07/2008:0043
corrected 6.5

MAGNESIUM CARBONATE, HEAVY

Magnesii subcarbonas ponderosus

DEFINITION

Hydrated basic magnesium carbonate.

Content: 40.0 per cent to 45.0 per cent, calculated as MgO (M_r 40.30).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water. It dissolves in dilute acids with effervescence.

IDENTIFICATION

A. Bulk density (*2.9.34*): minimum 0.25 g/mL.

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

C. Dissolve about 15 mg in 2 mL of *dilute nitric acid R* and neutralise with *dilute sodium hydroxide solution R*. The solution gives the reaction of magnesium (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in 100 mL of *dilute acetic acid R*. When the effervescence has ceased, boil for 2 min, allow to cool and dilute to 100 mL with *dilute acetic acid R*. Filter, if necessary, through a previously ignited and tared porcelain or silica filter crucible of suitable porosity to give a clear filtrate.

Appearance of solution. Solution S is not more intensely coloured than reference solution B_4 (*2.2.2, Method II*).

Soluble substances: maximum 1.0 per cent.

Mix 2.00 g with 100 mL of *water R* and boil for 5 min. Filter whilst hot through a sintered-glass filter (40) (*2.1.2*), allow to cool and dilute to 100 mL with *water R*. Evaporate 50 mL of the filtrate to dryness and dry at 100-105 °C. The residue weighs not more than 10 mg.

Substances insoluble in acetic acid: maximum 0.05 per cent.

Any residue obtained during the preparation of solution S, washed, dried, and ignited at 600 ± 50 °C, weighs not more than 2.5 mg.

Chlorides (*2.4.4*): maximum 700 ppm.

Dilute 1.5 mL of solution S to 15 mL with *water R*.

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

Dilute 0.5 mL of solution S to 15 mL with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 10 mL of solution S.

Calcium (*2.4.3*): maximum 0.75 per cent.

Dilute 2.6 mL of solution S to 150 mL with *distilled water R*. 15 mL of the solution complies with the test.

Iron (*2.4.9*): maximum 400 ppm.

Dissolve 0.1 g in 3 mL of *dilute hydrochloric acid R* and dilute to 10 mL with *water R*. Dilute 2.5 mL of the solution to 10 mL with *water R*.

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

To 20 mL of solution S add 15 mL of *hydrochloric acid R1* and shake with 25 mL of *methyl isobutyl ketone R* for 2 min. Allow to stand, separate the aqueous lower layer and evaporate to dryness. Dissolve the residue in 1 mL of *acetic acid R* and dilute to 20 mL with *water R*. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

ASSAY

Dissolve 0.150 g in a mixture of 2 mL of *dilute hydrochloric acid R* and 20 mL of *water R*. Carry out the complexometric titration of magnesium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 4.030 mg of MgO.

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 heavy magnesium carbonate used as filler in tablets.

Particle-size distribution (*2.9.31* or *2.9.38*).

Bulk and tapped density (*2.9.34*).

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MAGNESIUM CARBONATE, LIGHT

Magnesii subcarbonas levis

[546-93-0]

DEFINITION

Hydrated basic magnesium carbonate.

Content: 40.0 per cent to 45.0 per cent, calculated as MgO (M_r 40.30).

CHARACTERS

Appearance: white or almost white powder.

Solubility: practically insoluble in water. It dissolves in dilute acids with effervescence.

IDENTIFICATION

A. Bulk density (*2.9.34*): maximum 0.15 g/mL.

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

C. Dissolve about 15 mg in 2 mL of *dilute nitric acid R* and neutralise with *dilute sodium hydroxide solution R*. The solution gives the reaction of magnesium (*2.3.1*).

TESTS

Solution S. Dissolve 5.0 g in 100 mL of *dilute acetic acid R*. When the effervescence has ceased, boil for 2 min, allow to cool and dilute to 100 mL with *dilute acetic acid R*. Filter, if necessary, through a previously ignited and tared porcelain or silica filter crucible of suitable porosity to give a clear filtrate.

Appearance of solution. Solution S is not more intensely coloured than reference solution B_4 (*2.2.2, Method II*).

Soluble substances: maximum 1.0 per cent.

Mix 2.00 g with 100 mL of *water R* and boil for 5 min. Filter whilst hot through a sintered-glass filter (40) (*2.1.2*), allow to cool and dilute to 100 mL with *water R*. Evaporate 50 mL of the filtrate to dryness and dry at 100-105 °C. The residue weighs a maximum of 10 mg.

Substances insoluble in acetic acid: maximum 0.05 per cent.

Any residue obtained during the preparation of solution S, washed, dried and ignited at 600 ± 50 °C, weighs a maximum of 2.5 mg.

Chlorides (*2.4.4*): maximum 700 ppm.

Dilute 1.5 mL of solution S to 15 mL with *water R*.

Sulfates (*2.4.13*): maximum 0.3 per cent.

