Repaglinide and Voglibose Tablets

Repaglinide and Voglibose Tablets contain not less than 90.0 per cent and not more than 110.0 per cent of the stated amounts of repaglinide, $C_{27}H_{36}N_2O_4$ and voglibose, $C_{10}H_{21}NO_7$.

Usual strengths. Repaglinide, 0.5 mg and Voglibose 0.2 mg; Repaglinide, 0.5 mg and Voglibose 0.3 mg; Repaglinide, 1.0 mg and Voglibose, 0.2 mg; Repaglinide, 1.0 mg and Voglibose, 0.3 mg.

Identification

In the Assay of repaglinide, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution and in the Assay of voglibose, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution

Tests

Dissolution (2.5.2).

For Repaglinide

Apparatus No. 2 (Paddle),
Medium. 900 ml of a buffer solution prepared by dissolving 10.3 g of *citric acid monohydrate* and 18.1 g of *disodium hydrogen phosphate dihydrate* in 1000 ml of *water*, adjusted to pH 5.0.
Speed and time. 75 rpm and 30 minutes.

Withdraw a suitable volume of the medium and filter.

Determine by liquid chromatography (2.4.14).

Test solution. Dilute the filtrate, if necessary, with the dissolution medium.

Reference solution. A 0.0011 per cent w/v solution of *repaglinide IPRS* in *methanol.* To 5.0 ml of the solution, add 6 ml *methanol* and dilute to 100.0 ml with the dissolution medium.

Chromatographic system

- a stainless steel column 5 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- column temperature: 40º,
- mobile phase: a mixture of 30 volumes of a buffer solution prepared by dissolving 2 g of *ammonium dihydrogen phosphate* in 950 ml of *water*, adjusted to pH 2.5 with *orthophosphoric acid*, dilute to 1000 ml with *water* and 70 volumes of *methanol*,
- flow rate: 1 ml per minute,
- spectrophotometer set at 245 nm,
- injection volume: 50 µl.

Inject the reference solution. The test is not valid unless 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 $C_{27}H_{36}N_2O_4$ in the medium.

Q. Not less than 70 per cent of the stated amount of $C_{27}H_{36}N_2O_4$.

Related substances. Determine by liquid chromatography (2.4.14).

For Repaglinide

Solvent mixture: 30 volumes of a buffer solution prepared by dissolving 2 g of *ammonium dihydrogen phosphate* in 950 ml of *water*, adjusted to pH 4.0 with *orthophosphoric acid,* dilute to 1000 ml with *water* and 70 volumes of *methanol*.

Test solution. Disperse a suitable quantity of the intact tablets containing 8 mg of Repaglinide in the solvent mixture, with the aid of mechanical shaker and dilute with the solvent mixture to obtain a solution containing 0.008 per cent w/v of Repaglinide.

Reference solution. A 0.08 per cent w/v solution of *repaglinide IPRS* in *methanol.* Dilute 10.0 ml of the solution to 100.0 ml with the solvent mixture. Dilute 1.0 ml of the solution to 100.0 ml with the solvent mixture

Use the chromatographic system as described under dissolution with the following modification.

- spectrophotometer set at 210 nm,
- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 5.0 per cent.

Inject the reference solution and the test solution. In the chromatogram obtained with test solution, the area of any secondary peak is not more than 0.5 times the area of the principal peak in the chromatogram obtained with the reference solution (0.5 per cent) and the sum of the areas of all the secondary peaks is not more than twice the area of the principal peak in the chromatogram obtained with the reference solution (2.0 per cent). Ignore the peak due to voglibose 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).

Uniformity of content. Determine by liquid chromatography (2.4.14),

For Repaglinide.

Solvent mixture: 30 volumes of a buffer solution prepared by dissolving 2 g of *ammonium dihydrogen phosphate* in 950 ml of *water*, adjusted to pH 4.0 with *orthophosphoric acid,* dilute to 1000 ml with *water* and 70 volumes of *methanol*.

Test solution. Disperse 1 intact tablet in the solvent mixture, with the aid of ultrasound with intermittent shaking and dilute with the solvent mixture to obtain a solution containing 0.005 per cent w/v of Repaglinide and filter.

Reference solution. A 0.05 per cent w/v solution of *repaglinide IPRS* in *methanol.* Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Use the chromatographic system as described under dissolution with the following modification.

- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless 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 $C_{27}H_{36}N_2O_4$ in the tablet.

For Voglibose

Determine by liquid chromatography (2.4.14).

Test solution. Disperse 1 intact tablet in the mobile phase, with the aid of ultrasound with intermittent shaking and dilute to 25.0 ml with the mobile phase, filter.

Reference solution. Dissolve an accurately weighed quantity of *voglibose IPRS* in the mobile phase to obtain a solution of the same concentration as that of the test solution.

Chromatographic system

- a stainless steel column 25 cm x 4.6 mm, packed with aminopropylsilane bonded to porous silica (5 µm) (Such as Hypersil APS-2),
- column temperature: 20º,
- mobile phase: a mixture of 30 volumes of a buffer solution prepared by dissolving 0.6 g of *potassium dihydrogen phosphate* and 0.28 g of *dipotassium hydrogen phosphate* in 1000 ml of *water* and 70 volumes of *acetonitrile*,
- flow rate: 0.8 ml per minute,
- spectrophotometer set at 205 nm,
- injection volume: 100 µl.

[Note: Equilibrate the column with the mobile phase for at least 4 hours.]

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 3.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{21}NO_7$ in the tablet.

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

For Repaglinide

Solvent mixture: 30 volumes of a buffer solution prepared by dissolving 2 g of *ammonium dihydrogen phosphate* in 950 ml of *water*, adjusted to pH 4.0 with *orthophosphoric acid,* dilute to 1000 ml with *water* and 70 volumes of *methanol*.

Test solution. Disperse a sufficient quantity of intact tablets containing 8 mg of Repaglinide in the solvent mixture, with the aid of ultrasound with intermittent shaking and dilute with the solvent mixture to obtain a solution containing 0.008 per cent w/v of Repaglinide.

Reference solution. A 0.08 per cent w/v solution of *repaglinide IPRS* in *methanol.* Dilute 5.0 ml of the solution to 50.0 ml with the solvent mixture.

Use the chromatographic system as described under dissolution with the following modification.

- injection volume: 20 µl.

Inject the reference solution. The test is not valid unless 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 $C_{27}H_{36}N_2O_4$ in the tablets.

For Voglibose -

Test solution. Disperse a sufficient quantity of intact tablets containing 2.4 mg of Voglibose in the mobile phase, with the aid of ultrasound with intermittent shaking and dilute with the mobile phase to obtain a solution containing 0.0012 per cent w/v of Voglibose.

Reference solution. A 0.0012 per cent w/v solution of *voglibose IPRS* in the mobile phase.

Use the chromatographic system as described under Uniformity of content.

Inject the reference solution. The test is not valid unless the tailing factor is not more than 2.0 and the relative standard deviation for replicate injections is not more than 3.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{10}H_{21}NO_7$ in the tablets.

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