H_{26}N_{2}O_{3}S

dexcadotrilum

dexcadotril

\[\text{\((+)-N-[(R)\alpha-(mercaptopmethyl)hydrocinnamoyl]glycine, benzyl ester, acetate (ester)\}}\]

dexécadotril

\[\text{\((+)-(R)-2-[[2-(acétylsulfanyl)méthyl]-3-phénylpropanoyl]amino]acétate de benzyle}\]

dexcadotrio

\[\text{\((+)-N-(R)\alpha-(mercaptopmethyl)hidrocinamol]glicina, éster bencílico, acetato (ester)\}}\]

C_{21}H_{23}NO_{4}S

dexsotalolum

dexsotalol

\[\text{\((+)-(S)-4'-[1-hydroxy-2-(isopropylamino)ethyl]methanesulfonanilide}\]

dексotalol

\[\text{\((+)-N-[4-[(1S)-1-hydroxy-2-[(1-méthyléthyl)amino]éthyl]phényl= methanesulfonamide}\]

dexsotaloi

\[\text{\((+)-(S)-4'-[1-hidroxi-2-(isoproplamino)otil]metanosulfonanilida}\]

C_{12}H_{20}N_{2}O_{3}S

dimadectinum

dimadectin

mixture of:

\[
\]

\[
\]

\[
\]

\[
\]
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**dimadectina**

 mezcla de

\[(\text{2aE,4E,5'S,6S,6'R,7,8,8,9,10,11,14,16,17,17a,20,20a,20b,20b,20b,20b)-6'-(S)-secbutil-3',4',5',6,7,10,11,14,15,16,17a,20,29a,20b-tetradecahidro-20,20b-dihidroxi-7'-(2-metoxietoxi)metoxi)-5',6,8,19-tetrametilespiro[11,15-metano-2H,13H,17H-furo[4,3,2-pq][2,6]benzodioxaciclooctadecin-13,2'-[2H]piran]-17-ona (constituyente principal) y
\[(\text{2aE,4E,5'S,6S,6'R,7,8,8,9,10,11,14,16,17,17a,20,20a,20b,20b,20b,20b)-3',4',5',6,7,10,11,14,15,16,17a,20,29a,20b-tetradecahidro-20,20b-dihidroxi-6'-isopropil-7'-(2-metoxietoxi)metoxi)-5',6,8,19-tetrametilespiro[11,15-metano-2H,13H,17H-furo[4,3,2-pq][2,6]benzodioxaciclooctadecin-13,2'-[2H]piran]-17-ona\]

\[C_{38}H_{58}O_{10}\]

**droxinavirum**

**droxinavir**

3-3-tert-butyl-1-\{(\text{2R,3S})-3-\{(\text{2S})-3,3-dimethyl-2-[\text{methylaminoacetamido}=butramid]-\text{2-hydroxy-4-phenyl}1-[1-isopentylurea}

3-3-\{(\text{1,1-diméthyléthyl})-1-\{(\text{2R,3S})-3-\{(\text{2S})-3,3-diméthyl-2-[\text{methylamino}=acétyl]amino}butanoyl]amino\text{-2-hydroxy-4-phénylbutyl}]\text{-1-(3-méthylbutyl)uree}

3-3-3-terc-buti\{-1-\{(\text{2R,3S})-3-\{(\text{2S})-3,3-dimetil-2-[\text{2-(metilamino)acetamido} =butiramida}\text{-2-hidroxi-4-fenilbutyl}]-1-(3-méthylbutyl)uree\}

\[C_{39}H_{51}N_{5}O_{4}\]

**edaravonum**

**edaravone**

3-methyl-1-phenyl-2-pyrazolin-5-one

5-méthyl-2-phényl-2,4-dihydropyrrol-3-one

3-metil-1-fenil-2-pirazolin-5-ona

\[C_{10}H_{10}N_{2}O\]

**edrecolomabum**

**edrecolomab**

immunoglobulin G 2a (mouse monoclonal 17-1A γ-chain anti-human colon cancer tumor-associated antigen), disulfide with mouse monoclonal 17-1A light chain, dimer

édrécolomab: immunoglobulin G 2a (chaîne γ de l’anticorps monoclonal de souris 17-1A anti-antigène tumoral associé au cancer du colon humain), dimère du disulfure avec la chaîne légère de l’anticorps monoclonal de souris 17-1A

edrecolomab: immunoglobulina 2a (cadena γ del anticuerpo monoclonal de ratón 17-1A anti-antigeno tumoral asociado al cáncer de colon humano), dimero del disulfuro con la cadena ligera del anticuerpo monoclonal de ratón 17-1A

**eletriptanum**

**eletriptan**

3-\{[(\text{R})-1-methyl-2-pyrrolidinyl]methyl\}-5-[2-(phenylsulfonyl)ethyl]indole

\[C_{22}H_{26}N_{2}O_{2}S\]

**emoctakinum**

**emoctakin**

interleukin 8 (human)

émoctakine: interleukin 8 humaine

emoctakin: interleukina 8 humana

\[C_{27}H_{39}N_{5}O_{5}\]
epoetin omega

1-165-erythropoietin (human clone λ-HEP0FL13 protein moiety), glycoform ω

epoétine oméga

1-165-érythropoïétine (partie protéique de la substance issue du clone de cellules humaines λ-HEPOFL13), forme glycosylée ω

epoetina omega

1-165-entropoietina (fracción protéica del clon humano λ-HEPOFL13) glicofíorma ω

C_{809}H_{1301}N_{229}O_{210}S_{5}

eprinomectin

mixture of:


eprinomectine

mélange de:


epninectina

mezcla de:


C_{50}H_{72}NO_{14} + C_{49}H_{70}NO_{14}
**Recommended INN List**

<table>
<thead>
<tr>
<th>INN</th>
<th>Chemical Name</th>
<th>Molecular Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>fabesetronum</td>
<td>(+)-(R)-8,9-dihydro-10-methyl-7-[(5-methylimidazol-4-yl)methyl]pyridol-6(7H)-one</td>
<td>C_{12}H_{14}N_{3}O</td>
</tr>
<tr>
<td>fabésétron</td>
<td>(+)-(7R)-10-méthyl-7-[(5-méthyl-1H-imidazol-4-yl)méthyl]-9,9-dihydropyrindol-6(7H)-one</td>
<td>C_{12}H_{14}N_{3}O</td>
</tr>
<tr>
<td>fabesetrón</td>
<td>(+)-(R)-8,9-dihidro-10-metil-7-[(5-metilimidazol-4-il)metil]piridol-6(7H)-ona</td>
<td>C_{12}H_{14}N_{3}O</td>
</tr>
<tr>
<td>falecalcitriolum</td>
<td>(+)-(5Z,7E)-26,26,27,27,27-hexafluoro-9,10-secocholesta-5,7,10(19)-triene-1α,3β,25-triol</td>
<td>C_{27}H_{38}F_{6}O_{3}</td>
</tr>
<tr>
<td>falecalcitriol</td>
<td>(+)-(5Z,7E)-26,26,27,27,27-hexafluoro-9,10-sécocholesta-5,7,10(19)-triène-1α,3β,25-triol</td>
<td>C_{27}H_{38}F_{6}O_{3}</td>
</tr>
<tr>
<td>falecalcitríol</td>
<td>(+)-(5Z,7E)-26,26,27,27,27-hexafluoro-9,10-secocholesta-5,7,10(19)-triene-1α,3β,25-triol</td>
<td>C_{27}H_{38}F_{6}O_{3}</td>
</tr>
<tr>
<td>fasidotrum</td>
<td>N-[(S)-α-(mercaptopethyl)-3,4-(methyleneoxy)hydrocinnamoyl]-L-alanine. benzyl ester, acetate</td>
<td>C_{23}H_{29}NO_{6}S</td>
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<tr>
<td>fasidotril</td>
<td>(2S)-2-[[2S]-2-[(acétylsulfanyl)méthyl]-3-(1,3-benzodioxol-5-yl)propanoyl]amino]propanoate de benzyle</td>
<td>C_{23}H_{25}NO_{6}S</td>
</tr>
<tr>
<td>fasidotril</td>
<td>N-[(S)-α-(mercaptopemetyl)-3,4-(metilenodioxi)hidrocinnarnoíl]-L-alanina, éster benčlico, acetato (éster)</td>
<td>C_{23}H_{25}NO_{6}S</td>
</tr>
<tr>
<td>fexofenadinum</td>
<td>(4)-p-[1-hydroxy-4-{4-(hydroxydiphenylmethyl)piperidino}butyl]-α-methylhydratropic acid</td>
<td>C_{32}H_{39}NO_{4}</td>
</tr>
<tr>
<td>fexofénadine</td>
<td>acide 2-[4-[(1RS)-1-hydroxy-4-{4-(hydroxydiphenylméthyl)pipéridin-1-yl]butyl]phényl]-2-méthylpropanoïque</td>
<td>C_{32}H_{39}NO_{4}</td>
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<tr>
<td>fexofenadina</td>
<td>ácido (1z)-p-[1-hidroxi-4-{4-(hidroxidifenilmetil)piperidino}butil]-α-metilhidratropico</td>
<td>C_{32}H_{39}NO_{4}</td>
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<tr>
<td>forasartanum</td>
<td>5-{[3,5-dibutyl-1H-1,2,4-triazol-1-yl]methyl}-2-{(o-1H tetrazol-5-ylphenyl)pyridine</td>
<td>C_{23}H_{26}N_{8}</td>
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<tr>
<td>forasartan</td>
<td>5-{[3,5-dibutyl-1H-1,2,4-triazol-1-yl]méthyl}-2-{[2-(1H-tétrazol-5-yl)phényl]pyridine</td>
<td>C_{23}H_{26}N_{8}</td>
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<tr>
<td>forasartán</td>
<td>5-{[3,5-dibutil-1H-1,2,4-triazol-1-il]metil}-2-{(a-1H-tetrazol-5-ilfenil)pirindine</td>
<td>C_{23}H_{26}N_{8}</td>
</tr>
</tbody>
</table>
**fozivudinum tidoxilum**

fozivudine tidoxil

(2RS)-2-(decyloxy)-3-(dodecylthio)propyl hydrogen 3'-azido-3'-deoxy-5'-thymidylate

