Teneligliptin and Metformin Hydrochloride Prolonged-release Tablets

Teneligliptin and Metformin Hydrochloride Sustained-release Tablets; Teneligliptin and Metformin Hydrochloride Extended-release Tablets

Teneligliptin and Metformin Hydrochloride Prolonged-release Tablets contain teneligliptin hydrobromide hydrate equivalent to not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of teneligliptin, $C_{22}H_{30}N_6OS$ and metformin hydrochloride, $C_4H_{11}N_5$ HC1.

Usual strengths. Teneligliptin, 20 mg and Metformin hydrochloride, 500 mg; Teneligliptin, 20mg and Metformin hydrochloride, 1000 mg.

Identification

A. In the Assay for teneligliptin, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution.

B. In the Assay for metformin hydrochloride, the absorbance maxima obtained with the test solution corresponds to the absorbance maxima at same wavelength obtained with the reference solution.

Tests

Dissolution (2.5.2).

For Teneligliptin-

Apparatus. No 2 (Paddle),
Medium. 1000 ml of phosphate buffer pH 6.8 prepared by dissolving 6.8 g of *potassium dihydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 6.8 with *1M sodium hydroxide*,
Speed and time. 75 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14)

Solvent mixture. Equal volumes of *isopropyl alcohol* and *water.*

Test solution. Use the filtrate, dilute if necessary, with the dissolution medium.

Reference solution. A 0.02 per cent w/v solution of *teneligliptin hydrobromide hydrate IPRS* in the solvent mixture. Dilute a suitable volume of the solution with the dissolution medium to obtain a solution having similar concentration as that of the test solution.

Chromatographic system
- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Hypersil BDS),
- mobile phase: a mixture of 60 volumes of a buffer solution prepared by dissolving 3.48 g of *dipotassium hydrogen orthophosphate* in 1000 ml of *water*, adjusted to pH 7.2 with *orthophosphoric acid* and 40 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{22}H_{30}N_6OS$ in the medium.

Q. Not less than 70 per cent of the stated amount of $C_{22}H_{30}N_6OS$.

For Metformin Hydrochloride-
Apparatus No. 2 (Paddle),
Medium. 1000 ml of *phosphate buffer pH 6.8*,
Speed and time. 100 rpm and 1st hour, 3rd hour and 10th hour.
Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, suitably diluted with the dissolution medium to obtain a solution of similar concentration as that of the reference solution, at the maximum at about 232 nm (2.4.7). Calculate the content of $C_4H_{11}N_5$, HCl in the medium from the absorbance obtained from a solution of known concentration of *metformin hydrochloride IPRS,* in the dissolution medium.

At 1 hour, not less than 20 per cent and not more than 40 per cent; at 3 hour, not less than 45 per cent and not more than 65 per cent and at 10 hour, not less than 85 per cent.

Related substances. Determine by liquid chromatography (2.4.14).

For Teneligliptin-

Solvent mixture. 70 volumes of *water* and 30 volumes of *acetonitrile*.

Test solution. Disperse a quantity of the powdered tablets containing 50 mg of teneligliptin in 70 ml of *water,* with the aid of ultrasound for 25 minutes and dilute to 100.0 ml with *water*. Centrifuge the solution at 3000 rpm for 10 minutes. Use the supernatant liquid.

Reference solution. A solution containing 0.05 per cent w/v, each of, *teneligliptin impurity A IPRS, teneligliptin impurity B IPRS* and *teneligliptin hydrobromide hydrate IPRS* in the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm) (Such as Inertsil, ODS-3V),
- mobile phase: a mixture of 60 volumes of a buffer solution prepared by dissolving 2.16 g of *octane sulphonic acid sodium salt* in 1000 ml of *water*, adjusted to pH 3.5 with *dilute orthophosphoric acid* and 40 volumes of *acetonitrile*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 210 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to teneligliptin impurity A and teneligliptin impurity B, each of, is not more than 0.5 times the area of the corresponding peaks in the chromatogram obtained with the reference solution (0.5 per cent), the area of any other secondary peak is not more than 0.3 times the area of the principal peak in the chromatogram obtained with the reference solution (0.3 per cent) and the sum of the areas of all the secondary peaks is not more than 1.5 times the area of the principal peak in the chromatogram obtained with the reference solution (1.5 per cent). Ignore the peak due to metformin hydrochloride and any peak with an area less than 0.05 times the area of the principal peak in the chromatogram obtained with the reference solution (0.05 per cent).

