LUBRIZOL LIFE SCIENCE

HEALTH

Trimetazidine Dihydrochloride Extended Release Tablets

The extended release film coated tablet contains **Trimetazidine Dihydrochloride 35 mg**. The formulation features use of **Carbopol® 974P NF polymer** as the extended release matrix ingredient. Formulation demonstrates roller compaction as alternative processing technique.

Number	Ingredients	% w/w	mg / Tablet
	Intra-Granular Phase:		
1.	Trimetazidine Dihydrochloride	14.29	35.0
2.	**Carbopol® 974P NF polymer**	20.41	50.0
3.	Dibasic calcium phosphate - Anhydrous granular (A Tab®)	36.73	90.0
4.	Lactose (Anhydrous) (SuperTab® 30 GR)	22.04	54.0
5.	Colloidal silicon dioxide	0.41	1.0
6.	Magnesium stearate	0.41	1.0
	Extra-Granular Phase:		
7.	Colloidal silicon dioxide	0.41	1.0
8.	Magnesium stearate	0.41	1.0
9.	Talc	0.82	2.0
10.	Conventional aqueous film coat	4.08	10.0
	TOTAL:	**100.00**	**245.00**

Lab batch size – 500 tablets (Roll compaction process)

Process:

Core Tablets:

1. Weigh Trimetazidine Dihydrochloride, **Carbopol® 974P NF polymer**, dibasic calcium phosphate (anhydrous granular), lactose (Anhydrous), colloidal silicon dioxide and magnesium stearate. Pass through 60 mesh sieve. Add all the ingredients to high shear mixer and blend for 10 minutes at 15 RPM impeller speed.

2. Pass the blend through a roller compactor. Conduct roller compaction process and, if necessary, recycle the fines below 20 mesh (850 µm) to form granules of 250 - 425 µm size and about 0.6 g/cc bulk density (bulk density 0.4 g/cc for the uncompacted powder).

3. Pass the granules through a 20-mesh sieve and blend them with magnesium stearate, talc and colloidal silicon dioxide (passed through a 60 mesh sieve) in a V-blender for 5 minutes.

4. Compress the blend into tablets on a tablet press at using 8.5 mm round standard concave punches to achieve following parameters:

- Target weight: 235 mg
- Mechanical Strength: 11 to 15 kP
- Friability (100 revolutions): NMT 0.5 % W/W

Coating:

5. The tablets are coated with an aqueous solution of hypromellose substitution type 2910 to a weight gain of 10 mg/tablet.

Trimetazidine Dihydrochloride Extended Release Tablets

Final Tablet Properties:
Appearance: Film coated biconvex tablets
Weight (mg)*: 244 ± 2
Thickness (mm)*: 3.8 ± 0.10
Mechanical Strength (kP)*: 15.01 ± 1.12
Friability (100 revolutions) (%): 0.21

*Average ± SD

Dissolution**(% average of 6 tablets)	
Time (h)	**Lubrizol**
1	38.0
4	71.0
10	95.0

**USP Apparatus 2, 50 rpm, 0 - 1 hour: 750 ml 0.1N HCl 1 - 10 hours: 1000 ml pH 6.8 phosphate buffer.

Summary:

Carbopol® polymers have demonstrated to be useful and highly efficient as extended release matrix former for roller compaction process. Another example of roller compaction application is that Carbopol® 71G NF is produced by roller compaction of Carbopol® 971P NF polymer.

The Lubrizol Life Science Health website **www.lubrizol.com/Health** provides additional information:

- Bulletin 30 - Controlled Release Tablets and Capsules; Bulletin 31 - Formulating Controlled Release Tablets and Capsules with Carbopol; Bulletin 32 - Application of Carbopol 71G NF Polymer in Controlled Release Tablets
- Aqueous and non- aqueous granulation videos under video gallery
- Technical Papers, Technical Data Sheets, Test Procedures, Certificates, and other Formulations

Please contact your Lubrizol representative to get samples, quotations or further technical assistance.

LUBRIZOL LIFE SCIENCE
9911 Brecksville Road
Cleveland, OH 44141-3201 USA

Lubrizol.com/Health