UNIVERSITÀ DEGLI STUDI DI TORINO

ESAME DI STATO PER L'ABILITAZIONE ALL'ESERCIZIO DELLA PROFESSIONE DI FARMACISTA

PRIMA SESSIONE 2015

PROVA SCRITTA

Tema n. 1
Distribuzione in nome e per conto (DPC): finalità e modalità operative.

Tema n. 2
La contraccezione ormonale in farmacia: principi farmacologici, indicazioni d'uso e rischi di interazioni.

Tema n. 3
Le preparazioni oftalmiche: definizione, tipologie e requisiti.

PROVA PRATICA

Prova n.1
Dosamento del farmaco.
Vedi allegato di seguito.

Prova n.2
Riconoscimento del farmaco.
Vedi allegato di seguito.

Prova n.3
Spedizione della ricetta.
Vedi allegato di seguito.

UNIVERSITÀ DEGLI STUDI DI TORINO

ESAME DI STATO PER L'ABILITAZIONE ALL'ESERCIZIO DELLA PROFESSIONE DI FARMACISTA

PRIMA SESSIONE 2015

PROVA PRATICA: Dosamento del Farmaco

Cognome e nome.....

Una compressa del peso di 1,6000 grammi contenente calcio lattato (PM: 218,0) ed eccipienti inerti è stata sciolta in un matraccio da 150,00 mL e portata a volume ottenendo la soluzione A.

25,00 mL della soluzione A sono stati prelevati e titolati secondo Ph. Eur. 8. La titolazione ha richiesto 9,935 mL di EDTA sodico 0,1000 M.

75,00 mL di soluzione A sono stati prelevati e trasportati in un matraccio da 200,00 mL. Dopo aver portato a volume si è ottenuta la soluzione B.

Si calcoli:

a) i grammi di calcio lattato contenuti nella compressa

b) la concentrazione molare di calcio lattato nella soluzione A

c) il % p/v della soluzione B

Risposte ai quesiti:

a) _____

b) _____

c) _____

N.B. Insieme alla prova al candidato viene fornita copia della monografia ufficiale di Ph. Eur. 8 del calcio lattato monoidrato.

01/2008:20510

2.5.10. OXYGEN-FLASK METHOD

Unless otherwise prescribed the combustion flask is a conical flask of at least 500 mL capacity of borosilicate glass with a ground-glass stopper fitted with a suitable carrier for the sample, for example in platinum or platinum-iridium.

Finely grind the substance to be examined, place the prescribed quantity in the centre of a piece of filter paper measuring about 30 mm by 40 mm provided with a small strip about 10 mm wide and 30 mm long. If paper impregnated with lithium carbonate is prescribed, moisten the centre of the paper with a saturated solution of *lithium carbonate R* and dry in an oven before use. Envelop the substance to be examined in the paper and place it in the sample carrier. Introduce into the flask *water R* or the prescribed solution designed to absorb the combustion products, displace the air with oxygen by means of a tube having its end just above the liquid, moisten the neck of the flask with *water R* and close with its stopper. Ignite the paper strip by suitable means with the usual precautions. Keep the flask firmly closed during the combustion. Shake the flask vigorously to completely dissolve the combustion products. Cool and after about 5 min, unless otherwise prescribed, carefully unstopper the flask. Wash the ground parts and the walls of the flask, as well as the sample carrier, with *water R*. Combine the combustion products and the washings and proceed as prescribed in the monograph.

01/2008:20511
corrected 8.0

2.5.11. COMPLEXOMETRIC TITRATIONS

ALUMINIUM

Introduce 20.0 mL of the prescribed solution into a 500 mL conical flask, add 25.0 mL of *0.1 M sodium edetate* and 10 mL of a mixture of equal volumes of a 155 g/L solution of *ammonium acetate R* and *dilute acetic acid R*. Boil for 2 min, then cool. Add 50 mL of *ethanol R* and 3 mL of a freshly prepared 0.25 g/L solution of *dithizone R* in *ethanol R*. Titrate the excess of sodium edetate with *0.1 M zinc sulfate* until the colour changes from greenish-blue to reddish-violet.

1 mL of *0.1 M sodium edetate* is equivalent to 2.698 mg of Al.

BISMUTH

Introduce the prescribed solution into a 500 mL conical flask. Dilute to 250 mL with *water R* and then, unless otherwise prescribed, add dropwise, with shaking, *concentrated ammonia R* until the mixture becomes cloudy. Add 0.5 mL of *nitric acid R*. Heat to about 70 °C until the cloudiness disappears completely. Add about 50 mg of *xylenol orange triturate R* and titrate with *0.1 M sodium edetate* until the colour changes from pinkish-violet to yellow.

1 mL of *0.1 M sodium edetate* is equivalent to 20.90 mg of Bi.

CALCIUM

Introduce the prescribed solution into a 500 mL conical flask, and dilute to 300 mL with *water R*. Add 6.0 mL of *strong sodium hydroxide solution R* and about 200 mg of *calconecarboxylic acid triturate R*. Titrate with *0.1 M sodium edetate* until the colour changes from violet to full blue.

1 mL of *0.1 M sodium edetate* is equivalent to 4.008 mg of Ca.

MAGNESIUM

Introduce the prescribed solution into a 500 mL conical flask and dilute to 300 mL with *water R*. Add 10 mL of *ammonium chloride buffer solution pH 10.0 R* and about 50 mg of *mordant black 11 triturate R*. Heat to about 40 °C then titrate at this temperature with *0.1 M sodium edetate* until the colour changes from violet to full blue.

1 mL of *0.1 M sodium edetate* is equivalent to 2.431 mg of Mg.

LEAD

Introduce the prescribed solution into a 500 mL conical flask and dilute to 200 mL with *water R*. Add about 50 mg of *xylenol orange triturate R* and *hexamethylenetetramine R* until the solution becomes violet-pink. Titrate with *0.1 M sodium edetate* until the violet-pink colour changes to yellow.

1 mL of *0.1 M sodium edetate* is equivalent to 20.72 mg of Pb.

ZINC

Introduce the prescribed solution into a 500 mL conical flask and dilute to 200 mL with *water R*. Add about 50 mg of *xylenol orange triturate R* and *hexamethylenetetramine R* until the solution becomes violet-pink. Add 2 g of *hexamethylenetetramine R* in excess. Titrate with *0.1 M sodium edetate* until the violet-pink colour changes to yellow.

1 mL of *0.1 M sodium edetate* is equivalent to 6.54 mg of Zn.

01/2013:20512

2.5.12. WATER: SEMI-MICRO DETERMINATION

The semi-micro determination of water is based upon the quantitative reaction of water with sulfur dioxide and iodine in a suitable anhydrous medium in the presence of a base with sufficient buffering capacity.

Apparatus

The apparatus consists of a titration vessel with:

- 2 identical platinum electrodes;
- tight inlets for introduction of solvent and titrant;
- an inlet for introduction of air via a desiccant;
- a sample inlet fitted with a stopper or, for liquids, a septum.

Inlet systems for introduction of dry nitrogen or for aspiration of solvents may also be fitted.

The titration is carried out according to the instrument supplier's instructions. Care is taken throughout the determination to avoid exposure of reagents and solvents to atmospheric moisture. The end-point is determined using 2 identical indicator electrodes connected to an electrical source that maintains between the electrodes either a constant current (*2.2.65. Voltametric titration*) or a constant voltage (*2.2.19. Amperometric titration*). Where direct titration is used (method A), addition of titrant causes either a decrease in voltage where constant current is maintained or an increase in current where constant voltage is maintained, until the end-point is reached. Instruments with automatic end-point detection are commonly used.

Standardisation. To the titration vessel, add *methanol R*, dried if necessary, or the solvent recommended by the supplier of the titrant. Where applicable for the apparatus used, eliminate residual water from the measurement cell or carry out a pre-titration. Introduce a suitable amount of water in an appropriate form (*water R* or a certified reference material) and carry out the titration, stirring for the necessary time. The water equivalent is not less than 80 per cent of that indicated by the supplier. Standardise the titrant before the first use and at suitable intervals thereafter.

Unless otherwise prescribed, use Method A.

Method A. Introduce into the titration vessel *methanol R*, or the solvent indicated in the monograph or recommended by the supplier of the titrant. Where applicable for the apparatus used, eliminate residual water from the measurement cell or carry out a pre-titration. Introduce the substance to be examined rapidly and carry out the titration, stirring for the necessary extraction time.

Method B. Introduce into the titration vessel *methanol R*, or the solvent indicated in the monograph or recommended by the supplier of the titrant. Where applicable for the apparatus

and rapidly add 40 mL of hot *ammonium oxalate solution R*. Allow to stand for 4 h, dilute to 100.0 mL with *water R* and filter. To 50.0 mL of the filtrate add 0.5 mL of *sulfuric acid R*. Evaporate to dryness and ignite the residue to constant mass at 600 ± 50 °C. The residue weighs a maximum of 5 mg.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve 2.0 g in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): maximum 3.0 per cent, determined on 0.500 g by drying in an oven at 125 °C.

ASSAY

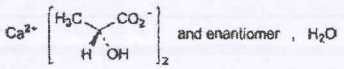
Dissolve 0.200 g in *water R* and dilute to 300 mL with the same solvent. Carry out the complexometric titration of calcium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 21.82 mg of $C_6H_{10}CaO_6$.

01/2008:2117
corrected 6.0

CALCIUM LACTATE MONOHYDRATE

Calcii lactas monohydricus



$C_6H_{10}CaO_6,H_2O$ M_r 236.0

DEFINITION

Calcium bis(2-hydroxypropanoate) or mixture of calcium (2*R*)-, (2*S*)- and (2*RS*)-2-hydroxypropanoates monohydrates.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline or granular powder.

Solubility: soluble in water, freely soluble in boiling water, very slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Loss on drying (see Tests).

B. It gives the reaction of lactates (*2.3.1*).

C. It gives reaction (b) of calcium (*2.3.1*).

TESTS

Solution S. Dissolve 5.4 g (equivalent to 5.0 g of the dried substance) with heating in *carbon dioxide-free water R* prepared from *distilled water R*, allow to cool and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *phenolphthalein solution R* and 0.5 mL of *0.01 M hydrochloric acid*. The solution is colourless. Not more than 2.0 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Chlorides (*2.4.4*): maximum 200 ppm.

Dilute 5 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 400 ppm.

Dilute 7.5 mL of solution S to 15 mL with *distilled water R*.

Barium. To 10 mL of solution S add 1 mL of *calcium sulfate solution R*. Allow to stand for 15 min. Any opalescence in the solution is not more intense than that in a mixture of 1 mL of *distilled water R* and 10 mL of solution S.

Iron (*2.4.9*): maximum 50 ppm.

Dilute 4 mL of solution S to 10 mL with *water R*.

Magnesium and alkali salts: maximum 1 per cent.

To 20 mL of solution S add 20 mL of *water R*, 2 g of *ammonium chloride R* and 2 mL of *dilute ammonia R1*. Heat to boiling and rapidly add 40 mL of hot *ammonium oxalate solution R*. Allow to stand for 4 h, dilute to 100.0 mL with *water R* and filter. To 50.0 mL of the filtrate add 0.5 mL of *sulfuric acid R*. Evaporate to dryness and ignite the residue to constant mass at 600 ± 50 °C. The residue weighs a maximum of 5 mg.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve a quantity equivalent to 2.0 g of the dried substance in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): 5.0 per cent to 8.0 per cent, determined on 0.500 g by drying in an oven at 125 °C.

ASSAY

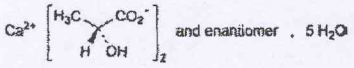
Dissolve a quantity equivalent to 0.200 g of the dried substance in *water R* and dilute to 300 mL with the same solvent. Carry out the complexometric titration of calcium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 21.82 mg of $C_6H_{10}CaO_6$.

