Oxytocin injection (Oxytocini injectio)

2015-01

Description. A clear, colourless liquid.

Category. Uterine-stimulating (Oxytocic).

Storage. Oxytocin injection should be kept protected from light and, unless otherwise indicated on the label, stored at a temperature between 2 ºC and 8 ºC. The manufacturer may provide additional information on the label regarding storage conditions for a specified period which may differ from the long-term storage conditions.

Labelling. The label states the content in IU per mL and the oxytocin peptide ($C_{43}H_{66}N_{12}O_{12}S_2$) content in mg per mL.

Additional information. Strength in the current WHO Model list of essential medicines (EML): 10 IU per mL in 1 mL ampoule.

Oxytocin injection is normally intended for intravenous or intramuscular administration.

Requirements

Oxytocin injection complies with the monograph for *Parenteral preparations*.

Definition. Oxytocin injection is a sterile solution of Oxytocin in a suitable diluent. Oxytocin injection contains not less than 90.0% and not more than 110.0% of the amount of oxytocin ($C_{43}H_{66}N_{12}O_{12}S_2$) stated on the label.

Identity tests

-Either test A or test B may be applied.

A. Carry out the test as described under *1.14.1 Chromatography*, Thin-layer chromatography using silica gel R5 as the coating substance and a mixture of 70 volumes of dichloromethane R, 30 volumes of methanol R, 6 volumes of water R and 1 volume of glacial acetic acid R as the mobile phase. Apply separately to the plate 20 µL of each of the following two solutions. For solution (A) evaporate 10.0 mL of oxytocin injection to dryness at 30 °C under reduced pressure (not exceeding 0.6 kPa or 5 mm of mercury) and dissolve the residue in 1.0 mL of methanol R. Prepare solution (B) in methanol R containing 165.0 µg per mL of oxytocin RS. After removing the plate from the chromatographic chamber allow it to dry exhaustively in a current of cool air. Expose the plate to iodine vapour and examine in daylight.

The principal spot obtained with solution A corresponds in position, appearance and intensity with that obtained with solution B.

B. Examine the chromatograms obtained in the assay. The principal peak in the chromatogram obtained with the test solution is similar in retention time to the principal peak in the chromatogram obtained with the reference solution.

pH value (*1.13*). pH of the injection, 3.0–5.0.

Related substances

Carry out the test as described under *1.14.1 Chromatography*, High-performance liquid chromatography using the chromatographic conditions as described under “Assay”, with the following modifications.

Prepare the following solutions using mobile phase A as diluent. For solution (1) use the undiluted injection. For solution (2) dilute 1 mL of solution (1) to 50 mL. For solution (3) weigh 100 mg of chlorbutol R into a 20 mL volumetric flask, dissolve in 0.25 mL of acetic acid, glacial R and dilute with mobile phase A.

For the system suitability test: prepare solution (4) using 3 mL of solution (1) and 2 mL of sulfuric acid (~10 g/L) TS, heat carefully in a boiling water-bath for 20 minutes.

Inject 50 µL of solution (4). The test is not valid unless the resolution between the peak due to oxytocin (retention time about 25 minutes) and the major peak with a relative retention of about 0.9 is at least 1.4.

Inject alternatively 50 µL each of solutions (1) and (2).

In the chromatogram obtained with solution (1) the area of not more than one peak, other than the principal peak, is greater than the area of the principal peak obtained with solution (2) (2%). No such peak, other than the principal peak, is greater than 2.5 times the area of the principal peak obtained with solution (2) (5%). Disregard any peak obtained in the chromatogram with solution (3).

Assay. Carry out the test under *1.14.1 Chromatography*, High-performance liquid chromatography using a stainless steel column (25 cm x 4.6 mm) packed with particles of silica gel, the surface of which has been modified with chemically-bonded octadecylsilyl groups (5 µm).

Use the following conditions for gradient elution:

mobile phase A: 15 volumes of acetonitrile R, 15 volumes of phosphate buffer and 70 volumes of water R;

mobile phase B: 70 volumes of acetonitrile R, 15 volumes of phosphate buffer and 15 volumes of water R.

Prepare the phosphate buffer by dissolving 31.2 g of sodium dihydrogen phosphate dihydrate R in 1000 mL of water R.

Time (min)	Mobile phase A (% v/v)	Mobile phase B (% v/v)	Comments
0–5	100	0	Isocratic
5–20	100 to 94	0 to 6	Linear gradient
20–50	94 to 60	6 to 40	Linear gradient
50–51	60 to 100	40 to 0	Return to initial composition
51–65	100	0	Re-equilibration

Use the following solutions.

For solution (1) use the undiluted injection. For solution (2) dissolve the contents of a vial of oxytocin RS in the mobile phase A to obtain a concentration of 16.7 µg per mL. Prepare solution (3) using 3 mL of solution (1) and 2 mL of sulfuric acid (~10 g/L) TS, heat carefully in a boiling water-bath for 20 minutes.

Operate with a flow rate of 1.0 mL per minute. As a detector use an ultraviolet spectrophotometer set at a wavelength of 220 nm.

Maintain the column temperature at 40 °C.

Inject 50 µL of solution (3). The assay is not valid unless the resolution between the peak due to oxytocin (retention time about 25 minutes) and the peak with a relative retention of about 0.9 is at least 1.4.

Inject alternatively 50 µL each of solutions (1) and (2).

Calculate the content of oxytocin ($C_{43}H_{66}N_{12}O_{12}S_2$) from the declared content of $C_{43}H_{66}N_{12}O_{12}S_2$ in oxytocin RS.

Bacterial endotoxins. Carry out the test as described under *3.4 Test for bacterial endotoxins*; contains less than 0.5 IU of endotoxin per IU of oxytocin.