**fozivudine tidoxil**

hydrogéno(3'-azido-3'-désoxy-5'-thymidylate) de (2RS)-2-(décyloxy)-3-(dédécylylsulfanyl)proppyle

**fozivudina tidoxilo**

3'-azido-3'-desoxi-5'-timidilato de (2RS)-2-(deciloxi)-3-(dodecitio)propil hidrógeno

$C_{35}H_{64}N_{5}O_{8}PS$

**gatifloxacinum**

gatifloxacin

(±)-1-cyclopropyl-6-fluoro-1,4-dihydro-8-methoxy-7-(3-methyl-1-piperazinyl)-4-oxo-3-quinolinecarboxylic acid

**gatifloxacine**

acide 1-cyclopropyl-6-fluoro-8-méthoxy-7-[3(RS)-3-méthylpipérazin-1-yl]-4-oxo-1,4-dihydroquinoléine-3-carboxylique

**gatifloxacino**

ácido (±)-1-ciclopropil-6-fluoro-1,4-dihidro-8-metoxi-7-(3-metil-1-piperazinil)-4-oxo-3-quinolina carboxílico

$C_{19}H_{22}FN_{3}O_{4}$

**glaspimodum**

glaspimod


**glaspimod**

$N_{2}N'[(2S,7S)-2,7-bis[[5-oxo-L-prolyl]-L-glutarnyl-L-aspartyl]amino]=octanedioyl][di-L-lysine$


$C_{48}H_{74}N_{12}O_{22}$

**igovomabum**

igovomab

immunoglobulin G 1 (mouse monoclonal OC125 F(ab')2 fragment anti-human ovarian cancer antigen CA 125), disulfide with mouse monoclonal OC125 F(ab')2 light chain

**igovomab**

immunoglobuline G1 fragment F(ab')2 de l’anticorps monoclonal OC 125 anti-antigène CA 125 associé à certaines tumeurs ovariennes

**igovomab**

immunoglobulin G1 fragmento F(ab')2 del anticuerpo monoclonal OC 125 anti-antígeno CA 125 asociado a ciertos tumores ováricos

**ilomastatum**

ilomastat

(2R)-N'-hydroxy-N'-(S)-2-indol-3-yl-1-(methylcarbamoyl)ethyl]-2-isobutylsuccinamide

**ilomastat**

(2R)-N'-hydroxy-N'-(1H-indol-3-yl)méthyl]-2-(méthylamino)-2-oxoéthyl]-3-(2-méthylpropyl)butanediamide

**ilomastat**

(2R)-N'-hidroxi-N'-(S)-2-indol-3-il-1-(metilcarbamoil)etil]-2-isobutil succinamida

$C_{20}H_{36}N_{4}O_{4}$
indinavirum
indinavir \((\alpha R,\gamma S,2 S)-\alpha\text{-benzyl-2-(\text{tert-butylcarbamoyl})-}\gamma\text{-hydroxy-N-}[(1 S,2 R)-2\text{-hydroxy-1-indanyl}]\text{-}4\text{-}((3\text{-pyridyl})\text{methyl})\text{-}1\text{-}piperazinvaleramide}\)

indinavir \([2 R,4 S\text{-}2\text{-benzyl-5\text{-}([2 S\text{-}2\text{-}(1,1\text{-dimethyléthyl})\text{carbomoyl})\text{-}4\text{-}((3\text{-pyridyl})=\text{méthyl})\text{pipérazin-1-yl}]\text{-}4\text{-hydroxy-N-}[(1 S,2 R)-2\text{-hydroxy-2,3\text{-dihydro-1H\text{-}indén-1-yl}]\text{pentanamide}}\)

indinavir \((\alpha R,\gamma S,2 S)-\alpha\text{-bencil-2-(terc-buticarbonamoi)}\text{-}\gamma\text{-hidroxi-N-}[(1 S,2 R)-2\text{-hidroxi-1\text{-indanil}]\text{-}4\text{-}((3\text{-pírdilimetil})\text{-}1\text{-piperazinvaleraramida}}\)

ioloipridum \((1 2 3)\)
ioloipride \((1 2 3)\)
ioloipride \((1 2 3)\)
ioloiprida \((1 2 3)\)
imidacrinum
imidacrine
imidacrine
imidacrina
imroplactum
imroplact
imroplact
imroplact
lenapenemum
lenapenem
lenapénem
acide \((+-)(4 R,5 S,6 S)-6\{[R]-1\text{-hydroxyethyl]}\text{-}3\{([S,5 S]-5\{[R]-1\text{-hydroxy-3\text{-}(methylamino)propyl]}\text{-}3\text{-pyrrolidiny}[thio]}\text{-}4\text{-methyl-7-oxo-1\text{-azabicyclo}[3.2.0]hept-2-ène-2-carboxylique}\)

lenapenem
ácido \((+-)(4 R,5 S,6 S)-6\{[R]-1\text{-hidroxiétil]}\text{-}3\{([S,5 S]-5\{[R]-1\text{-hidroxi-3\text{-}(metilamino)propil]}\text{-}3\text{-pirrolidínil]cilicio]}\text{-}4\text{-metil-7-oxo-1-azabicyclo[3.2.0]hept-2-én-2-carboxílico}\)
lepirudinum
lepirudin
lépirudine
lepirudina
levobupivacainum
levobupivacaine
lévobupivacaine
levobupivacaina
levormeloxifenum
levormeloxifene
lévorméloxifène
levormeloxifeno
linetastinum
linetastine
linéastine
linetastina
lintontriptum
lintitript
lintitript
lirexapridum
lirexaprde
lirexaprida

1-L-leucine-2-L-threonine-63-desulfotirudin (Hirudo medicinalis isoform HV1)
1-L-leucine-2-L-thréonine-63-désulfotirudine (Hirudo medicinalis, variant HV1)
1-L-leucina-2-L-treonina-63-desulfotirudina (Hirudo medicinalis, isoforma HV1)

C_{287}H_{440}N_{82}O_{111}S_{9}

(5S)-1-butyl-2',6'-pipecoloxylidide
(2S)-1-butyl-N-(2,6-diméthylphényl)pipéridine-2-carboxamide
(S)-1-butyl-2',6'-pipecoloxylidide

C_{188}H_{28}N_{2}O

(2E,4E)-N-[2-[4-(diphenylmethoxy)pipéridino]éthyl]-5-(4-hydroxy-3-méthoxyphenyl)-2,4-pentadiénamide éthyl carbonate (ester)

C_{35}H_{40}N_{2}O_{6}

2-[4-(o-clorofenil)-2-thiazolyl]carbamoylindole-1-acetic acid

C_{20}H_{14}ClN_{3}O_{2}S

4-amino-5-chloro-α-cyclopropyl-N-[(1R,2R)-2-[(4-méthylpipéridino)méthyl]-cyclohexyl]-o-anisamida

C_{22}H_{36}ClN_{3}O_{2}

<table>
<thead>
<tr>
<th>INN</th>
<th>Name</th>
<th>Molecular Formula</th>
</tr>
</thead>
<tbody>
<tr>
<td>lurtotecanum</td>
<td>lurtotecan</td>
<td>(8S)-8-ethyl-2,3-dihydro-8-hydroxy-15-[(4-methyl-1-piperazinyl)methyl]-11H-p-dioxino[2,3-g]pyrano[3',4':6,7]indolizino[1,2-b]quinoline-9,12(8H,14H)-dione</td>
</tr>
<tr>
<td></td>
<td>lurtotécan</td>
<td>(8S)-8-éthyl-8-hydroxy-15-[(4-méthylpípérazin-1-yl)méthyl]-2,3,11,14-tétrahydro-12H-1,4-dioxino[2,3-g]pyrano[3',4':6,7]indolizino-[1,2-b]quinoline-9,12(8H,14H)-dione</td>
</tr>
<tr>
<td></td>
<td>lurtotecán</td>
<td>(8S)-8-etil-2,3-dihidro-8-hidroxi-15-[(4-metil-1-piperazinil)metil]-11H-p-dioxino[2,3-g]pirano[3',4':6,7]indolizino[1,2-b]quinolina-9,12(8H,14H)-diona</td>
</tr>
<tr>
<td></td>
<td>mélagatran</td>
<td>acide 2-[(1R)-2-[2(S)-2-[4-carbamidoylbenzyl]carbamoyl]azétidin-1-y]-1-cyclohexyl-2-oxéthyl]aminoacétique</td>
</tr>
<tr>
<td>milamelinum</td>
<td>milaméline</td>
<td>1,2,5,6-tetrahydro-1-methylnicotinaldehyde (E)-O-méthylloxime</td>
</tr>
<tr>
<td></td>
<td>milamelina</td>
<td>(E)-1-méthyl-1 2,5,6-tétrahydropyndine-3-carbaldéhyde O-méthylxime</td>
</tr>
<tr>
<td></td>
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<td>C_{1336}H_{2116}N_{362}O_{410}S_{13}</td>
</tr>
</tbody>
</table>
### minolteparinum natricum
**minolteparin sodium**

Sodium salt of depolymerized heparin obtained by nitrous acid degradation of heparin from pork intestinal mucosa, the majority of the components have a 2-O-sulfo-α-L-idopyranosuronic acid structure at the non-reducing end and a 6-O-sulfo-2,5-anhydro-α-mannitol structure at the reducing end of their chain; the average relative molecular mass is between 1700 and 3300, 90 per cent of which ranging between 1000 and 8000; the degree of sulfatation is about 2,1 per disaccharide unit.

