Overview of the requirements for homoeopathic products of chemical origin

A Guide Through The Different Sections

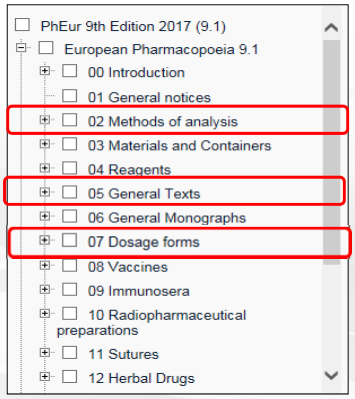
Catherine Lang

Scientific Officer

European Pharmacopoeia Department

General chapters of the Ph. Eur. supporting HOM chemical monographs (HOM + Vol 2&3)

- 2.2 Physical and physicochemical methods (ex. loss on drying)
- 2.3.1 Identification reactions of ions and functional groups (ex. magnesium)
- 2.4 Limit tests (chlorides, sulfates, aluminium, iron, etc)
- 2.9 Pharmeceutical technical procedures (ex. ethanol content)
- 5.1 General texts on microbiology (ex. microbiological quality, viral safety)



etc

General monographs of the Ph. Eur. supporting HOM monographs

ALL HOM preparations

- ***Pharmaceutical preparations (2619)***

Viral safety 5.1.7 and TSE 5.2.8 (**biologicals**)
PRODUCTION: ref. to General monograph
Microbiological quality (5.1.4. & 5.1.1)
Containers 3.1 & 3.2.
TESTS/ASSAY/LABELLING & STORAGE

- ***Homoeopathic preparations (1038)***

DEFINITION: Raw materials, Vehicles, Stocks, Potentisation, Dosage forms and Manufacturing methods (2371) - Table 1038.-1

Inorganics (non-HOM Chap)

- **Substances for pharmaceutical use (2034)**

Herbals PPH

- Herbal drug FHP (2045)
- Mother tincture FHP (2029)

Biological PPH

- Mother tincture FHP (2029)

Individual INC monographs

- Title
- Relative atomic and molecular masses
- CAS registry number

- Definition
- Production (mandatory for manufacturer)

- Potential adulteration (fraudulent activities)
- Characters (for information only)

Individual INC monographs

- Identification
- Tests
- Assay

- Storage (information and recommendation, but competent authority may make it mandatory)
- Labelling

- Impurities – transparency list
- Functionality-related characteristics (not mandatory)
  → Excipients monographs

KEY TO MONOGRAPHS

Available Ph. Eur. online

http://online6.edqm.eu/ep901/NetisUtils/srvrutil_getdoc.aspx/2L34qC3anEJ5SNqDITcLoS65dPNDVHIveT6g0/key_E.pdf?ts=0waGdJZv69zedmZKX-CCKzWZtDWaqiye~JUeO0EK3hkd~qF2nDbe-nXzH&sid=a10f8b29

Carbimazole EUROPEAN PHARMACOPOEIA 9.1

Version date of the text

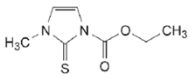
01/2012:0884 corrected 9.1 — *Text reference number*

Modification to be taken into account as soon as possible and not later than the end of the month following the month of publication of Supplement 9.1

Link to further information on the text (e.g. Knowledge database) for smartphones/tablets with camera and barcode reader app

CARBIMAZOLE(1)

Carbimazolum



$C_7H_{10}N_2O_2S$

[22232-54-8] — *CAS number*

M_r 186.2

DEFINITION

Ethyl 3-methyl-2-thioxo-2,3-dihydro-1*H*-imidazole-1-carboxylate. — *Chemical name in accordance with IUPAC nomenclature rules*

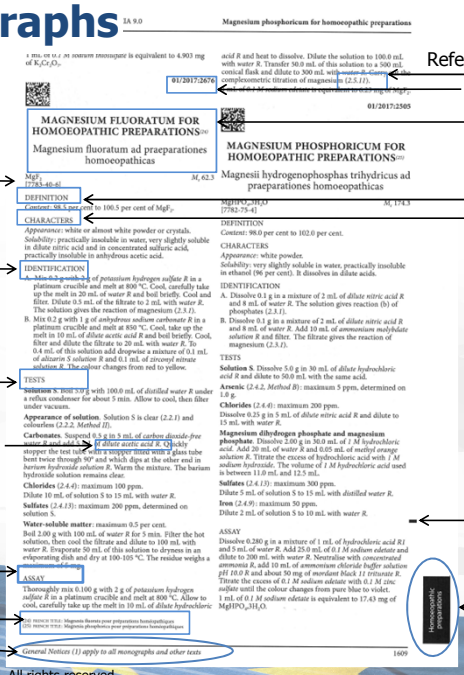
Content: 98.0 per cent to 102.0 per cent (dried substance).

