01/2008:0438
corrected 6.0

TALC

Talcum

[14807-96-6]

DEFINITION

Powdered, selected, natural, hydrated magnesium silicate. Pure talc has the formula $Mg_3Si_4O_{10}(OH)_2$ (M_r 379.3). It may contain variable amounts of associated minerals among which chlorites (hydrated aluminium and magnesium silicates), magnesite (magnesium carbonate), calcite (calcium carbonate) and dolomite (calcium and magnesium carbonate) are predominant.

PRODUCTION

Talc derived from deposits that are known to contain associated asbestos is not suitable for pharmaceutical use. The manufacturer is responsible for demonstrating by the test for amphiboles and serpentines that the product is free from asbestos. The presence of amphiboles and of serpentines is revealed by X-ray diffraction or by infrared spectrophotometry (see A and B). If detected, the specific morphological criteria of asbestos are investigated by a suitable method of optical microscopy to determine whether tremolite asbestos or chrysotile is present, as described below.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs of *potassium bromide R*.

In the range 740 cm^{-1} to 760 cm^{-1} using scale expansion, any absorption band at 758 ± 1 cm^{-1} may indicate the presence of tremolite or of chlorite. If the absorption band remains after ignition of the substance to be examined at 850 ± 50 °C for at least 30 min, it indicates the presence of the tremolite. In the range 600 cm^{-1} to 650 cm^{-1} using scale expansion, any absorption band or shoulder may indicate the presence of serpentines.

B. X-ray diffraction.

Preparation: place the sample on the sample holder; pack and smooth its surface with a polished glass microscope slide.

Radiation: Cu Kα monochromatic, 40 kV, 24-30 mA.

Incident slit: 1°.

Detection slit: 0.2°.

Goniometer speed: 1/10° 2θ/min.

Scanning range: 10-13° 2θ and 24-26° 2θ.

Sample: not oriented.

Results: the presence of amphiboles is detected by a diffraction peak at 10.5 ± 0.1° 2θ, the presence of serpentines is detected by diffraction peaks at 24.3 ± 0.1° 2θ and at 12.1 ± 0.1° 2θ.

If, by one of the 2 methods, amphiboles and/or serpentine are detected, examine by a suitable method of optical microscopy to determine the asbestos character.

The presence of asbestos is shown if the following 2 criteria are met:

– a range of length to width ratios of 20:1 to 100:1, or higher for fibres longer than 5 µm,
– capability of splitting into very thin fibrils,

and if at least 2 of the following 4 criteria are met:

– parallel fibres occurring in bundles,
– fibre bundles displaying frayed ends,
– fibres in the form of thin needles,
– matted masses of individual fibres and/or fibres showing curvature.

CHARACTERS

Appearance: light, homogeneous, white or almost white powder, greasy to the touch (non abrasive).

Solubility: practically insoluble in water, in ethanol (96 per cent) and in dilute solutions of acids and alkali hydroxides.

IDENTIFICATION

First identification: A.

Second identification: B, C.

A. Infrared absorption spectrophotometry (*2.2.24*).

Preparation: discs of *potassium bromide R*.

Absorption bands: at 3677 ± 2 cm^{-1}, 1018 ± 2 cm^{-1} and 669 ± 2 cm^{-1}.

B. In a platinum crucible, melt a mixture of 0.2 g of *anhydrous sodium carbonate R* and 2.0 g of *potassium carbonate R*. To the melted mass add 0.1 g of the substance to be examined and heat until the mixture is completely melted. Allow to cool and transfer the melted mass into an evaporating dish with 50 ml of hot *water R*. Add *hydrochloric acid R* until effervescence ceases. Add 10 ml of *hydrochloric acid R* and evaporate to dryness on a water-bath. Allow to cool. Add 20 ml of *water R*, heat to boiling and filter (the residue is used for identification test C). To 5 ml of the filtrate add 1 ml of *ammonia R* and 1 ml of *ammonium chloride solution R* and filter. To the filtrate add 1 ml of *disodium hydrogen phosphate solution R*. A white, crystalline precipitate is formed.

