Chlorides (*2.4.4*): maximum 1 per cent.

Dissolve 0.1 g with heating in 10 mL of *dilute nitric acid R* and dilute to 100 mL with *water R*. Dilute 5 mL of the solution to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 1 per cent.

Dilute 4 mL of solution S to 100 mL with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 4 ppm, determined on 10 mL of solution S.

Heavy metals (*2.4.8*): maximum 60 ppm.

Neutralise 20 mL of solution S with *concentrated ammonia R,* using *metanil yellow solution R* as an external indicator. Filter, if necessary, and dilute to 30 mL with *water R*. 12 mL of the solution complies with test A. Prepare the reference solution using 10 mL of *lead standard solution (1 ppm Pb) R*.

Microbial contamination

TAMC: acceptance criterion 10^3 CFU/g (*2.6.12*).

TYMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

Absence of bile-tolerant gram-negative bacteria (*2.6.13*).

Absence of *Escherichia coli* (*2.6.13*).

ASSAY

Dissolve 0.800 g in 10 mL of *hydrochloric acid R1,* heating on a water-bath. Cool and dilute to 50.0 mL with *water R*. To 10.0 mL of the solution add *dilute ammonia R1* until a precipitate begins to appear. Add the smallest quantity of *dilute hydrochloric acid R* needed to dissolve the precipitate and dilute to 20 mL with *water R*. Carry out the complexometric titration of aluminium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 5.098 mg of Al_2O_3.

STORAGE

In an airtight container, at a temperature not exceeding 30 °C.

FUNCTIONALITY-RELATED CHARACTERISTICS

This section provides information on characteristics that are recognised as being relevant control parameters for one or more functions of the substance when used as an excipient (see chapter 5.15). This section is a non-mandatory part of the monograph and it is not necessary to verify the characteristics to demonstrate compliance. Control of these characteristics can however contribute to the quality of a medicinal product by improving the consistency of the manufacturing process and the performance of the medicinal product during use. Where control methods are cited, they are recognised as being suitable for the purpose, but other methods can also be used. Wherever results for a particular characteristic are reported, the control method must be indicated.

The following characteristics may be relevant for hydrated aluminium oxide used as adsorbent.

Particle-size distribution (*2.9.31*).

Specific surface area (*2.9.26*).

01/2009:2166

ALUMINIUM PHOSPHATE GEL

Aluminii phosphatis liquamen

DEFINITION

Hydrated $AlPO_4$ in gel form.

Content: 19.0 per cent to 21.0 per cent of $AlPO_4$.

CHARACTERS

Appearance: gel.

Solubility: practically insoluble in water, in ethanol (96 per cent) and in methylene chloride. It dissolves in dilute solutions of mineral acids.

IDENTIFICATION

A. Solution S (see Tests) gives reaction (b) of phosphates (*2.3.1*).

B. Solution S gives the reaction of aluminium (*2.3.1*).

C. It complies with the assay.

TESTS

Solution S. Dissolve 2.00 g in *dilute hydrochloric acid R* and dilute to 100 mL with the same acid.

pH (*2.2.3*): 6.0 to 8.0.

Peroxides: maximum 150 ppm, expressed as hydrogen peroxide.

Test solution. Dissolve with heating 1.0 g of the substance to be examined in 5 mL of *dilute hydrochloric acid R*, then add 5 mL of *water R* and 2 mL of *divanadium pentoxide solution in sulfuric acid R*.

Reference solution. Dilute 1.0 mL of *dilute hydrogen peroxide solution R* to 200.0 mL with *water R*. To 1 mL of this solution add 9 mL of *water R* and 2 mL of *divanadium pentoxide solution in sulfuric acid R*.

The test solution is not more intensely coloured than the reference solution.

Chlorides (*2.4.4*): maximum 500 ppm.

Dissolve 1.3 g in 5 mL of *dilute nitric acid R* and dilute to 200 mL with *water R*.

Soluble phosphates: maximum 0.5 per cent, expressed as PO_4.

Test solution. Centrifuge 10.0 g until a clear supernatant is obtained. To 2.00 mL of the supernatant add 20.0 mL of a 10.3 g/L solution of *hydrochloric acid R* and dilute to 100.0 mL with *water R*. To 10.0 mL of this solution add 10.0 mL of *nitro-molybdovanadic reagent R* and dilute to 50.0 mL with *water R*. Allow to stand protected from light for 15 min.

