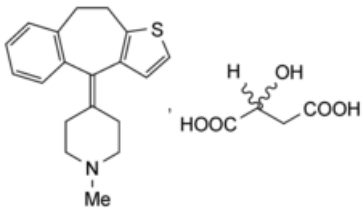
Edition: BP 2025 (Ph. Eur. 11.6 update)

Pizotifen Malate

General Notices



$C_{19}H_{21}NS,C_4H_6O_5$ 429.5 *5189-11-7*

Action and use

Serotonin (5HT) receptor partial agonist; prophylaxis of migraine.

Preparation

Pizotifen Tablets

DEFINITION

Pizotifen Malate is 9,10-dihydro-4-(1-methylpiperidin-4-ylidene)-4*H*-benzo[4,5]cyclohepta[1,2-*b*]thiophene hydrogen malate. It contains not less than 98.5% and not more than 101.5% of $C_{19}H_{21}NS,C_4H_6O_5$, calculated with reference to the dried substance.

CHARACTERISTICS

A white or slightly yellowish white, crystalline powder.

Very slightly soluble in *water*; slightly soluble in *ethanol (96%)*; sparingly soluble in *methanol*.

IDENTIFICATION

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of pizotifen malate *(RS 277)*.
B. In the test for Related substances, the principal spot in the chromatogram obtained with solution (2) corresponds to that in the chromatogram obtained with solution (5).
C. Carry out the method for *thin-layer chromatography*, Appendix III A, using *silica gel G* as the coating substance and a mixture of 70 volumes of *isopropyl ether*, 25 volumes of *anhydrous formic acid* and 5 volumes of *water* as the mobile phase. Apply separately to the plate 5 µL of each of the following solutions. For solution (1) dissolve 30 mg of the substance being examined in 1 mL of *ethanol (80%)*, heating if necessary. Solution (2) contains 1% w/v of *malic acid* in *ethanol (80%)*. After removal of the plate, dry it at 100° for 30 minutes, cool, spray with 0.02M *potassium permanganate* and dry in a current of warm air for about 1 minute. The chromatogram obtained with solution (1) exhibits a spot corresponding in position, colour and size to the spot in the chromatogram obtained with solution (2).

TESTS

Clarity and colour of solution

A 1.0% w/v solution in a mixture of equal volumes of *ethanol (96%)* and *water* is *clear*, Appendix IV A, and not more intensely coloured than *reference solution* BY_6, Appendix IV B, Method II.

Related substances

Carry out the method for *thin-layer chromatography*, Appendix III A, using *silica gel G* as the coating substance and a mixture of 100 volumes of *toluene*, 60 volumes of *butan-1-ol*, 40 volumes of *hexane* and 3 volumes of 13.5M *ammonia* as the mobile phase. Apply separately to the plate 5 µL of each of five solutions in a mixture of 9 volumes of *dichloromethane* and 1 volume of *methanol* containing (1) 2.0% w/v, (2) 0.20% w/v, (3) 0.010% w/v and (4) 0.0050% w/v of the substance being examined and (5) 0.20% w/v of *pizotifen malate BPCRS*. After removal of the plate, dry it in a current of cold air for 5 minutes, spray with a mixture of 1 volume of *potassium iodobismuthate solution* and 10 volumes of 2M *acetic acid* and then with *hydrogen peroxide solution (10 vol)*, cover immediately with a glass plate and examine in daylight. Any *secondary spot* in the chromatogram obtained with solution (1) is not more intense than the spot in the chromatogram obtained with solution (3) and not more than one such spot is more intense than the spot in the chromatogram obtained with solution (4). Disregard any yellow spot or band remaining on the line of application.

Loss on drying

When dried to constant weight at 100° to 105°, loses not more than 0.5% of its weight. Use 1 g.

Sulfated ash

Not more than 0.2%, Appendix IX A, Method II. Use the residue obtained in the test for Loss on drying.

ASSAY

Dissolve 0.35 g in 60 mL of *anhydrous acetic acid* and carry out Method I for *non-aqueous titration*, Appendix VIII A, determining the end point potentiometrically. Each mL of *0.1M perchloric acid VS* is equivalent to 42.95 mg of $C_{19}H_{21}NS,C_4H_6O_5$.

STORAGE

Pizotifen Malate should be protected from light.