### mnoltéparine sodique

Sel de sodium d’héparine dépolymérisée obtenue par fragmentation au moyen d’acide nitreux d’héparine de muqueuse intestinale de porc. La majorité des composants présentent une structure acide 2-O-sulfo-α-L-idopyranosuronique à l’extrémité non réductrice et une structure 6-O-sulfo-2,5-anhydro-α-mannitol à l’extrémité réductrice de leur chaîne. La masse moléculaire relative moyenne est de 1700 à 3300, 90% de celle-ci se situant entre 1000 et 8000. Le degré de sulfatation est d’environ 2,1.

### minoltepanna sodica

Sal sódica de la heparina despolymerizada obtenida por fragmentación con ácido nitroso de la heparina de la mucosa intestinal del cerdo; la mayoría de los componentes tienen una estructura de ácido 2-O-sulfo-α-L-idopiranosurónico en el extremo no reductor y una estructura de 6-O-sulfo-2,5-anhidro-α-mannitol en el extremo reductor de la cadena, la masa molecular relativa media está entre 1700 y 3300, con 90% entre 1000 y 8000, el grado de sulfatación es aproximadamente de 2,1 por unidad de disacárido.

### mipitrobanum
**mipitroban**

6-chloro-3-(p-chlorobenzyl)-β,β-dimethyl-3H-imidazo[4,5-b]pyridine-2-butynic acid

### mipitroban

ácido 6-cloro-3-(p-clorobencil)-β,β-dimetil-3H-imidazo[4,5-b]piridina-2-butírico

\[C_{19}H_{19}Cl_{2}N_{3}O_{2}\]

### miproxifenum
**miproxfene**

(Z)-α-[p-[2-(dimethylamino)ethoxy]phenyl]-α’-ethyl-4’-isopropyl-4-stilbenol

### miproxfeno

(Z)-α-[p-[2-(díméthylamino)etoxi]fenil]-α’-etil-4’-isopropil-4-estilbenol

\[C_{29}H_{35}NO_{2}\]

### montelukastum
**montelukast**

1-[[[(R)-m-[(E)-2-(7-chloro-2-quinolyl)vinyl]-α-[1-hydroxy-1-méthyléthyl]phényl]benzyl][thio]méthyl]cyclopropaneacetic acid

### montélukast

ácide 2-1-[[[(R)-1-3-[(E)-2-(7-chloroquinoléin-2-yl)éthénylephényl]-3-[(1-hydroxy-1-méthyléthyl)phényl]sulfanyl]méthyl]cyclopropyleacytique

### montelukast

ácido 1-[[[(R)-m-[(E)-2-(7-cloro-2-quinolil)vinil]-α-[1-hidroxi-1-metiletíleno]fenetil]bencil][thio]metil]ciclopropanoacético

\[C_{35}H_{36}ClNO_{3}\]
<table>
<thead>
<tr>
<th>INN</th>
<th>Molecular Structure</th>
<th>Formula</th>
</tr>
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<tbody>
<tr>
<td>napitanum</td>
<td>$\pm$-(3R*)-3-phenyl-1-[[6(R*)-6,7,8,9-tetrahydronaph[1,2-c]-1,3-dioxol-6-yl]methyl]pyrroldine</td>
<td>$C_{22}H_{25}NO_2$</td>
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<tr>
<td>napitane</td>
<td>(3RS)-3-phényl-1-[[6RS]-6,7,8,9-tétrahydronapht[1,2-d]-1,3-dioxol-6-yl]méthyl]pyrrolidine</td>
<td></td>
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<tr>
<td>napitano</td>
<td>(±)-(3R*)-3-fenil-1-[[6(R*)-6,7,8,9-tetrahidronaft[1,2-d]-1,3-dioxol-6-il]metil]pirrolidina</td>
<td></td>
</tr>
<tr>
<td>nateplasum</td>
<td>mixture of $N$-${N^2-$N-glycyl-L-alanyl-L-arginyl]-plasminogen activator (human tissue-type 1-chain form, protein moiety), glycoform $\beta$</td>
<td></td>
</tr>
<tr>
<td>nateplase</td>
<td>mélaun de $N$-${N^2-$N-glycyl-L-alanyl-L-arginyl]activateur du plasminogène (type tissulaire humain constituté d'une chaîne, partie protéique), forme glycosylée $\beta$</td>
<td></td>
</tr>
<tr>
<td>nateplasa</td>
<td>mezcla de $N$-${N^2-$N-glicil-L-alanil]-L-arginil]activador del plasminógeno (tipo tisular humano forma monocatenaria, fracción proteica), forma glicosilada $\beta$</td>
<td></td>
</tr>
<tr>
<td>nepaprazolum</td>
<td>$\pm$-(9R*)-9-[[SS*]-2-benzipimidazolylsulfínyl]-6,7,8,9-tetrahydro-4-methoxy-5H-ciclohepta[b]piridina</td>
<td>$C_{18}H_{19}N_3O_2S$</td>
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<tr>
<td>nepaprazole</td>
<td>(9RS)-9-[[SR]-1H-benzimidazol-2-ylsulfínyl]-4-méthoxy-6,7,8,9-tétrahydro-5H-cyclohepta[b]pyridine</td>
<td></td>
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<tr>
<td>nepaprazol</td>
<td>(±)-(9R*)-9-[[SS*]-2-benzipimidazolilisulfínil]-6,7,8,9-tetrahydro-4-metoxy-5H-ciclohepta[b]piridina</td>
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<tr>
<td>octocogum alfa</td>
<td>blood-coagulation factor VIII (human), glycoform $\alpha$</td>
<td></td>
</tr>
<tr>
<td>octocog alfa</td>
<td>facteur VIII de coagulation sanguine (humain), forme glycosylée $\alpha$</td>
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</tr>
<tr>
<td>octocog alfa</td>
<td>factor de coagulación VIII (humano) forma glicosilada $\alpha$</td>
<td></td>
</tr>
<tr>
<td>odulimomabum</td>
<td>immunoglobulin G1 (mouse monoclonal 25.3 heavy chain anti-human antigen CD 11 $\alpha$-chain), disulfide with mouse 25.3 light chain, dimer</td>
<td></td>
</tr>
<tr>
<td>odulimomab</td>
<td>immunoglobuline G1 (chaîne lourde de l'anticorps monoclonal de souris 25 3 anti-chaîne $\alpha$ de l'antigène CD11 humain), dimère du disulfure avec la chaîne légère de l'anticorps monoclonal de souris 25 3</td>
<td></td>
</tr>
<tr>
<td>odulimomab</td>
<td>immunoglobulin G1 (cadena pesada del anticuerpo monoclonal de ratón 25 3 anti-cadena $\alpha$ del antígeno CD11 humano), dimero del disulfuro con la cadena ligera del anticuerpo monoclonal de ratón 25 3</td>
<td></td>
</tr>
</tbody>
</table>
osanetantum  
\[N\{1-\{3-\{\{R\}-1-benzoyl-3-\{(3,4-dichlorophenyl)-3-piperidyl\}propyl\}-4-phenyl-4-piperidyl\}-N-methylacetamide\]

osanétant  
\[N\{1-\{3-\{3R\}-1-benzoyl-3-\{(3,4-dichlorophényl)pipérìdin-3-yl\}propyl\}-4-phénylpipérìdin-4-yl\}-N-méthylacétamide\]

osanetant  
\[N\{1-\{3-\{\{R\}-1-bencil-3-\{(3,4-diclorofenil)-3-piperidil\}propil\}-4-fenil-4-piperidil\}-N-metilacetamida\]

C_{30}H_{71}ClN_{3}O_{2}

pagoclonum  
\[\text{(+)-2-\{7-chloro-1,8-naphtyridin-2-yl\}-3-\{(5-méthyl-2-oxohexyl\}phthalimidine}\]

pagoclone  
\[\text{(+)-2-\{7-chloro-1,8-naphtyridin-2-yl\}-3-\{(5-méthyl-2-oxohexyl\}-2,3-dihydro-1H-sindol-1-one}\]

pagoclonia  
\[\text{(+)-2-\{7-cloro-1,8-naftiridin-2-il\}-3-\{(5-metil-2-oxohexil\}italimidina}\]

