## Cutaneous patches

DEFINITION

Cutaneous patches are flexible preparations containing 1 or more active substances. They are intended to be applied to the skin. They are designed to maintain the active substance(s) in close contact with the skin such that these may act locally.

Cutaneous patches consist of an adhesive basis, which may be coloured, containing 1 or more active substances, spread as a uniform layer on an appropriate support made of natural or synthetic material. The adhesive basis is not irritant or sensitising to the skin. The adhesive layer is covered by a suitable protective liner, which is removed before applying the patch to the skin. When removed, the protective liner does not detach the preparation from the outer, supporting layer.

Cutaneous patches are presented in a range of sizes adapted to their intended use. They adhere firmly to the skin when gentle pressure is applied and can be peeled off without causing appreciable injury to the skin or detachment of the preparation from the outer, supporting layer.

TESTS

**Dissolution**. A suitable test may be required to demonstrate the appropriate release of the active substance(s), for example one of the tests described in *Dissolution test for transdermal patches* (*2.9.4*).

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# STICKS

## Styli

*Additional requirements for sticks may be found, where appropriate, in other general monographs, for example Nasal preparations (0676).*

DEFINITION

Sticks are solid preparations intended for local application. They may be single-dose or multidose preparations. They are rod-shaped or conical preparations consisting of one or more active substances, either alone or dissolved or dispersed in a suitable basis, and are usually intended to dissolve or melt at body temperature. They may be inserted into a body cavity or wound, or be applied cutaneously.

Urethral sticks and sticks for insertion into wounds are sterile.

PRODUCTION

In the manufacture, packaging, storage and distribution of sticks, suitable measures are taken to ensure their microbial quality; recommendations on this aspect are provided in general chapter *5.1.4. Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use*.

Urethral sticks and other sterile sticks are prepared using materials and methods designed to ensure sterility and to avoid the introduction of contaminants and the growth of micro-organisms; recommendations on this aspect are provided in general chapter *5.1.1. Methods of preparation of sterile products*.

TESTS

**Uniformity of dosage units** (*2.9.40*). Single-dose sticks comply with the test or, where justified and authorised, with the tests for uniformity of content and/or uniformity of mass shown below. Herbal drugs and herbal drug preparations present in the dosage form are not subject to the provisions of this paragraph.

**Uniformity of content** (*2.9.6*). Unless otherwise prescribed or justified and authorised, single-dose sticks with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test B. If the preparation contains more than one active substance, this requirement applies only to those substances that correspond to the above conditions.

**Uniformity of mass** (*2.9.5*). Single-dose sticks comply with the test. If the test for uniformity of content is prescribed for all active substances, the test for uniformity of mass is not required.

**Sterility** (*2.6.1*). Urethral sticks and sticks for insertion into wounds comply with the test for sterility.

LABELLING

The label states, for urethral sticks and sticks to be inserted into wounds, that they are sterile.

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# TABLETS

## Compressi

*The requirements of this monograph do not necessarily apply to preparations that are presented as tablets intended for use other than by oral administration. Requirements for such preparations may be found, where appropriate, in other general monographs; for example Rectal preparations (1145), Vaginal preparations (1164) and Oromucosal preparations (1807). This monograph does not apply to lozenges, oral pastes and oral gums. Where justified and authorised, the requirements of this monograph do not apply to tablets for veterinary use. Tablets for use in the mouth comply with the requirements of the monograph Oromucosal preparations (1807).*

DEFINITION

Tablets are solid preparations each containing a single dose of one or more active substances. They are obtained by compressing uniform volumes of particles or by another suitable manufacturing technique, such as extrusion, moulding or freeze-drying (lyophilisation). Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated.

The particles consist of one or more active substances with or without excipients such as diluents, binders, disintegrating agents, glidants, lubricants, substances capable of modifying the behaviour of the preparation in the digestive tract, colouring matter authorised by the competent authority and flavouring substances.

Tablets are usually straight, solid cylinders, the end surfaces of which are flat or convex and the edges of which may be bevelled. They may have break-marks and may bear a symbol or other markings. Tablets may be coated.

Where applicable, containers for tablets comply with the requirements for materials used for the manufacture of containers (*3.1* and subsections) and containers (*3.2* and subsections).

Several categories of tablets for oral use may be distinguished:

- uncoated tablets;
- coated tablets;
- gastro-resistant tablets;
- modified-release tablets;
- effervescent tablets;
- soluble tablets;
- dispersible tablets;

- orodispersible tablets;
- chewable tablets;
- oral lyophilisates.

