Tablets are solid dosage forms containing one or more drug substances. They are obtained by single or multiple compression or they are moulded and may be uncoated or coated. They are intended for oral administration. Different categories of tablets include soluble and effervescent tablets, tablets for use in the mouth and extended release tablets. Unless otherwise indicated in the individual monograph, tablets are normally circular in shape, their surfaces are flat or convex. Tablets may have lines or break-marks, symbols or other markings. They are sufficiently hard to withstand handling, including packaging and transportation, without crumbling or breaking.

Tablets may contain pharmaceutical aids such as diluents, binders, disintegrating agents, gildants, lubricants, substances capable of modifying the behaviour of the dosage forms in the digestive tract, colouring matter and flavouring substances. When such pharmaceutical aids are used, it is necessary to ensure that they do not adversely affect the efficacy, bioavailability, dissolution rate, stability, and safety of the drug substance; incompatibility between any of the components of the dosage form should be avoided.

Manufacture

The manufacturing processes for tablets should meet the general requirements on Good Manufacturing Practices (GMP). The following information is intended to provide very broad guidelines concerning the main steps during production with an indication of certain critical factors:

The particle size of the drug substance is primarily significant in terms of dissolution rate and extent, bioavailability and uniformity, especially for substances of low solubility in aqueous media. In order to obtain an

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1. Preparations intended for use other than by oral administration (implants, solution tablets for injections, vaginal tablets etc.) may also be presented in this form. These preparations may require a special formulation, methods of manufacture or form of presentation appropriate to the particular use. For this reason they may not comply with certain parts of this monograph.

2. A separate section in the International Pharmacopoeia will deal with pharmaceutical aids.

3. Adopted in World Health Assembly WHA28.65 and text reproduced in PHARM/82.4/Rev.2 Certification Scheme on the Quality of Pharmaceutical Products moving in International Commerce (periodically updated).
appropriate formulation, it is usually necessary to mix the drug substance with a number of suitable pharmaceutical aids. It is essential that such mixing is carried out in a manner to ensure homogeneity. In some cases the physical characteristics of the mixture are such that it may be directly compressed. Sometimes, it is necessary to granulate before compression, e.g. by wet granulation or precompression (slugging).

The granulate and powders normally need to be mixed with lubricants and/or disintegrating agents. The use of excessive amounts of lubricants should be avoided since these will deleteriously affect the tablets. The final tablet mixture is volumetrically fed into the die cavity to assure tablets of uniform mass and compressed at an adequate pressure. When necessary, the tablets may be coated, e.g. in coating pans or by the air suspension technique.

Throughout the manufacturing procedure critical steps should be monitored by carrying out appropriate in-process controls. Such tests (validation) should be designed to provide assurance of the effectiveness of each stage of production. Important in-process controls for different stages of tablet production are: particle size of the drug substance, homogeneity of the mixture, moisture content of the mixture and/or granulate, size of granules, flowability of final mixture, uniformity of mass, hardness, abrasion, disintegration, or dissolution rate (if appropriate), of the tablets.

The packing of tablets should protect them from light, moisture, and damage during transportation.

GENERAL REQUIREMENTS

Visual inspection

Visually inspect at least 20 tablets. They should be without any damage, smooth and usually of uniform colour. Evidence of physical instability may consist of the following:

- presence of excessive powder and/or pieces of tablets at the bottom of the container (from abraded, crushed or broken tablets);
- cracks or chips in the tablet surfaces of coatings, swelling, mottling, discoloration, fusion between tablets;
- the appearance of crystals on the container walls or on the tablets.

Labelling

Every pharmaceutical preparation must comply with the labelling requirements established in the GMP.

1. the name of the drug;
2. a list of the active drug substances, showing the amount of each present, and a statement of the net contents, e.g., number of dosage units, weight or volume;
3. the batch (lot) number assigned by the manufacturer;
4. the expiry date, if required;
5. any special storage conditions or handling precautions that may be necessary;
6. directions for use, warnings and precautions that may be necessary; and
7. the name and address of the manufacturer or the person responsible for placing the drug on the market.
Storage

Tablets should throughout their shelf-life maintain their integrity by storage in well-closed containers, protected from light, crushing and mechanical shock, kept at temperatures compatible with its stability, and whenever necessary in areas of low humidity. They should withstand handling, including packaging and transportation without losing their pharmaceutical integrity. Moisture sensitive forms, such as effervescent tablets should be stored in tightly closed containers or moisture proof packs and may require the use of separate packages containing water-adsorbent agents, such as silica gel.

Additional special packaging, storage and transportation recommendations are given in individual monographs.

Uniformity of mass

Tablets comply with the test for "Uniformity of mass for single dose preparations", unless otherwise specified in the monograph.

