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Propranolol Prolonged-release Capsules

General Notices

Prolonged-release Propranolol Capsules

Details for the public consultation of this monograph are as follows:

EAG/Panel/Working Party	Medicinal Chemicals 2
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Deadline for Comment	31st March 2025
Target Publication Date (subject to change)	BP 2026
Notes	Revised monograph **Identification** UV (A) and TLC (B) test replaced with IR. **Related substances** Solution concentrations & injection volume aligned with revised Injection monograph and the USP. Quantitative limits introduced. **Assay** Harmonised with the existing Related substances test and the USP monograph test.

Propranolol Prolonged-release Capsules from different manufacturers, whilst complying with the requirements of the monograph, are not interchangeable unless otherwise justified and authorised.

Action and use

Beta-adrenoceptor antagonist.

DEFINITION

Propranolol Prolonged-release Capsules contain Propranolol Hydrochloride. They are formulated so that the medicament is released over a period of several hours.

PRODUCTION

A suitable dissolution test is carried out to demonstrate the appropriate release of Propranolol Hydrochloride. The dissolution profile reflects the *in vivo* performance which in turn is compatible with the dosage schedule recommended by the manufacturer.

The capsules comply with the requirements stated under Capsules and with the following requirements.

Content of propranolol hydrochloride, $C_{16}H_{21}NO_2$,HCl

95.0 to 105.0% of the stated amount.

IDENTIFICATION

Suspend a quantity of the prolonged-release capsules containing 100 mg of Propranolol Hydrochloride in 20 mL of *water*, filter, make the filtrate alkaline with 1M *sodium hydroxide* and extract with three 10 mL quantities of *light petroleum R1*. Wash the combined extracts with water until the washings are free from alkali, dry with *anhydrous sodium sulfate*, filter, evaporate the filtrate to dryness and dry the residue at 50° at a pressure of 2 kPa for 1 hour. The *infrared absorption spectrum* of the residue, Appendix II A, is concordant with the *reference spectrum* of propranolol *RS 298*.

TESTS

Related substances

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) Add 100 mL of *methanol* to a quantity of the powdered capsule contents containing 50 mg of Propranolol Hydrochloride, mix with the aid of ultrasound for 15 minutes, shaking occasionally, filter through a glass-microfibre filter (Whatman GF/C is suitable) and use the filtrate.
(2) Dilute 1 volume of solution (1) to 50. Further dilute 1 volume to 10 volumes.
(3) 0.05% w/v of *propranolol for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *octadecylsilyl silica gel for chromatography* (5 µm) (Hypersil ODS 5 µm is suitable).
(b) Use isocratic elution and the mobile phase described below.
(c) Use a flow rate of 1.8 mL per minute.
(d) Use an ambient column temperature.
(e) Use a detection wavelength of 292 nm.
(f) Inject 50 µL of each solution.
(g) For solution (1), allow the chromatography to proceed for 8 times the retention time of the principal peak.

MOBILE PHASE

Add 1.6 g of *sodium laurilsulfate* and 0.31 g of *tetrabutylammonium dihydrogen orthophosphate* to a mixture of 1 mL of *sulfuric acid*, 450 mL of *water* and 550 mL of *acetonitrile*, adjusted to pH 3.3 with 2 M *sodium hydroxide*.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and propranolol is at least 1.5.

CALCULATION OF IMPURITIES

For each impurity, use the concentration of propranolol hydrochloride in solution (2).

For the reporting threshold, use the concentration of propranolol hydrochloride in solution (2).

For peak identification, use solution (3).

Propranolol retention time: about 3 minutes.

Relative retention: impurity A, about 0.6; impurity B, about 4.5 and impurity C, about 6.2.

LIMITS

— unspecified impurities: for each impurity, not more than 0.2%;

— total impurities: not more than 0.8%;

— reporting threshold: 0.1%.

ASSAY

Weigh the contents of 20 capsules. Mix and powder if necessary. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions prepared in the mobile phase.

(1) To a quantity of the capsule contents containing 80 mg of Propranolol Hydrochloride add about 150 mL of *methanol*, heat to boiling and boil for 2 minutes. Remove from the heat, shake for 20 minutes and allow to cool. Add sufficient *methanol* to produce 200 mL. Filter (Whatman No. 1 paper is suitable) and dilute 1 volume of the filtrate to 20 volumes with the mobile phase.
(2) 0.002% w/v of *propranolol hydrochloride BPCRS*.
(3) 0.05% w/v of *propranolol for system suitability EPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic procedure described under Related substances may be used, with the exception of the run time.

SYSTEM SUITABILITY

The test is not valid unless, in the chromatogram obtained with solution (3), the *resolution* between the peaks due to impurity A and propranolol is at least 1.5.

DETERMINATION OF CONTENT

Calculate the content of propranolol hydrochloride, $C_{16}H_{21}NO_2$,HCl, in the capsules from the chromatograms obtained and using the declared content of $C_{16}H_{21}NO_2$,HCl in *propranolol hydrochloride BPCRS*.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed under Propranolol Hydrochloride.