PRODUCTION

Tablets are usually prepared by compressing uniform volumes of particles or particle aggregates produced by granulation methods. In the manufacture of tablets, measures are taken to ensure that they possess a suitable mechanical strength to avoid crumbling or breaking on handling or subsequent processing. This may be demonstrated using the tests described in general chapters *2.9.7. Friability of uncoated tablets* and *2.9.8. Resistance to crushing of tablets*.

In the manufacture, packaging, storage and distribution of tablets, suitable measures are taken to ensure their microbiological quality; recommendations on this aspect are provided in general chapter *5.1.4. Microbiological quality of non-sterile pharmaceutical preparations and substances for pharmaceutical use*.

*Subdivision of tablets*. Tablets may bear a break-mark or break-marks for the purpose of being subdivided into parts, either to ease the intake of the medicinal product or to deliver fractional doses. In cases where fractions of tablets are necessary to deliver the intended dose stated on the label, the efficacy of the breakmark is assessed during product development or for validation purposes by determining the uniformity of mass of the sub-divided parts using the following test.

Take 30 tablets at random, break them by hand and, from all the parts obtained from 1 tablet, take 1 part for the test and reject the other part(s). Weigh each of the 30 parts individually and calculate the average mass. The tablets comply with the test if not more than 1 individual mass is outside the limits of 85 per cent to 115 per cent of the average mass. The tablets fail to comply with the test if more than 1 individual mass is outside these limits, or if 1 individual mass is outside the limits of 75 per cent to 125 per cent of the average mass.

TESTS

**Uniformity of dosage units** (*2.9.40*). Tablets comply with the test or, where justified and authorised, with the tests for uniformity of content and/or uniformity of mass shown below. Herbal drugs and herbal drug preparations present in the dosage form are not subject to the provisions of this paragraph.

**Uniformity of content** (*2.9.6*). Unless otherwise prescribed or justified and authorised, tablets with a content of active substance less than 2 mg or less than 2 per cent of the total mass comply with test A. If the preparation has more than 1 active substance, the requirement applies only to those substances that correspond to the above conditions.

Unless otherwise justified and authorised, coated tablets other than film-coated tablets comply with test A irrespective of their content of active substance(s).

**Uniformity of mass** (*2.9.5*). Uncoated tablets and, unless otherwise justified and authorised, film-coated tablets comply with the test. If the test for uniformity of content is prescribed or justified and authorised for all the active substances, the test for uniformity of mass is not required.

**Dissolution**. Unless otherwise justified and authorised, a suitable test is carried out, for example one of the tests described in general chapter *2.9.3. Dissolution test for solid dosage forms*.

Where a dissolution test is prescribed, a disintegration test may not be required.

## Uncoated tablets

DEFINITION

Uncoated tablets include single-layer tablets resulting from a single compression of particles and multi-layer tablets consisting of concentric or parallel layers obtained by successive compression of particles of different composition. The excipients used are not specifically intended to modify the release of the active substance in the digestive fluids.

Uncoated tablets conform to the general definition of tablets. 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.

TESTS

**Disintegration** (*2.9.1*). Uncoated tablets comply with the test using *water R* as the liquid medium. Add a disc to each tube. Operate the apparatus for 15 min, unless otherwise justified and authorised, and examine the state of the tablets. If the tablets fail to comply because of adherence to the discs, the results are invalid. Repeat the test on a further 6 tablets, omitting the discs.

## Coated tablets

DEFINITION

Coated tablets are tablets covered with one or more layers of mixtures of various substances such as natural or synthetic resins, gums, gelatin, inactive and insoluble fillers, sugars, plasticisers, polyols, waxes, colouring matter authorised by the competent authority and sometimes flavouring substances and active substances. The substances used as coatings are usually applied as a solution or suspension in conditions in which evaporation of the vehicle occurs. When the coating is a very thin polymeric coating, the tablets are known as film-coated tablets.

Coated tablets have a smooth surface, which is often coloured and may be polished; a broken section, when examined under a lens, shows a core surrounded by one or more continuous layers with a different texture.

PRODUCTION

Where justified, uniformity of mass or uniformity of content of coated tablets other than film-coated tablets may be ensured by control of the cores.

TESTS

**Disintegration** (*2.9.1*). Coated tablets other than film-coated tablets comply with the test using *water R* as the liquid medium. Add a disc to each tube. Operate the apparatus for 60 min, unless otherwise justified and authorised, and examine the state of the tablets. If any of the tablets has not disintegrated, repeat the test on a further 6 tablets, replacing *water R* with *0.1 M hydrochloric acid*. If 1 or 2 tablets fail to disintegrate, repeat the test on 12 additional tablets.

