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Notes: Revised monograph **Title:** Title amended to reflect BP policy on the naming of pharmaceutical products under internationally recognised standard terms. **Content** limits revised to "95-105 % of the stated amount." **Identification**. Test utilising Infra-red spectroscopy included in place of TLC method. **Related Substances**. Improved LC method, harmonised with the Ph. Eur. Impurity limits revised to mirror the improvement in the method capabilities. **Assay**. Harmonised with the Related Substances procedure.	

Minocycline Prolonged-release Capsules

Minocycline Preparations

Action and use
Tetracycline antibacterial.

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

DEFINITION
Minocycline Prolonged-release Capsules contain Minocycline Hydrochloride Dihydrate. 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 minocycline 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 minocycline, $C_{23}H_{27}N_3O_7$
95.0 to 105.0% of the stated amount.

IDENTIFICATION
Dissolve a quantity of the contents of the capsules containing the equivalent of 50 mg of minocycline with 10 mL of *methanol*, filter (a 0.45 µm nylon filter is suitable), evaporate the filtrate to dryness under a stream of nitrogen at 60 °. The infrared absorption spectrum of the dried residue, Appendix II A, is concordant with the reference spectrum of minocycline (RS xxx).

TESTS

Related substances
Carry out the test protected from light. Store the solutions at a temperature of 2 to 8 ° and use them within 3 hours of preparation.

Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions. Mix 18 volumes of a 0.375% w/v solution of *sodium edetate* and 60 volumes of a 2.83% w/v solution of *ammonium oxalate* and adjust to pH 7.2 with *dilute ammonia* (Solution A).

(1) Dissolve a quantity of the contents of the capsules containing the equivalent of 50 mg of minocycline in *water*, dilute to 100 mL with the same solvent, filter and use the filtrate.

(2) Dilute 1 volume of solution (1) to 100 volumes with *water*.

(3) Dissolve 2 mg of *Minocycline for system suitability EPCRS* (containing impurities A, B, C, E, F, G and H) in *water* and dilute to 5 mL with the same solvent.

(4) Dilute 1 volume of solution (2) to 10 volumes with *water*.

CHROMATOGRAPHIC CONDITIONS

(a) Use a stainless steel column (25 cm × 4.6 mm) packed with *base-deactivated end-capped octadecylsilyl silica gel for chromatography* (5 µm) (ChromaNik Technologies Inc, Sunniest C18 is suitable is suitable).

(b) Use isocratic elution and the mobile phase described below.

(c) Use a flow rate of 1.5 mL per minute.

(d) Use a column temperature of 40°.

(e) Use a detection wavelength of 280 nm.

(f) Inject 20 µL of each solution.

(g) Allow the chromatography to proceed for about 3 times the retention time of minocycline.

MOBILE PHASE

8 volumes of *tetrahydrofuran*, 12 volumes of *dimethylformamide* and 78 volumes of solution A.

When the chromatograms are recorded under the prescribed conditions the retention times relative to minocycline (retention time about 11 minutes) are impurity C, about 0.52; impurity H, about 0.55; impurity B, about 0.66; impurity A, about 0.74; impurity G, about 0.79; impurity F, about 0.92 and impurity E, about 2.1.

SYSTEM SUITABILITY

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

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

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

LIMITS

Identify the peaks due to impurity E, impurity F and impurity G using the chromatogram obtained with solution (3) and multiply the areas of these peaks by the corresponding correction factors: impurity E, 1.60; impurity F, 1.6; and impurity G, 1.4.

In the chromatogram obtained with solution (1):

the area of any peak corresponding to impurity A is not greater than twice the area of the principal peak in the chromatogram obtained with solution (2) (2.0%);

the area of any peak corresponding to impurity B is not greater than 0.8 times the area of the principal peak in the chromatogram obtained with solution (2) (0.8%);

the area of any peak corresponding to impurity C or impurity E is not greater than 0.6 times the area of the principal peak in the chromatogram obtained with solution (2) (0.6% of each);

the area of any peak corresponding to impurity F or impurity G is not greater than 0.5 times the area of the principal peak in the chromatogram obtained with solution (2) (0.5% of each);

the area of any other *secondary peak* is not greater than 0.2 times the principal peak in the chromatogram obtained with solution (2) (0.2%).

the sum of the areas of any *secondary peaks* is not greater than 3.5 times the principal peak in the chromatogram obtained with solution (2) (3.5%).

Disregard any peak with an area less than the area of the principal peak in the chromatogram obtained with solution (4) (0.1%).

ASSAY

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

(1) Dissolve a quantity of the contents of the capsules containing the equivalent of 28 mg of minocycline in *mobile phase*, dilute to 50 mL, filter and use the filtrate.

(2) 0.060% w/v *Minocycline Hydrochloride BPCRS*.

CHROMATOGRAPHIC CONDITIONS

The chromatographic conditions described under Related substances may be used

DETERMINATION OF CONTENT

Calculate the total content of minocycline, $C_{23}H_{27}N_3O_7$, in the capsules using the declared content of $C_{23}H_{27}N_3O_7$,HCl in *minocycline hydrochloride BPCRS*. Each mg of $C_{23}H_{27}N_3O_7$,HCl is equivalent to 0.9261 mg of $C_{23}H_{27}N_3O_7$.

LABELLING

The quantity of active ingredient is stated in terms of the equivalent amount of minocycline.

IMPURITIES

The impurities limited by the requirements of this monograph include those listed in the monograph for Minocycline Hydrochloride Dihydrate.