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Ribavirin Powder for Nebuliser Solution

General Notices

Ribavirin Nebuliser Solution

Action and use

Antiviral (Hepatitis C, respiratory syncytial virus).

DEFINITION

Ribavirin Powder for Nebuliser Solution consists of Ribavirin with or without excipients. It is supplied in a sealed container and it is reconstituted with an appropriate liquid in accordance with the manufacturer's instructions to obtain a nebuliser solution intended to be converted into aerosols by a nebuliser.

The contents of the sealed container comply with the requirements stated under Preparations for Inhalation and with the following requirements.

Content of ribavirin, $C_8H_{12}N_4O_5$

95.0 to 105.0% of the stated amount.

IDENTIFICATION

A. Carry out the method for *thin-layer chromatography*, Appendix III A, using *silica gel* as the coating substance and a mixture of 20 volumes of 0.1M *ammonium chloride* and 90 volumes of *acetonitrile* as the mobile phase. Apply separately to the plate 10 µL of each of two solutions in *water* containing (1) 1% w/v Ribavirin and (2) 1% w/v of *ribavirin BPCRS*. After removal of the plate, allow the spots to dry in air for 15 minutes and spray the plate with mixture of 0.5 mL of *anisaldehyde*, 0.5 mL of *sulfuric acid*, 0.1 mL of *glacial acetic acid* and 9 mL of *ethanol* (*96%*). Heat the plate at 105° for 40 minutes. The principal spot in the chromatogram obtained with solution (1) is similar in position, colour and size to that in the chromatogram obtained with solution (2).
B. In the Assay the retention time of the principal peak in the chromatogram obtained with solution (1) is similar to that of the principal peak in the chromatogram obtained with solution (2).

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using two solutions of the contents of the container in the mobile phase containing (1) 0.050% w/v and (2) 0.000125% w/v of Ribavirin respectively. Solution (3) contains 0.050% w/v of *ribavirin impurity standard BPCRS* in the mobile phase.

The chromatographic procedure may be carried out using (a) a stainless steel column (10 cm × 7.8 mm) packed with a strong cation-exchange resin of sulfonated, cross-linked *styrene-divinylbenzene co-polymer* in the hydrogen form (7 to 11 µm) (Aminex HPAH is suitable) and maintained at 40°, (b) *water* adjusted to pH 2.5 with *sulfuric acid* as the mobile phase with a flow rate of 1 mL per minute and (c) a detection wavelength of 207 nm. Inject separately 10 µL of each solution. For solution (1) allow the chromatography to proceed for ten times the retention time of the principal peak.

The test is not valid unless the *symmetry factor* for the principal peak in the chromatogram obtained with solution (1) is at least 0.7 and not more than 1.5 and unless the chromatogram obtained with solution (3) closely resembles the reference chromatogram supplied with *ribavirin impurity standard BPCRS*.

In the chromatogram obtained with solution (1) the area of any *secondary peak* is not greater than that of the principal peak in the chromatogram obtained with solution (2) (0.25%) and the sum of the areas of any such peaks is not greater than 4 times the area of the principal peak in the chromatogram obtained with solution (2) (1%).

ASSAY

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in the mobile phase. For solution (1) reconstitute the contents of one container as instructed on the label using an accurately measured volume of diluent, dilute a suitable volume of the solution to 200 volumes with the mobile phase to produce a solution containing 0.10% w/v of Ribavirin; mix and dilute 5 volumes of the resulting solution to 20 volumes with the mobile phase. Solution (2) contains 0.0025% w/v of *ribavirin BPCRS*.

The chromatographic procedure described under Related substances may be used.

Calculate the content of $C_8H_{12}N_4O_5$ in the container using the declared content of $C_8H_{12}N_4O_5$ in *ribavirin BPCRS*.