C. The residue obtained in identification test B gives the reaction of silicates (*2.3.1*).

TESTS

Solution S1. Weigh 10.0 g into a conical flask fitted with a reflux condenser, add 50 ml of *0.5 M hydrochloric acid* gradually while stirring and heat on a water-bath for 30 min. Allow to cool. Transfer the mixture to a beaker and allow the undissolved material to settle. Filter the supernatant through medium-speed filter paper into a 100 ml volumetric flask, retaining as much as possible of the insoluble material in the beaker. Wash the residue and the beaker with 3 quantities, each of 10 ml, of hot *water R*. Wash the filter with 15 ml of hot *water R*, allow the filtrate to cool and dilute to 100.0 ml with the same solvent.

Solution S2. *Perchlorates mixed with heavy metals are known to be explosive. Take proper precautions while performing this procedure.* Weigh 0.5 g in a 100 ml polytetrafluoroethylene dish, add 5 ml of *hydrochloric acid R*, 5 ml of *lead-free nitric acid R* and 5 ml of *perchloric acid R*. Stir gently then add 35 ml of *hydrofluoric acid R* and evaporate slowly to dryness on a hot plate. To the residue, add 5 ml of *hydrochloric acid R*, cover with a watch-glass, heat to boiling and allow to cool. Rinse the watch-glass and the dish with *water R*. Transfer into a volumetric flask, rinse the dish with *water R* and dilute to 50.0 ml with the same solvent.

Acidity or alkalinity. Boil 2.5 g with 50 ml of *carbon dioxide-free water R* under reflux. Filter *in vacuo*. To 10 ml of the filtrate add 0.1 ml of *bromothymol blue solution R1*; not more than 0.4 ml of *0.01 M hydrochloric acid* is required to change the colour of the indicator to green. To 10 ml of the filtrate add 0.1 ml of *phenolphthalein solution R1*; not more than 0.3 ml of *0.01 M sodium hydroxide* is required to change the colour of the indicator to pink.

Water-soluble substances: maximum 0.2 per cent.

To 10.0 g add 50 ml of *carbon dioxide-free water R*, heat to boiling and maintain boiling under a reflux condenser for 30 min. Allow to cool, filter through a medium-speed filter paper and dilute to 50.0 ml with *carbon dioxide-free water R*. Take 25.0 ml of the filtrate, evaporate to dryness and heat at 105 °C for 1 h. The residue weighs a maximum of 10 mg.

Aluminium: maximum 2.0 per cent.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. To 5.0 ml of solution S2 add 10 ml of a 25.34 g/l solution of *caesium chloride R*, 10.0 ml of *hydrochloric acid R* and dilute to 100.0 ml with *water R*.

Reference solutions. Into 4 identical volumetric flasks, each containing 10.0 ml of *hydrochloric acid R* and 10 ml of a 25.34 g/l solution of *caesium chloride R*, introduce respectively 5.0 ml, 10.0 ml, 15.0 ml and 20.0 ml of *aluminium standard solution (100 ppm Al) R* and dilute to 100.0 ml with *water R*.

Source: aluminium hollow-cathode lamp.

Wavelength: 309.3 nm.

Atomisation device: nitrous oxide-acetylene flame.

Calcium: maximum 0.90 per cent.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. To 5.0 ml of solution S2 add 10.0 ml of *hydrochloric acid R*, 10 ml of *lanthanum chloride solution R* and dilute to 100.0 ml with *water R*.

Reference solutions. Into 4 identical volumetric flasks, each containing 10.0 ml of *hydrochloric acid R* and 10 ml of *lanthanum chloride solution R*, introduce respectively 1.0 ml, 2.0 ml, 3.0 ml and 4.0 ml of *calcium standard solution (100 ppm Ca) R1* and dilute to 100.0 ml with *water R*.

Source: calcium hollow-cathode lamp.

Wavelength: 422.7 nm.

Atomisation device: nitrous oxide-acetylene flame.

