3.2.P.8.1 RESUMEN DE ESTABILIDAD Y CONCLUSIONES

CLARITROMICINA COMPRIMIDOS RECUBIERTOS 500 mg

A Subdepartamento Registros y Autorizaciones Sanitarias

3.2.P.8 Stability

3.2.P.8.1 Stability Summary and Conclusions

Stress testing and formal stability studies (accelerated and long-term stability testings) were performed according to the relevant guidelines and protocols. Detailed Stability testing protocol is described in Section 3.2.P.8.1.1. The actual study results are showed in Section 3.2.P.8.3. At present, only the Stress testing of clarithromycin Film-coated Tablets has been completed, and the stability studies are still in progress

3.2.P.8.1.1 Stability Study Protocol

The purpose of stability testing is to provide evidence on how the quality of a drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity, and light, and to establish a shelf life for the drug product and recommended storage conditions. Three consecutive commercial batches for process validation (detailed information see the below table) are selected for stability study.

Test	Condition	Batch of product	Completed testing intervals	Sample amount	Packaging
Stress testing	60℃	008a201201	0, 5, 10 and 30 days	6 samples (50 tablets per sample)	Clarithromycin Film-coated tablets in aluminum-plastic packaging
	Temperature: 25℃, Related Humidity: 90%±5%	008a201201	0, 5 and 10 days	4 samples (50 tablets per sample)	
	25 ℃ and RH 75±5% (Reserve)	008a201201	0, 5 and 10 days	4 samples (50 tablets per sample)	
	4500Lx±500Lx	008a201201	0, 5 and 10 days	4 samples (50 tablets per sample)	
Long-term testing	Temperature: 30℃±2℃, Relative Humidity: 65%±5%;	008a201201; 008a201202; 008a201203	0, 3, 6, 9, 12, 18, 24, 36,48 and 60 months	80 tablets×2×5 times, 120 tablets×2×4times	Simulate commercial packaging, packed in 10 pieces / plate and aluminum plastic
Accelerated testing	Temperature: 40℃±2℃, Related Humidity: 75%±5%	008a201201; 008a201202; 008a201203	0, 1, 2, 3, 6months	80 tablets×2×3 times, 120 tablets×2×1 times	Simulate commercial packaging, packed in 10 pieces / plate and aluminum plastic

A. Test Items for Stability Study

No.	Test items	Acceptance criteria	
※1	Character Ⅰ	White, capsule-shaped, Film-coated tablets, scored on one side and plain on the other side.	
2	Character Ⅱ	Diameter: 18.8-19.0mm Width: 9.0-9.2mm Thickness: 5.8-6.3mm	
3	Identification	The retention time of the major peak of the sample solution corresponds to that of the Standard solution, as obtained in the Assay	
※4	Assay	Not less than 90.0 % and not more than 110.0 % of the labeled amount of clarithromycin ($C_{38}H_{69}NO_{13}$)	
※5	Dissolution	NLT Q(Q=80%) of the labeled amount of clarithromycin ($C_{38}H_{69}NO_{13}$) is dissolved.	
※6	Uniformity of dosage units (By weight variation)	AV ≤ L1 % (L1 = 15.0)	
※7	Loss on drying	NMT 6.0%	
※8	Organic Impurities	Any individual unspecified impurity	≤1.0%
		Impurities exceed 0.4%	≤4
		Total impurities	≤3.5%
9	Microbial limit	TAMC	≤10^3cfu/g
		TYMC	≤10^2cfu/g
		E. coli	Not detected

Note:
1. The above 9 test items are full test items of Clarithromycin Film-coated Tablets.
2. The test items with asterisk are critical observation items of the stability testing.
   They will be tested every time according to the predefined test frequency.
3. Full test (all 9 test items) will be performed at the following time points.
   Accelerated stability test: 6 months
   Long-term stability test: 24 ,36,48 and 60 months
   At other time points, only critical observation items will be tested.
4. In stress testing, on the 5th, 10th and 30th days, only critical observation items will be tested.

3.2.P.8.1.2 Stability Study Report

A. Summary of Stability Test Results

Stress Test:

1. Clarithromycin Film-coated Tablets was stable under high temperature, hunmidity and light exposure, except results of uniformity of dosage units was increased.

Accelerated Stability Test:
After 6 months, Clarithromycin Film-coated Tablets are still stable, all test results meet the requirement.

Long-term Stability Test:
After 6 months, Clarithromycin Film-coated Tablets are still stable, all test results meet the requirement.

For full details refer to Section **3.2.P.8.3 Stability Data**

Recommended Shelf-life

The recommended shelf life is tentative 2 years.