Amphotericin B for injection (Amphotericini B ad injectionem)

Description. A yellow to orange powder; odourless or almost odourless.

Category. Antifungal drug.

Storage. Amphotericin B powder for injections should be protected from light and stored at a temperature between 2 and 8 °C.

Labelling. The label should state whether any buffering agents and preservatives are added. Further, it should indicate that it is intended for intravenous or intrathecal administration, and that it should be protected from light. Expiry date.

Additional information. Strength in the current WHO Model list of essential medicines: 50 mg.

Requirements

The powder for injections and the reconstituted solution for injections comply with the monograph for "Parenteral preparations".

Definition. Amphotericin B powder for injections is a sterile powder of amphotericin B mixed with sodium desoxycholate. In water, it yields a colloidal dispersion.

Amphotericin B powder for injections may contain suitable buffers and preservatives. The powder is sterilized by a suitable method (see 5.8 Methods of sterilization).

Identity tests

A. Dissolve a quantity of the powder for injections equivalent to 25 mg of Amphotericin B in 5 mL of dimethyl sulfoxide R, add sufficient methanol R to produce 50 mL, and dilute 2 mL to 200 mL with methanol R. The absorption spectrum of the resulting solution, when observed between 300 nm and 450 nm, exhibits three maxima at about 362 nm, 381 nm, and 405 nm. The ratio of the absorbance of a 1-cm layer at 362 nm to that at 381 nm is about 0.6; the ratio of the absorbance at 381 nm to that at 405 nm is about 0.9.

B. Dissolve a quantity of the powder for injections equivalent to 1 mg of Amphotericin B in 2 mL of dimethyl sulfoxide R and introduce 5 mL of phosphoric acid (~1440 g/l) TS to form a lower layer; a blue ring is immediately formed at the interface of the two liquids. Mix the two liquids; a strong blue colour is produced. Add 15 mL of water and mix; the colour of the solution changes to pale yellow.

Loss on drying. Dry the powder for injections to constant mass at 60 °C under reduced pressure (not exceeding 0.6 kPa or 5 mm of mercury); it loses not more than 80 mg/g.

pH value. pH of a suspension of the powder for injections containing 10 mg of Amphotericin B per mL of carbon-dioxide-free water R, 7.2-8.0.

Assay

Mix the contents of 10 containers and carry out the assay as described.

Triturate a quantity of the powder for injections equivalent to about 0.06 g of Amphotericin B, accurately weighed, with dimethylformamide R and add, with shaking, sufficient dimethylformamide R to produce 100 mL. Dilute 10 mL to 100 mL with dimethylformamide R and carry out the assay as described under 3.1 Microbiological assay of antibiotics, using *Saccharomyces cerevisiae* (NCTC 10716, or ATCC 9763) as the test organism, culture medium Cm3 with a final pH of 6.1, sterile phosphate buffer, pH 10.5, TS1, an appropriate concentration of Amphotericin B (usually between 0.5 and 10.0 µg/mL), and an incubation temperature of 29-33 °C. The precision of the assay is such that the fiducial limits of error of the estimated potency (P = 0.95) are not less than 95% and not more than 105% of the estimated potency.

The upper fiducial limit of error is not less than 750 µg/g, calculated with reference to the dried substance.

Bacterial endotoxins. Carry out the test as described under 3.4 Test for bacterial endotoxins; contains not more than 1.0 IU of endotoxin RS per mg.

Sterility. Complies with 3.2 Test for sterility.