Uniformity of content

A requirement for the "Uniformity of content for single dose preparations" is specified in certain monographs for sugar-coated or enteric coated tablets, where the test for uniformity of mass does not apply. In addition a requirement is specified in certain monographs where the drug substance is 5% or less of the total formulation. In such cases the test for uniformity of mass may be omitted.

Disintegration test

Uncoated tablets, except effervescent tablets and tablets for use in the mouth comply with the "Disintegration test for tablets and capsules". Operate the apparatus for 15 minutes and examine the state of the tablets.

Dissolution test

Where a requirement for the "Dissolution test"4 is specified in the individual monograph the "Disintegration test for tablets and capsules" may be omitted.

Requirements for specific types of tablets

1. Uncoated tablets

The majority of uncoated tablets are made in such a way that the release of drug substances is unmodified. A broken section, when examined under a lens, shows either a relatively uniform texture (single-layer tablets) or a stratified texture (multi-layer tablets) but no signs of coating.

4 To be developed
1.1 Soluble tablets

Soluble tablets are uncoated tablets that dissolve in water to give a clear solution (see International Pharmacopoeia, third edition, volume 2, p. 11).

Disintegration test

Use water at room temperature, and operate the apparatus for 3 minutes.

1.2 Effervescent tablets

Effervescent tablets are uncoated tablets generally containing acid substances and carbonates or hydrogen carbonates which react rapidly in the presence of water to release carbon dioxide. They are intended to be dissolved or dispersed in water before administration.

Disintegration test

Place a tablet in a 250 ml beaker containing 200 ml of water at room temperature. Numerous bubbles of gas are evolved. When the evolution of gas around the tablet or its fragments ceases, the tablet should have disintegrated, being either dissolved or dispersed in the water so that no agglomerates of particles remain. Repeat the operation on 5 other tablets. The tablets comply with the test if each of the 6 tablets used in the test disintegrate within 5 minutes, unless otherwise specified in the individual monographs.

Packaging and storage

Effervescent tablets should be stored in tightly closed containers or moisture proof packs and are labelled not to be swallowed directly. It is advisable to include a separate package of water-adsorbent agent, such as silica gel.

1.3 Tablets for use in the mouth (sublingual and buccal)

Tablets for use in the mouth are usually uncoated tablets. They are formulated to effect a slow release and local action of the drug substance or substances (for example, compressed lozenges) or the release and absorption of the drug substance under the tongue (sublingual tablets) or in other parts of the mouth for systemic action.

2. Coated tablets

Coated tablets are tablets covered with one or more layers of mixtures of various substances such as natural or synthetic resins, gums, fillers, sugar, plasticisers, polyols, waxes, colouring matters and flavouring substances, and drug substances. A broken section, when examined under a lens shows a core surrounded by a continuous layer of a different texture.
The tablets may be coated for a variety of pharmaceutical reasons including protection of the drug substances from air, moisture or light, masking of unpleasant tastes and odours, or improvement of appearance. The substances used for coatings are usually applied as a solution or suspension.

Three main categories of coated tablets may be distinguished: sugar-coated, film-coated and certain extended release tablets.

2.1 Sugar-coated tablets

Sugar-coated tablets are coated tablets in which the major coating agent is sugar. The hydrophobic subcoat applied to the core can diminish dissolution from the core especially on storage.

Uniformity of mass

The test does not apply to sugar-coated tablets.

Disintegration test

Operate the apparatus for 60 minutes, unless otherwise specified in the monograph, and examine the state of the tablets. If any of the tablets has not disintegrated, repeat the test on a further 6 tablets.

To pass the test 11 out of 12 tablets must have disintegrated.

2.2 Film-coated tablets

A film-coated tablet is covered with a thin layer of resins, polymers and plasticisers capable of forming a film.

Disintegration test

Operate the apparatus for 30 minutes, and examine the state of the tablets.

2.3 Extended release tablets

Extended release tablets are coated or uncoated tablets containing pharmaceutical aids or prepared by procedures which, separately or together, are designed to modify the rate or the site at which the drug substance(s) are released in the gastro-intestinal tract.

The specialized nature of these dosage forms is such that all the requirements are given in the individual monographs.

Enteric-coated tablets

Enteric-coated tablets are tablets covered with one or more layers intended to resist the gastric fluid but to permit disintegration in the intestinal fluid. These properties are achieved using substances such as cellulose acetate phthalate, and anionic copolymers of methacrylic acid and its esters in the coating. It may be necessary to apply an additional protective coat.
Uniformity of mass

The test does not apply to enteric-coated tablets.

Disintegration test

Use hydrochloric acid (0.1 mol/l)VS as the immersion fluid. Operate the apparatus for 2 hours and examine the state of the tablets. No tablet shows signs of either disintegration (apart from fragments of coating) or cracks that would allow the escape of the contents. Replace the acid by phosphate buffer solution, pH 6.8, TS. Operate the apparatus for 60 minutes and examine the state of the tablets.

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