Dilute 1 mL of solution S to 15 mL with *distilled water R*.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 10 mL of solution S.

Calcium (*2.4.3*): maximum 0.75 per cent.

Dilute 2.6 mL of solution S to 150 mL with *distilled water R*. 15 mL of the solution complies with the test.

Iron (*2.4.9*): maximum 400 ppm.

Dissolve 0.1 g in 3 mL of *dilute hydrochloric acid R* and dilute to 10 mL with *water R*. Dilute 2.5 mL of this solution to 10 mL with *water R*.

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

To 20 mL of solution S add 15 mL of *hydrochloric acid R1* and shake with 25 mL of *methyl isobutyl ketone R* for 2 min. Allow to stand, separate the aqueous lower layer and evaporate to dryness. Dissolve the residue in 1 mL of *acetic acid R* and dilute to 20 mL with *water R*. 12 mL of the solution complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

ASSAY

Dissolve 0.150 g in a mixture of 2 mL of *dilute hydrochloric acid R* and 20 mL of *water R*. Carry out the complexometric titration of magnesium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 4.030 mg of MgO.

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 characteristic may be relevant for light magnesium carbonate used as filler in oral solid dosage forms.

Particle-size distribution (*2.9.31* or *2.9.38*).

Bulk and tapped density (*2.9.34*).

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MAGNESIUM CHLORIDE 4.5-HYDRATE

Magnesii chloridum 4.5-hydricum

$MgCl_2,xH_2O$ with $x \approx 4.5$ M_r 95.21 (anhydrous substance)

DEFINITION

Content: 98.5 per cent to 101.0 per cent (anhydrous substance).

CHARACTERS

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

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

IDENTIFICATION

A. Water (see Tests).

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

C. It gives the reaction of magnesium (*2.3.1*).

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100.0 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 5 mL of solution S add 0.05 mL of *phenol red solution R*. Not more than 0.3 mL of *0.01 M hydrochloric acid* or *0.01 M sodium hydroxide* is required to change the colour of the indicator.

Bromides: maximum 500 ppm.

Dilute 2.0 mL of solution S to 10.0 mL with *water R*. To 1.0 mL of the solution add 4.0 mL of *water R*, 2.0 mL of *phenol red solution R3* and 1.0 mL of *chloramine solution R2* and mix immediately. After exactly 2 min, add 0.30 mL of *0.1 M sodium thiosulfate*, mix and dilute to 10.0 mL with *water R*. The absorbance (*2.2.25*) of the solution measured at 590 nm, using *water R* as the compensation liquid, is not greater than that of a standard prepared at the same time and in the same manner using 5.0 mL of a 3 mg/L solution of *potassium bromide R*.

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

Aluminium (*2.4.17*): maximum 1 ppm, if intended for use in the manufacture of peritoneal dialysis solutions, haemodialysis solutions, or haemofiltration solutions.

Prescribed solution. Dissolve 4 g in 100 mL of *water R* and add 10 mL of *acetate buffer solution pH 6.0 R*.

Reference solution. Mix 2 mL of *aluminium standard solution (2 ppm Al) R*, 10 mL of *acetate buffer solution pH 6.0 R* and 98 mL of *water R*.

Blank solution. Mix 10 mL of *acetate buffer solution pH 6.0 R* and 100 mL of *water R*.

Arsenic (*2.4.2, Method A*): maximum 2 ppm, determined on 0.5 g.

Calcium (*2.4.3*): maximum 0.1 per cent.

Dilute 1 mL of solution S to 15 mL with *distilled water R*.

Iron (*2.4.9*): maximum 10 ppm, determined on solution S.

Potassium: maximum 500 ppm, if intended for use in the manufacture of parenteral preparations.

Atomic emission spectrometry (*2.2.22, Method I*).

Test solution. Dissolve 1.00 g in *water R* and dilute to 100.0 mL with the same solvent.

Reference solutions. Prepare the reference solutions using the following solution, diluted as necessary with *water R*: dissolve 1.144 g of *potassium chloride R*, previously dried at 100-105 °C for 3 h, in *water R* and dilute to 1000.0 mL with the same solvent (600 µg of K per millilitre).

Wavelength: 766.5 nm.

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

12 mL of solution S complies with test A. Prepare the reference solution using *lead standard solution (1 ppm Pb) R*.

Water (*2.5.12*): 44.0 per cent to 48.0 per cent, determined on 50.0 mg.

ASSAY

Dissolve 0.250 g in 50 mL of *water R*. Carry out the complexometric titration of magnesium (*2.5.11*).

1 mL of *0.1 M sodium edetate* is equivalent to 9.521 mg of $MgCl_2$.

STORAGE

In an airtight container.

LABELLING

The label states:

– where applicable, that the substance is suitable for use in the manufacture of peritoneal dialysis solutions, haemodialysis solutions or haemofiltration solutions,

– where applicable, that the substance is suitable for use in the manufacture of parenteral preparations.