01/2008:0468
corrected 6.0

CALCIUM LACTATE PENTAHYDRATE

Calcii lactas pentahydricus



$C_6H_{10}CaO_6,5H_2O$ M_r 308.3

DEFINITION

Calcium bis(2-hydroxypropanoate) or mixture of calcium (2*R*)-, (2*S*)- and (2*RS*)-2-hydroxypropanoates pentahydrates.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline or granular powder, slightly efflorescent.

Solubility: soluble in water, freely soluble in boiling water, very slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Loss on drying (see Tests).

B. It gives the reaction of lactates (*2.3.1*).

C. It gives reaction (b) of calcium (*2.3.1*).

TESTS

Solution S. Dissolve 7.1 g (equivalent to 5.0 g of the dried substance) with heating in *carbon dioxide-free water R* prepared from *distilled water R*, allow to cool and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *phenolphthalein solution R* and 0.5 mL of *0.01 M hydrochloric acid*. The solution is colourless. Not more than 2.0 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Chlorides (*2.4.4*): maximum 200 ppm.

Dilute 5 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 400 ppm.

Dilute 7.5 mL of solution S to 15 mL with *distilled water R*.

Barium. To 10 mL of solution S add 1 mL of *calcium sulfate solution R*. Allow to stand for 15 min. Any opalescence in the solution is not more intense than that in a mixture of 1 mL of *distilled water R* and 10 mL of solution S.

Iron (*2.4.9*): maximum 50 ppm.

Dilute 4 mL of solution S to 10 mL with *water R*.

Magnesium and alkali salts: maximum 1 per cent.

To 20 mL of solution S add 20 mL of *water R*, 2 g of *ammonium chloride R* and 2 mL of *dilute ammonia R1*. Heat to boiling and rapidly add 40 mL of hot *ammonium oxalate solution R*. Allow to stand for 4 h, dilute to 100.0 mL with *water R* and filter. To 50.0 mL of the filtrate add 0.5 mL of *sulfuric acid R*. Evaporate to dryness and ignite the residue to constant mass at 600 ± 50 °C. The residue weighs a maximum of 5 mg.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve a quantity equivalent to 2.0 g of the dried substance in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): 22.0 per cent to 27.0 per cent, determined on 0.500 g by drying in an oven at 125 °C.

ASSAY

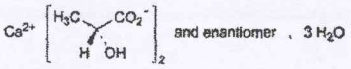
Dissolve a quantity equivalent to 0.200 g of the dried substance in *water R* and dilute to 300 mL with the same solvent. Carry out the complexometric titration of calcium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 21.82 mg of $C_6H_{10}CaO_6$.

01/2008:0469
corrected 6.0

CALCIUM LACTATE TRIHYDRATE

Calcii lactas trihydricus



$C_6H_{10}CaO_6,3H_2O$ M_r 272.3

DEFINITION

Calcium bis(2-hydroxypropanoate) or mixture of calcium (2*R*)-, (2*S*)- and (2*RS*)-2-hydroxypropanoates trihydrates.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline or granular powder.

Solubility: soluble in water, freely soluble in boiling water, very slightly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Loss on drying (see Tests).

B. It gives the reaction of lactates (*2.3.1*).

C. It gives reaction (b) of calcium (*2.3.1*).

TESTS

Solution S. Dissolve 6.2 g (equivalent to 5.0 g of the dried substance) with heating in *carbon dioxide-free water R* prepared from *distilled water R*, allow to cool and dilute to 100 mL with the same solvent.

Appearance of solution. Solution S is not more opalescent than reference suspension II (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *phenolphthalein solution R* and 0.5 mL of *0.01 M hydrochloric acid*. The solution is colourless. Not more than 2.0 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Chlorides (*2.4.4*): maximum 200 ppm.

Dilute 5 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 400 ppm.

Dilute 7.5 mL of solution S to 15 mL with *distilled water R*.

Barium. To 10 mL of solution S add 1 mL of *calcium sulfate solution R*. Allow to stand for 15 min. Any opalescence in the solution is not more intense than that in a mixture of 1 mL of *distilled water R* and 10 mL of solution S.

Iron (*2.4.9*): maximum 50 ppm.

Dilute 4 mL of solution S to 10 mL with *water R*.

Magnesium and alkali salts: maximum 1 per cent.

To 20 mL of solution S add 20 mL of *water R*, 2 g of *ammonium chloride R* and 2 mL of *dilute ammonia R1*. Heat to boiling and rapidly add 40 mL of hot *ammonium oxalate solution R*. Allow to stand for 4 h, dilute to 100.0 mL with *water R* and filter. To 50.0 mL of the filtrate add 0.5 mL of *sulfuric acid R*. Evaporate to dryness and ignite the residue to constant mass at 600 ± 50 °C. The residue weighs a maximum of 5 mg.

Heavy metals (*2.4.8*): maximum 10 ppm.

Dissolve a quantity equivalent to 2.0 g of the dried substance in *water R* and dilute to 20 mL with the same solvent. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Loss on drying (*2.2.32*): 15.0 per cent to 20.0 per cent, determined on 0.500 g by drying in an oven at 125 °C.

ASSAY

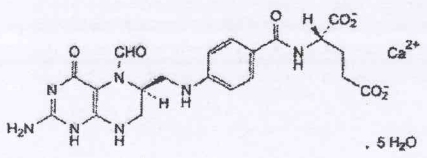
Dissolve a quantity equivalent to 0.200 g of the dried substance in *water R* and dilute to 300 mL with the same solvent. Carry out the complexometric titration of calcium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 21.82 mg of $C_6H_{10}CaO_6$.

01/2008:1606
corrected 7.0

CALCIUM LEVOFOLINATE PENTAHYDRATE

Calcii levofolinas pentahydricus



$C_{20}H_{21}CaN_7O_7,5H_2O$ M_r 511.5 (anhydrous substance)
[80433-71-2]

UNIVERSITÀ DEGLI STUDI DI TORINO

ESAME DI STATO PER L'ABILITAZIONE ALL'ESERCIZIO DELLA PROFESSIONE DI FARMACISTA

PRIMA SESSIONE 2015

PROVA PRATICA: Prova di riconoscimento del farmaco

Cognome e nome.....

La prova consiste nel ***riconoscimento di due farmaci.***

Per ogni farmaco viene fornito il profilo sperimentale (sequenza delle analisi effettuate) ed una indicazione di possibili farmaci candidati corredati dalle rispettive monografie provenienti dalla Farmacopea Europea (Ph. Eur. 8.).

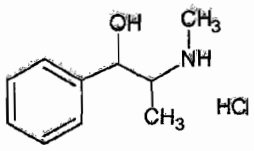
Al candidato viene richiesto di:

- individuare il farmaco che meglio corrisponde al profilo fornito;
- motivare brevemente la propria scelta;
- proporre un'ulteriore prova sperimentale a conferma della scelta effettuata.

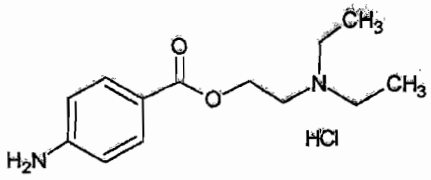
Riconoscimento del farmaco: *primo riconoscimento*

Il farmaco in esame si presenta come una polvere cristallina bianca o quasi bianca ed ha una solubilità in acqua pari a 1 g/ml.
Quando la soluzione acquosa del farmaco acidificata con HNO_3 diluito viene trattata con $AgNO_3$ si origina un precipitato bianco caseoso.

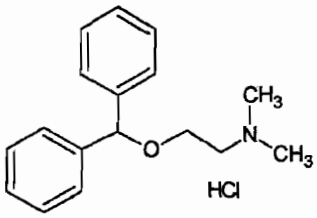
In base a queste caratteristiche ed a tale comportamento sono stati individuati tra i farmaci a disposizione 3 possibili candidati: **efedrina cloridrato, procaina cloridrato, difenidramina cloridrato.**



efedrina cloridrato



procaina cloridrato



difenidramina cloridrato

Tenendo presente che:

- trattando la soluzione del farmaco in questione in HCl diluito con $NaNO_2$ e successivamente con una soluzione di β-naftolo non si osserva alcun cambiamento di colorazione;
- la soluzione acquosa del farmaco in questione non mostra reattività in presenza di $CuSO_4$ in ambiente basico;

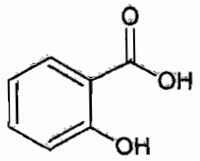
indicare quale farmaco corrisponde al profilo sperimentale fornito motivando brevemente tale scelta e proporre almeno un'ulteriore prova sperimentale per validare la scelta effettuata.

Riconoscimento del farmaco: *secondo riconoscimento*

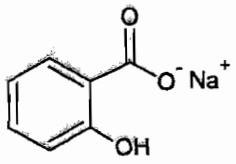
Il farmaco in esame si presenta come polvere cristallina bianca o quasi bianca con una solubilità in acqua pH dipendente (diminuisce a pH acido).

Quando la soluzione del farmaco in NaOH diluito viene trattata con $FeCl_3$ si sviluppa una colorazione violetta che persiste anche dopo aggiunta di CH_3COOH.

In base a queste caratteristiche ed a tale comportamento sono stati individuati tra i farmaci a disposizione 2 possibili candidati: **acido salicilico** e **salicilato sodico.**



acido salicilico



sodio salicilato

Tenendo presente che:

- il farmaco in questione ha una solubilità pari a circa 1 g/l in acqua e che questa risulta decisamente più elevata (circa 1 g/ml) in EtOH

indicare a quale dei due farmaci corrisponde il profilo sperimentale fornito motivando tale scelta e proporre almeno un'ulteriore prova sperimentale per validare la scelta effettuata.

2.3. IDENTIFICATION

01/2008:20301

2.3.1. IDENTIFICATION REACTIONS OF IONS AND FUNCTIONAL GROUPS

ACETATES

a) Heat the substance to be examined with an equal quantity of *oxalic acid R*. Acid vapours with the characteristic odour of acetic acid are liberated, showing an acid reaction (*2.2.4*).

b) Dissolve about 30 mg of the substance to be examined in 3 mL of *water R* or use 3 mL of the prescribed solution. Add successively 0.25 mL of *lanthanum nitrate solution R*, 0.1 mL of *0.05 M iodine* and 0.05 mL of *dilute ammonia R2*. Heat carefully to boiling. Within a few minutes a blue precipitate is formed or a dark blue colour develops.

ACETYL

In a test-tube about 180 mm long and 18 mm in external diameter, place about 15 mg of the substance to be examined, or the prescribed quantity, and 0.15 mL of *phosphoric acid R*. Close the tube with a stopper through which passes a small test-tube about 100 mm long and 10 mm in external diameter containing *water R* to act as a condenser. On the outside of the smaller tube, hang a drop of *lanthanum nitrate solution R*. Except for substances hydrolysable only with difficulty, place the apparatus in a water-bath for 5 min, then take out the smaller tube. Remove the drop and mix it with 0.05 mL of *0.01 M iodine* on a tile. Add at the edge 0.05 mL of *dilute ammonia R2*. After 1 min to 2 min, a blue colour develops at the junction of the two drops; the colour intensifies and persists for a short time.

For *substances hydrolysable only with difficulty* heat the mixture slowly to boiling over an open flame and then proceed as prescribed above.

ALKALOIDS

Dissolve a few milligrams of the substance to be examined, or the prescribed quantity, in 5 mL of *water R*, add *dilute hydrochloric acid R* until an acid reaction occurs (*2.2.4*), then 1 mL of *potassium iodobismuthate solution R*. An orange or orange-red precipitate is formed immediately.

ALUMINIUM

Dissolve about 15 mg of the substance to be examined in 2 mL of *water R* or use 2 mL of the prescribed solution. Add about 0.5 mL of *dilute hydrochloric acid R* and about 0.5 mL of *thioacetamide reagent R*. No precipitate is formed. Add dropwise *dilute sodium hydroxide solution R*. A gelatinous white precipitate is formed which dissolves on further addition of *dilute sodium hydroxide solution R*. Gradually add *ammonium chloride solution R*. The gelatinous white precipitate is re-formed.