C_{26}H_{32}ClN_{3}O_{2}

palinavirum  
\[N\{1,3\}-1-\{\{1S,2R\}-1-benzyl-3-\{2S,4R\}-2-((tert-butyl)carbamoil)\}-4-(4-pyridylmethoxy)pipendino\}-2-hydroxypropyl\}carbamoil\}-2-méthylpropyl\}quinaldarmide\]

palinavir  
\[N\{1,3\}-1-\{\{1S,2R\}-1-benzyl-3-\{2S,4R\}-2-\{1,1-diméthyléthyl\}carbamoil\}-4-(4-pyridylméthoxy)pipéridín-1-yl\}-2-hydroxypropyl\}carbamoil\}-2-méthylpropyl\}quínoléine-2-carboxamid\]

palinavir  
\[N\{1,3\}-1-\{\{1S,2R\}-1-bencil-3-\{2S,4R\}-2-\{terc-butilcarbamoil\}-4-(4-pridilmeteo)pipendino\}-2-hidroxipropil\}carbamoil\}-2-metilpropil\}quinaldamida\]

C_{41}H_{52}N_{6}O_{5}

palonosetronum  
\[2,4,5,6-tetrahydro-2-\{(3S)-3-quinuclidinyl\}-1H-benz[de]isoquinolin-1-one\]

palonosétron  
\[2-\{(3S)-1-azabicyclo[2.2.2]oct-3-yl\}-2,4,5,6-tetrahydro-1H-benzol[de]isoquinolén-1-one\]

palonosetróhn  
\[2,4,5,6-tetrahdro-2-\{(3S)-3-quinuclidinil\}-1H-benzol[de]isoquinolin-1-ona\]

C_{19}H_{22}N_{2}O

pamaquesidium  
\[11-oxo-(25R)-5α-spirostan-3\}įl\}-4-Ó-β-o-glucopyranosyl-β-o-glucopyranoside\]

pamaquéside  
\[3β\{-4-O-β-o-glucopyranosyl-β-o-glucopyranosyl\}oxy\}-(25R)-5α-spirostan-11-one\]

pamaquesida  
\[11-oxo-(25R)-5α-esprostan-3\}įl\}-4-Ó-β-o-glucopiranosoβ-o-glucopranósido\]

C_{59}H_{62}O_{14}
**Recommended INN: List 36**

- **panamesinum**
- **panamesine**
- **panamésine**
- **panamesina**
- **piclamilastum**
- **piclamilast**
- **piclarnilast**
- **piclamilast**
- **plusonerminum**
- **plusonermin**
- **plusonermine**
- **plusonermina**
- **pomisartanum**
- **pomisartan**
- **pomisartan**
- **povidonum**
- **povidone**
- **povidone**
- **povidone**

- **(5S)-5-[[4-hydroxy-4-[3,4-(methylenedioxy)phenyl]piperidino]methyl]-3-(p-methoxyphenyl)-2-oxazolidinone**
- **(1S)-5-[[4-(1,3-benzodioxol-5-yl)-4-hydroxypiperidin-1-yl]methyl]-3-(4-méthoxyphényl)oxazolidin-2-one**
- **(5S)-5-[[4-Hidroxi-4-[3,4-(métilendioxi)fenil]piperidino]metil]-3-(p-metoxyfenil)-2-oxazolidinona**
- **3-(cyclopentyloxy)-N-(3,5-dichloro-4-pyridyl)-p-anisamide**
- **3-(cyclopentyloxy)-N-(3,5-dichloropyridin-4-yl)-4-méthoxybenzamide**
- **mixture of tumor necrosis factor proteins (human): 1-157-tumor necrosis factor, 3-157-tumor necrosis factor (major component), and 5-157-tumor necrosis factor**
- **mélange de protéines de facteur de nécrose tumorale (humain) 1-157-facteur de nécrose tumorale, 3-157-facteur de nécrose tumorale (constituant principal) et 5-157-facteur de nécrose tumorale**
- **mezcla de factor de necrosis tumoral proteinas: 1-157-factor de necrosis tumoral, 3-157-factor de necrosis tumoral (constituyente principal) y 5-157-factor de necrosis tumoral**
- **4'-[[2-ethyl-4-methyl-6-(5,6,7,8-tetrahydroimidazo[1,2-a]pyridin-2-yl)-1-benzimidazolyl]methyl]-2-biphenylcarboxylic acid**
- **acide 4'-[[2-éthyl-4-méthyl-6-(5,6,7,8-tétrahydroimidazo[1,2-a]pyridin-2-yl)-1H-benzimidazol-1-yl]methyl]biphénylé-2-carboxylique**
- **ácido 4'-[[2-etil-4-metil-6-(5,6,7,8-tetrahidroimidazol[1,2-a]píridin-2-il)-1-benzimidazolil]metil]-2-bifenilcarboxílico**
- **1-vinyl-2-pyrrolidinone polymer, linear**
- **poly[1-(2-oxopyrrolidin-1-yl)éthylène] linéaire**
- **polímero lineal de 1-vinil-2-pirrolidona**

\[C_{63}H_{99}N_4O_5\]
pramlintidum

pramlintide

\[
**Recommended INN: List 36**

**ramatrobanum**
ramatroban

\((+)-(3R)-3-(p\text{-fluorobenzenesulfonylamino})-1,2,3,4\text{-tetrahydrocarbazole-9-propionic acid}\)

**resocortolum**
resocortol

\(11\beta,17\alpha\text{-dihydroxy}-17\text{-propanoylandrost-4-en-3-one}\)

**revatropatum**
revatropate

\(11\beta,17\alpha\text{-dihydroxy}-17\text{-propanoylandrost-4\text{-en-3-one}}\)

**ripisartanum**
ripisartan

\(5\text{-methyl-7-propyl-8-[p-(1H-tetrazol-5-ylphenyl)benzyl]-s-triazolo-[1,5-c]pyrimidin-2(3H)-one}\)

**rismorelinum**
rismorelin

\(1-(p\text{-methylhippuric acid})-9\text{-L-asparagine}-12\text{-L-arginine}-15\text{-L-threonine}-21\text{-L-arginine}-27\text{-L-leucine}-51\text{-L-leucine}-56\text{-L-arginine}-58\text{-L-leucine}\) prosomatohberin (pig)

**ritonavirum**
ritonavir

\(5\text{-thiazolylmethyl}[(\alpha\text{-S})-\alpha\text{-[(1S,3S)-1-hydroxy-3-[2(S)-2-[3\text{-isopropyl-4thiazolyl}methyl]-3\text{-methylurido}-3\text{-methylbutyramidod}-4-phenylbutylylphényl]carbamate}\)
ribovir

ribovir

rufinamidum

rufinamide

rufinamido

rufinamide

rupatadinum

rupatadine

rupatadina

sainingedirum

sainingedin

sainingedina

samarin (153Sm) lexidronumum

samanum (153Sm) lexidronum

samanum (153Sm) lexidronum

samanato (153Sm) lexidronum

sampatriatulum

sampatriat

sampatriolate

sampatriat
**sildenafilum**
sildenafil
sildénafil
sildenafilo
sinitrodilum
sinitrodil
sinitrodil
sipatriginum
sipatrigine
sipatrigina
stacofyllinum
stacofylline
stacofylline
estacofilina
susalimodum
susalimod
sipatriginum
sipatrigine
sipatrigina
stacofyllinum
stacofylline
stacofylline
estacofilina
susalimodum
susalimod
sipatriginum
sipatrigine
sipatrigina
stacofyllinum
stacofylline
stacofylline
estacofilina
susalimodum
susalimod

1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-ethoxyphenyl]sulfonyl]-4-methylpiperazine
1-[[4-éthoxy-3-[1-méthyl-7-oxo-3-propyl-6,7-dihydro-1H-pyrazolo[4,3-d]pyrimidin-5-yl]phénoxy]sulfonyle]-4-méthylpipérazine
1-[[3-(6,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]pyrimidin-5-yl)-4-etoxifenil]sulfonil]-4-metilpiperazina

C$_{22}$H$_{30}$N$_{6}$O$_{4}$S

2,3-dihydro-3-(2-hydroxyethyl)-4H-1,3-benzoxazin-4-one nitrate (ester)
nitrato de 2-[4-oxo-2H-1,3-benzoxazin-3(4H)-yl]éthyle
nitrato de 2-(4-oxo-2H-1,3-benzoxazin-3(4H)-yl)éthyle

C$_{15}$H$_{16}$N$_{2}$O$_{5}$

4-amino-2-[4-methyl-1-piperazinyl]-5-(2,3,5-trichlorophenyl)pyrimidine
4-amino-2-[4-méthylpipérazin-1-yl]-5-(2,3,5-trichlorophenyl)pyrimidina

C$_{15}$H$_{16}$Cl$_{3}$N$_{5}$

N,N-diethyl-4-[3-(1,2,3,6-tetrahydro-1,3,7-trimethyl-2,6-dioxopurin-8-yl)propyl]-1-piperazinecarboxamide
N,N-diéthyl-4-[3-(1,3,7-triméthyl-2,6-dioxo-2,3,6,7-tétrahydro-1H-purin-8-yl)propyl]pipérazine-1-carboxamide
N,N-dietil-4-[3-{1,2,3,6-tetrahidro-1,3,7-trimetil-2,6-dioxopurín-8-il}propil]-1-piperazinacarboxamida