♦CHARACTERS — *For the meaning of black and white diamonds see chapter 5.8. Pharmacopoeial harmonisation*

Appearance: white or yellowish-white, crystalline powder.

Solubility: slightly soluble in water, soluble in acetone and in

Key to monographs



- Molecular (and graphic) formulae
- Relative atomic or molecular mass
- CAS number

Identification tests

Tests

Reagent described in the Ph.Eur.: *dilute acetic acid R*

Assay

Foot note French (or English) title

Reference to the General Notices

Reference to general Chapters: *2.5.11*

Version date & text reference number

English (or French) **title**
and foot note
Latin subtitle

Official definition
Characters
Section for information
e.g. appearance, solubility

Further information provided on Knowledge database

(http://www.edqm.eu/en/Knowledge-Database-707.html)

Vertical/horizontal line where a part of the text has been modified/deleted.

Homoeopathy part

Monograph number

unique **01/2017:0185** **POTASSIUM CHLORIDE**

Kalii chloridum

KCl
[7447-40-7]

M_r 74.6

TITLE

INNs used almost universally

Includes degree of hydration

- «*x* hydrate»: if well-defined form (*x* = hemi, mono, di, tri, tetra, etc)
- «hydrate»: if a mixture of hydrates

DEFINITION

DEFINITION

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

- Chemical nomenclature
- Assay limits

➢ Content expressed on anhydrous or dried basis

➢ Solvent-free substance is implied, even where not stated

(see *Substances for Pharmaceutical Use, Residual solvents*)

➢ Volumetric titration: usually 99.0% to 101.0 % (cf Technical guide)

VOLUMETRIC TRITRATION	CONTENT LIMITS (%)	REPEATABILITY (RSD)	RELATIVE ACCURACY (%)
Acid/base	± 1.0	0.33	± 0.67
Non-aqueous	± 1.0	0.33	± 0.67
Conjugate acid of base	± 1.0	0.33	± 0.67
Redox	± 1.5	0.5	± 1.0
Argentometric	± 1.5	0.5	± 1.0
Complexometric	± 2.0	0.67	± 1.33

CHARACTERS

CHARACTERS

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

Solubility: freely soluble in water, practically insoluble in anhydrous ethanol.

➢ Not analytical requirement

➢ Useful information for the analyst

➢ Physical properties may be mentioned (melting point, density)

➢ See also chapter 5.11: Characters section in monographs

(methods to determine hygroscopicity, crystallinity, solubility)

IDENTIFICATION

IDENTIFICATION
A. It gives the reactions of chlorides (*2.3.1*).
B. Solution S (see Tests) gives the reactions of potassium (*2.3.1*).

First and Second identifications → defined in General Notices

Sometimes cross-reference to "Tests"

Reference to Water/ Loss on drying (applicable for a hydrate)

1st identification alone → always sufficient

2nd identification → never mandatory

2nd identification →usually less sophisticated;

may be performed in pharmacies (not performed by manufacturers)

POTASSIUM CHLORIDE

Kalii chloridum

KCl M_r 74.6
[7447-40-7]

TESTS

Solution S. Dissolve 10.0 g in *carbon dioxide-free water R* prepared from *distilled water R* and dilute to 100 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 50 mL of solution S add 0.1 mL of *bromothymol blue solution R1*. Not more than 0.5 mL of *0.01 M hydrochloric acid* or *0.01 M sodium hydroxide* is required to change the colour of the indicator.

Bromides: maximum 0.1 per cent.
Dilute 1.0 mL of solution S to 50 mL with *water R*. To 5.0 mL of the solution add 2.0 mL of *phenol red solution R2* and 1.0 mL of *chloramine solution R1* and mix immediately. After exactly 2 min add 0.15 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 mL of a 3.0 mg/L solution of *potassium bromide R*.

TESTS

Iodides. Moisten 5 g by the dropwise addition of a freshly prepared mixture of 0.15 mL of *sodium nitrite solution R*, 2 mL of *0.5 M sulfuric acid*, 25 mL of *iodide-free starch solution R* and 25 mL of *water R*. After 5 min, examine in daylight. The substance shows no blue colour.