Reference solution. Add 10.0 mL of *nitro-molybdovanadic reagent R* to 10.0 mL of a 143 mg/L solution of *potassium dihydrogen phosphate R* and dilute to 50.0 mL with *water R*. Allow to stand protected from light for 15 min.

Measure the absorbances (*2.2.25*) of the 2 solutions at 400 nm. The absorbance of the test solution is not greater than that of the reference solution.

Sulfates (*2.4.13*): maximum 0.2 per cent.

Dilute 25 mL of solution S to 100 mL with *distilled water R*.

Soluble aluminium: maximum 50 ppm.

To 16.0 g add 50 mL of *water R*. Heat to boiling for 5 min. Cool and centrifuge. Separate the supernatant. Wash the residue with 20 mL of *water R* and centrifuge. Separate the supernatant and add to the first supernatant. To the combined supernatants add 5 mL of *hydrochloric acid R* and 20 mL of *water R*. Introduce all of this solution into a 500 mL conical flask and carry out the complexometric titration of aluminium (*2.5.11*) using *0.01 M sodium edetate*.

Arsenic (*2.4.2, Method A*): maximum 1 ppm, determined on 1.0 g.

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

Dissolve 4.0 g in *dilute hydrochloric acid R* and dilute to 20 mL with the same acid. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (2 ppm Pb) R*.

Acid neutralising capacity. Add 2.0 g to 30 mL of *0.1 M hydrochloric acid R* heated to 37 °C and maintain at 37 °C while shaking. Determine the pH after 15 min. The pH (*2.2.3*) of the mixture is 2.0 to 2.5.

Residue on ignition: 19.0 per cent to 23.0 per cent.

Heat 0.500 g at 50 °C for 5 hours, then ignite at 500 ± 50 °C until constant mass.

Microbial contamination

TAMC: acceptance criterion 10^3 CFU/g (*2.6.12*).

TYMC: acceptance criterion 10^2 CFU/g (*2.6.12*).

Absence of bile-tolerant gram-negative bacteria (*2.6.13*).

Absence of *Escherichia coli* (*2.6.13*).

ASSAY

Dissolve with heating 0.300 g in 5 mL of *dilute hydrochloric acid R*. Add 45 mL of *water R*, 10.0 mL of *0.1 M sodium edetate* and 30 mL of a mixture of equal volumes of *ammonium acetate solution R* and *dilute acetic acid R*. Heat to boiling and maintain boiling for 3 min. Cool, then add 25 mL of *ethanol (96 per cent) R*. Titrate with *0.1 M zinc sulfate*, determining the end-point potentiometrically (*2.2.20*).

1 mL of *0.1 M zinc sulfate* is equivalent to 12.2 mg of $AlPO_4$.

STORAGE

In an airtight container.

01/2008:1598
corrected 6.0

ALUMINIUM PHOSPHATE, HYDRATED

Aluminii phosphas hydricus

$AlPO_4,x\ H_2O$ M_r 122.0 (anhydrous substance)

DEFINITION

Content: 94.0 per cent to 102.0 per cent of $AlPO_4$ (M_r 122.0) (ignited substance).

CHARACTERS

Appearance: white or almost white powder.

Solubility: very slightly soluble in water, practically insoluble in alcohol. It dissolves in dilute solutions of mineral acids and alkali hydroxides.

IDENTIFICATION

A. Solution S (see Tests) gives reaction (b) of phosphates (*2.3.1*).

B. Solution S gives the reaction of aluminium (*2.3.1*).

TESTS

Solution S. Dissolve 2.00 g in *dilute hydrochloric acid R* and dilute to 100 mL with the same acid.

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

pH (*2.2.3*): 5.5 to 7.2

Shake 4.0 g with *carbon dioxide-free water R* and dilute to 100 mL with the same solvent.

Chlorides (*2.4.4*): maximum 1.3 per cent.

Dissolve 50.0 mg in 10 mL of *dilute nitric acid R* and dilute to 200 mL with *water R*. 15 mL of the solution complies with the limit test for chlorides.

Soluble phosphates: maximum 1.0 per cent, calculated as PO_4^{3-}.

