Government of Nepal
Ministry of Health and Population
Department of Drug Administration
National Medicines Laboratory
Quality and Method Validation Section

Analytical profile of Atorvastatin and Ezetimibe Tablets

Analytical Profile No.: Ator Eze 080/81/AP 146

Atorvastatin and Ezetimibe Tablets contains not less than 90.0% and not more than 110.0% of the stated amount of Atorvastatin and Ezetimibe.

Usual Strength: Each film coated tablet contains

Atorvastatin Calcium eqv. to Atorvastatin 10 mg

Ezetimibe 10 mg

A. Method of Analysis for Atorvastatin

1. Identification:

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.

2. Dissolution: *Determine by liquid chromatography*

2.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml of Phosphate Buffer pH 6.8 (Dissolve 47.6 gm. Potassium dihydrogen orthophosphate and 6.3 gm. Sodium Hydroxide pellets in sufficient water to produce 7000 ml and mix well. Measure and adjust the pH 6.80 with 1 N NaOH or 10% orthophosphoric acid.

Speed and Time: 75 rpm and 30 minutes

Withdraw a suitable volume of the medium and filter.

2.3 Test Solution: Use the filtrate.

2.4 Reference Solution: Weigh accurately 24 mg of Atorvastatin Calcium WS and transfer in 100 ml completely dries volumetric flask. Add about 70 ml methanol and sonicate to dissolve. Cool to room temperature and make up the volume to mark with methanol. Further dilute 5 ml of this solution with dissolution media and mix.

2.5 Procedure: Use the chromatographic system as described in the Assay. Inject the reference solution and the test solution.

Calculate the percent release of Atorvastatin.

2.6 Limit: Not less than 75% (Q) of the stated amount of Atorvastatin.

3. Uniformity of Content

Determine by liquid chromatography, as described in the Assay, using the following test solution.

3.1 Test Solution: Place one tablet in 50 ml completely dried volumetric flask. Add 5 ml of water and 25 ml of methanol, sonicate for 10 minutes. Allow to cool to room temperature and make up the volume with diluent.

4. Assay: *Determine by liquid chromatography*

4.1 Diluent: Dissolve 13.6 gm. of Potassium dihydrogen phosphate and 1.8 gm. of NaOH pellets in 2000 ml water. Adjust pH with 10% Phosphoric acid or 1 N NaOH solution to 6.8.

4.2 Test solution: Weigh 20 tablets and calculate average weight. Weigh intact 1 tablet (equivalent to 10 mg of Atorvastatin) and transfer to 50 ml completely dried volumetric flask. Add 5 ml water and 25 ml methanol, sonicate for 10 minutes. Cool down to room temperature and make up the volume with diluent.

4.3 Reference solution: Weigh accurately 22 mg of Atorvastatin Calcium WS and transfer in 100 ml completely dries volumetric flask. Add 50 ml of methanol, sonicate to dissolve. Cool to room temperature and make up the volume with diluent.

4.4 Chromatographic system:

Column: C18 (4.6mmX 100-mm, 3.5µ)

Flow rate: 2.0 ml/min

Wavelength: 246 nm

Injection volume: 5µl

Column Temperature: 30ºC

Mobile Phase: Buffer: Mobile Phase A: 60:40

Buffer: Dissolve 0.77 gm. Of Ammonium acetate in 500 ml water. Adjust pH with 25% glacial acetic acid solution to 4.0.

Mobile Phase A: 92.5:7.5: Acetonitrile: Tetrahydrofuran

4.5 Procedure: Inject the reference solution five times and sample solutions. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, and the

relative standard deviation for replicate injections is not more than 2.0%. Measure the peak responses. Calculate the content of Atorvastatin in Atorvastatin and Ezetimibe Tablets.

B. Method of analysis for Ezetimibe

5. Identification:

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.

6. Dissolution: *Determine by liquid chromatography*

6.1 Dissolution Parameters:

Apparatus: Paddle

Medium: 900 ml of 1% Sodium Lauryl Sulphate

Speed and Time: 75 rpm and 45 minutes

Withdraw a suitable volume of the medium and filter.

6.2 Test Solution: Use the filtrate.

6.3 Reference Solution: Weigh accurately 22 mg of Ezetimibe WS and transfer to 100 ml completely dries volumetric flask. Add about 70 ml of mobile phase and sonicate to dissolve. Cool to room temperature and make up the volume with mobile phase. Further dilute 5 ml of this solution to 100 ml with dissolution media.

6.4 Procedure: Use the chromatographic system as described in the Assay. Inject the reference solution and the test solution.

Calculate the percent release of Ezetimibe.

6.5 Limit: Not less than 75% (Q) of the stated amount of Ezetimibe.

7. Uniformity of Content

Determine by liquid chromatography, as described in the Assay, using the following test solution.

7.1Test Solution: Place one tablet in 50 ml completely dried volumetric flask. Add 30 ml of mobile phase and sonicate for 10 minutes. Allow to cool to room temperature and make up the volume with mobile phase.

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8. Assay: *Determine by liquid chromatography*

8.1 Test solution: Weigh 20 tablets and calculate average weight. Weigh intact 1 tablet (equivalent to 10 mg of Ezetimibe) and transfer to 50 ml completely dried volumetric flask. Add 30 ml of mobile phase, sonicate for 10 minutes. Allow to cool to room temperature and make up the volume with mobile phase.

8.2 Reference solution: Weigh accurately 20 mg of Ezetimibe WS and transfer to 100 ml completely dried volumetric flask. Add 60 ml of mobile phase and sonicate to dissolve. Allow to cool to room temperature and make up the volume with mobile phase.

8.3 Chromatographic system:

Column: C8 (4.6mmX 100-mm, 3.5µ)

Flow rate: 1.0 ml/min

Wavelength: 230 nm

Injection volume: 5µl

Column Temperature: 30ºC

Mobile Phase: Buffer: Acetonitrile: 55:45

Buffer: Dissolve 0.77 gm. Of Ammonium acetate in 500 ml water. Adjust pH with 25% glacial or 5M ammonia solution to 6.7 if necessary.

8.4 Procedure: Inject the reference solution five times and sample solutions. The test is not valid unless the column efficiency is not less than 2000 theoretical plates, tailing factor is not more than 2.0, and the relative standard deviation for replicate injections is not more than 2.0%. Measure the peak responses. Calculate the content of Ezetimibe in Atorvastatin and Ezetimibe Tablets.

9. Other tests: As per pharmacopoeial requirements.