Sulfates (*2.4.13*): maximum 300 ppm.
Dilute 5 mL of solution S to 15 mL with *distilled water R*.

Aluminium (*2.4.17*): maximum 1.0 ppm, if intended for use in the manufacture of haemodialysis 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*.

Barium. To 5 mL of solution S add 5 mL of *distilled water R* and 1 mL of *dilute sulfuric acid R*. After 15 min, any opalescence in the solution is not more intense than that in a mixture of 5 mL of solution S and 6 mL of *distilled water R*.

TESTS (cont.)

POTASSIUM CHLORIDE

Kalii chloridum

KCl M_r 74.6
[7447-40-7]

Iron (*2.4.9*): maximum 20 ppm.
Dilute 5 mL of solution S to 10 mL with *water R*.

Magnesium and alkaline-earth metals (*2.4.7*): maximum 200 ppm, calculated as Ca, determined on 10.0 g using 0.15 g of *mordant black 11 triturate R*. The volume of *0.01 M sodium edetate* used does not exceed 5.0 mL.

Sodium: maximum 0.1 per cent, if intended for use in the manufacture of parenteral preparations or haemodialysis solutions.
Atomic emission spectrometry (*2.2.22, Method I*).
Test solution. Dissolve 1.00 g of the substance to be examined in *water R* and dilute to 100.0 mL with the same solvent.
Reference solutions. Prepare the reference solutions by diluting as required a solution containing 200 µg of Na per millilitre, prepared as follows: dissolve in *water R* 0.5084 g of *sodium chloride R*, previously dried at 105 °C for 3 h, and dilute to 1000.0 mL with the same solvent.
Wavelength: 589 nm.

Loss on drying (*2.2.32*): maximum 1.0 per cent, determined on 1.000 g by drying in an oven at 105 °C for 3 h.

ASSAY

ASSAY
Dissolve 60.0 mg in *water R*, add 5 mL of *dilute nitric acid R* and dilute to 50 mL with *water R*. Titrate with *0.1 M silver nitrate*, determining the end-point potentiometrically (*2.2.20*).
1 mL of *0.1 M silver nitrate* is equivalent to 7.46 mg of KCl.

Often Unspecific but precise assay (titration)

STORAGE

Not mantadory section

→

Competent authority decides on storage

→ may decide to make it mandatory

Storage of the product
→ to ensure compliance with the monographs

Conventional expressions
→ defined in the General Notices
(e. g. *in an airtight container, protected from light)*

LABELLING

LABELLING
The label states:
- where applicable, that the substance is suitable for use in the manufacture of parenteral preparations;
- where applicable, that the substance is suitable for use in the manufacture of haemodialysis solutions.

Covered by national and international regulations

Information provided with the product included in "labelling":

package, leaflet, certificate of analysis

Labelling items needed for the application of monographs,

e.g. nominal values (especially excipients)

Informational items or recommendations included

FUNCTIONALITY-RELATED CHARACTERISTICS (FRCs)

Described in monographs on Excipients

Section is not mandatory

Provides information on important parameters

→ Chapter on FRCs 5.15

Tests are linked to use

(lubricant, tablet compression, etc.)

CALCIUM SULFATE DIHYDRATE

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). Some of the characteristics described in the Functionality-related characteristics section may also be present in the mandatory part of the monograph since they also represent mandatory quality criteria. In such cases, a cross-reference to the tests described in the mandatory part is included in the Functionality-related characteristics section. Control of the characteristics can 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 calcium sulfate dihydrate used as filler in tablets and capsules.

Calcium sulphate dihydrate (0982)

- Characteristics may be relevant for anhydrous calcium hydrogen phosphate used as filler in tablets and capsules.
- *Particle-size distribution (2.9.31 or 2.9.38).*
- *Bulk and tapped density (2.9.34).*
- *Powder flow (2.9.36).*

Technical Guides

Download for free the latest technical guides

https://www.edqm.eu/en/technical-guides-589.html

Take home messages

- Complementarity of individual and general monographs/chapters
  - *2619 Pharmaceutical preparations*, *2034 Substances for Pharmaceutical use*, etc
  - 5.4 Residual solvants, etc
  - 2.2.46 Chromatographic separation techniques, etc
- Not mandatory sections: Characters, Storage, FRC
- Chemical monographs used for homoeopathy only : individual monograph in Ph. Eur. HOM part ;
- Chemical monographs used for allopathy only OR for allopathy & homoeopathy: individual monograph in Ph. Eur. Volumes 2&3.