AMINES, PRIMARY AROMATIC

Acidify the prescribed solution with *dilute hydrochloric acid R* and add 0.2 mL of *sodium nitrite solution R*. After 1 min to 2 min, add 1 mL of *β-naphthol solution R*. An intense orange or red colour and usually a precipitate of the same colour are produced.

AMMONIUM SALTS

To the prescribed solution add 0.2 g of *magnesium oxide R*. Pass a current of air through the mixture and direct the gas that escapes just beneath the surface of a mixture of 1 mL of *0.1 M hydrochloric acid* and 0.05 mL of *methyl red solution R*. The colour of the indicator changes to yellow. On addition of 1 mL of a freshly prepared 100 g/L solution of *sodium cobaltinitrite R* a yellow precipitate is formed.

AMMONIUM SALTS AND SALTS OF VOLATILE BASES

Dissolve about 20 mg of the substance to be examined in 2 mL of *water R* or use 2 mL of the prescribed solution. Add 2 mL of *dilute sodium hydroxide solution R*. On heating, the solution gives off vapour that can be identified by its odour and by its alkaline reaction (*2.2.4*).

ANTIMONY

Dissolve with gentle heating about 10 mg of the substance to be examined in a solution of 0.5 g of *sodium potassium tartrate R* in 10 mL of *water R* and allow to cool: to 2 mL of this solution, or to 2 mL of the prescribed solution, add *sodium sulfide solution R* dropwise; an orange-red precipitate is formed which dissolves on addition of *dilute sodium hydroxide solution R*.

ARSENIC

Heat 5 mL of the prescribed solution on a water-bath with an equal volume of *hypophosphorous reagent R*. A brown precipitate is formed.

BARBITURATES, NON-NITROGEN SUBSTITUTED

Dissolve about 5 mg of the substance to be examined in 3 mL of *methanol R*, add 0.1 mL of a solution containing 100 g/L of *cobalt nitrate R* and 100 g/L of *calcium chloride R*. Mix and add, with shaking, 0.1 mL of *dilute sodium hydroxide solution R*. A violet-blue colour and precipitate are formed.

BENZOATES

a) To 1 mL of the prescribed solution add 0.5 mL of *ferric chloride solution R1*. A dull-yellow precipitate, soluble in *ether R*, is formed.

b) Place 0.2 g of the substance to be examined, treated if necessary as prescribed, in a test-tube. Moisten with 0.2 mL to 0.3 mL of *sulfuric acid R*. Gently warm the bottom of the tube. A white sublimate is deposited on the inner wall of the tube.

c) Dissolve 0.5 g of the substance to be examined in 10 mL of *water R* or use 10 mL of the prescribed solution. Add 0.5 mL of *hydrochloric acid R*. The precipitate obtained, after crystallisation from warm *water R* and drying *in vacuo*, has a melting point (*2.2.14*) of 120 °C to 124 °C.

BISMUTH

a) To 0.5 g of the substance to be examined add 10 mL of *dilute hydrochloric acid R* or use 10 mL of the prescribed solution. Heat to boiling for 1 min. Cool and filter if necessary. To 1 mL of the solution obtained add 20 mL of *water R*. A white or slightly yellow precipitate is formed which on addition of 0.05 mL to 0.1 mL of *sodium sulfide solution R* turns brown.

b) To about 45 mg of the substance to be examined add 10 mL of *dilute nitric acid R* or use 10 mL of the prescribed solution. Boil for 1 min. Allow to cool and filter if necessary. To 5 mL of the solution obtained add 2 mL of a 100 g/L solution of *thiourea R*. A yellowish-orange colour or an orange precipitate is formed. Add 4 mL of a 25 g/L solution of *sodium fluoride R*. The solution is not decolorised within 30 min.

BROMIDES

a) Dissolve in 2 mL of *water R* a quantity of the substance to be examined equivalent to about 3 mg of bromide (Br^-) or use 2 mL of the prescribed solution. Acidify with *dilute nitric acid R* and add 0.4 mL of *silver nitrate solution R1*. Shake and allow to stand. A curdled, pale yellow precipitate is formed. Centrifuge and wash the precipitate with three quantities, each of 1 mL, of *water R*. Carry out this operation rapidly in subdued light disregarding the fact that the supernatant solution may not become perfectly clear. Suspend the precipitate obtained in 2 mL of *water R* and add 1.5 mL of *ammonia R*. The precipitate dissolves with difficulty.

b) Introduce into a small test-tube a quantity of the substance to be examined equivalent to about 5 mg of bromide (Br^-) or the prescribed quantity. Add 0.25 mL of *water R*, about 75 mg

of *lead dioxide R*, 0.25 mL of *acetic acid R* and shake gently. Dry the inside of the upper part of the test-tube with a piece of filter paper and allow to stand for 5 min. Prepare a strip of suitable filter paper of appropriate size. Impregnate it by capillarity, by dipping the tip in a drop of *decolorised fuchsin solution R* and introduce the impregnated part immediately into the tube. Starting from the tip, a violet colour appears within 10 s that is clearly distinguishable from the red colour of fuchsin, which may be visible on a small area at the top of the impregnated part of the paper strip.

CALCIUM

a) To 0.2 mL of a neutral solution containing a quantity of the substance to be examined equivalent to about 0.2 mg of calcium (Ca^{2+}) per millilitre or to 0.2 mL of the prescribed solution add 0.5 mL of a 2 g/L solution of *glyoxalhydroxyanil R* in *ethanol (96 per cent) R*, 0.2 mL of *dilute sodium hydroxide solution R* and 0.2 mL of *sodium carbonate solution R*. Shake with 1 mL to 2 mL of *chloroform R* and add 1 mL to 2 mL of *water R*. The chloroform layer is coloured red.

b) Dissolve about 20 mg of the substance to be examined or the prescribed quantity in 5 mL of *acetic acid R*. Add 0.5 mL of *potassium ferrocyanide solution R*. The solution remains clear. Add about 50 mg of *ammonium chloride R*. A white, crystalline precipitate is formed.

CARBONATES AND BICARBONATES

Introduce into a test-tube 0.1 g of the substance to be examined and suspend in 2 mL of *water R* or use 2 mL of the prescribed solution. Add 3 mL of *dilute acetic acid R*. Close the tube immediately using a stopper fitted with a glass tube bent twice at right angles. The solution or the suspension becomes effervescent and gives off a colourless and odourless gas. Heat gently and collect the gas in 5 mL of *barium hydroxide solution R*. A white precipitate is formed that dissolves on addition of an excess of *hydrochloric acid R1*.

CHLORIDES

a) Dissolve in 2 mL of *water R* a quantity of the substance to be examined equivalent to about 2 mg of chloride (Cl^-) or use 2 mL of the prescribed solution. Acidify with *dilute nitric acid R* and add 0.4 mL of *silver nitrate solution R1*. Shake and allow to stand. A curdled, white precipitate is formed. Centrifuge and wash the precipitate with three quantities, each of 1 mL, of *water R*. Carry out this operation rapidly in subdued light, disregarding the fact that the supernatant solution may not become perfectly clear. Suspend the precipitate in 2 mL of *water R* and add 1.5 mL of *ammonia R*. The precipitate dissolves easily with the possible exception of a few large particles which dissolve slowly.

b) Introduce into a test-tube a quantity of the substance to be examined equivalent to about 15 mg of chloride (Cl^-) or the prescribed quantity. Add 0.2 g of *potassium dichromate R* and 1 mL of *sulfuric acid R*. Place a filter-paper strip impregnated with 0.1 mL of *diphenylcarbazide solution R* over the opening of the test-tube. The paper turns violet-red. The impregnated paper must not come into contact with the potassium dichromate.

CITRATES

Dissolve in 5 mL of *water R* a quantity of the substance to be examined equivalent to about 50 mg of citric acid or use 5 mL of the prescribed solution. Add 0.5 mL of *sulfuric acid R* and 1 mL of *potassium permanganate solution R*. Warm until the colour of the permanganate is discharged. Add 0.5 mL of a 100 g/L solution of *sodium nitroprusside R* in *dilute sulfuric acid R* and 4 g of *sulfamic acid R*. Make alkaline with *concentrated ammonia R*, added dropwise until all the sulfamic acid has dissolved. Addition of an excess of *concentrated ammonia R* produces a violet colour, turning to violet-blue.

ESTERS

To about 30 mg of the substance to be examined or the prescribed quantity add 0.5 mL of a 70 g/L solution of *hydroxylamine hydrochloride R* in *methanol R* and 0.5 mL of a 100 g/L solution of *potassium hydroxide R* in *ethanol (96 per cent) R*. Heat to boiling, cool, acidify with *dilute hydrochloric acid R* and add 0.2 mL of *ferric chloride solution R1* diluted ten times. A bluish-red or red colour is produced.

IODIDES

a) Dissolve a quantity of the substance to be examined equivalent to about 4 mg of iodide (I^-) in 2 mL of *water R* or use 2 mL of the prescribed solution. Acidify with *dilute nitric acid R* and add 0.4 mL of *silver nitrate solution R1*. Shake and allow to stand. A curdled, pale-yellow precipitate is formed. Centrifuge and wash with three quantities, each of 1 mL, of *water R*. Carry out this operation rapidly in subdued light disregarding the fact that the supernatant solution may not become perfectly clear. Suspend the precipitate in 2 mL of *water R* and add 1.5 mL of *ammonia R*. The precipitate does not dissolve.

b) To 0.2 mL of a solution of the substance to be examined containing about 5 mg of iodide (I^-) per millilitre, or to 0.2 mL of the prescribed solution, add 0.5 mL of *dilute sulfuric acid R*, 0.1 mL of *potassium dichromate solution R*, 2 mL of *water R* and 2 mL of *chloroform R*. Shake for a few seconds and allow to stand. The chloroform layer is coloured violet or violet-red.

IRON

a) Dissolve a quantity of the substance to be examined equivalent to about 10 mg of iron (Fe^{2+}) in 1 mL of *water R* or use 1 mL of the prescribed solution. Add 1 mL of *potassium ferricyanide solution R*. A blue precipitate is formed that does not dissolve on addition of 5 mL of *dilute hydrochloric acid R*.

b) Dissolve a quantity of the substance to be examined equivalent to about 1 mg of iron (Fe^{3+}) in 30 mL of *water R*. To 3 mL of this solution or to 3 mL of the prescribed solution, add 1 mL of *dilute hydrochloric acid R* and 1 mL of *potassium thiocyanate solution R*. The solution is coloured red. Take two portions, each of 1 mL, of the mixture. To one portion add 5 mL of *isoamyl alcohol R* or 5 mL of *ether R*. Shake and allow to stand. The organic layer is coloured pink. To the other portion add 2 mL of *mercuric chloride solution R*. The red colour disappears.

c) Dissolve a quantity of the substance to be examined equivalent to not less than 1 mg of iron (Fe^{3+}) in 1 mL of *water R* or use 1 mL of the prescribed solution. Add 1 mL of *potassium ferrocyanide solution R*. A blue precipitate is formed that does not dissolve on addition of 5 mL of *dilute hydrochloric acid R*.

LACTATES

Dissolve a quantity of the substance to be examined equivalent to about 5 mg of lactic acid in 5 mL of *water R* or use 5 mL of the prescribed solution. Add 1 mL of *bromine water R* and 0.5 mL of *dilute sulfuric acid R*. Heat on a water-bath until the colour is discharged, stirring occasionally with a glass rod. Add 4 g of *ammonium sulfate R* and mix. Add dropwise and without mixing 0.2 mL of a 100 g/L solution of *sodium nitroprusside R* in *dilute sulfuric acid R*. Still without mixing add 1 mL of *concentrated ammonia R*. Allow to stand for 30 min. A dark green ring appears at the junction of the two liquids.

