Edition: BP 2025 (Ph. Eur. 11.6 update)

Omeprazole for Injection

General Notices

Action and use

Proton pump inhibitor; treatment of peptic ulcer disease.

DEFINITION

Omeprazole for Injection is a sterile material consisting of Omeprazole Sodium with or without excipients. It is supplied in a sealed container.

The contents of the sealed container comply with the requirements for Powders for Injections or Infusions stated under Parenteral Preparations and with the following requirements.

Content of omeprazole, $C_{17}H_{19}N_3O_3S$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

In the Assay, record the UV spectrum of the principal peak in the chromatograms obtained with solutions (1) and (2) with a diode array detector in the range of 210 to 400 nm.

The UV spectrum of the principal peak in the chromatogram obtained with solution (1) is concordant with that of the peak in the chromatogram obtained with solution (2);

the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the peak in the chromatogram obtained with solution (2).

TESTS

Alkalinity

pH of a solution containing the equivalent of 0.8% w/v of omeprazole in 0.9% w/v of sodium chloride in water for injections, 9.0 to 11.0, Appendix V L.

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in solution A. All solutions should be freshly prepared and injected within 15 minutes.

Solution A 0.068% w/v of *trisodium orthophosphate* and 0.062% w/v *disodium hydrogen orthophosphate dihydrate*.

(1) Dilute the volume of the injection containing the equivalent of 0.2 g of omeprazole in 100 mL and dilute to 1 volume to 20 volumes.

(2) Dilute 1 volume of solution (1) to 200 volumes.
(3) 0.0005% w/v each of *omeprazole BPCRS* and *omeprazole impurity D EPCRS*.
(4) 0.01% w/v of *omeprazole impurity BPCRS*.
(5) Dilute 1 volume of solution (2) to 5 volumes.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (10 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (3 µm) (Microspher C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 280 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Solution B 0.017% w/v of *sodium dihydrogen orthophosphate monohydrate* and 0.053% w/v of *disodium hydrogen orthophosphate dihydrate*, adjusted to pH 7.4.

50 volumes of 0.02M *tetrabutylammonium hydrogen sulfate*, 260 volumes of *acetonitrile* and 690 volumes of solution B.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between omeprazole and impurity D and is at least 3.0.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of omeprazole in solution (2).

For the reporting threshold, use the concentration of omeprazole in solution (5).

For peak identification, use solutions (3) and (4).

Omeprazole retention time: about 7 minutes.

Relative retention: impurity 5, about 0.25; impurity 3, about 0.3; impurity A, about 0.35; impurity E, about 0.45; impurity D; about 1.25; impurity 2, about 1.45.

LIMITS

— impurities 2 and 5: not more than 0.6%;

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 2.5%;

— reporting threshold: 0.1%.

ASSAY

Determine the weight of the contents of 10 containers as described in the test for *uniformity of weight*, Appendix XII C1, Powders for Parenteral Administration.

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions.

Solution C 11 volumes of 0.25M *trisodium orthophosphate*, 22 volumes of 0.5M *disodium hydrogen orthophosphate* and dilute to 100 volumes with *water*. Adjust to pH 11.0 with *orthophosphoric acid* or 10M *sodium hydroxide*.

(1) Dilute a quantity of the mixed contents of 10 containers containing the equivalent of 20 mg of omeprazole with 20 mL of *ethanol*, dilute to 100 mL with solution C and filter (a 0.45-µm glass fibre filter is suitable). Dilute 1 volume to 5 volumes with *water*.
(2) 0.02% w/v of *omeprazole BPCRS* in a mixture of 1 volume of *ethanol* and 4 volumes of solution C. Dilute 1 volume to 5 volumes with *water*.

(3) 0.1% w/v of *omeprazole BPCRS* and 0.0005% w/v *omeprazole impurity D EPCRS*, each prepared by dissolving the reference material in 1 volume of *ethanol* and diluting to 5 volumes with solution C. Mix 1 volume of each solution and dilute to 10 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (15 cm × 4.6 mm) packed with *end-capped extra-dense bonded octadecylsilyl silica gel for chromatography* (5 µm) (Zorbax Eclipse XDB-C18 is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 302 nm.
(f) Inject 20 µL of each solution.

MOBILE PHASE

Solution D 10.5 volumes of 1M *sodium dihydrogen orthophosphate monohydrate*, 60 volumes of 0.5M *disodium hydrogen orthophosphate dihydrate* and dilute to 100 volumes with *water*. Adjust to pH 7.3 with *orthophosphoric acid* or 10M *sodium hydroxide*.

35 volumes of *acetonitrile*, 50 volumes of solution D and dilute to 100 volumes with *water*.

When the chromatograms are recorded under the prescribed conditions, the retention time of omeprazole is about 4 minutes.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between impurity D and omeprazole is greater than 5.0.

DETERMINATION OF CONTENT

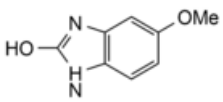
Calculate the content of $C_{17}H_{19}N_3O_3S$ in the powder for injection using the declared content of $C_{17}H_{19}N_3O_3S$ in *omeprazole BPCRS*.

LABELLING

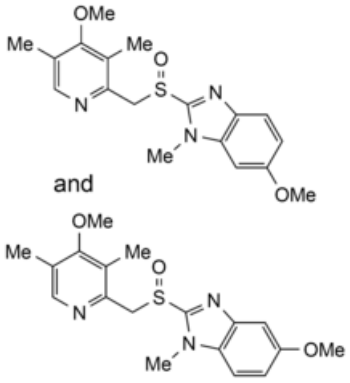
The quantity of active ingredient is stated in terms of the equivalent amount of omeprazole.

IMPURITIES

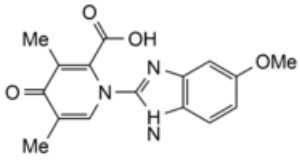
The impurities limited by the requirements of this monograph include those listed under Omeprazole Sodium and:



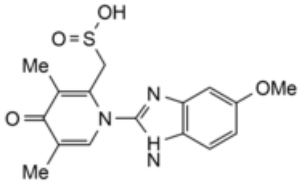
1. 2-hydroxy-5-methoxybenzimidazole (5-methoxy-2-benzimidazolinone),



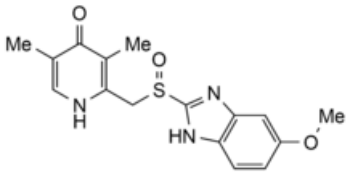
2. 5-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1-methyl-1*H*-benzimidazole and 6-methoxy-2-[[(4-methoxy-3,5-dimethyl-2-pyridinyl)-methyl]sulfinyl]-1-methyl-1*H*-benzimidazole, regioisomers



3. 1,4-dihydro-1-(5-methoxy-1*H*-benzimidazol-2-yl)-3,5-dimethyl-4-oxo-2-pyridinecarboxylic acid



4. [1-(5-methoxy-1*H*-benzimidazol-2-yl)-3,5-dimethyl-4-oxo-1,4-dihydropyridin-2-yl] methanesulfinic acid



5. 2{[(5-methoxy-1*H*-benzimidazol-2-yl)sulfinyl]methyl}-3,5-dimethyl-4(1*H*)-pyridone