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<b>Deadline for Comment</b>	30 June 2018
<b>Target Publication (subject to change)</b>	BP 2020
<p><b>Notes:</b> Revised monograph <b>Content</b> limits revised to “95-105 % of the stated amount.” <b>Identification.</b> Test utilising Infra-red spectroscopy included in place of TLC method. <b>Dissolution.</b> New test with limit of 75% (Q) in 45 minutes. Harmonised with USP <b>Related Substances.</b> Improved LC method, harmonised with the Ph. Eur. Impurity limits revised to mirror the improvement in the method capabilities. <b>Assay.</b> Harmonised with the Related Substances procedure.</p>	

## Minocycline Tablets

### Minocycline Preparations

#### Action and use

Tetracycline antibacterial.

#### DEFINITION

Minocycline Tablets contain Minocycline Hydrochloride Dihydrate.

*The tablets comply with the requirements stated under Tablets and with the following requirements.*

#### Content of minocycline, C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>

95.0 to 105.0% of the stated amount.

#### IDENTIFICATION

Dissolve a quantity of the tablets 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

##### Dissolution

Comply with the *dissolution test for tablets and capsules*, Appendix XII B1.

##### TEST CONDITIONS

- Use Apparatus 2, rotating the paddle at 50 revolutions per minute.
- Use 900 mL of water, at a temperature of 37°, as the medium.

##### PROCEDURE

- After 45 minutes withdraw a sample of the medium and measure the *absorbance* of the filtered sample, suitably diluted with the dissolution medium if necessary, at the maximum at 348 nm, Appendix II B using *water* in the reference cell.
- Measure the *absorbance* of a suitable solution of minocycline hydrochloride *BPCRS* using *water* in the reference cell.

##### DETERMINATION OF CONTENT

Calculate the total content of minocycline, C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>, in the medium from the *absorbance* obtained using the

declared content of C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>.HCl in *minocycline hydrochloride BPCRS*. Each mg of C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>.HCl is equivalent to 0.9261 mg of C<sub>23</sub>H<sub>27</sub>N<sub>3</sub>O<sub>7</sub>.

#### LIMITS

The amount of minocycline released in not less than 75% (Q) of the stated amount.

#### 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).

- Dissolve a quantity of the powdered tablets containing the equivalent of 50 mg of minocycline in *water*, dilute to 100 mL with the same solvent, filter and use the filtrate.
- Dilute 1 volume of solution (1) to 100 volumes with *water*.
- Dissolve 2 mg of *minocycline for system suitability EPCRS* in *water* and dilute to 5 mL with the same solvent.
- Dilute 1 volume of solution (2) to 10 volumes with *water*.

#### CHROMATOGRAPHIC CONDITIONS

- 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).
- Use isocratic elution and the mobile phase described below.
- Use a flow rate of 1.5 mL per minute.
- Use a column temperature of about 40°.
- Use a detection wavelength of 280 nm.
- Inject 20 µL of each solution.
- 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

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.

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

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

Weigh and powder 20 tablets. Carry out the method for *liquid chromatography*, Appendix III D, using the following solutions in water.

(1) Shake a quantity of the powdered tablets containing the equivalent of 28 mg of minocycline in *water*, 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 tablets using the declared content of  $C_{23}H_{27}N_3O_7 \cdot HCl$  in *minocycline hydrochloride BPCRS*. Each mg of  $C_{23}H_{27}N_3O_7 \cdot HCl$  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.