LEAD

a) Dissolve 0.1 g of the substance to be examined in 1 mL of *acetic acid R* or use 1 mL of the prescribed solution. Add 2 mL of *potassium chromate solution R*. A yellow precipitate is formed that dissolves on addition of 2 mL of *strong sodium hydroxide solution R*.

b) Dissolve 50 mg of the substance to be examined in 1 mL of *acetic acid R* or use 1 mL of the prescribed solution. Add 10 mL of *water R* and 0.2 mL of *potassium iodide solution R*. A yellow precipitate is formed. Heat to boiling for 1 min to 2 min. The precipitate dissolves. Allow to cool. The precipitate is re-formed as glistening, yellow plates.

MAGNESIUM

Dissolve about 15 mg of the substance to be examined in 2 mL of *water R* or use 2 mL of the prescribed solution. Add 1 mL of *dilute ammonia R1*. A white precipitate is formed that dissolves on addition of 1 mL of *ammonium chloride solution R*. Add 1 mL of *disodium hydrogen phosphate solution R*. A white crystalline precipitate is formed.

MERCURY

a) Place about 0.1 mL of a solution of the substance to be examined on well-scraped copper foil. A dark-grey stain that becomes shiny on rubbing is formed. Dry the foil and heat in a test-tube. The spot disappears.

b) To the prescribed solution add *dilute sodium hydroxide solution R* until strongly alkaline (*2.2.4*). A dense yellow precipitate is formed (mercuric salts).

NITRATES

To a mixture of 0.1 mL of *nitrobenzene R* and 0.2 mL of *sulfuric acid R*, add a quantity of the powdered substance equivalent to about 1 mg of nitrate (NO_3^-) or the prescribed quantity. Allow to stand for 5 min. Cool in iced water and add slowly and with mixing 5 mL of *water R*, then 5 mL of *strong sodium hydroxide solution R*. Add 5 mL of *acetone R*. Shake and allow to stand. The upper layer is coloured deep violet.

PHOSPHATES (ORTHOPHOSPHATES)

a) To 5 mL of the prescribed solution, neutralised if necessary, add 5 mL of *silver nitrate solution R1*. A yellow precipitate is formed whose colour is not changed by boiling and which dissolves on addition of *ammonia R*.

b) Mix 1 mL of the prescribed solution with 2 mL of *molybdovanadic reagent R*. A yellow colour develops.

POTASSIUM

a) Dissolve 0.1 g of the substance to be examined in 2 mL of *water R* or use 2 mL of the prescribed solution. Add 1 mL of *sodium carbonate solution R* and heat. No precipitate is formed. Add to the hot solution 0.05 mL of *sodium sulfide solution R*. No precipitate is formed. Cool in iced water and add 2 mL of a 150 g/L solution of *tartaric acid R*. Allow to stand. A white crystalline precipitate is formed.

b) Dissolve about 40 mg of the substance to be examined in 1 mL of *water R* or use 1 mL of the prescribed solution. Add 1 mL of *dilute acetic acid R* and 1 mL of a freshly prepared 100 g/L solution of *sodium cobaltinitrite R*. A yellow or orange-yellow precipitate is formed immediately.

SALICYLATES

a) To 1 mL of the prescribed solution add 0.5 mL of *ferric chloride solution R1*. A violet colour is produced that persists after the addition of 0.1 mL of *acetic acid R*.

b) Dissolve 0.5 g of the substance to be examined in 10 mL of *water R* or use 10 mL of the prescribed solution. Add 0.5 mL of *hydrochloric acid R*. The precipitate obtained, after recrystallisation from hot *water R* and drying *in vacuo*, has a melting point (*2.2.14*) of 156 °C to 161 °C.

SILICATES

Mix the prescribed quantity of the substance to be examined in a lead or platinum crucible by means of a copper wire with about 10 mg of *sodium fluoride R* and a few drops of *sulfuric acid R* to give a thin slurry. Cover the crucible with a thin, transparent plate of plastic under which a drop of *water R* is suspended and warm gently. Within a short time a white ring is rapidly formed around the drop of water.

SILVER

Dissolve about 10 mg of the substance to be examined in 10 mL of *water R* or use 10 mL of the prescribed solution. Add 0.3 mL of *hydrochloric acid R1*. A curdled, white precipitate is formed that dissolves on addition of 3 mL of *dilute ammonia R1*.

SODIUM

a) Dissolve 0.1 g of the substance to be examined in 2 mL of *water R* or use 2 mL of the prescribed solution. Add 2 mL of a 150 g/L solution of *potassium carbonate R* and heat to boiling. No precipitate is formed. Add 4 mL of *potassium pyroantimonate solution R* and heat to boiling. Allow to cool in iced water and if necessary rub the inside of the test-tube with a glass rod. A dense white precipitate is formed.

b) Dissolve a quantity of the substance to be examined equivalent to about 2 mg of sodium (Na^+) in 0.5 mL of *water R* or use 0.5 mL of the prescribed solution. Add 1.5 mL of *methoxyphenylacetic reagent R* and cool in ice-water for 30 min. A voluminous, white, crystalline precipitate is formed. Place in water at 20 °C and stir for 5 min. The precipitate does not disappear. Add 1 mL of *dilute ammonia R1*. The precipitate dissolves completely. Add 1 mL of *ammonium carbonate solution R*. No precipitate is formed.

SULFATES

a) Dissolve about 45 mg of the substance to be examined in 5 mL of *water R* or use 5 mL of the prescribed solution. Add 1 mL of *dilute hydrochloric acid R* and 1 mL of *barium chloride solution R1*. A white precipitate is formed.

b) To the suspension obtained during reaction (a), add 0.1 mL of *0.05 M iodine*. The suspension remains yellow (distinction from sulfites and dithionites), but is decolorised by adding dropwise *stannous chloride solution R* (distinction from iodates). Boil the mixture. No coloured precipitate is formed (distinction from selenates and tungstates).

TARTRATES

a) Dissolve about 15 mg of the substance to be examined in 5 mL of *water R* or use 5 mL of the prescribed solution. Add 0.05 mL of a 10 g/L solution of *ferrous sulfate R* and 0.05 mL of *dilute hydrogen peroxide solution R*. A transient yellow colour is produced. After the colour has disappeared add *dilute sodium hydroxide solution R* dropwise. A violet or purple colour is produced.

b) To 0.1 mL of a solution of the substance to be examined containing the equivalent of about 15 mg of tartaric acid per millilitre or to 0.1 mL of the prescribed solution add 0.1 mL of a 100 g/L solution of *potassium bromide R*, 0.1 mL of a 20 g/L solution of *resorcinol R* and 3 mL of *sulfuric acid R*. Heat on a water-bath for 5 min to 10 min. A dark-blue colour develops. Allow to cool and pour the solution into *water R*. The colour changes to red.

XANTHINES

To a few milligrams of the substance to be examined or the prescribed quantity add 0.1 mL of *strong hydrogen peroxide solution R* and 0.3 mL of *dilute hydrochloric acid R*. Heat to dryness on a water-bath until a yellowish-red residue is obtained. Add 0.1 mL of *dilute ammonia R2*. The colour of the residue changes to violet-red.

ZINC

Dissolve 0.1 g of the substance to be examined in 5 mL of *water R* or use 5 mL of the prescribed solution. Add 0.2 mL of *strong sodium hydroxide solution R*. A white precipitate is formed. Add a further 2 mL of *strong sodium hydroxide solution R*. The precipitate dissolves. Add 10 mL of *ammonium chloride solution R*. The solution remains clear. Add 0.1 mL of *sodium sulfide solution R*. A flocculent white precipitate is formed.

Solubility. In statements of solubility in the Characters section, the terms used have the following significance, referred to a temperature between 15 °C and 25 °C.

Descriptive term	Approximate volume of solvent in millilitres per gram of solute		
Very soluble	less than 1		
Freely soluble	from 1	to	10
Soluble	from 10	to	30
Sparingly soluble	from 30	to	100
Slightly soluble	from 100	to	1000
Very slightly soluble	from 1000	to	10 000
Practically insoluble	more than		10 000

The term 'partly soluble' is used to describe a mixture where only some of the components dissolve. The term 'miscible' is used to describe a liquid that is miscible in all proportions with the stated solvent.

IDENTIFICATION

Scope. The tests given in the Identification section are not designed to give a full confirmation of the chemical structure or composition of the product; they are intended to give confirmation, with an acceptable degree of assurance, that the article conforms to the description on the label.

First and second identifications. Certain monographs have subdivisions entitled 'First identification' and 'Second identification'. The test or tests that constitute the 'First identification' may be used in all circumstances. The test or tests that constitute the 'Second identification' may be used in pharmacies provided it can be demonstrated that the substance or preparation is fully traceable to a batch certified to comply with all the other requirements of the monograph.

Certain monographs give two or more sets of tests for the purpose of the first identification, which are equivalent and may be used independently. One or more of these sets usually contain a cross-reference to a test prescribed in the Tests section of the monograph. It may be used to simplify the work of the analyst carrying out the identification and the prescribed tests. For example, one identification set cross-refers to a test for enantiomeric purity while the other set gives a test for specific optical rotation: the intended purpose of the two is the same, that is, verification that the correct enantiomer is present.

Powdered herbal drugs. Monographs on herbal drugs may contain schematic drawings of the powdered drug. These drawings complement the description given in the relevant identification test.

TESTS AND ASSAYS

Scope. The requirements are not framed to take account of all possible impurities. It is not to be presumed, for example, that an impurity that is not detectable by means of the prescribed tests is tolerated if common sense and good pharmaceutical practice require that it be absent. See also below under Impurities.

Calculation. Where the result of a test or assay is required to be calculated with reference to the dried or anhydrous substance or on some other specified basis, the determination of loss on drying, water content or other property is carried out by the method prescribed in the relevant test in the monograph. The words 'dried substance' or 'anhydrous substance' etc. appear in parentheses after the result. Where a quantitative determination of a residual solvent is carried out and a test for loss on drying is not carried out, the content of residual solvent is taken into account for the calculation of the assay content of the substance, the specific optical rotation and the specific absorbance. No further indication is given in the specific monograph.

Limits. The limits prescribed are based on data obtained in normal analytical practice; they take account of normal analytical errors, of acceptable variations in manufacture and compounding and of deterioration to an extent considered acceptable. No further tolerances are to be applied to the limits prescribed to determine whether the article being examined complies with the requirements of the monograph.

In determining compliance with a numerical limit, the calculated result of a test or assay is first rounded to the number of significant figures stated, unless otherwise prescribed. The limits, regardless of whether the values are expressed as percentages or as absolute values, are considered significant to the last digit shown (for example 140 indicates 3 significant figures). The last figure of the result is increased by one when the part rejected is equal to or exceeds one half-unit, whereas it is not modified when the part rejected is less than a half-unit.

Indication of permitted limit of impurities. The acceptance criteria for related substances are expressed in monographs either in terms of comparison of peak areas (comparative tests) or as numerical values. For comparative tests, the approximate content of impurity tolerated, or the sum of impurities, may be indicated in brackets for information only. Acceptance or rejection is determined on the basis of compliance or non-compliance with the stated test. If the use of a reference substance for the named impurity is not prescribed, this content may be expressed as a nominal concentration of the substance used to prepare the reference solution specified in the monograph, unless otherwise described.

Herbal drugs. For herbal drugs, the sulfated ash, total ash, water-soluble matter, alcohol-soluble matter, water content, content of essential oil and content of active principle are calculated with reference to the drug that has not been specially dried, unless otherwise prescribed in the monograph.

Equivalents. Where an equivalent is given, for the purposes of the Pharmacopoeia only the figures shown are to be used in applying the requirements of the monograph.

Culture media. The culture media described in monographs and general chapters have been found to be satisfactory for the intended purpose. However, the components of media, particularly those of biological origin, are of variable quality, and it may be necessary for optimal performance to modulate the concentration of some ingredients, notably:

- peptones and meat or yeast extracts, with respect to their nutritive properties;
- buffering substances;
- bile salts, bile extract, deoxycholate, and colouring matter, depending on their selective properties;
- antibiotics, with respect to their activity.