C$_{20}$H$_{33}$N$_{7}$O$_{3}$

5-[[p]-[(3-methyl-2-pyndyl)sulfamoyl]phenyl]ethynyl]salicylic acid
ácido 2-hydroxy-5-[[4-[(3-méthylpiridin-2-yl)sulfamoyl]phényl]=éthynyl]benzoique
ácido 5-[[p]-[(3-metil-2-pindil)sulfamoil]fenil]etilico

C$_{28}$H$_{28}$N$_{2}$O$_{5}$

N(5,6,7 8-tetrahdro-5,5,8,8-tetramethy-2-naphtyl)terephthalamic acid
acide 4-[[5,6,8,8-tétraméthyl-5,8,7,8-tétrahydronaphtalén-2-yl]carbamoyl]=benzoique
ácido N-(5,6,7,9-tetrahdro-5,5,8,8-tetrametil-2-naftil)tereftalámico

C$_{26}$H$_{33}$NO$_{3}$
tazofelone

\((\pm)-5\{3,5\text{-di-tert-butyl-4-hydroxybenyl}\}-4\text{-thiazolidinone}\)

tazofélone

\((RS)-5\{3,5\text{-bis(1,1-diméthyléthyl)}-4\text{-hydroxybenyl}\}\text{thiazolidin-4-one}\)

tazofelona

\((\pm)-5\{3,5\text{-di-terc-butil-4-hidroxibencil}\}-4\text{-thiazolidinona}\)

\(C_{18}H_{27}NO_{2}S\)

telinavirum
telinavir

\((2S)-N\{[1S,2R]-1\text{-benzyl-3-}(3\text{-tert-butyl-1-isobutylureido)}-2\text{-hydroxypropyl}]\}-2\text{-quinaldamidosuccinamide}\)

télinavir

\((2S)-N\{[1S,2R]-1\text{-benzil-3-}[3,(1,1\text{-diméthyléthyl)}\]-1\text{-}(2\text{-méthylpropyl})uréido]-2\text{-hydroxypropyl}]\}-2\text{-[quinoléin-2-ylcarbonyl]amino}butanédiamide\)

telinavir

\((2S)-N\{[1S,2R]-1\text{-bencil-3-}(3\text{-terc-butil-1-isobutilureido)}-2\text{-hidroxipropl}\}-2\text{-quinaldamidosuccinamida}\)

\(C_{23}H_{44}N_{6}O_{5}\)

thymalfasinum
thymalfasin


\(C_{129}H_{215}N_{23}O_{56}\)

tilnoprofenum arbamelum

tilnoprofem arbamelm

\((\pm)\text{-2-dimethyl-5H}\{1\}\text{-benzopyrano}\{2,3-b\}\text{pyridine-7-acetic acid}, \text{ ester with} \ N,N\text{-dimethylglycolalamide}\)

tilnoprofène arbamelm

\((2RS)-2\{2\text{-méthyl-5H}\{1\}\text{-benzopyrano}\{2,3-b\}\text{pyridine-7-yl}\}\text{propanoate de} \ 2\text{-}(\text{diméthylamino})-2\text{-oxoéthyle}\)

tilnoprofeno arbamelm

\(\text{ácido (±)-2-dimetil-5H}\{1\}\text{-benzopirano}\{2,3-b\}\text{piridina-7-acético, éster con} \ N,N\text{-dimetilglicolalamida}\)

\(C_{20}H_{22}N_{2}O_{4}\)

tirofibanum
tirofiban

\(N\{\text{butylsulfonyl}\}-4\{4\text{-}(4\text{-piperidil})\text{butoxyl}\}\text{-fenilalanina}\)

tirofiban

acide \((2S)-2\{[\text{butylsulfonyl}]\text{amino}\}-3\{4\text{-}(4\text{-pipérindin-4-yl})\text{butoxy}\}\text{phényl}=\text{propanoïque}\)

tirofibán

\(N\{\text{butisulfonil}\}-4\{4\text{-}(4\text{-piperidil})\text{butoxi}\}\text{-fenilalanina}\)

\(C_{22}H_{36}N_{2}O_{5}\)

tivirapinum

tivirapine

\((S)-8\text{-chlooro-4,5,6,7-tetrahydro-5-methyl-6\{3\text{-methyl-2-butenyl}\}\text{imidazolo}=\} [4,5,1-f]\{1,4\}\text{benzdiazepine-2(1H)}\text{-thione}\)
tivirapine

(trans)-5S)-8-chloro-5-methyl-6-(3-methylbut-2-ényle)-4,5,6,7-tétrahydroimidazo[4,5,1-jk][1,4]benzodiazépine-2(1H)-thione

traferminum

2-155-basic fibroblast growth factor (human clone λKB7/λHFL1 precursor reduced)

trifosminum

tris(3-méthoxypropyl)phosphane

trofloxacinum

7-[(1R,5S,6s)-6-amino-3-azabicyclo[3.1.0]hex-3-yl]-1-(2,4-difluorophenyl)-6-fluoro-1,4-dihydro-4-oxo-1,8-naphtyridine-3-carboxylic acid

troviridinum

1-(5-bromo-2-pyridyl)-3-[2-(2-pyridyl)éthyl]-2-thiourea

valnemulinum

[[2-[(R)-2-amino-3-methylbutyramido]-1,1-diméthylethyl][thio]acétate acid, 8-éster con (3aS,4R,5S,6s,8R,9R,9aR,10R)-octahidro-5,8-dihydroxy-4,6,9,10-tétraméthyl-6-vinyl-3a,9-propano-3aH-cyclopentacycloocten-1(4H)-thione

valnemuline

2-[[2-(2R)-2-amino-3-méthylbutanoyl][amino]-1,1-diméthyléthyl]-sulfanylacétate de (1S,2R,3S,4S,6R,7R,8R,9R,10R)-octahidro-5,8-dihydroxy-4,6,9,10-tétraméthyl-9-octocycl[5.4.3.0,8]tétradé-6-ylo
AMENDMENTS TO PREVIOUS LISTS

Recommended International Nonproprietary Names (Rec. INN): List 19
(WHO Chronicle Vol. 33, No. 10, 1979)

p. 8  zinostatinum  zinostatin

replace the description by the following:

(4S, 6R, 11R, 12R)-11-[(α-D-2,6-dideoxy-2-methylaminogalactopyranosyl)oxy]-
12-[[2-hydroxy-7-methoxy-5-methyl-1-naphtyl]carbonyl]oxy]-4-[(4R)-2-oxo-
1,3-dioxolan-4-yl]-5-oxatricyclo[8 3.0.0 4,6]tridec-9,13-dien-2,7-dyne
and apoprotein
Recommended International Nonproprietary Names (Rec. INN): List 25
(Who Chronicle Vol. 39, No. 5, 1985)

p.14 interferonum beta
interferon beta

Replace the description by the following:
A secreted protein known previously as fibroblast interferon, that is produced according to the information coded by a specis of interferon gene.
Sub species of human beta gene produce protein variants designated by the hyphenated addition of a number, e.g. interferon beta-1
The numbers conform with the recommendations of the Interferon Nomenclature Committee.
Human interferon beta has the following amino acid sequence:

H→X-Ser-Tyr-Asn-Leu-Leu-Gly-Phe-Leu-Gln-Arg-Ser-Ser-Asn-Phe-
Gln-Y-Gln-Lys-Leu-Leu-Trp-Gln-Leu-Asn-Gly-Arg-Leu-Glu-Tyr-
Cys-Leu-Lys-Asp-Arg-Met-Asn-Phe-Asp-Ile-Pro-Glu-Glu-Ile-Lys-
Gln-Leu-Gln-Gln-Phe-Gln-Lys-Glu-Asp-Ala-Ala-Leu-Thr-Ile-Tyr-
Glu-Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-Asp-Ser-Ser-
Ser-Thr-Gly-Trp-Asn-Glu-Thr-Ile-Val-Glu-Asn-Leu-Leu-Ala-Asn-
Val-Tyr-His-Gln-Ile-Asn-Glu-Leu-Thr-Val-Leu-Glu-Glu-Lys-
Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-Lys-Leu-Met-Ser-Ser-Leu-
His-Leu-Lys-Arg-Tyr-Tyr-Gly-Arg-Ile-Leu-His-Tyr-Leu-Lys-Ala-
Lys-Glu-Tyr-Ser-His-Cys-Ala-Tyr-Thr-Ile-Val-Arg-Val-Glu-Ile-
Leu-Arg-Asn-Phe-Tyr-Phe-Ile-Asn-Arg-Leu-Thr-Gly-Tyr-Leu-Arg-
Asn-CH

* glycosylation site

In the case of interferon beta-1 it is necessary to qualify the number by a letter depending on the amino-acid residues at positions 1 and 17 in the protein chain and to whether or not glycosylation is present at a specified glycosylation site:

<table>
<thead>
<tr>
<th>Amino acid structure</th>
<th>Glycosylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positions</td>
<td></td>
</tr>
<tr>
<td>1(X)</td>
<td>17(Y)</td>
</tr>
<tr>
<td>beta-1a</td>
<td>Met</td>
</tr>
<tr>
<td>beta-1b</td>
<td>-</td>
</tr>
</tbody>
</table>

Mixtures of interferon beta proteins will be designated as interferon beta-n1, interferon beta-n2 etc.
Recommended International Nonproprietary Names (Rec. INN): List 26
(WHO Chronicle Vol. 40, No. 6, 1986)

p.13 interferonum alfa interferon alfa

replace the description by the following:

A family of secreted proteins, known previously as leucocyte interferon or lymphoblastoid interferon, that is produced according to the information coded by multiple interferon alfa genes

Sub-species of human alfa gene are variants designated by the hyphenated addition of a number, e.g. interferon alfa-2

The numbers conform with the recommendations of the Interferon Nomenclature Committee.