For Metformin hydrochloride-

Test solution. Disperse a quantity of the powdered tablets containing 0.5 g of Metformin Hydrochloride in 70 ml of *water,* with the aid of ultrasound for 20 minutes and dilute to 100.0 ml with *water*.

Reference solution (a). Dilute 1.0 ml of the test solution to 100.0 ml with *water.* Dilute 1.0 ml of the solution to 10.0 ml with *water*.

Reference solution (b). A 0.0001 per cent w/v solution of *dicyandiamide IPRS* in *water*.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a buffer solution prepared by dissolving 0.87 g of *pentane sulphonic acid sodium* salt and 1.2 g of *sodium chloride* in 1000 ml of *water*, adjusted to pH 3.5 with *dilute orthophosphoric acid*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 218 nm,
- injection volume: 20 µl.

Inject reference solution (a), (b) and the test solution. Run the chromatogram 3 times the retention time of the principal peak for test solution. The area of any peak corresponding to dicyandiamide is not more than the area of the principal peak in the chromatogram obtained with reference solution (b) (0.02 per cent), the area of any other secondary peak is not more than the area of the principal peak in the chromatogram obtained with reference solution (a) (0.1 per cent). Ignore any peak due to teneligliptin.

Uniformity of content. Complies with the test stated under Tablets.

For Teneligliptin - Determine by liquid chromatography (2.4.14), as described under Assay with the following modifications.

Test solution. Disperse 1 tablet in sufficient quantity of the solvent mixture, with the aid of ultrasound for 20 minutes with intermittent shaking and dilute with the solvent mixture to obtain a solution containing 0.02 per cent w/v of teneligliptin.

Inject the reference solution and the test solution.

Calculate the content of $C_{22}H_{30}N_6OS$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14), as described under dissolution for Teneligliptin with following modifications.

For Teneligliptin-

Test solution. Weigh and powder 20 tablets. Disperse a quantity of the powder containing 20 mg of teneligliptin in 70 ml of the solvent mixture, with the aid of ultrasound for 25 minutes and dilute to 100.0 ml with the solvent mixture.

Reference solution. A 0.02 per cent w/v solution of *teneligliptin hydrobromide hydrate IPRS* in the solvent mixture.

Inject the reference solution. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the contents of $C_{22}H_{30}N_6OS$ in the tablets.

For Metformin hydrochloride-

Test solution. To a quantity of the powdered tablets containing 0.5 g of Metformin Hydrochloride. add 10 g of *sodium dihydrogen orthophosphate* and 80 ml of *water,* stir the solution on magnetic stirrer for 1 hour with intermittent shaking and dilute to 1000.0 ml with *water*. Dilute 2.0 ml of the solution to 100.0 ml with *water*.

Reference solution. To 100 mg of *metformin hydrochloride IPRS*, add 1 g of *sodium dihydrogen orthophosphate* and 80 ml of *water*, sonicate for 2 minutes and dilute to 100.0 ml with *water*. Dilute 1.0 ml of the solution to 100.0 ml with *water*.

Measure the absorbance of the reference solution and the test solution at 233 nm (2.4.7) Calculate the content of $C_4H_{11}N_5$, HC1 in tablets.

Storage. Store protected from moisture, at a temperature not exceeding 30°.

Labelling. The label states the strength in terms of the equivalent amount of teneligliptin and metformin hydrochloride.