

# KEY TO MONOGRAPHS

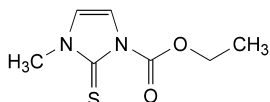
Carbimazole

EUROPEAN PHARMACOPOEIA 6.0

Version date of the text **01/2008:0884**  
corrected 6.0

Text reference number **CARBIMAZOLE**  
Carbimazolum

Modification to be taken into account from the publication date of volume 6.0



CAS number  $C_7H_{10}N_2O_2S$   
**[22232-54-8]**  $M_r$  186.2

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

Content: 98.0 per cent to 102.0 per cent (dried substance).  
CHARACTERS  
Appearance: white or yellowish-white, crystalline powder.  
Solubility: slightly soluble in water, soluble in acetone and in ethanol (96 per cent).

Application of the first and second identification is defined in the General Notices (chapter 1)  
IDENTIFICATION  
First identification: B.  
Second identification: A, C.  
A. Melting point (2.2.14): 122 °C to 125 °C.  
B. Infrared absorption spectrophotometry (2.2.24).

Preparation: discs.  
Comparison: carbimazole CRS.  
C. Thin-layer chromatography (2.2.27).  
Test solution. Dissolve 10 mg of the substance to be examined in methylene chloride R and dilute to 10 ml with the same solvent.  
Reference solution. Dissolve 10 mg of carbimazole CRS in methylene chloride R and dilute to 10 ml with the same solvent.

Plate: TLC silica gel GF<sub>254</sub> plate R.  
Mobile phase: acetone R / methylene chloride R (20:80 V/V).  
Application: 10 µl.  
Development: over a path of 15 cm.  
Drying: in air for 30 min.

Reagents described in chapter 4  
Further information available on www.edqm.eu (KNOWLEDGE)  
Detection: examine in ultraviolet light at 254 nm.  
Results: the principal spot in the chromatogram obtained with the test solution is similar in position and size to the principal spot in the chromatogram obtained with the reference solution.

TESTS  
Related substances. Liquid chromatography (2.2.29).  
Test solution. Dissolve 5.0 mg of the substance to be examined in 10.0 ml of a mixture of 20 volumes of acetonitrile R and 80 volumes of water R. Use this solution within 5 min of preparation.  
Reference solution (a). Dissolve 5 mg of thiamazole R and 0.10 g of carbimazole CRS in a mixture of 20 volumes of acetonitrile R and 80 volumes of water R and dilute to 100.0 ml with the same mixture of solvents. Dilute 1.0 ml

Reference to a general chapter

Line in the margin indicating where part of the text has been modified (technical modification)

of this solution to 10.0 ml with a mixture of 20 volumes of acetonitrile R and 80 volumes of water R.

Reference solution (b). Dissolve 5.0 mg of thiamazole R in a mixture of 20 volumes of acetonitrile R and 80 volumes of water R and dilute to 10.0 ml with the same mixture of solvents. Dilute 1.0 ml of this solution to 100.0 ml with a mixture of 20 volumes of acetonitrile R and 80 volumes of water R.

Column:

– size:  $l = 0.15$  m,  $\varnothing = 3.9$  mm,

– stationary phase: octadecylsilyl silica gel for chromatography R (5 µm).

Mobile phase: acetonitrile R, water R (10:90 V/V).

Flow rate: 1 ml/min.

Detection: spectrophotometer at 254 nm.

Injection: 10 µl.

Run time: 1.5 times the retention time of carbimazole.

Retention time: carbimazole = about 6 min.

System suitability: reference solution (a):

– resolution: minimum 5.0 between the peaks due to impurity A and carbimazole.

Limits:

– impurity A: not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.5 per cent),

– unspecified impurities: for each impurity, not more than 0.1 times the area of the principal peak in the chromatogram obtained with reference solution (b) (0.10 per cent).

Loss on drying (2.2.32): maximum 0.5 per cent, determined on 1.000 g by drying in a desiccator over diphosphorus pentoxide R at a pressure not exceeding 0.7 kPa for 24 h.

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

ASSAY

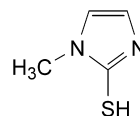
Dissolve 50.0 mg in water R and dilute to 500.0 ml with the same solvent. To 10.0 ml add 10 ml of dilute hydrochloric acid R and dilute to 100.0 ml with water R. Measure the absorbance (2.2.25) at the absorption maximum at 291 nm.

Calculate the content of  $C_7H_{10}N_2O_2S$  taking the specific absorbance to be 557.

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-methyl-1H-imidazole-2-thiol (thiamazole),