Human interferon alfa-2 has the following amino acid sequence:

```
H-(Met)-Cys-Asp-Leu-Pro-Gln-Thr-His-Ser-Leu-Gly-Ser-Arg-Arg-Thr-Arg-Leu-Leu-Ala-Gln-Met-Arg-X-Ile-Ser-Leu-Phe-Ser-Cys-
 Leu-Lys-Asp-Arg-Y-Asp-Phe-Gly-Phe-Pro-Gin-Glu-Glu-Phe-Gly-
 Asn-Gln-Phe-Gln-Lys-Asn-Val-Thr-Ile-Pro-Val-Leu-His-Glu-Met-
 Ile-Gln-Gln-Ile-Phe-Asn-Leu-Phe-Ser-Thr-Lys-Arg-Ser-Ser-Ala-
 Ala-Trp-Asp-Glu-Thr-Leu-Leu-Asp-Lys-Phe-Tyr-Thr-Glu-Leu-Thr-
 Gln-Gln-Leu-Asn-Asp-Leu-Glu-Ala-Cys-Val-Ile-Gln-Gly-Val-Gly-
 Val-Thr-Glu-Thr-Pro-Leu-Met-Lys-Glu-Asp-Ser-Ile-Leu-Ala-Val-
 Arg-Lys-Tyr-Phe-Gln-Arg-Ile-Thr-Leu-Tyr-Leu-Lys-Glu-Lys-Lys-
 Tyr-Ser-Pro-Cys-Ala-Trp-Glu-Val-Val-Arg-Ala-Glu-Ile-Met-Arg-
 Ser-Phe-Ser-Leu-Ser-Thr-Asn-Leu-Gln-Glu-Ser-Leu-Arg-Ser-Lys-
 Glu-OH
```

In the case of interferon alfa-2 it is necessary to qualify the number by a letter depending on the amino-acid group occupying positions 23 and 34 respectively in the protein chain:

<table>
<thead>
<tr>
<th>Amino acid structure</th>
<th>Positions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>23(X)</td>
</tr>
<tr>
<td>alfa-2a</td>
<td>Lys</td>
</tr>
<tr>
<td>alfa-2b</td>
<td>Arg</td>
</tr>
<tr>
<td>alfa-2c</td>
<td>Arg</td>
</tr>
</tbody>
</table>

Mixtures of interferon alfa proteins will be designated as interferon alfa-n1, interferon alfa-n2 etc.
A secreted protein known previously as immune interferon, that is produced according to the information coded by a species of interferon gene.

Sub-species of human gamma gene produce protein variants designated by the hyphenated addition of a number, e.g. interferon gamma-1a. The numbers conform with the recommendations of the Interferon Nomenclature Committee.

Human interferon gamma has the following amino acid sequence:

\[
\begin{align*}
X & = \text{Gln-Asp-Pro-Tyr-Val-Lys-Glu-Ala-Glu-Asn-Leu-Lys-Tyr-Phe-} \\
\text{Asn-Ala-Gly-His-Ser-Asp-Val-Ala-Asp-Asn-Gly-Thr-Leu-Phe-Leu-} \\
\text{Gly-Ile-Leu-Lys-Asn-Trp-Glu-Glu-Ser-Asp-Arg-Lys-Ile-Met-} \\
\text{Gln-Ser-Gln-Ile-Val-Ser-Phe-Tyr-Phe-Lys-Leu-Phe-Lys-Asn-Phe-} \\
\text{Lys-Asp-Asp-Gln-Ile-Gln-Lys-Ser-Val-Glu-Thr-Ile-Lys-Glu-} \\
\text{Asp-Met-Asn-Val-Lys-Phe-Phe-Asn-Ser-Asn-Lys-Lys-Arg-Asp-} \\
\text{Asp-Phe-Glu-Lys-Leu-Thr-Asn-Tyr-Val-Thr-Asp-Leu-Asn-Val-} \\
\text{Gln-Arg-Lys-Ala-Ile-His-Glu-Leu-Ile-Gln-Val-Met-Ala-Glu-Leu-} \\
\text{Ser-Pro-Ala-Ala-Lys-Thr-Gly-Lys-Arg-Lys-Arg-Ser-Gln-Met-Leu-} \\
\text{Phe-Arg-Gly-Arg-Y}
\end{align*}
\]

In the case of interferon gamma-1 it is necessary to qualify the number by a letter depending on the nature of the termini X and Y at positions 1 and 139 in the protein chain:

<table>
<thead>
<tr>
<th>Amino acid structure</th>
<th>Glycosylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>terminal group</td>
<td>terminal group</td>
</tr>
<tr>
<td>X(1)</td>
<td>Y(139)</td>
</tr>
<tr>
<td>gamma-1a</td>
<td>H-Cys-Tyr-Cys</td>
</tr>
<tr>
<td>gamma-1b*</td>
<td>H-Met</td>
</tr>
<tr>
<td>gamma-1c</td>
<td>H-Met</td>
</tr>
</tbody>
</table>

*formerly interferon gamma-2a

Mixtures of interferon gamma proteins will be designated as interferon gamma-n1, interferon gamma-n2 etc.

Replace the molecular formula by the following:

\[C_{979}H_{1537}N_{265}O_{236}S_{9}\]

Replace the molecular formula by the following:

\[C_{978}H_{1527}N_{265}O_{297}S_{9}\]
Recommended International Nonproprietary Names (Rec. INN): List 27
(WHO Drug Information, Vol. 1, No. 4, 1987)
p.10

somatropinum  
replace the chemical name:
somatropin  
growth hormon (human), r-DNA derived

Recommended International Nonproprietary Names (Rec. INN): List 30
p.3

ciclesonidum  
replace the chemical name by the following:
ciclesonide  
(\(R\))-11\(\beta\),16\(\alpha\),17,21-tetrahydroxyprogna-1,4-diene-3,20-dione cyclic 16,17-acetal with cyclohexanecarboxaldehyde, 21-isobutyrate

p.4
dosmaltatum  
replace the chemical name by the following:
dosmalfate  
125-L-serine-2-133-interleukin 2 (human reduced), reaction product with glutaric anhydride, esters with polyethylene glycol monomethyl ether

Recommended International Nonproprietary Names (Rec. INN): List 33
p.6

pegaldesleukinum  
pegaldesleukin  
replace the chemical name by the following:

Recommended International Nonproprietary Names (Rec. INN): List 35

(Dénominations communes internationales recommandées (DCI Rec.): Liste 35
Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 35
(WHO Drug Information, Vol. 9, No. 3, 1995)
p.16

mangafodipirum  
mangafodipir  
sustituyase la descripción por la siguiente:

p.18

muplestimum  
muplestim  
replace the description and molecular formula by the following:
muplestim  
interleukin 3 (human protein moiety)
muplestim  
replace the description and molecular formula by the following:
muplestim  
interleukine 3 (partie protéique humaine)
muplestim  
reemplácase la descripción y la fórmula empírica por
interleukina 3 (fracción proteica humana)

\(C_{670}H_{1974}N_{184}O_{193}S_{5}\)
MODIFICATIONS APPORTÉES AUX LISTES ANTÉRIEURES

Dénominations communes internationales recommandées (DCI Rec.): Liste 19
(Supplément à la Chronique OMS, Vol. 33, No. 10, 1979)

p. 8  zinostatinum  remplacer la description par:

zinostatin  combinaison de

2-hydroxy-7-méthoxy-5-méthynaphtalène-1-carboxylate de
(4S,6R,11R,12R)-11-[[2-(méthylamino)-2,6-didésoxy-α-D-

galactopyranosyl]oxy]-4-[[4R]-2-oxo-1,3-dioxolane-4-yl]-5-

oxatricycle[8.3.0.04,6]tridéca-1(13),8-diène-2,7-diyn-12-yle avec

l'apoproteïne dont la structure suit

Dénominations communes internationales recommandées (DCI Rec.): Liste 25
(Supplément à la Chronique OMS, Vol. 39, No. 5, 1985)

p.14  interferonum beta  remplacer la description par:

interféron bêta  Protéine diffusible, antérieurement connue sous le nom d'interféron

fibroblastique, produite selon l'information codée par une espèce de gène

interféron

Des sous-espèces du gène bêta humain produisent des variants de la

protéine designés par l'adjonction d'un nombre relié par un tiret, par
e

exemple interféron bêta-1.

Les nombres sont conformes aux recommandations du Comité de nomen-

cature pour l'interféron.