Iron: maximum 0.25 per cent.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. To 2.5 ml of solution S1, add 50.0 ml of *0.5 M hydrochloric acid* and dilute to 100.0 ml with *water R*.

Reference solutions. Into 4 identical volumetric flasks, each containing 50.0 ml of *0.5 M hydrochloric acid*, introduce respectively 2.0 ml, 2.5 ml, 3.0 ml and 4.0 ml of *iron standard solution (250 ppm Fe) R* and dilute to 100.0 ml with *water R*.

Source: iron hollow-cathode lamp.

Wavelength: 248.3 nm.

Atomisation device: air-acetylene flame.

Correction: deuterium lamp.

Lead: maximum 10.0 ppm.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Use solution S1.

Reference solutions. Into 4 identical volumetric flasks, each containing 50.0 ml of *0.5 M hydrochloric acid*, introduce respectively 5.0 ml, 7.5 ml, 10.0 ml and 12.5 ml of *lead standard solution (10 ppm Pb) R1* and dilute to 100.0 ml with *water R*.

Source: lead hollow-cathode lamp.

Wavelength: 217.0 nm.

Atomisation device: air-acetylene flame.

Magnesium: 17.0 per cent to 19.5 per cent.

Atomic absorption spectrometry (*2.2.23, Method I*).

Test solution. Dilute 0.5 ml of solution S2 to 100.0 ml with *water R*. To 4.0 ml of the solution, add 10.0 ml of *hydrochloric acid R*, 10 ml of *lanthanum chloride solution R* and dilute to 100.0 ml with *water R*.

Reference solutions. Into 4 identical volumetric flasks, each containing 10.0 ml of *hydrochloric acid R* and 10 ml of *lanthanum chloride solution R*, introduce respectively 2.5 ml, 3.0 ml, 4.0 ml and 5.0 ml of *magnesium standard solution (10 ppm Mg) R1* and dilute to 100.0 ml with *water R*.

Source: magnesium hollow-cathode lamp.

Wavelength: 285.2 nm.

Atomisation device: air-acetylene flame.

Loss on ignition: maximum 7.0 per cent, determined on 1.00 g by ignition to constant weight at 1050-1100 °C.

Microbial contamination. If intended for topical administration, the total viable aerobic count (*2.6.12*) is not more than a total of 10^2 bacteria and fungi per gram.

If intended for oral administration, the total viable aerobic count (*2.6.12*) is not more than 10^3 bacteria and not more than 10^2 fungi per gram.

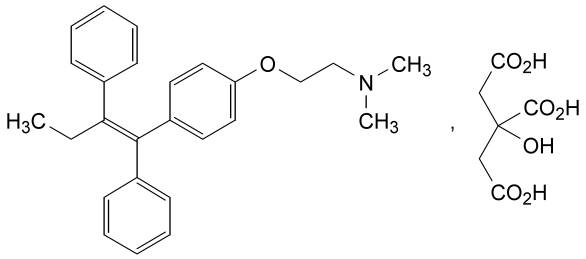
LABELLING

The label states, where applicable, that the substance is suitable for oral or topical administration.

01/2008:1046

TAMOXIFEN CITRATE

Tamoxifeni citras



$C_{32}H_{37}NO_8$ M_r 563.6

[54965-24-1]

DEFINITION

2-[4-[(*Z*)-1,2-Diphenylbut-1-enyl]phenoxy]-*N*,*N*-dimethylethanamine dihydrogen 2-hydroxypropane-1,2,3-tricarboxylate.

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

CHARACTERS

Appearance: white or almost white, crystalline powder.

Solubility: slightly soluble in water, soluble in methanol, slightly soluble in acetone.

It shows polymorphism (*5.9*).

IDENTIFICATION

First identification: B.

Second identification: A, C, D.

A. Ultraviolet and visible absorption spectrophotometry (*2.2.25*).

Test solution. Dissolve 20 mg in *methanol R* and dilute to 50.0 ml with the same solvent. Dilute 5.0 ml of this solution to 100.0 ml with *methanol R*.

Spectral range: 220-350 nm.

Absorption maxima: at 237 nm and 275 nm.