STORAGE

The information and recommendations given under the heading Storage do not constitute a pharmacopoeial requirement but the competent authority may specify particular storage conditions that must be met.

The articles described in the Pharmacopoeia are stored in such a way as to prevent contamination and, as far as possible, deterioration. Where special conditions of storage are recommended, including the type of container (see section 1.3. General chapters) and limits of temperature, they are stated in the monograph.

The following expressions are used in monographs under Storage with the meaning shown.

In an airtight container means that the product is stored in an airtight container (3.2). Care is to be taken when the container is opened in a damp atmosphere. A low moisture content may be maintained, if necessary, by the use of a desiccant in the container provided that direct contact with the product is avoided.

Sulfates (*2.4.13*): maximum 300 ppm.

To 25 mL of solution S, add 5 mL of *distilled water R* and 10 mL of *hydrochloric acid R* and dilute to 50 mL with *distilled water R*. Shake and filter. Dilute 10 mL of the filtrate to 15 mL with *distilled water R*.

Heavy metals (*2.4.8*): maximum 10 ppm.

2.0 g complies with test C. Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Water (*2.5.12*): maximum 5.0 per cent, determined on 0.500 g.

ASSAY

Liquid chromatography (*2.2.29*) as described in the test for related substances with the following modification.

Injection: test solution and reference solution (b).

Calculate the percentage content of $C_{10}H_{11}NaO_3$ from the declared content of *propyl parahydroxybenzoate CRS*, multiplied by a correction factor of 1.122.

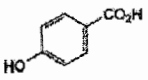
STORAGE

In an airtight container.

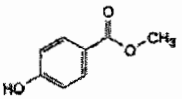
IMPURITIES

Specified impurities: *A*.

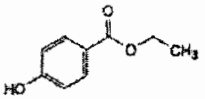
Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): *B, C, D*.



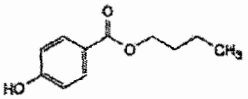
A. 4-hydroxybenzoic acid,



B. methyl 4-hydroxybenzoate (methyl parahydroxybenzoate),



C. ethyl 4-hydroxybenzoate (ethyl parahydroxybenzoate),

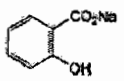


D. butyl 4-hydroxybenzoate (butyl parahydroxybenzoate).

01/2008:0413
corrected 6.0

SODIUM SALICYLATE

Natrii salicylas



$C_7H_5NaO_3$ M_r 160.1
[54-21-7]

DEFINITION

Sodium 2-hydroxybenzenecarboxylate.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder or small, colourless crystals or shiny flakes.

Solubility: freely soluble in water, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: *A, C*.

Second identification: *B, C*.

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *sodium salicylate CRS*.

B. Solution S (see Tests) gives the reactions of salicylates (*2.3.1*).

C. It gives reaction (b) of sodium (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 50 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Acidity. To 20 mL of solution S add 0.1 mL of *phenol red solution R*. The solution is yellow. Not more than 2.0 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to violet-red.

Chlorides (*2.4.4*): maximum 200 ppm.

To 5 mL of solution S add 5 mL of *water R* and 10 mL of *dilute nitric acid R* and filter. Dilute 10 mL of the filtrate to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 600 ppm.

Dilute 2.5 mL of solution S to 15 mL with *distilled water R*.

Heavy metals (*2.4.8*): maximum 20 ppm.

Dissolve 1.6 g in 16 mL of a mixture of 5 volumes of *water R* and 10 volumes of *ethanol (96 per cent) R*. 12 mL of the solution complies with test B. Prepare the reference solution using lead standard solution (2 ppm Pb) obtained by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 5 volumes of *water R* and 10 volumes of *ethanol (96 per cent) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.00 g by drying in an oven at 105 °C.

ASSAY

Dissolve 0.130 g in 30 mL of *anhydrous acetic acid R*. Titrate with *0.1 M perchloric acid*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M perchloric acid* is equivalent to 16.01 mg of $C_7H_5NaO_3$.

STORAGE

In an airtight container, protected from light.

01/2008:1677

SODIUM SELENITE PENTAHYDRATE

Natrii selenis pentahydricus

$Na_2SeO_3,5H_2O$ M_r 263.0
[26970-82-1]

DEFINITION

Content: 98.5 per cent to 101.5 per cent.

CHARACTERS

Appearance: white or almost white, crystalline powder, hygroscopic.

- *impurity C*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (f) (0.02 per cent);
- *any other impurity*: for each impurity, not more than the area of the peak due to impurity B in the chromatogram obtained with reference solution (f) (0.05 per cent);
- *total*: not more than twice the area of the peak due to impurity A in the chromatogram obtained with reference solution (f) (0.2 per cent);
- *disregard limit*: 0.01 times the area of the principal peak in the chromatogram obtained with reference solution (f).

Chlorides (*2.4.4*): maximum 100 ppm.

Dilute 10 mL of solution S to 15 mL with *water R*.

Sulfates: maximum 200 ppm.

Dissolve 1.0 g in 5 mL of *dimethylformamide R* and add 4 mL of *water R*. Mix thoroughly. Add 0.2 mL of *dilute hydrochloric acid R* and 0.5 mL of a 25 per cent *m/m* solution of *barium chloride R*. After 15 min any opalescence in the solution is not more intense than that in a standard prepared as follows: to 2 mL of *sulfate standard solution (100 ppm SO_4) R* add 0.2 mL of *dilute hydrochloric acid R*, 0.5 mL of a 25 per cent *m/m* solution of *barium chloride R*, 3 mL of *water R* and 5 mL of *dimethylformamide R*.

Heavy metals (*2.4.8*): maximum 20 ppm.

Dissolve 2.0 g in 15 mL of *ethanol (96 per cent) R* and add 5 mL of *water R*. 12 mL of the solution complies with test B. Prepare the reference solution using lead standard solution (2 ppm Pb) prepared by diluting *lead standard solution (100 ppm Pb) R* with a mixture of 5 volumes of *water R* and 15 volumes of *ethanol (96 per cent) R*.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in a desiccator.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 2.0 g.

ASSAY

Dissolve 0.120 g in 30 mL of *ethanol (96 per cent) R* and add 20 mL of *water R*. Titrate with *0.1 M sodium hydroxide*, using 0.1 mL of *phenol red solution R* as indicator.

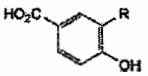
1 mL of *0.1 M sodium hydroxide* is equivalent to 13.81 mg of $C_7H_6O_3$.

STORAGE

Protected from light.

IMPURITIES

Specified impurities: A, B, C.



A. R = H: 4-hydroxybenzoic acid,

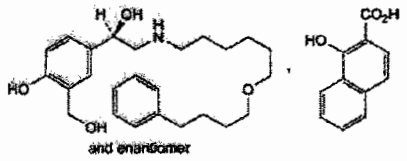
B. R = CO_2H: 4-hydroxyisophthalic acid,

C. phenol.

01/2008:1765

SALMETEROL XINAFOATE

Salmeteroli xinafoas



$C_{36}H_{45}NO_7$ M_r 604
[94749-08-3]

DEFINITION

(1*RS*)-1-[4-Hydroxy-3-(hydroxymethyl)phenyl]-2-[[6-(4-phenylbutoxy)hexyl]amino]ethanol 1-hydroxynaphthalene-2-carboxylate.

Content: 97.0 per cent to 102.0 per cent (anhydrous substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water, soluble in methanol, slightly soluble in anhydrous ethanol.

IDENTIFICATION

Infrared absorption spectrophotometry (*2.2.24*).

Comparison: salmeterol xinafoate CRS.

TESTS

Related substances. Liquid chromatography (*2.2.29*). *Protect the solutions from light.*

Solvent mixture: acetonitrile R, water R (50:50 *V/V*).

Test solution. Dissolve 50.0 mg of the substance to be examined in the solvent mixture and dilute to 10.0 mL with the solvent mixture.

Reference solution (a). Dissolve 11 mg of *salmeterol xinafoate for system suitability CRS* (salmeterol containing impurities E and G) in the solvent mixture and dilute to 2 mL with the solvent mixture.

Reference solution (b). Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

Column:

- *size*: *l* = 0.15 m, Ø = 4.6 mm,
- *stationary phase: octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase:

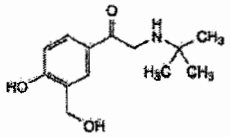
- *mobile phase A*: mix 24 volumes of a 7.71 g/L solution of *ammonium acetate R* with 24 volumes of a 28.84 g/L solution of *sodium dodecyl sulfate R* and adjust to pH 2.7 with *glacial acetic acid R*; mix with 52 volumes of *acetonitrile R*;
- *mobile phase B: acetonitrile R*;

Time (min)	Mobile phase A (per cent *V/V*)	Mobile phase B (per cent *V/V*)
0 - 16	100	0
16 - 36	100 → 30	0 → 70
36 - 45	30	70
45 - 50	30 → 100	70 → 0

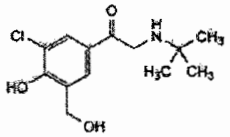
Flow rate: 2 mL/min.

Detection: spectrophotometer at 278 nm.

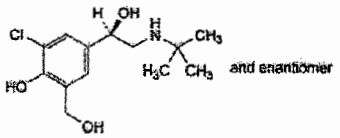
Injection: 20 µL; inject the solvent mixture as a blank solution.



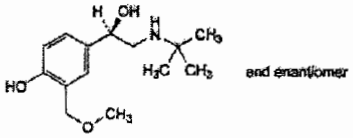
J. 2-[(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(hydroxymethyl)phenyl]ethanone (salbutamone),



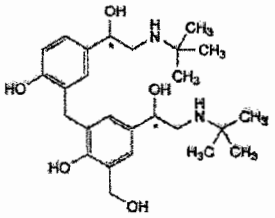
K. 2-[(1,1-dimethylethyl)amino]-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl]ethanone,



L. (1*RS*)-2-[(1,1-dimethylethyl)amino]-1-[3-chloro-4-hydroxy-5-(hydroxymethyl)phenyl]ethanol,



M. (1*RS*)-2-[(1,1-dimethylethyl)amino]-1-[4-hydroxy-3-(methoxymethyl)phenyl]ethanol,



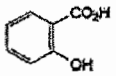
N. 2-[(1,1-dimethylethyl)amino]-1-[3-[[5-[2-[(1,1-dimethylethyl)amino]-1-hydroxyethyl]-2-hydroxyphenyl]methyl]-4-hydroxy-5-(hydroxymethyl)phenyl]-ethanol,

O. unknown structure.

01/2008:0366
corrected 6.0

SALICYLIC ACID

Acidum salicylicum



$C_7H_6O_3$ M_r 138.1
[69-72-7]

DEFINITION

2-Hydroxybenzenecarboxylic acid.

Content: 99.0 per cent to 100.5 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder or white or colourless, acicular crystals.

Solubility: slightly soluble in water, freely soluble in ethanol (96 per cent), sparingly soluble in methylene chloride.

IDENTIFICATION

First identification: A, B.

Second identification: A, C.

A. Melting point (*2.2.14*): 158 °C to 161 °C.

B. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *salicylic acid CRS*.

C. Dissolve about 30 mg in 5 mL of *0.05 M sodium hydroxide*, neutralise if necessary and dilute to 20 mL with *water R*. 1 mL of the solution gives reaction (a) of salicylates (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in 50 mL of boiling *distilled water R*, cool and filter.

Appearance of solution. The solution is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Dissolve 1 g in 10 mL of *ethanol (96 per cent) R*.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 0.50 g of the substance to be examined in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (a). Dissolve 10 mg of *phenol R* (impurity C) in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (b). Dissolve 5 mg of *salicylic acid impurity B CRS* in the mobile phase and dilute to 20.0 mL with the mobile phase.

