DEPARTMENT OF DRUG ADMINISTRATION

National Medicines Laboratory

ANALYTICAL METHOD VALIDATION COMMITTEE

Linezolid and Dextrose IV Injection

Analytical Profile No.: Linez 076/077/AP 066

Linezolid and Dextrose IV Injection contain not less than 90 % and not more than 110 % of the stated amount of Linezolid and Dextrose.

1. Identification:

1.1 Linezolid: In the assay, the principle peak in the chromatogram obtained with the test solution corresponds to the peak in the chromatogram obtained with the reference solution of Linezolid.

1.2. Dextrose: The solution prepared as directed in the assay is dextrorotatory.

Tests:

2. pH: 4.0 to 6.0

3. Particulate matter: As per IP (latest edition)

4. Sterility: As per IP (latest edition) by membrane filtration method.

5. Bacterial Endotoxins: As per IP (latest edition)

Limit: Less than 0.58 EU/mg of Linezolid

6. Assay:

6.1 Linezolid: *Determine by Liquid Chromatography*

6.1.1 Solvent mixture: A mixture of 75 volumes of buffer solution prepared by diluting 1.0 ml of triethylamine to 1000 ml with water, adjusted to pH 3.0 with orthophosphoric acid and 25 volumes of methanol.

6.1.2 Test solution: Weigh and transfer 20 ml of injection (equivalent to 40 mg of Linezolid) into a 50 ml volumetric flask, add about 35 ml of solvent mixture, sonicate for 20 minutes, cool to room temperature and make up the volume to 50.0 ml with the same solvent. Dilute 5.0 ml of this solution to 50.0 ml with the solvent mixture.

6.1.3 Reference Solution: A 0.08 per cent w/v solution of Linezolid reference standard in solvent mixture. Dilute 5.0 ml of this solution to 50.0 ml with the same solvent.

6.1.4 Chromatographic system

Column: C18 (15 cm x 4.6 mm), 5 µm,

Column temperature: 40 ^{O}C

Flow rate: 1.5 ml per minute

Wavelength: 250 nm

Injection volume: 10 µl

Detector: UV

Mobile phase: A mixture of 70 volumes of buffer solution prepared by mixing 1.0 ml of triethylamine in 1000 ml water, adjusted to pH 3.0 with orthophosphoric acid and 30 volumes of methanol.

6.1.5 Procedure: Inject reference solution five times and test solution. The test is not valid unless the column efficiency determined from the major peak is not less than 2000 theoretical plates, the tailing factor is not more than 2.0 and the relative standard deviation of replicate injections is not more than 2.0 %. Inject the test solution. Calculate the content of Linezolid in injection.

6.2 Dextrose:

6.2.1 Test solution: In 100 ml sample, add 0.2 ml of 5 M ammonia, mix well and set aside for 30 minutes. Measure the placebo also.

Placebo preparation: Take a 100 ml volumetric flask and weigh 200 mg linezolid, 180 mg sodium citrate, and 109.32 mg citric acid (monohydrate) and dissolve in water for injection and make up the volume to 100 ml mark. Adjust the pH of this solution between 4.5 to 5.5 with HCl or NaOH (if required).

6.2.2 Procedure: Measure the optical rotation of the infusion at 25 ^{0}C. Take the blank correction by taking placebo in the polarimeter tube at 25 ^{0}C.

6.2.3 Calculation:

Content of dextrose in % w/v

Dextrose (in % w/v) = OR 25 ^{0}C x 0.9477 (On anhydrous basis)

Where OR $_{25\,^{0}C}$ = Optical rotation of the sample at 25 ^{0}C – Optical rotation of the blank

7. Other tests: As per pharmacopoeial requirement.