Minocycline Tablets

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Manufacturers, regulatory authorities, health authorities, researchers, and other stakeholders are invited to provide their feedback and comments on this draft proposal. Manufacturers are also invited to submit samples of their products to the IPC to ensure that the proposed monograph adequately controls the quality of the product(s) they manufacture. Comments and samples received after the last date will not be considered by the IPC before finalizing the monograph.

Please send any comments you may have on this draft document to lab.ipc@gov.in, with a copy to Dr. Gaurav Pratap Singh (email: gpsingh.ipc@gov.in) before the last date for comments.

Document History and Schedule for the Adoption Process

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Further follow-up action as required.	

Minocycline Tablets

Minocycline Hydrochloride Tablets

Minocycline Tablets contain not less than 95.0 per cent and not more than 105.0 per cent of the stated amount of minocycline, $C_{23}H_{27}N_3O_7$.

Usual strengths. 50 mg; 100 mg.

Identification

In the Assay, the principal peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with reference solution.

Tests

Dissolution (2.5.2).
Apparatus No. 2 (Paddle),
Medium. 900 ml of *water*,
Speed and time. 50 rpm and 45 minutes.

Withdraw a suitable volume of the medium and filter. Measure the absorbance of the filtrate, dilute suitably if necessary with the medium, at the maximum at about 348 nm (2.4.7). Calculate the content of $C_{23}H_{27}N_3O_7$ in the medium from the absorbance obtained from a solution of known concentration of *minocycline hydrochloride IPRS* in the dissolution medium.

Calculate the contents of $C_{23}H_{27}N_3O_7$ in the medium.

Q. Not less than 75 per cent of the stated amount of $C_{23}H_{27}N_3O_7$.

Related substances. Determine by liquid chromatography (2.4.14).

NOTE — Carry out the test protected from light. Store the solution at 2° to 8° and use within 3 hours of preparation.

Buffer solution. Mix 18 volumes of 0.38 per cent w/v solution of *sodium edetate* and 60 volumes of 0.28 per cent w/v solution of *ammonium oxalate*, adjusted to pH 7.2 with *dilute ammonia.*

Test solution. Disperse a quantity of the powdered tablets containing 50 mg of Minocycline in *water*, with the aid of ultrasound with intermittent shaking and dilute to 100.0 ml with *water*, filter.

Reference solution (a). a solution of *minocycline hydrochloride IPRS* containing 0.0005 per cent w/v of minocycline in *water*.

Reference solution (b). Dissolve 2 mg of *minocycline for system suitability IPRS* (Containing A, B, C, E, F, G and H) in water and dilute to 5.0 ml of *water*.

Reference solution (c). Dilute 1.0 ml of reference solution (a) to 10.0 ml with *water*.

Chromatographic system
- a stainless steel column 20 cm × 4.6 mm, packed with base-deactivated, end-capped octadecylsilane bonded to porous silica (5 µm) (Such as Sunniest C18),
- column temperature: 40º,
- mobile phase: a mixture of 78 volumes of the buffer solution, 12 volumes of *dimethylformamide* and 8 volumes of *tetrahydrofuran*,
- flow rate: 1.5 ml per minute,

– spectrophotometer set at 280 nm,
– injection volume: 20 µl.

Name	Relative retention time	Correction factor
Minocycline impurity C[1]	0.52	---
Minocycline impurity H[2]	0.55	---
Minocycline impurity B[3]	0.66	---
Minocycline impurity A[4]	0.74	---
Minocycline impurity G[5]	0.8	1.4
Minocycline impurity F[6]	0.9	1.6
Minocycline (Retention time: about 11 minutes)	1.0	---
Minocycline impurity E[7]	2.1	1.6