Reference solution (c). Dissolve 50 mg of *4-hydroxybenzoic acid R* (impurity A) in the mobile phase and dilute to 100.0 mL with the mobile phase.

Reference solution (d). Dilute 1.0 mL of reference solution (a) to 10.0 mL with the mobile phase.

Reference solution (e). Dilute a mixture of 1.0 mL of each of reference solutions (a), (b) and (c) to 10.0 mL with the mobile phase.

Reference solution (f). Dilute a mixture of 0.1 mL of each of reference solutions (a), (b) and (c) to 10.0 mL with the mobile phase.

Column:
- *size*: *l* = 0.15 m, Ø = 4.6 mm;
- *stationary phase*: non-deactivated *octadecylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: *glacial acetic acid R, methanol R, water R* (1:40:60 *V/V/V*).

Flow rate: 0.5 mL/min.

Detection: spectrophotometer at 270 nm.

Injection: 10 µL of the test solution and reference solutions (d), (e) and (f).

Relative retention with reference to impurity C: impurity A = about 0.70; impurity B = about 0.90.

System suitability: reference solution (e):
- the 3rd peak in the chromatogram corresponds to the peak due to phenol in the chromatogram obtained with reference solution (d);
- *resolution*: minimum 1.0 between the peaks due to impurities B and C; if necessary, adjust the quantity of acetic acid in the mobile phase.

Limits:
- *impurity A*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (f) (0.1 per cent);
- *impurity B*: not more than the area of the corresponding peak in the chromatogram obtained with reference solution (f) (0.05 per cent);

phase. Dilute 2.0 mL of the solution to 10.0 mL with the mobile phase.

Reference solution (a). Dilute 1.0 mL of the test solution to 10.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 20.0 mL with the mobile phase.

Reference solution (b). Dissolve 5 mg of *diphenhydramine impurity A CRS* and 5 mg of *diphenylmethanol R* in the mobile phase and dilute to 10.0 mL with the mobile phase. To 2.0 mL of this solution add 1.5 mL of the test solution and dilute to 10.0 mL with the mobile phase.

Column:

- *size*: *l* = 0.25 m, Ø = 4.6 mm,
- *stationary phase*: *base-deactivated octylsilyl silica gel for chromatography R* (5 µm).

Mobile phase: mix 35 volumes of *acetonitrile R* and 65 volumes of a 5.4 g/L solution of *potassium dihydrogen phosphate R* adjusted to pH 3.0 using *phosphoric acid R*.

Flow rate: 1.2 mL/min.

Detection: spectrophotometer at 220 nm.

Injection: 10 µL.

Run time: 7 times the retention time of diphenhydramine.

Relative retention with reference to diphenhydramine (retention time = about 6 min): impurity A = about 0.9; impurity B = about 1.5; impurity C = about 1.8; impurity D = about 2.6; impurity E = about 5.1.

System suitability: reference solution (b):

- *resolution*: minimum 2.0 between the peaks due to diphenhydramine and to impurity A.

Limits:

- *correction factor*: for the calculation of content, multiply the peak area of impurity D by 0.7,
- *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent),
- *any other impurity*: not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.3 per cent),
- *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (1.0 per cent),
- *disregard limit*: 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.250 g in 50 mL of *alcohol R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

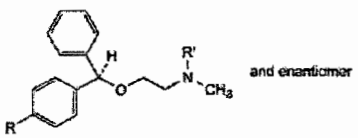
1 mL of *0.1 M sodium hydroxide* is equivalent to 29.18 mg of $C_{17}H_{22}ClNO$.

STORAGE

Protected from light.

IMPURITIES

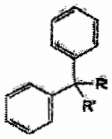
Specified impurities: *A, B, C, D, E.*



A. R = R′ = H: 2-(diphenylmethoxy)-*N*-methylethanamine,

B. R = R′ = CH_3: 2-[(*RS*)-(4-methylphenyl)phenylmethoxy]-*N*,*N*-dimethylethanamine,

C. R = Br, R′ = CH_3: 2-[(*RS*)-(4-bromophenyl)phenylmethoxy]-*N*,*N*-dimethylethanamine,



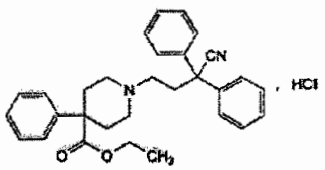
D. R = OH, R′ = H: diphenylmethanol (benzhydrol),

E. R + R′ = O: diphenylmethanone (benzophenone).

04/2012:0819

DIPHENOXYLATE HYDROCHLORIDE

Diphenoxylati hydrochloridum



$C_{30}H_{33}ClN_2O_2$ M_r 489.1
[3810-80-8]

DEFINITION

Ethyl 1-(3-cyano-3,3-diphenylpropyl)-4-phenylpiperidine-4-carboxylate hydrochloride.

Content: 98.0 per cent to 102.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very slightly soluble in water, freely soluble in methylene chloride, sparingly soluble in ethanol (96 per cent).

IDENTIFICATION

A. Infrared absorption spectrophotometry (*2.2.24*).
Comparison: *diphenoxylate hydrochloride CRS.*

B. Dissolve about 30 mg in 5 mL of *methanol R*. Add 0.25 mL of *nitric acid R* and 0.4 mL of *silver nitrate solution R1*. Shake and allow to stand. A curdled precipitate is formed. Centrifuge and rinse the precipitate with 3 quantities, each of 2 mL, of *methanol R*. Carry out this operation rapidly and protected from bright light. Suspend the precipitate in 2 mL of *water R* and add 1.5 mL of *ammonia R*. The precipitate dissolves easily.

TESTS

Appearance of solution. The solution is clear (*2.2.1*) and not more intensely coloured than reference solution Y_6 (*2.2.2, Method II*).

Dissolve 1.0 g in *methylene chloride R* and dilute to 10 mL with the same solvent.

Related substances. Liquid chromatography (*2.2.29*).

Solution A. Adjust 900 mL of *water R* to pH 2.3 with *phosphoric acid R* and dilute to 1000.0 mL with *water R*.

Solvent mixture: *acetonitrile R1*, solution A (50:50 *V/V*).

Test solution. Dissolve 25 mg of the substance to be examined in 20 mL of the solvent mixture, sonicate for 2 min, cool and dilute to 25.0 mL with the solvent mixture.

Reference solution (a). Dilute 1.0 mL of the test solution to 100.0 mL with the solvent mixture. Dilute 1.0 mL of this solution to 10.0 mL with the solvent mixture.

- *impurity F*: not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (b) (3 per cent),
- *any other impurity*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent),
- *total of other impurities and impurity A*: not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (b) (1 per cent),
- *total*: not more than twice the area of the principal peak in the chromatogram obtained with reference solution (b) (10 per cent),
- *disregard limit*: 0.02 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.1 per cent).

Heavy metals (*2.4.8*): maximum 20 ppm.

2.0 g complies with test C. Prepare the reference solution using 4.0 mL of *lead standard solution (10 ppm Pb) R*.

Water (*2.5.12*): maximum 6.0 per cent, determined on 0.300 g.

Sulfated ash (*2.4.14*): maximum 0.2 per cent, determined on 1.0 g.

ASSAY

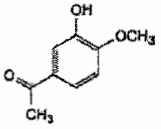
Liquid chromatography (*2.2.29*), as described in the test for related substances.

Injection: test solution and reference solution (a).

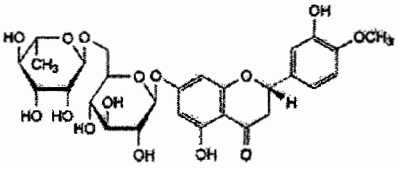
STORAGE

In an airtight container.

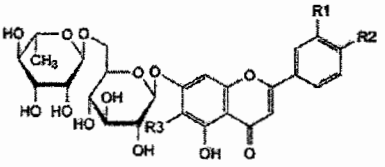
IMPURITIES



A. 1-(3-hydroxy-4-methoxyphenyl)ethanone (acetoisovanillone),



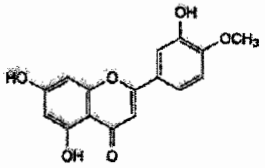
B. (2*S*)-7-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-2,3-dihydro-4*H*-1-benzopyran-4-one (hesperidin),



C. R1 = R3 = H, R2 = OH: 7-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(4-hydroxyphenyl)-4*H*-1-benzopyran-4-one (isorhoifolin),

D. R1 = OH, R2 = OCH_3, R3 = I: 7-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(3-hydroxy-4-methoxyphenyl)-6-iodo-4*H*-1-benzopyran-4-one (6-iododiosmin),

E. R1 = R3 = H, R2 = OCH_3: 7-[[6-*O*-(6-deoxy-α-L-mannopyranosyl)-β-D-glucopyranosyl]oxy]-5-hydroxy-2-(4-methoxyphenyl)-4*H*-1-benzopyran-4-one (linarin),

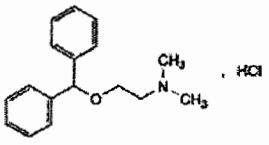


F. 5,7-dihydroxy-2-(3-hydroxy-4-methoxyphenyl)-4*H*-1-benzopyran-4-one (diosmetin).

01/2008:0023
corrected 6.0

DIPHENHYDRAMINE HYDROCHLORIDE

Diphenhydramini hydrochloridum



$C_{17}H_{22}ClNO$ M_r 291.8
[147-24-0]

DEFINITION

2-(Diphenylmethoxy)-*N*,*N*-dimethylethanamine hydrochloride.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: very soluble in water, freely soluble in alcohol.

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D.

A. Melting point (*2.2.14*): 168 °C to 172 °C.

B. Dissolve 50 mg in *alcohol R* and dilute to 100.0 mL with the same solvent. Examined between 230 nm and 350 nm, the solution shows 3 absorption maxima (*2.2.25*), at 253 nm, 258 nm and 264 nm. The ratio of the absorbance measured at the maximum at 258 nm to that measured at the maximum at 253 nm is 1.1 to 1.3. The ratio of the absorbance measured at the maximum at 258 nm to that measured at the maximum at 264 nm is 1.2 to 1.4.

C. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs.

Comparison: *diphenhydramine hydrochloride CRS*.

D. It gives the reactions of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 1.0 g in *carbon dioxide-free water R* and dilute to 20 mL with the same solvent.

Appearance of solution. Solution S and a fivefold dilution of solution S are clear (*2.2.1*). Solution S is not more intensely coloured than reference solution BY_6 (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.15 mL of *methyl red solution R* and 0.25 mL of *0.01 M hydrochloric acid*. The solution is pink. Not more than 0.5 mL of *0.01 M sodium hydroxide* is required to change the colour of the indicator to yellow.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 70 mg of the substance to be examined in the mobile phase and dilute to 20.0 mL with the mobile

ASSAY

Dissolve 0.150 g in 50 mL of *ethanol (96 per cent) R* and add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the 2 points of inflexion.

1 mL of *0.1 M sodium hydroxide* is equivalent to 20.17 mg of $C_{10}H_{16}ClNO$.

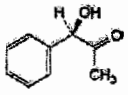
STORAGE

Protected from light.

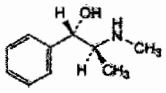
IMPURITIES

Specified impurities: A.

Other detectable impurities (the following substances would, if present at a sufficient level, be detected by one or other of the tests in the monograph. They are limited by the general acceptance criterion for other/unspecified impurities and/or by the general monograph *Substances for pharmaceutical use (2034)*. It is therefore not necessary to identify these impurities for demonstration of compliance. See also *5.10. Control of impurities in substances for pharmaceutical use*): B.