L'interféron bêta humain présente la séquence d'acides aminés suivante:

H-X-Ser-Tyr-Asn-Leu-Leu-Gly-Pha-Leu-Gin-Arg-Ser-Ser-Asn-Pha-

Gin-Y-Gin-Lys-Leu-Leu-Trp-Gln-Leu-Asn-Gly-Arg-Leu-Glu-Tyr-

Cys-Leu-Lys-Asp-Arg-Met-Asn-Pha-Asp-Isa-Phe-Glu-Glu-Ile-Lys-

Gln-Leu-Gin-Gln-Pha-Gln-Lys-Glu-Asp-Ala-Leu-Thr-Ile-Tyr-

Glu-Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-Glu-Ser-Ser-

Ser-Thr-Gly-Trp-Asn-Glu-Thr-Ile-Val-Glu-Asn-Leu-Ala-Asn-

Val-Tyr-His-Gln-Ile-Asn-His-Leu-Lys-Thr-Trp-Leu-Glu-Glu-Lys-

Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-Lys-Leu-Met-Ser-Ser-Leu-

His-Leu-Lys-Arg-Tyr-Gly-Arg-Ile-Leu-His-Tyr-Leu-Lys-Ala-

Lys-Glu-Tyr-Ser-His-Cys-Ala-Trp-Thr-Ile-Val-Arg-Glu-Ile-

Leu-Arg-Asn-Phe-Tyr-Phe-Ile-Asn-Arg-Leu-Thr-Gly-Tyr-Leu-Arg-

Asn-OH

* site de glycosylation
Dans le cas de l'interféron bêta-1, il est nécessaire de faire suivre le nombre par une lettre selon les restes d'acides aminés qui occupent respectivement les positions 1 et 17 dans la chaîne peptidique et selon qu'une glycosylation est présente ou non à un site de glycosylation spécifié.

<table>
<thead>
<tr>
<th>Nature des acides aminés</th>
<th>Glycosylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positions</td>
<td>80</td>
</tr>
<tr>
<td>bêta-1a</td>
<td>Met</td>
</tr>
</tbody>
</table>
bêta-1b| -|Ser| -|

Les mélanges des protéines d'interféron bêta seront désignés comme interféron bêta-n1, interféron bêta-n2, etc.

Dénominations communes internationales recommandées (DCI Rec.): Liste 26

(Supplément à la Chronique OMS, Vol. 40, No. 6, 1986)

| p 13 | interferonum alfa | interféron alfa |

Remplacer la description par:

Famille de protéines diffusibles, antérieurement connue sous le nom d'interféron leucocytaire ou lymphoblastoïde, produites selon l'information codée par plusieurs gènes interféron alfa.

Des sous-espèces du gène alfa humain produisent des variants de la protéine désignés par l'adjonction d'un nombre relié par un tiret, par exemple interféron alfa-2.

Les nombres sont conformes aux recommandations du Comité de nomenclature pour l'interféron.

L'interféron alfa-2 humain présente la sequence d'acides aminés suivante:

H-(Met)-Cys-Asp-Leu-Pro-Gln-Thr-His-Ser-Leu-Gly-Ser-Arg-Arg-Thr-

Leu-Met-Leu-Leu-Ala-Gln-Met-Arg-X-Ile-Ser-Leu-Phe-Ser-Cys-

Leu-Lys-Asp-Arg-Y-Asp-Phe-Gly-Phe-Pro-Gln-Glu-Glu-Phe-Gly-

Asn-Gln-Phe-Gln-Lys-Arg-Leu-Thr-Ile-Pro-Val-Leu-His-Glu-Met-

Ile-Gln-Ile-Phe-Asn-Leu-Phe-Ser-Thr-Lys-Asp-Ser-Ser-Ala-

Ala-Tyr-Asp-Glu-Thr-Leu-Leu-Asp-Lys-Phe-Tyr-Thr-Glu-Leu-Tyr-

Gln-Gln-Leu-Asn-Asp-Leu-Glu-Ala-Cys-Val-Ile-Gln-Gly-Val-Gly-

Val-Thr-Glu-Thr-Pro-Leu-Met-Lys-Glu-Asp-Ser-Ile-Leu-Ala-Val-

Arg-Lys-Tyr-Phe-Gln-Arg-Ile-Thr-Leu-Tyr-Leu-Lys-Gly-Lys-

Tyr-Ser-Pro-Cys-Ala-Tpr-Glu-Val-Arg-Ala-Ile-Met-Arg-

Ser-Phe-Ser-Leu-Ser-Thr-Asn-Leu-Gln-Glu-Ser-Leu-Arg-Ser-Lys-

Dans le cas de l'interféron alfa-2, il est nécessaire de faire suivre le nombre par une lettre selon les restes d'acides aminés qui occupent respectivement les positions 23 et 34 dans la chaîne peptidique.
Les mélanges des protéines de l'interféron alpha seront désignés comme interféron alpha-n1, interféron alpha-n2, etc.

<table>
<thead>
<tr>
<th>Nature des acides amnés</th>
<th>Positions</th>
</tr>
</thead>
<tbody>
<tr>
<td>alfa-2a</td>
<td>23(X) Lys</td>
</tr>
<tr>
<td>alfa-2b</td>
<td>23(X) Arg</td>
</tr>
<tr>
<td>alfa-2c</td>
<td>23(X) Arg</td>
</tr>
</tbody>
</table>

Les nombres sont conformes aux recommandations du Comité de nomenclature pour l'interféron.

L'interféron gamma humain présente la séquence d'acides aminés suivante:

X-Gln-Asp-Pro-Tyr-Val-Lys-Ala-Glu-Asn-Leu-Lys-Lys-Tyr-Phe-
Asn-Ala-Gly-His-Ser-Asp-Val-Ala-Asp-Asn-Gly-Thr-Leu-Phe-Leu-
Gly-Ile-Leu-Lys-Asn-Trp-Lys-Glu-Glu-Ser-Asp-Arg-Lys-Ile-Met-
Gln-Ser-Gln-Ile-Val-Ser-Phe-Tyr-Phe-Lys-Leu-Phe-Lys-Asn-Phe-
Lys-Asp-Asp-Gln-Ser-Ile-Gln-Lys-Ser-Val-Glu-Thr-Ile-Lys-Glu-
Asp-Met-Asn-Val-Lys-Phe-Phe-Asn-Ser-Asn-Lys-Lys-Arg-Asp-
Asp-Phe-Glu-Lys-Leu-Thr-Asn-Tyr-Val-Thr-Asp-Leu-Asn-Val-
Glu-Arg-Lys-Ala-Ile-His-Glu-Leu-Ile-Gln-Val-Met-Ala-Glu-Leu-
Ser-Pro-Ala-Ala-Lys-Thr-Gly-Lys-Arg-Lys-Arg-Glu-Met-Leu-
Phe-Arg-Gly-Arg-Y

Dans le cas de l'interféron gamma-1, il est nécessaire de faire suivre le nombre par une lettre selon la nature des acides aminés qui composent les groupes terminaux X et Y fixés respectivement sur les positions 1 et 139 de la chaîne peptidique.

<table>
<thead>
<tr>
<th>Nature des acides aminés</th>
<th>Glycosylation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Groupe terminal X(1)</td>
<td>Groupe terminal Y (139)</td>
</tr>
<tr>
<td>gamma-1a</td>
<td>H-Cys-Tyr-Cys</td>
</tr>
<tr>
<td>gamma-1b</td>
<td>H-Met</td>
</tr>
<tr>
<td>gamma-1c</td>
<td>H-Met</td>
</tr>
</tbody>
</table>

*précédemment interféron gamma-2a
Les mélanges des protéines d'interféron gamma seront désignés comme interféron gamma-n1, interféron gamma-n2, etc.

p. 9  sometribove
      remplacer la formule brute par:
      C_{578}H_{1537}N_{265}O_{286}S_{9}

p. 9  sométripor
      remplacer la formule brute par:
      C_{577}H_{1527}N_{265}O_{287}S_{8}

Dénominations communes internationales recommandées (DCI Rec.): Liste 27
(Informations pharmaceutiques OMS, Vol. 1, No. 4, 1987)

p. 10
somatropine
remplacer la description :
hormone de croissance (humaine), obtenue par génie génétique

Dénominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 30
(Suplemento de Crónica de la OMS, Vol. 4, No. 3, 1990)

p. 3  ciclosonide
remplacer le nom chimique par
21-[(2-méthylpropanoate) de 16α,17-[[[(R)-cyclohexylméthyléne]bis(oxy)]-11β,21-dihydroxyprégalna-1,4-diéne-3,20-dione

p. 5  dosmaltate
remplacer le nom chimique et la formule brute par:
[[μ₇-[diosmine heptasulfato](7-)][tétracontahydroxytétradécaaluminium
C_{28}H_{60}Al_{14}O_{71}S_{7}

Pour toutes modifications apportées aux Dénominaciones communes internacionales recomendadas (DCI Rec.):
Liste 35 voir page 166, section AMENDMENTS TO PREVIOUS LISTS.

