LUBRIZOL LIFE SCIENCE

HEALTH

Quetiapine Fumarate Extended Release Tablets

The extended release film coated tablet contains **Quetiapine fumarate 230 mg equivalent to 200 mg Quetiapine**. The formulation features use of **Carbopol® 971P NF polymer** as the extended release matrix ingredient and methacrylic acid copolymer dispersion providing porous enteric film coating. The formula uses a low drug to Carbopol® polymer ratio of about 9:1.

Number	Ingredients	% w/w	mg / Tablet
	Intra-Granular Phase:		
1.	Quetiapine fumarate (Eqv. to Quetiapine 200 mg)	40.64	230.00
2.	Lactose monohydrate (200 mesh)	53.00	230.00
3.	**Carbopol® 971P NF polymer**	4.42	25.00
	Extra-Granular Phase:		
4.	Talc	0.97	5.50
5.	Magnesium stearate	0.97	5.50
	TOTAL (core tablets):	**100.00**	**566.00**

Lab batch size – 1000 Tablets (water used as binder)

Number	Ingredients	% w/w	mg / Tablet
	Intra-Granular Phase:		
1.	Methacrylic acid copolymer (Eudragit® L 30 D-55)	23.00 (equiv. to solid content of 6.90)	30.00 (equiv. to solid content of 9.00)
2.	Lactose monohydrate (200 mesh)	11.46	15.00
3.	Talc	0.69	0.90
4.	Triethyl citrate	1.72	2.24
5.	FD&C Yellow #6	0.46	0.60
6.	Titanium dioxide	0.28	0.37
7.	Deionized water (removed during processing)	62.46	(81.50 gm/1000 tablets)
	TOTAL (coating):	**100.00**	**28.00**
	TOTAL (coated tablets):	**-**	**594.00 (566 + 28)**

*Coating process should be conducted till 5% weight gain is achieved.

Process:

Core Tablets:

1. Pass quetiapine fumarate, Carbopol® 971P NF polymer and lactose through 40 mesh screen.

2. Granulate the blend with water in high shear granulator - using about 100 g water for 555 g powder blend – adding the water as a thin stream, as droplets using peristaltic pump or as a spray and impeller speed above 250 to 300 RPM during wet massing.

3. Dry the granules in fluid bed drier (inlet temperature at 60 °C) to loss on drying (LOD) of about 2%.

4. Mill the granules through 18 mesh screen.

5. Pass magnesium stearate and talc through 40 mesh and blend with the granules in V cone blender for 5 minutes.

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Core Tablets (continued):

6. Compress the blend into tablets on a tablet press at 30 rpm using 15.3 X 7.8 mm capsule shaped biconvex punches to achieve following parameters:

• Target weight: 566 mg • Mechanical Strength: 12 to 15 kP • Friability (100 revolutions): NMT 0.5 %

Film Coating:

1. Dissolve triethyl citrate and lactose in 60g water heated at about 45 °C. Add talc, titanium dioxide and FD&C Yellow #6, and homogenize.

2. Add solution to Eudragit L 30 D 55 dispersion and mix using propeller stirrer.

3. Pass the dispersion through 100 mesh nylon filter.

4. Coat the tablets using this coating dispersion with suitable coating pan (tablet bed temperature to about 40 °C) to achieve a weight gain of 5% w/w (average tablet weight of 594 mg).

5. Cure the tablets in tray drier for 3 hours at 50 °C.

Final Tablet Properties:
Appearance: Film coated biconvex tablets
Weight (mg)*: 599 ± 3
Thickness (mm)*: 5.5 ± 0.02
Mechanical Strength (kP)*: 15.29 ± 0.66
Friability (100 revolutions) (%): 0.03

*Average ± SD

Dissolution**(% average of 6 tablets)		
Time (h)	**Lubrizol**	**Innovator**
1	20	21
2	36	36
4	50	43
8	58	54
16	80	85
24	96	102

**Dissolution method per US Patent 5,948,437: USP Apparatus 1 100 RPM, 0-2 hours: 750 ml 0.1 N HCl, 2-24 hours: 1000 ml pH 6.2 phosphate buffer.

Summary:

Carbopol® polymers have demonstrated to be useful and highly efficient as extended release matrix former making them a polymer of choice when formulating high drug load extended release tablets.

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
- Wet granulation videos from 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.

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