Test solution. Stir 5.0 g with 150 mL of *water R* for 2 h. Filter and wash the filter with 50 mL of *water R*. Combine the filtrate and the washings and dilute to 250.0 mL with *water R*. Dilute 10.0 mL of this solution to 100.0 mL with *water R*.

Reference solution (a). Dissolve 2.86 g of *potassium dihydrogen phosphate R* in *water R* and dilute to 100 mL with the same solvent.

Reference solution (b). Dilute 1 mL of reference solution (a) to 5 mL with *water R*.

Reference solution (c). Dilute 3 mL of reference solution (a) to 5 mL with *water R*.

Treat each solution as follows. To 5.0 mL add 4 mL of *dilute sulfuric acid R*, 1 mL of *ammonium molybdate solution R*, 5 mL of *water R* and 2 mL of a solution containing 0.10 g of *4-methylaminophenol sulfate R*, 0.5 g of *anhydrous sodium sulfite R* and 20.0 g of *sodium metabisulfite R* in 100 mL of *water R*. Shake and allow to stand for 15 min. Dilute to 25.0 mL with *water R* and allow to stand for a further 15 min. Measure the absorbance (*2.2.25*) at 730 nm. Calculate the content of soluble phosphates from a calibration curve prepared using reference solutions (a), (b) and (c) after treatment.

Sulfates (*2.4.13*): maximum 0.6 per cent.

Dilute 8 mL of solution S to 100 mL with *distilled water R*. 15 mL of the solution complies with the limit test for sulfates.

Arsenic (*2.4.2*): maximum 1 ppm.

1.0 g complies with limit test A.

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

Dissolve 1.0 g in *dilute hydrochloric acid R* and dilute to 20 mL with the same acid. 12 mL of the solution complies with limit test A. Prepare the standard using *lead standard solution (1 ppm Pb) R*.

Loss on ignition. 10.0 per cent to 20.0 per cent, determined on 1.000 g at 800 ± 50 °C.

Neutralising capacity. Add 0.50 g to 30 mL of *0.1 M hydrochloric acid* previously heated to 37 °C and maintain at this temperature for 15 min while stirring. The pH (*2.2.3*) of the mixture after 15 min at 37 °C is 2.0 to 2.5.

ASSAY

Dissolve 0.400 g in 10 mL of *dilute hydrochloric acid R* and dilute to 100.0 mL with *water R*. To 10.0 mL of the solution, add 10.0 mL of *0.1 M sodium edetate* and 30 mL of a mixture of equal volumes of *ammonium acetate solution R* and *dilute acetic acid R*. Boil for 3 min, then cool. Add 25 mL of *alcohol R* and 1 mL of a freshly prepared 0.25 g/L solution of *dithizone R* in *alcohol R*. Titrate the excess of sodium edetate with *0.1 M zinc sulfate* until the colour changes to pink.

1 mL of *0.1 M sodium edetate* is equivalent to 12.20 mg of $AlPO_4$.

STORAGE

In an airtight container.

01/2009:1676
corrected 7.0

ALUMINIUM SODIUM SILICATE

Aluminii natrii silicas

DEFINITION

Silicic acid aluminium sodium salt of synthetic origin.

Content:

- *aluminium* (Al; M_r 26.98): 2.7 per cent to 7.9 per cent (dried substance);
- *sodium* (Na; M_r 22.99): 3.7 per cent to 6.3 per cent (dried substance).

CHARACTERS

Appearance: white or almost white, fine, light, amorphous powder.

Solubility: practically insoluble in water and in organic solvents.

IDENTIFICATION

A. Transfer 1.0 g to a 100 mL beaker and add 10 mL of *dilute hydrochloric acid R*. Mix, cover with a watch glass and boil for 15 min. Allow to cool to room temperature, mix and centrifuge the solution. 2 mL of the supernatant gives the reaction of aluminium (*2.3.1*).

B. 2 mL of the supernatant obtained in identification test A gives reaction (a) of sodium (*2.3.1*).

C. 0.2 g gives the reaction of silicates (*2.3.1*).

TESTS

pH (*2.2.3*): 9.5 to 11.5.

Disperse 5.0 g in 100 mL of *carbon dioxide-free water R*.