[1](4*S*,4a*S*,5a*R*,12a*S*)-4-(dimethylamino)-3,10,12,12a-tetrahydroxy-7-(methylamino)-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide(7-monodemethylDapagliflozin),
[2](4*S*,4a*S*,12a*S*)-4,7-bis(dimethylamino)-3,10,11,12a-tetrahydroxy-1,12-dioxo-1,4,4a,5,12,12a-hexahydrotetracene-2-carboxamide,
[3](4*S*,4a*S*,5a*R*,12a*S*)-4-(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide (sancycline),
[4](4*R*,4a*S*,5a*R*,12a*S*)-4,7-bis(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide(4-epiDapagliflozin),
[5](4*S*,4a*S*,5a*R*,12a*S*)-4,7,9-tris(dimethylamino)-3,10,12,12a-tetrahydroxy-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide,
[6](4*S*,4a*S*,5a*R*,12a*S*)-4,7-bis(dimethylamino)-3,10,12,12a-tetrahydroxy-*N*-(hydroxymethyl)-1,11-dioxo-1,4,4a,5,5a,6,11,12a-octahydrotetracene-2-carboxamide,
[7](4*S*,4a*S*,5a*R*,12a*S*)-4,7-bis(dimethylamino)-3,10,12a-trihydroxy-12-imino-1,11-dioxo-1,4,4a,5,5a,6,11,11a,12,12a-decahydrotetracene-2-carboxamide,

Inject reference solution (b) to identify the peaks due to Minocycline impurity A, B, C, E, F, G and H.

Inject reference solution (b) and (c). The test is not valid unless the resolution between the peaks due to minocycline impurity C and minocycline impurity H is not less than 1.5, between the peaks due to minocycline impurity A and minocycline impurity G is not less than 1.5 and between the peaks due to minocycline impurity F and minocycline is not less than 1.5 in the chromatogram obtained with reference solution (b) and the signal- to- noise ratio is not less than 20 in the chromatogram obtained with reference solution (c).

Inject reference solution (a) (c) and the test solution. Run the chromatogram 3 times the retention time of the principal peak. In the chromatogram obtained with the test solution, the area of any peak corresponding to minocycline impurity A is not more than twice the area of the principal peak in the chromatogram obtained with reference solution (a) (2.0 per cent), the area of any peak corresponding to minocycline impurity B is not more than 0.8 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.8 per cent), the area of any peak corresponding minocycline impurity C and minocycline impurity E, each of, is not more than 0.6 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.6 per cent), the area of any peak corresponding minocycline impurity F and minocycline impurity G, each of, is not more than 0.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.5 per cent), the area of any other secondary peak is not more than 0.2 times the area of the principal peak in the chromatogram obtained with reference solution (a) (0.2 per cent) and the sum of areas of all the secondary peaks is not more than 3.5 times the area of the principal peak in the chromatogram obtained with reference solution (a) (3.5 per cent). Ignore any peak with an area less than the area of the principal peak in the chromatogram obtained with reference solution (c) (0.1 per cent).

Other tests. Comply with the tests stated under Tablets.

Assay. Determine by liquid chromatography (2.4.14).

NOTE — Carry out the test protected from light. Store the solution at 2° to 8° and use within 3 hours of preparation.

Test solution. Weigh and powder 20 tablets. Disperse a quantity of powder containing 100 mg of Minocycline in *water* with the aid of ultrasound for 15 minutes with intermittent shaking and dilute to 200.0 ml with *water*, filter.

Reference solution. a solution of *minocycline hydrochloride IPRS* containing 0.05 per cent w/v of minocycline in *water*.

Use chromatographic system as described under Related substances.

Inject the reference solution. The test is not valid unless the relative standard deviation for replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of $C_{23}H_{27}N_3O_7$ in the tablets.

1 mg of minocycline in $C_{23}H_{28}N_3O_7$. HCl is equivalent to 0.9261 mg of minocycline, $C_{23}H_{27}N_3O_7$.

Storage. Store protected from light and moisture, at temperature not exceeding 30º.

Labelling. The label states the strength in terms of the equivalent amount of minocycline.