Risperidone Syrup

Risperidone Oral Solution

Risperidone Syrup contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of risperidone, $C_{23}H_{27}FN_4O_2$. It may contain suitable preservative.

Usual strength. 1 mg per ml.

Identification

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

Tests

pH (2.4.24). 2.0 to 4.0.

Related substances. Determine by liquid chromatography (2.4.14).

Buffer solution. A 0.5 per cent w/v solution of *ammonium acetate* in *water.*

Test solution. Transfer a quantity of the syrup containing 10 mg of Risperidone to a 50-ml volumetric flask, add 25 ml of buffer solution, fill with *methanol* almost to volume and mix. Allow to cool to room temperature and dilute with *methanol* to volume.

Reference solution (a). Dissolve 2.5 mg of *risperidone related compounds mixture IPRS* in 2 ml of *methanol*. Add 2 ml of *water* and 5 ml of the buffer solution and allow to cool to room temperature, dilute to 10.0 ml with *methanol.*

Reference solution (b). A 0.0005 per cent w/v solution of *risperidone IPRS* in *methanol.*

Reference solution (c). Transfer 10.0 ml of reference solution (b) to a 50-ml volumetric flask. Add 10 ml of *water* and 25 ml of the buffer solution and allow to cool to room temperature, dilute with *methanol* to volume.

Reference solution (d). Transfer 2.0 ml of reference solution (b) to a 50-ml volumetric flask. Add 10 ml of *water* and 25 ml of the buffer solution and allow to cool to room temperature, dilute with *methanol* to volume.

Chromatographic system
- a stainless steel column 10 cm x 4.6 mm, packed with octadecylsilane bonded to porous silica (3 µm),
- mobile phase: a mixture of 78 volumes of buffer solution and 22 volumes of *acetonitrile,*
- flow rate: 1.5 ml per minute,
- spectrophotometer set at 275 nm,
- injection volume: 10 µl.

Name	Relative retention time	Correction factor
Risperidone *cis*-*N*-oxide[1]	0.33	1.03
Bicyclorisperidone[2]	0.43	1.49
Risperidone *Z*-oxime[3*]	0.53	—
Risperidone	1.0	—

[1]*cis*-3-{2-[4-(6-Fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]ethyl}-2-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one *N*-oxide.
[2]3-(4-Fluoro-2-hydroxyphenyl)-1-{2-(6,7,8,9-tetrahydro-2-methyl-4-oxo-4*H*pyrido-[1,2-*a*]pyrimidin-3-yl)ethyl}-2-aza-1-azoniabicyclo[2.2.2]oct-2-ene iodide.
[3]3-(2-{4-[(*Z*)-(2,4-Difluorophenyl)(hydroxyimino)methyl]piperidin-1-yl}ethyl)-2-methyl-6,7,8,9-tetrahydro-4*H*-pyrido[1,2-*a*]pyrimidin-4-one.
*Process impurity included for identification only. Process impurities are controlled in the drug substance, and are not to be reported or included in the total impurities for the drug product.

Inject reference solution (a), (c) and (d). The test is not valid unless the resolution between the peaks due to bicyclorisperidone and risperidone *Z*-oxime is not less than 1.5 in the chromatogram obtained with reference solution (a), the relative standard deviation for replicate injections is not more than 5.0 per cent in the chromatogram obtained with reference solution (c) and signal-to-noise ratio for the principal peak is not less than 10.0 in the chromatogram obtained with reference solution (d).

Inject reference solution (c) and the test solution. In the chromatogram obtained with the test solution, the area of any peak corresponding to risperidone *cis*-*N*-oxide and bicyclorisperidone, each of, is not more than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.5 per cent), the area of any other secondary peak is not more than 0.4 times the area of the principal peak in the chromatogram obtained with reference

solution (c) (0.2 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 reference solution (c) (1.0 per cent). Ignore any peak with an area less than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent).

Microbial contamination (2.2.9). Total aerobic microbial count is not more than 100 CFU/ml and total combined molds and yeasts is not more than 10 CFU/ml. It meets the requirements of the test for absence of *Escherichia coli.*

Other tests. Comply with the tests stated under Oral Liquids.

Assay. Determine by liquid chromatography (2.4.14), as described under Related substances with the following modifications.

Reference solution (a). Dissolve 2.5 mg *risperidone related compounds mixture IPRS* in 2 ml of *methanol*. Add 2 ml of *water* and 5 ml of the buffer solution and allow to cool to room temperature, dilute to 10.0 ml with *methanol*.

Reference solution (b). A 0.1 per cent w/v solution of *risperidone IPRS* in *methanol.* Transfer 10.0 ml of the solution to a 50-ml volumetric flask. Add 10 ml of *water* and 25 ml of the buffer solution and allow to cool to room temperature, dilute to volume with *methanol.*

Inject reference solution (a) and (b). The test is not valid unless the resolution between the peaks due to bicyclorisperidone and risperidone 2-oxime is not less than 1.5 in the chromatogram obtained with reference solution (a) and the relative standard deviation for replicate injections is not more than 1.0 per cent in the chromatogram obtained with reference solution (b).

Inject reference solution (b) and the test solution.

Determine the weight per ml of the oral solution (2.4.29) and calculate the content of $C_{23}H_{27}FN_4O_2$.

Storage. Store protected from light, at a temperature not exceeding 30°. Do not freeze.

Note (Preeti): the monograph was drafted as per USP 2021. CHECKED