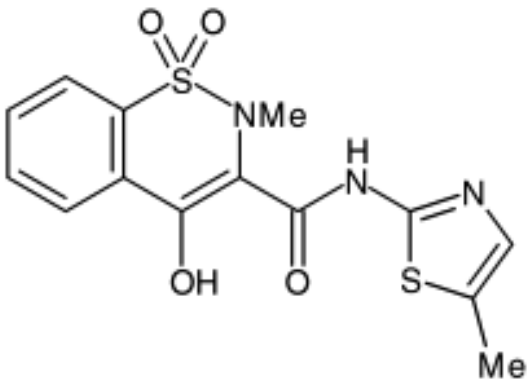
Meloxicam

General Notices



$C_{14}H_{13}N_3O_4S_2$ 351.4 *71125-38-7*

Definition Meloxicam is 4-hydroxy-2-methyl-*N*-(5-methyl-1,3-thiazol-2-yl)-2 *H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide. It contains not less than 99.0% and not more than 100.5% of $C_{14}H_{13}N_3O_4S_2$, calculated with reference to the dried substance.

Characteristics A pale yellow powder.

Practically insoluble in *water*; slightly soluble in *acetone*; soluble in *dimethylformamide*; very slightly soluble in *ethanol (96%)* and in *methanol*.

Identification

A. The *infrared absorption spectrum*, Appendix II A, is concordant with the *reference spectrum* of meloxicam *(RS 374)*.

B. The *light absorption*, Appendix II B, in the range 240 nm to 450 nm of a 0.0015% w/v solution in *methanol* exhibits a maximum at 354 nm. The *absorbance* at 354 nm is about 0.8.

Clarity of solution A 5.0% w/v solution in *dimethylformamide* is *clear*, Appendix IV A.

Related substances Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. For solution (1) prepare a 0.4% w/v of the substance being examined in a mixture of 50 volumes of *methanol (40%)* and 3 volumes of 0.4M *sodium hydroxide* and dilute a portion of this solution with an equal volume of *methanol (40%)*. For solution (2) dilute 1 volume of solution (1) to 100 volumes with *methanol (40%)* and further dilute 1 volume of this solution to 10 volumes with *methanol (40%)*. Prepare solution (3) in the same manner as solution (1) using *meloxicam impurity standard BPCRS*.

The chromatographic procedure may be carried out using a stainless steel column (15 cm × 4.6 mm) packed with *stationary phase C* (5 µm) (Inertsil ODS-2 is suitable). Carry out a linear gradient elution at 45° with a flow rate of 1 ml per minute using the following conditions.

Mobile phase A: A 0.1% w/v solution of *potassium dihydrogen orthophosphate* adjusted to pH 6.0 with *dilute sodium hydroxide solution.*

Mobile phase B: Methanol.

Time (minutes)	Mobile phase A % v/v	Mobile phase B % v/v
0	60	40
2.5	60	40
12	30	70

Use detection wavelengths of 260 and 350 nm. Allow the chromatography to proceed for 15 minutes.

Inject 10 µl of each solution. The test is not valid unless, at each wavelength, the chromatogram obtained with solution (3) closely resembles the corresponding chromatogram supplied with *meloxicam impurity standard BPCRS.*

In the chromatogram obtained with solution (1) at 350 nm, the areas of any peaks corresponding to impurity A and impurity C are not greater than half the area of the peak in the chromatogram obtained with solution (2) at 350 nm (0.1% of impurity A assuming a relative response factor of 0.5, and 0.05% for impurity C). In the chromatogram obtained with solution (1) at 260 nm, the area of any peak corresponding to impurity B is not greater than the area of the peak in the chromatogram obtained with solution (2) at 350 nm (0.1%). In both the chromatograms obtained with solution (1) at 350 nm and at 260 nm, the area of any other *secondary peak* is not greater than the area of the peak in the chromatogram obtained with solution (2) at 350 nm (0.1%). Calculate the percentage content of impurities A and C at 350 nm, the percentage content of impurity B at 260 nm and the percentage content of any other *secondary peaks* at the wavelength of higher response. The nominal total content of any such impurities is not greater than 0.3%.

Heavy metals 2.0 g complies with *limit test C for heavy metals*, Appendix VII (10 ppm). Prepare the standard using 2 ml of *lead standard solution (10 ppm Pb)*.

Loss on drying When dried to a constant weight at 105°, loses not more than 0.5% of its weight. Use 3 g.

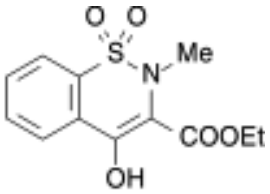
Sulphated ash Not more than 0.1%, Appendix IX A. Use 1 g.

Assay Dissolve 0.25 g in a mixture of 50 ml of *anhydrous acetic acid* and 5 ml of *anhydrous formic acid* and carry out the method for *non-aqueous titration*, Appendix VIII A, determining the end-point potentiometrically. Each ml of 0.1M *perchloric acid VS* is equivalent to 35.14 mg of $C_{14}H_{13}N_3O_4S_2$.

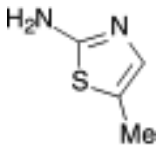
Storage Meloxicam should be kept in a well-closed container.

Action and use Analgesic; anti-inflammatory.

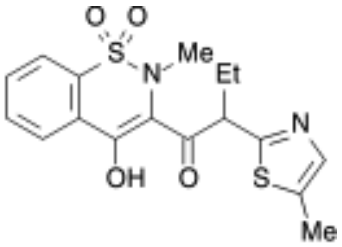
IMPURITIES



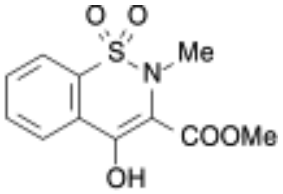
A. ethyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide



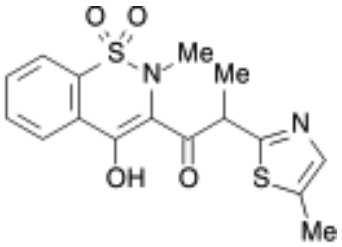
B. 5-methylthiazol-2-ylamine



C. 4-hydroxy-2-methyl- *N*-ethyl-*N´*-(5-methyl-1,3-thiazol-2-yl)-2 *H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide



D. methyl 4-hydroxy-2-methyl-2*H*-1,2-benzothiazine-3-carboxylate 1,1-dioxide,



E. 4-hydroxy-2-methyl- *N*-methyl-*N´*-(5-methyl-1,3-thiazol-2-yl)-2 *H*-1,2-benzothiazine-3-carboxamide 1,1-dioxide