MODIFICACIONES A LAS LISTAS ANTERIORES

Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Lista 19
(Suplemento de Crónica de la OMS, Vol. 33, No. 10, 1979)

p. 8  zinostatina
sustituyase la descripción por la siguiente:
(4S, 6R,11R,12R)-11-[[((α-D-2,6-didesoxi-2-metilaminogalactopiranosil)oxi]-12-
[[2-hidroxi-7-metoxi-5-metil-1-naftilcarbonil]oxi]-4-((4R)-2-oxo-1,3-dioxolan-
4-4)-5-oxitriciclo[8.3.0.0^{3,8}]tridec-9,13-dien-2,7-diene
y apoproteína
Una proteína secretada, previamente conocida como interferón fibroblástico, que está producida de acuerdo con la información codificada por un tipo gen de interferón.

Las subespecies del gen beta humano constituyen variantes, que se designan añadiendo un número precedido de un guión, p ej. interferón beta-1.

Los números se ajustan a las recomendaciones del Comité para la Nomenclatura de interferones.

El interferón beta humano tiene la siguiente secuencia de aminoácidos:

H-X-Ser-Tyr-Asn-Leu-Leu-Gly-Phe-Leu-Gln-Arg-Ser-Ser-Asn-Phe-
Gln-Y-Gin-Lys-Leu-Leu-Trp-Gln-Leu-Aas-Gly-Arg-Leu-Glu-Tyr-
Cys-Leu-Lys-Asp-Arg-Met-Asn-Phe-Asp-Ile-Pro-Glu-Ile-Lys-
Gln-Leu-Gln-Gln-Leu-Gly-Asp-Ala-Ala-Leu-Thr-Ile-Tyr-
Glu-Met-Leu-Gln-Asn-Ile-Phe-Ala-Ile-Phe-Arg-Gln-Asp-Ser-Ser-
Ser-Thr-Gly-Trp-Asn-Glu-Thr-Ile-Val-Glu-Asn-Leu-Val-Ala-
Val-Tyr-His-Gln-Ile-Asn-His-Leu-Lys-Thr-Val-Leu-Glu-Lys-
Leu-Glu-Lys-Glu-Asp-Phe-Thr-Arg-Gly-Lys-Leu-Met-Ser-Ser-Leu-
His-Leu-Lys-Arg-Tyr-Tyr-Gly-Arg-Ile-Leu-His-Tyr-Leu-Lys-Ala-
Lys-Glu-Tyr-Ser-His-Cys-Ala-Trp-Thr-Ile-Val-Arg-Val-Glu-Ile-
Leu-Arg-Asn-Phe-Tyr-Phe-Ile-Asn-Arg-Leu-Thr-Gly-Tyr-Leu-Arg-
Asn-OH

* posición de glicosilación

En el caso del interferón beta-1 será necesario añadir al número una letra, dependiendo del aminoácido que ocupe las posiciones 1 y 17, respectivamente, en la cadena de proteína:

<table>
<thead>
<tr>
<th>Estructura de aminoácidos</th>
<th>Glicosilación</th>
</tr>
</thead>
<tbody>
<tr>
<td>Posiciones</td>
<td></td>
</tr>
<tr>
<td>1(X) 17(Y) 8C</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>beta-1a</th>
<th>Met</th>
<th>Cys</th>
<th>Asn</th>
</tr>
</thead>
<tbody>
<tr>
<td>beta-1b</td>
<td>-</td>
<td>Ser</td>
<td>-</td>
</tr>
</tbody>
</table>

Las mezclas de interferones beta se designarán como interferón beta-n1, interferón beta-n2 etc.
interferonum alfa
interferón alfa:

sustituyase la descripción por la siguiente:

Una familia de proteínas secretadas, previamente conocida como interferón leucocitario o linfoblástico producida de acuerdo con la información codificada por múltiples genes de interferón alfa.

Las subespecies del gen alfa humano constituyen variantes, que se designan añadiendo un número precedido de un guión, p ej. interferón alfa-2.

Los números se ajustan a las recomendaciones del Comité para la Nomenclatura de Interferones

El interferón alfa-2 humano tiene la siguiente secuencia de aminoácidos.

\[
\begin{array}{c}
\text{H-Met-Cys-Asp-Leu-Pro-Gln-Thr-His-Ser-Leu-Gly-Ser-Arg-Arg-Thr-} \\
\text{Leu-Met-Leu-Leu-Ala-Gln-Met-Arg-X-Thr-Ser-Leu-Phe-Ser-Cys-} \\
\text{Leu-Lys-Asp-Arg-Y-Asp-Phe-Gly-Phe-Pro-Gln-Glu-Phe-Gly-} \\
\text{Asn-Gln-Phe-Gln-Lys-Ala-Glu-Thr-Ile-Pro-Val-Leu-His-Glu-Met-} \\
\text{Ile-Gln-Gin-Ile-Phe-Asn-Leu-Phe-Ser-Thr-Lys-Asp-Ser-Ser-Ala-} \\
\text{Ala-Tyr-Asp-Glu-Thr-Leu-Leu-Asp-Lys-Phe-Tyr-Thr-Glu-Leu-Tyr-} \\
\text{Gln-Gln-Leu-Asn-Asp-Leu-Glu-Ala-Cys-Val-Ile-Gln-Gly-Val-Gly-} \\
\text{Val-Thr-Glu-Thr-Pro-Leu-Met-Lys-Glu-Asp-Ser-Ile-Leu-Ala-Val-} \\
\text{Arg-Lys-Tyr-Phe-Gln-Arg-Ile-Thr-Leu-Tyr-Leu-Lys-Glu-Lys-Lys-} \\
\text{Tyr-Ser-Pro-Cys-Ala-Trp-Glu-Val-Val-Arg-Ala-Glu-Ile-Met-Arg-} \\
\text{Ser-Phe-Ser-Leu-Ser-Thr-Asn-Leu-Gln-Glu-Ser-Leu-Arg-Ser-Lys-} \\
\text{Glu-OH}
\end{array}
\]

En el caso del interferón alfa-2 será necesario añadir al número una letra, dependiendo de los aminoácidos que ocupen las posiciones 23 y 34, respectivamente, en la cadena de proteína:

<table>
<thead>
<tr>
<th>Sinónimo</th>
<th>23(X)</th>
<th>34(Y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>alfa-2a</td>
<td>Lys</td>
<td>His</td>
</tr>
<tr>
<td>alfa-2b</td>
<td>Arg</td>
<td>His</td>
</tr>
<tr>
<td>alfa-2c</td>
<td>Arg</td>
<td>Arg</td>
</tr>
</tbody>
</table>

Las mezclas de interferones alfa se designarán como interferón alfa-n1, interferón alfa-n2 etc.
sustituya la descripción por la siguiente:

Una proteína secretada, previamente conocida como interferón inmune, que está producida de acuerdo con la información codificada por un tipo de gen de interferón.

Las subespecies del gen gamma humano producen variantes, que se designan añadiendo un número precedido de un guión, p.ej. interferón gamma-1a

Los números se ajustan a las recomendaciones del Comité para la Nomenclatura de Interferones.

El interferón gamma humano tiene la siguiente secuencia de aminoácidos:

\[
\begin{align*}
\text{Asn-Ala-Gly-His-Ser-Asp-Val-Ala-Asp-Asn-Gly-Thr-Leu-Phe-Leu-} \\
\text{Gly-Leu-Leu-Lys-Asn-Tyr-Lys-Glu-Glu-Ser-Asp-Arg-Lys-Ile-Met-} \\
\text{Gln-Ser-Gln-Ile-Val-Ser-Phe-Tyr-Phe-Lys-Leu-Phe-Lys-Asn-Phe-} \\
\text{Lys-Asp-Asp-Gln-Ser-Ile-Gln-Lys-Ser-Val-Glu-Thr-Ile-Lys-Glu-} \\
\text{Asp-Met-Asn-Val-Lys-Phe-Phe-Asn-Ser-Asn-Lys-Lys-Arg-Asp-} \\
\text{Asp-Phe-Glu-Lys-Leu-Thr-Asn-Tyr-Ser-Val-Thr-Asp-Leu-Asn-Val-} \\
\text{Gln-Arg-Lys-Ala-Ile-His-Glu-Leu-Ile-Gln-Val-Met-Ala-Glu-Leu-} \\
\text{Ser-Pro-Ala-Ala-Lys-Thr-Gly-Lys-Arg-Lys-Arg-Ser-Gln-Met-Leu-} \\
\text{Phe-Arg-Gly-Arg-Y}
\end{align*}
\]

En el caso del interferón gamma-1 será necesario añadir al número una letra, dependiendo de los aminoácidos que ocupen las posiciones 1 y 139, respectivamente, en la cadena de proteína:

<table>
<thead>
<tr>
<th>Estructura de aminoácidos</th>
<th>Glicosilación</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grupo extremo</td>
<td>Grupo extremo</td>
</tr>
<tr>
<td>X(1)</td>
<td>Y (139)</td>
</tr>
</tbody>
</table>

- gamma-1a: H-Cys-Tyr-Cys Arg-Ala-Ser-Gln-OH -
- gamma-1b*: H-Met OH -
- gamma-1c: H-Met Arg-Ala-Ser-Gln-OH -

*anteriormente interferón gamma-2a

Las mezclas de interferones gamma se designarán como interferón gamma-n1, interferón gamma-n2 etc.
Para cualquier modificación de las Denominaciones Comunes Internacionales Recomendadas (DCI Rec.): Listas 35 vease página 166, sección AMENDMENTS TO PREVIOUS LISTS