The requirements of the test are met if not fewer than 16 of the 18 tablets tested have disintegrated.

Film-coated tablets comply with the disintegration test prescribed above except that the apparatus is operated for 30 min, unless otherwise justified and authorised.

If coated tablets or film-coated tablets fail to comply because of adherence to the discs, the results are invalid. Repeat the test on a further 6 tablets, omitting the discs.

## Gastro-resistant tablets

DEFINITION

Gastro-resistant tablets are delayed-release tablets that are intended to resist the gastric fluid and to release their active substance(s) in the intestinal fluid. Usually they are prepared

by covering tablets with a gastro-resistant coating or from granules or particles already covered with a gastro-resistant coating.

Tablets covered with a gastro-resistant coating conform to the definition of coated tablets.

TESTS

**Disintegration** (*2.9.1*). Tablets covered with a gastro-resistant coating comply with the test with the following modifications. Use *0.1 M hydrochloric acid* as the liquid medium. Operate the apparatus for 2 h, or another such time as may be justified and authorised, without the discs, and examine the state of the tablets. The time of resistance to the acid medium varies according to the formulation of the tablets to be examined. It is typically 2 h to 3 h but even with authorised deviations is not less than 1 h. 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 R* and add a disc to each tube. Operate the apparatus for 60 min and examine the state of the tablets. If the tablets fail to comply because of adherence to the discs, the results are invalid. Repeat the test on a further 6 tablets, omitting the discs.

## Modified-release tablets

DEFINITION

Modified-release tablets are coated or uncoated tablets that contain special excipients or are prepared by special procedures, or both, designed to modify the rate, the place or the time at which the active substance(s) are released.

Modified-release tablets include prolonged-release tablets, delayed-release tablets and pulsatile-release tablets.

## Effervescent tablets

DEFINITION

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.

TESTS

**Disintegration**. Place 1 tablet in a beaker containing 200 mL of *water R* at 15-25 °C; numerous bubbles of gas are evolved. When the evolution of gas around the tablet or its fragments ceases the tablet has 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 disintegrates in the manner prescribed within 5 min, unless otherwise justified and authorised.

## Soluble tablets

DEFINITION

Soluble tablets are uncoated or film-coated tablets. They are intended to be dissolved in water before administration. The solution produced may be slightly opalescent due to the added excipients used in the manufacture of the tablets.

TESTS

**Disintegration** (*2.9.1*). Soluble tablets disintegrate within 3 min, using *water R* at 15-25 °C as the liquid medium.

## Dispersible tablets

DEFINITION

Dispersible tablets are uncoated or film-coated tablets intended to be dispersed in water before administration, giving a homogeneous dispersion.

TESTS

**Disintegration** (*2.9.1*). Dispersible tablets disintegrate within 3 min, using *water R* at 15-25 °C as the liquid medium.

**Fineness of dispersion**. Place 2 tablets in 100 mL of *water R* and stir until completely dispersed. A smooth dispersion is produced, which passes through a sieve screen with a nominal mesh aperture of 710 µm.

## Orodispersible tablets

DEFINITION

Orodispersible tablets are uncoated tablets intended to be placed in the mouth where they disperse rapidly before being swallowed.

TESTS

**Disintegration** (*2.9.1*). Orodispersible tablets disintegrate within 3 min, using *water R* as the liquid medium.

## Chewable tablets

DEFINITION

Chewable tablets are intended to be chewed before being swallowed.

PRODUCTION

Chewable tablets are prepared to ensure that they are easily crushed by chewing.

## Oral lyophilisates

DEFINITION

Oral lyophilisates are solid single-dose preparations made by freeze-drying of a liquid or semi-solid preparation. These fast-releasing preparations are intended to be placed in the mouth where their contents are released in saliva and swallowed or, alternatively, are intended to be dissolved or dispersed in water before oral administration.

PRODUCTION

Oral lyophilisates are obtained by freeze-drying (lyophilisation), involving division into single doses, freezing, sublimation and drying of usually aqueous, liquid or semi-solid preparations.

TESTS

**Disintegration**. Place 1 oral lyophilisate in a beaker containing 200 mL of *water R* at 15-25 °C. It disintegrates within 3 min. Repeat the test on 5 other oral lyophilisates. They comply with the test if all 6 have disintegrated.

**Water** (*2.5.12*). Oral lyophilisates comply with the test; the limits are approved by the competent authority.