A. (–)-(1*R*)-1-hydroxy-1-phenylpropan-2-one,

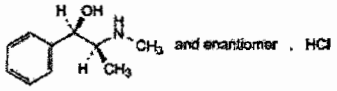


B. (1*S*,2*S*)-2-(methylamino)-1-phenylpropan-1-ol (pseudoephedrine).

01/2008:0715
corrected 6.0

EPHEDRINE HYDROCHLORIDE, RACEMIC

Ephedrini racemici hydrochloridum



$C_{10}H_{16}ClNO$ M_r 201.7
[134-71-4]

DEFINITION

Racemic ephedrine hydrochloride contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of (1*RS*,2*SR*)-2-(methylamino)-1-phenylpropan-1-ol hydrochloride, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, freely soluble in water, soluble in ethanol (96 per cent).

It melts at about 188 °C.

IDENTIFICATION

First identification: B, E.

Second identification: A, C, D, E.

A. Optical rotation (see Tests).

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *racemic ephedrine hydrochloride CRS*. Examine the substances prepared as discs.

C. Examine the chromatograms obtained in the test for related substances. The principal spot in the chromatogram obtained with test solution (b) is similar in position, colour and size to the principal spot in the chromatogram obtained with reference solution (a).

D. To 0.1 mL of solution S (see Tests) add 1 mL of *water R*, 0.2 mL of *copper sulfate solution R* and 1 mL of *strong sodium hydroxide solution R*. A violet colour is produced. Add 2 mL of *ether R* and shake. The ether layer is purple and the aqueous layer is blue.

E. To 5 mL of solution S add 5 mL of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 5.00 g in *distilled water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *methyl red solution R* and 0.1 mL of *0.01 M sodium hydroxide*; the solution is yellow. Add 0.2 mL of *0.01 M hydrochloric acid*; the solution is red.

Optical rotation (*2.2.7*): + 0.2° to – 0.2°, determined on solution S.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel G R* as the coating substance.

Test solution (a). Dissolve 0.20 g of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Test solution (b). Dilute 1 mL of test solution (a) to 10 mL with *methanol R*.

Reference solution (a). Dissolve 20 mg of *racemic ephedrine hydrochloride CRS* in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution (b). Dilute 1 mL of test solution (a) to 200 mL with *methanol R*.

Apply separately to the plate 10 µL of each solution. Develop over a path of 15 cm using a mixture of 5 volumes of *chloroform R*, 15 volumes of *concentrated ammonia R* and 80 volumes of *2-propanol R*. Allow the plate to dry in air. Spray with *ninhydrin solution R* and heat at 110 °C for 5 min. Any spot in the chromatogram obtained with test solution (a), apart from the principal spot, is not more intense than the spot in the chromatogram obtained with reference solution (b) (0.5 per cent). Disregard any spot of lighter colour than the background.

Sulfates (*2.4.13*). 15 mL of solution S complies with the limit test for sulfates (100 ppm).

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.170 g in 30 mL of *ethanol (96 per cent) R*. Add 5.0 mL of *0.01 M hydrochloric acid*. Carry out a potentiometric titration (*2.2.20*), using *0.1 M sodium hydroxide*. Read the volume added between the two points of inflexion.

1 mL of *0.1 M sodium hydroxide* corresponds to 20.17 mg of $C_{10}H_{16}ClNO$.

STORAGE

Store protected from light.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g in 5 mL of *alcohol R* and add 20.0 mL of *0.1 M hydrochloric acid*. Using 0.05 mL of *methyl red solution R* as indicator, titrate with *0.1 M sodium hydroxide* until a yellow colour is obtained.

1 mL of *0.1 M hydrochloric acid* is equivalent to 16.52 mg of $C_{10}H_{15}NO$.

STORAGE

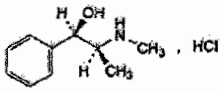
Store protected from light.

01/2008:0487
corrected 6.0

Monographs D-E

EPHEDRINE HYDROCHLORIDE

Ephedrini hydrochloridum



$C_{10}H_{16}ClNO$ M_r 201.7
[50-98-6]

DEFINITION

(1*R*,2*S*)-2-(Methylamino)-1-phenylpropan-1-ol hydrochloride.

Content: 99.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, crystalline powder or colourless crystals.

Solubility: freely soluble in water, soluble in ethanol (96 per cent).

mp: about 219 °C.

IDENTIFICATION

First identification: *B, E.*

Second identification: *A, C, D, E.*

A. Specific optical rotation (see Tests).

B. Infrared absorption spectrophotometry (*2.2.24*).

Comparison: *ephedrine hydrochloride CRS.*

C. Thin-layer chromatography (*2.2.27*).

Test solution. Dissolve 20 mg of the substance to be examined in *methanol R* and dilute to 10 mL with the same solvent.

Reference solution. Dissolve 10 mg of *ephedrine hydrochloride CRS* in *methanol R* and dilute to 5 mL with the same solvent.

Plate: *TLC silica gel plate R.*

Mobile phase: *methylene chloride R, concentrated ammonia R, 2-propanol R* (5:15:80 *V/V/V*).

Application: 10 µL.

Development: over 2/3 of the plate.

Drying: in air.

Detection: spray with *ninhydrin solution R*; heat at 110 °C for 5 min.

Results: the principal spot in the chromatogram obtained with the test solution is similar in position, colour and size to the principal spot in the chromatogram obtained with the reference solution.

D. To 0.1 mL of solution S (see Tests) add 1 mL of *water R*, 0.2 mL of *copper sulfate solution R* and 1 mL of *strong sodium hydroxide solution R*. A violet colour is produced. Add 2 mL of *methylene chloride R* and shake. The lower (organic) layer is dark grey and the upper (aqueous) layer is blue.

E. To 5 mL of solution S (see Tests) add 5 mL of *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

TESTS

Solution S. Dissolve 5.00 g in *distilled water R* and dilute to 50.0 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

Acidity or alkalinity. To 10 mL of solution S add 0.1 mL of *methyl red solution R* and 0.2 mL of *0.01 M sodium hydroxide*. The solution is yellow. Add 0.4 mL of *0.01 M hydrochloric acid*. The solution is red.

Specific optical rotation (*2.2.7*): − 33.5 to − 35.5 (dried substance).

Dilute 12.5 mL of solution S to 25.0 mL with *water R*.

Related substances. Liquid chromatography (*2.2.29*).

Test solution. Dissolve 75 mg of the substance to be examined in the mobile phase and dilute to 10 mL with the mobile phase.

Reference solution (a). Dilute 2.0 mL of the test solution to 100.0 mL with the mobile phase. Dilute 1.0 mL of this solution to 10.0 mL with the mobile phase.

Reference solution (b). Dissolve 5 mg of the substance to be examined and 5 mg of *pseudoephedrine hydrochloride CRS* in the mobile phase and dilute to 50 mL with the mobile phase.

Column:

- *size*: *l* = 0.15 m, Ø = 4.6 mm;
- *stationary phase*: spherical *phenylsilyl silica gel for chromatography R* (3 µm).

Mobile phase: mix 6 volumes of *methanol R* and 94 volumes of a 11.6 g/L solution of *ammonium acetate R* adjusted to pH 4.0 with *glacial acetic acid R*.

Flow rate: 1.0 mL/min.

Detection: spectrophotometer at 257 nm.

Injection: 20 µL.

Run time: 2.5 times the retention time of ephedrine.

Relative retention with reference to ephedrine (retention time = about 8 min): impurity B = about 1.1; impurity A = about 1.4.

System suitability: reference solution (b):

- *resolution*: minimum 2.0 between the peaks due to ephedrine and impurity B.

Limits:

- *correction factor*: for the calculation of content, multiply the peak area of impurity A by 0.4;
- *impurity A*: not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent);
- *unspecified impurities*: for each impurity, not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent);
- *sum of impurities other than A*: not more than 2.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent);
- *disregard limit*: 0.25 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.05 per cent).

Sulfates (*2.4.13*): maximum 100 ppm, determined on solution S.

Loss on drying (*2.2.32*): maximum 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*): maximum 0.1 per cent, determined on 1.0 g.

Heavy metals (2.4.8). Dissolve 1.0 g in *water R* and dilute to 25.0 mL with the same solvent. Carry out the prefiltration. 10 mL of the prefiltrate complies with test E (5 ppm). Prepare the reference solution using 5 mL of *lead standard solution (1 ppm Pb) R*.

Loss on drying (2.2.32). Not more than 0.5 per cent, determined on 1.00 g by drying in an oven at 105 °C.

Sulfated ash (2.4.14). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.400 g in 50 mL of *dilute hydrochloric acid R*. Carry out the determination of primary aromatic amino nitrogen (2.5.8).

1 mL of *0.1 M sodium nitrite* is equivalent to 27.28 mg of $C_{13}H_{21}ClN_2O_2$.

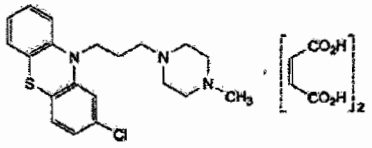
STORAGE

Store protected from light.

07/2010:0244

PROCHLORPERAZINE MALEATE

Prochlorperazini maleas



$C_{28}H_{32}ClN_3O_8S$ M_r 606
[84-02-6]

DEFINITION

2-Chloro-10-[3-(4-methylpiperazin-1-yl)propyl]-10*H*-phenothiazine bis[hydrogen (*Z*)-butenedioate].

Content: 98.0 per cent to 101.0 per cent (dried substance).

CHARACTERS

Appearance: white or pale-yellow, crystalline powder.

Solubility: very slightly soluble in water and in ethanol (96 per cent).

IDENTIFICATION

First identification: B, C, D.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (2.2.25). *Carry out the identification test protected from light and measure the absorbances immediately.*

Test solution (a). Dissolve 50 mg in *0.1 M hydrochloric acid* and dilute to 500.0 mL with the same acid.

Test solution (b). Dilute 10.0 mL of test solution (a) to 100.0 mL with *0.1 M hydrochloric acid.*

Spectral range: 280-350 nm for test solution (a); 230-280 nm for test solution (b).

Absorption maximum: at 305 nm for test solution (a); at 255 nm for test solution (b).

Specific absorbance at the absorption maximum at 255 nm: 525 to 575 for test solution (b).

B. Infrared absorption spectrophotometry (2.2.24).

Comparison: prochlorperazine maleate CRS.

C. Identification test for phenothiazines by thin-layer chromatography (2.3.3) with the following modifications.

Test solution. Dissolve 20 mg of the substance to be examined in a mixture of equal volumes of *methanol R* and *methylene chloride R* and and dilute to 20 mL with the same mixture of solvents.

Reference solution. Dissolve 20 mg of *prochlorperazine maleate CRS* in a mixture of equal volumes of *methanol R* and *methylene chloride R* and and dilute to 20 mL with the same mixture of solvents.

Application: 4 µL.

D. Triturate 0.2 g with a mixture of 1 mL of *strong sodium hydroxide solution R* and 3 mL of *water R*. Shake with 3 quantities, each of 5 mL, of *ether R*. To 0.1 mL of the aqueous layer add a solution of 10 mg of *resorcinol R* in 3 mL of *sulfuric acid R*. Heat in a water-bath for 15 min. No colour develops. To the remainder of the aqueous layer add 2 mL of *bromine solution R*. Heat in a water-bath for 15 min and then heat to boiling. Cool. To 0.1 mL of the solution add a solution of 10 mg of *resorcinol R* in 3 mL of *sulfuric acid R*. Heat in a water-bath for 15 min. A blue colour develops.

TESTS

pH (2.2.3): 3.0 to 4.0 for a freshly prepared saturated solution in *carbon dioxide-free water R*.

Related substances. Thin-layer chromatography (2.2.27). *Carry out the test protected from light.*

Solvent mixture: *diethylamine R, methanol R* (5:95 *V/V*).

Test solution. Dissolve 0.2 g of the substance to be examined in the solvent mixture and dilute to 10 mL with the solvent mixture. Prepare the solution immediately before use.

Reference solution. Dilute 1 mL of the test solution to 200 mL with the solvent mixture.

