September 2022

Public assessment summary report

Name of the Finished Pharmaceutical Product	DOVPRELA (Pretomanid Tablets 200 mg)
Manufacturer of Prequalified Product	**Mylan Laboratories Limited,** Plot No H12 & H13 MIDC, Waluj Industrial Estate,Aurangabad -431136, Maharashtra, INDIA
Active Pharmaceutical Ingredient	Pretomanid

1. Introduction

This is a summary of the public assessment report for DOVPRELA (Pretomanid Tablets 200 mg).

Pretomanid is a nitroimidazooxazine antimycobacterial drug, ATC Code: *not assigned.* Pretomanid tablet is a nitroimidazooxazine antimycobacterial drug. It kills actively replicating *M. tuberculosis* by inhibiting mycolic acid biosynthesis, thereby blocking cell wall production.

2. Assessment of quality

Active pharmaceutical Ingredient (API)

Pretomanid is a white to off-white to yellow color powder. The chemical name is (6*S*)-2-Nitro-6-{[4-(trifluoromethoxy) phenyl] methoxy}-6,7-dihydro-5*H*-imidazo[2,1-*b*] [1,3]oxazine.

The solubility of Pretomanid across the physiological pH range has been determined as shown in 2.3.S.1.3.2 and 3.2.P.2.1.1.2. The solubility has been determined by standard solubility determinations using a full pH range of buffer solutions as well as some simulated physiological media at gastric and duodenal pH's.

Critical process parameters are identified and appropriate controls are established for the intermediates in the manufacturing process of drug substance, Pretomanid.

A total of four different solid-state forms of pretomanid drug substance were identified and characterized. The proposed synthesis route produces a defined polymorphic form, Form I. Since Form I exhibits a reversible (endothermic) solid-solid phase transition at 100°C, Form I is enantio tropically related to a second polymorphic form, arbitrarily designated as Form II.

Finished pharmaceutical product (FPP)

Pharmaceutical development and manufacture:

The objective of the development programme was to formulate a safe efficacious, stable dosage form. Suitable pharmaceutical development data have been provided for this application. Dissolution profiles were comparable between the manufacturing sites. The Drug Substance and Drug Product Comparability Report were presented. The process chosen for Pretomanid tablet, 200 mg arose following a progression from a powder filled capsule, through a direct compression tablet to, finally, the wet granulation process. The latter is the most commonly used method of tablet production and for Pretomanid tablet, 200 mg it *uses conventional processing steps and equipment throughout.*

Manufacture of the product

A satisfactory description of the manufacturing process and batch formulae for product has been provided. The manufacturing process has been validated with full scale production scale batches and result found to be acceptable.

Specifications:

The finished product specification is satisfactory. Test methods have been described and adequately validated as appropriate. Batch data have been provided that complies with the release specification. Certificate of analysis have been provided for the standard used.

Other ingredients:

All excipients comply with their respective pharmacopoeia monographs.

Stability testing:

Finished product stability studies were performed in accordance with current guidelines on batches of finished product packaging proposed for marketing. The data from these studies support a shelf life.

3. Conclusion

Based on assessment of data on quality, non clinical and clinical studies the assessors considered that the benefit–risk profile of Pretomanid was acceptable for the following indication: as part of a combination regimen with bedaquiline and linezolid for the treatment of adults with pulmonary extensively drug resistant (XDR) or treatment-intolerant or nonresponsive multidrug-resistant (MDR) tuberculosis (TB).