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_{3}O_{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 in water, dilute to 100 mL with the same solvent, filter and use the filtrate.

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

(2) 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.

(3) 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).

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

(c) Use an injection volume of 20 µL.

(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, C23H27N3O7, in the capsules using the declared content of C23H27N3O7·HCl in minocycline hydrochloride BPCRS. Each mg of C23H27N3O7·HCl is equivalent to 0.9261 mg of C23H27N3O7.

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.