Plate: *TLC silica gel GF_{254} plate R.*

Mobile phase: *acetone R, diethylamine R, cyclohexane R* (10:10:80 *V/V/V*).

Application: 10 µL.

Development: over 2/3 of the plate.

Drying: in air.

Detection: examine in ultraviolet light at 254 nm.

Limit: any spot, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent); disregard any spots remaining at the points of application.

Loss on drying (2.2.32): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (2.4.14): maximum 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.200 g of the powdered substance to be examined in 50 mL of *anhydrous acetic acid R*, warming on a water-bath. Allow to cool to room temperature. Titrate with *0.1 M perchloric acid* determining the end-point potentiometrically (2.2.20).

1 mL of *0.1 M perchloric acid* is equivalent to 30.31 mg of $C_{28}H_{32}ClN_3O_8S$.

STORAGE

Protected from light.

CHARACTERS

A white or very slightly yellow, crystalline powder, hygroscopic, very soluble in water, freely soluble in alcohol, slightly soluble in acetone.

IDENTIFICATION

First identification: C, D.

Second identification: A, B, D, E.

A. Melting point (*2.2.14*): 166 °C to 170 °C.

B. Dissolve 10.0 mg in *0.1 M sodium hydroxide* and dilute to 100.0 mL with the same solvent. Dilute 10.0 mL of the solution to 100.0 mL with *0.1 M sodium hydroxide*. Examined between 220 nm and 350 nm (*2.2.25*), the solution shows an absorption maximum at 273 nm. The specific absorbance at the maximum is 580 to 610.

C. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *procainamide hydrochloride CRS*.

D. Dilute 1 mL of solution S to 5 mL with *water R*. The solution gives reaction (a) of chlorides (*2.3.1*).

E. Dilute 1 mL of solution S (see Tests) to 2 mL with *water R*. 1 mL of this solution gives the reaction of primary aromatic amines (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 25 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and not more intensely coloured than reference solution B_6 (*2.2.2, Method II*).

pH (*2.2.3*). The pH of solution S is 5.6 to 6.3.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 0.10 g of the substance to be examined in *alcohol R* and dilute to 10 mL with the same solvent.

Reference solution. Dilute 1 mL of the test solution to 200 mL with *alcohol R*.

Apply to the plate 5 µL of each solution. Develop over a path of 12 cm using a mixture of 15 volumes of *glacial acetic acid R*, 30 volumes of *water R* and 60 volumes of *butanol R*. Place the plate in a stream of cold air until the plate appears dry. Examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.5 per cent).

Heavy metals (*2.4.8*). 1.0 g complies with test C for heavy metals (20 ppm). Prepare the reference solution using 2 mL of *lead standard solution (10 ppm Pb) R*.

Loss on drying (*2.2.32*). Not more than 0.5 per cent, determined on 1.000 g by drying in an oven at 105 °C.

Sulfated ash (*2.4.14*). Not more than 0.1 per cent, determined on 1.0 g.

ASSAY

Dissolve 0.2500 g in 50 mL of *dilute hydrochloric acid R*. Carry out the determination of primary aromatic amino-nitrogen (*2.5.8*).

1 mL of *0.1 M sodium nitrite* is equivalent to 27.18 mg of $C_{13}H_{22}ClN_3O$.

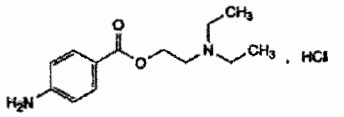
STORAGE

Store in an airtight container, protected from light.

01/2008:0050
corrected 7.0

PROCAINE HYDROCHLORIDE

Procaini hydrochloridum



$C_{13}H_{21}ClN_2O_2$ [51-05-8] M_r 272.8

DEFINITION

Procaine hydrochloride contains not less than 99.0 per cent and not more than the equivalent of 101.0 per cent of 2-(diethylamino)ethyl 4-aminobenzoate hydrochloride, calculated with reference to the dried substance.

CHARACTERS

A white or almost white, crystalline powder or colourless crystals, very soluble in water, soluble in ethanol (96 per cent).

IDENTIFICATION

First identification: A, B, E.

Second identification: A, C, D, E, F.

A. Melting point (*2.2.14*): 154 °C to 158 °C.

B. Examine by infrared absorption spectrophotometry (*2.2.24*), comparing with the spectrum obtained with *procaine hydrochloride CRS*.

C. To about 5 mg add 0.5 mL of *fuming nitric acid R*. Evaporate to dryness on a water-bath, allow to cool and dissolve the residue in 5 mL of *acetone R*. Add 1 mL of *0.1 M alcoholic potassium hydroxide*. Only a brownish-red colour develops.

D. To 0.2 mL of solution S (see Tests) add 2 mL of *water R* and 0.5 mL of *dilute sulfuric acid R* and shake. Add 1 mL of a 1 g/L solution of *potassium permanganate R*. The colour is immediately discharged.

E. It gives reaction (a) of chlorides (*2.3.1*).

F. Dilute 1 mL of solution S to 100 mL with *water R*. 2 mL of this solution gives the reaction of primary aromatic amines (*2.3.1*).

TESTS

Solution S. Dissolve 2.5 g in *carbon dioxide-free water R* and dilute to 50 mL with the same solvent.

Appearance of solution. Solution S is clear (*2.2.1*) and colourless (*2.2.2, Method II*).

pH (*2.2.3*). Dilute 4 mL of solution S to 10 mL with *carbon dioxide-free water R*. The pH of the solution is 5.0 to 6.5.

Related substances. Examine by thin-layer chromatography (*2.2.27*), using *silica gel* GF_{254} *R* as the coating substance.

Test solution. Dissolve 1.0 g of the substance to be examined in *water R* and dilute to 10 mL with the same solvent.

Reference solution. Dissolve 50 mg of *4-aminobenzoic acid R* in *water R* and dilute to 100 mL with the same solvent. Dilute 1 mL of the solution to 10 mL with *water R*.

Apply separately to the plate 5 µL of each solution. Develop over a path of 10 cm using a mixture of 4 volumes of *glacial acetic acid R*, 16 volumes of *hexane R* and 80 volumes of *dibutyl ether R*. Dry the plate at 100 °C to 105 °C for 10 min and examine in ultraviolet light at 254 nm. Any spot in the chromatogram obtained with the test solution, apart from the principal spot, is not more intense than the spot in the chromatogram obtained with the reference solution (0.05 per cent). The principal spot in the chromatogram obtained with the test solution remains on the point of application.

Cognome e Nome _____

SCHEDA DI PREPARAZIONE

Fonte di legittimazione: O Farmacopea _____

M Prescrizione medica del _____ N° _____

Forma farmaceutica: _____

Riferimento alla procedura tecnologica _____

Avvertenze e precauzioni: _____

Componenti	*Cod.Interno*	*Lotto**	*Quantità unitarie*	**

** Compilare se preparazione allestita un'unica volta e che dunque non richiede foglio di allestimento.*
*** Barrare se impiegato per motivi tecnici*

Controlli previsti _____

Contenitore _____

Periodo di validità _____

Disciplina di vendita (senza ricetta, RR, RNR, RRM) _____

Metodo di preparazione

_____
_____
_____
_____
_____
_____
_____
_____

OBBLIGO DI REGISTRAZIONE IN USCITA **SÌ** **NO**

Cognome e Nome _____

SCHEDA RICETTA

Tipologia

□ RR □ RNR □ RNR (tab 3) □ RRM □ SSN

La ricetta risulta spedibile?
□ sì
□ no perché?

Validità temporale ed eventuale ripetibilità della ricetta in oggetto:

Formalismi obbligatori per il **medico** per la ricetta in oggetto:

Formalismi obbligatori per il **farmacista** per la ricetta in oggetto:

Presenza di:
□ veleni, sostanze molto tossiche
□ sost. stupefacenti e psicotrope □ registrazione registro EU
□ coloranti o corrosivi
□ sostanze vietate per doping

Modalità e tempo di conservazione della ricetta

Data limite di utilizzo della preparazione

Uso
□ UI □ UE

Forma farmaceutica

Controllo di qualità obbligatori per le NBP:

Attività terapeutica della preparazione

n°……**li**……**Dott.**…… …… …… …… …… …… …… …… …… …… **Avvertenze**…… …… …… **Precauzioni**…… …… …… **Posologia**…… …… …… **Data limite di utilizzo**…… **Sig.**……	

Segue: **TABELLA N. 8**

Sostanza	Vie di somministrazione	Dosi abituali		Dosi massime	
		Per ogni dose grammi	Nelle 24 ore grammi	Per ogni dose grammi	Nelle 24 ore grammi
Acido mefenamico	per os	–	–	0,500	1,5
Acido nalidixico	per os	0,50	2	1	4
Acido nicotinico	per os s.c. e.v.	0,05-0,20 0,05-0,10 0,05-0,10	0,30 0,30 0,20	0,30 0,20 0,20	1 1 1
Acido ossolinico *	per os	–	–	0,75	1,5
Acido pipemidico triidrato	per os	–	–	0,471	0,942
Acido salicilico	top.	pom. (crema, ung., gel, ecc.), loz., cerotto, shampoo, sapone, ecc. 1%, 2%, 4%, 25%, 40%, 60%			
Acido tiaprofenico	per os rett.	–	–	0,6 0,3	0,6 0,6
Acido tolfenamico	per os	–	–	0,2	0,6
Acido tranexamico *	per os e.v. lenta	– –	– –	0,025/kg 0,015/kg	0,1/kg 0,045/kg
Acido tricloroacetico	top.	–	–	50%	
Acido undecilenico	top.	ung. 5% (in ass. con Zn undecilenato); polv. 2-5% (idem); aerosol 2% (idem)			
Acido ursodesossicolico	per os	–	–	–	0,012/kg
Acido valproico	per os	–	–	0,030/kg	0,060/kg
Acitretina *	per os	–	–	0,025	0,075
Aconitina	per os	0,0001	0,0002	0,0002	0,0005
Adenina	per os	0,015-0,03	0,15	0,03-0,06	0,3
Adenosina *	e.v. rapida	–	–	0,012	0,021
Adrenalina cloridrato	i.m. o s.c.	0,0002-0,001	0,001	0,001	0,003
Adrenalina tartrato acido	i.m. o s.c.	0,0002-0,001	0,001	0,001	0,003
Ajmalina	per os	0,05-0,10	0,15-0,60	0,30	0,60
Ajmalina monoetanolato	per os i.m. o e.v.	0,05-0,10 0,05-0,10	0,15-0,30 0,20	– –	0,40 0,20
Alanina	fleboclisi	In combinazione con altri amminoacidi nelle soluzioni perfusionali per la nutrizione parenterale			
Albendazolo *	per os	–	–	0,4	0,4
Alcool isopropilico	top.	sol. al 70%	–	–	–
Alcuronio cloruro	e.v.	–	–	0,000250/kg	0,000300/kg
Alfacalcidolo *	per os	–	–	–	0,000001
Alfentanile cloridrato *	e.v.	0,1	0,2	–	–
Alfuzosina cloridrato *	per os	–	–	0,0025	0,010
Allobarbital	per os	0,10-0,20	0,20	0,20	0,30
Allopurinolo	per os	0,10-0,20	0,20-0,60	0,30	0,80
Alluminio cloruro esaidrato	top.	sol. al 20%	–	–	–
Alluminio ossido idrato	per os	0,50-1	2	1	4

Dott. xxxxx xxxxxxxxx
Via xxxxxxx xxxxxxx, xx
Torino
Tel. xxx/xxxxxxxxxxx

Sig.ra xxxxxx xxxxxxx

R/	Acido salicilico		2	g
	Zinco ossido			
	Amido polvere (frumento)	ana	25	g
	Vaselina	q.b.	100	g

Zinco ossido e acido salicilico pasta cutanea (F.U. XII)

Spedire 30 g

2-3 applicazioni al dì

26/06/2015

UTILIZZARE IL FOGLIO PROTOCOLLO A QUADRETTI **UNICAMENTE** PER I CALCOLI