Tilmicosin Injection

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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.	

Tilmicosin Injection

Tilmicosin Injection is a sterile solution of Tilmicosin or Tilmicosin Phosphate in a mixture of propylene glycol and water for injection, and is solubilized with the aid of phosphoric acid.

Commented [SR1]: Comment from stakeholder

Tilmicosin Injection contains not less than 90.0 per cent and not more than 110.0 per cent of the stated amount of Tilmicosin, $C_{46}H_{80}N_2O_{13}$.

Usual strengths. 250 mg per ml, 300 mg per ml.

Identification

In the Assay, the peak due to tilmicosin *trans*-isomer and tilmicosin *cis*-isomer in the chromatogram obtained with the test solution corresponds to the peaks due to tilmicosin *trans*-isomer and tilmicosin *cis*-isomer in the chromatogram obtained with the reference solution.

Tests

pH (2.4.24). ~~5.5 to 6.5~~ 5.0 to 7.0.

Commented [SR2]: Specs to cover Tilmicosin phosphate base also

Propylene glycol. 80.0 to 120.0 per cent of the labeled amount.

Determine by gas chromatography (2.4.13).

Internal standard solution. A 0.05 per cent w/v solution of *pentadecane* in *acetone*.

Test solution. Dilute a suitable volume of injection with *acetone* to obtain a solution containing 0.125 per cent w/v of propylene glycol. Dilute 10.0 ml of the solution to 20.0 ml with the internal standard solution.

Reference solution. A 0.125 per cent w/v solution of *propylene glycol* in *acetone*. Dilute 10.0 ml of the solution to 20.0 ml with the internal standard solution.

Chromatographic system
– a fused silica column 15 m× 0.53 mm, packed with polyethylene glycol compound (mol. wt. about 15,000), (1µm)
– temperature:
~~column~~column. 100°,
inlet port 250° and detector 250°,
– flame ionization detector,
– flow rate 15 ml per minute using helium as carrier gas,
– injection volume: 1.0 µl.

The relative retention time with reference to propylene glycol for *pentadecane* is about 0.6.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to pentadecane (Internal standard) and propylene glycol is not less than 7.0 and the relative standard deviation of peak area ratio due to propylene glycol and internal standard and for the replicate injections is not more than 2.0 per cent.

Inject the reference solution and the test solution.

Calculate the content of propylene glycol using ratio of the peak area of propylene glycol to that of peak area of the internal standard.

Other tests. Comply with the tests stated under Parenteral Preparations (Injections).

Sterility (2.2.11). Complies with the test for sterility.

Bacterial endotoxins (2.2.3). Not more than 0.5 Endotoxin Unit per ml of tilmicosin.

Assay. Determine by liquid chromatography (2.4.14).

Buffer solution. A solution prepared by diluting 168 ml of *dibutylaminein* in 700 ml of *water*. Add *orthophosphoric acid* slowly until the *dibutylamine* is just dissolved, string vigorously during the addition. Allow to cool and adjusted to pH 2.55 with *orthophosphoric acid*, dilute to 1000 ml with *water*. Mix and filter under vacuum.

Solvent mixture. A 77.5 volumes of *water*, 20 volumes of *acetonitrile* and 2.5 volumes of buffer solution.

Test solution. Dilute a suitable volume of injection with the solvent mixture to obtain a solution containing 0.05 per cent w/v of
Tilmicosin.

Reference solution. A 0.25 per cent w/v solution of *tilmicosin IPRS* in *acetonitrile*. Transfer 4.0 ml of the solution to a 20-ml volumetric flask, add 10 ml of *water* and 0.5 ml buffer solution and dilute to volume with *water*

Chromatographic system
- a stainless steel column 25 cm × 4.6 mm, packed with octadecylsilane bonded to porous silica (5 µm),
- mobile phase: a mixture of 11.5 volumes of *acetonitrile*, 5.5 volumes of *tetrahydrofuran*, 25 volumes of a buffer solution and 80.5 volumes of *water*,
- flow rate: 1.1 ml per minute,
- spectrophotometer set at 280 nm,
- injection volume: 10 µl.

The relative retention time with reference to tilmicosin *cis* -isomers for tilmicosin *trans* -isomers form is about 0.8.

Inject the reference solution. The test is not valid unless the resolution between the peaks due to tilmicosin *trans*-isomers and tilmicosin *cis*-isomers is not less than 1.25, the tailing factor is not less than 0.7 and not more than 2.0 and the relative standard deviation for replicate injections is not more than 1.5 per cent.

Inject the reference solution and the test solution. Record the chromatograms, and measure the area responses for the major peaks. Calculate the quantity, in mg, each of the, tilmicosin isomer in each ml of the injection.

Calculate the content of $C_{46}H_{80}N_2O_{13}$ (in mg per ml) of the injection, taken by adding the quantities, in mg per ml, of tilmicosin *trans*-isomer and tilmicosin *cis*-isomer found.

Storage. Store protected from light, at temperature not exceeding 30°.