Summary of Stability Study of VB_1 (Thiamine Mononitrate)

1 Stability summary and conclusions

In accordance with ICH Guidance for industry: ICH Q1A (R2) Stability Testing of New Drug Substances and Products, and Q1E Evaluation of Stability Data, on-going stability studies performed in support of this application include lots of Thiamine Mononitrate drug substance stored under the recommended storage condition. One batch of each product manufactured in every year is added to long-term testing.

1.1 Recommended retest period

A re-test period of 4 years (48 months) is recommended.

1.2 Advice on storage

Preserve in a tight non-metallic container, protected from light.

2 Post-approval stability protocol and stability commitment

2.1 Long-term stability study

Duration 0, 3, 6, 9, 12, 18, 24, 36, 48 months.
Packaging The same as the actual packaging used for storage and distribution, i.e. polyethylene bags / carton system.
Storage conditions Temperature 30±2 °C; relative humidity 65±5%.
Test performed As listed below.

Test	Specification	Method
Appearance	White crystals or crystalline powder, usually having a slight, characteristic odor.	Visual observation
pH	6.0 ~ 7.5	USP
Related substances Impurity A Impurity B Impurity C Unspecified impurities Total impurities	 ≤0.15% ≤0.6% ≤0.4% ≤0.10% ≤1.0%	EP
Related compound	≤1.0%	USP
Loss on drying	≤1.0%	USP
Assay (on dry basis)	98.0% ~ 102.0%	USP

3 Tabulated stability data

3.1 Data from long-term stability study

Batch number	Manufacturing date
TN17012019	Jan 4, 2017
TN18012001	Dec 31, 2017
TN19012001	Jan 1, 2019

Tabulated Long Term Study Data for Thiamine Mononitrate -1

Batch No. TN17012019 | Date of initial test: Jan 5, 2017 | 30±2 °C, 65±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Appearance	White crystals or crystalline powder, usually having a slight, characteristic odor.	White crystalline powder							On-going	
pH	6.0 ~ 7.5	7.1	7.0	7.2	7.2	7.0	7.2	7.1		
Related substances	Impurity A≦0.15%	0.13%	0.14%	0.12%	0.13%	0.13%	0.13%	0.12%		
	Impurity B≦0.6%	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.		
	Impurity C≦0.4%	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.		
	Unspecified impurities≦0.10%	<0.05%	<0.05%	<0.05%	<0.05%	<0.05%	<0.05%	<0.05%		
	Total impurities≦1.0%	0.13%	0.14%	0.12%	0.13%	0.13%	0.13%	0.12%		
Related compound	≦1.0%	0.25%	0.27%	0.22%	0.21%	0.21%	0.22%	0.20%		
Loss on drying	≦1.0%	0.14%	0.12%	0.14%	0.14%	0.10%	0.12%	0.14%		
Assay	98.0% ~ 102.0%	99.7%	99.5%	99.6%	99.6%	99.6%	99.5%	99.5%		

* Remark: N. D. = Not Detected

Tabulated Long Term Study Data for Thiamine Mononitrate -2

Batch No. TN18012001 | Date of initial test: Jan 2, 2018 | 30±2 °C, 65±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Appearance	White crystals or crystalline powder, usually having a slight, characteristic odor.	White crystalline powder						On-going		
pH	6.0 ~ 7.5	7.1	7.1	7.2	7.2	7.1	7.2			
Related substances	Impurity A≦0.15%	0.11%	0.12%	0.12%	0.14%	0.12%	0.12%			
	Impurity B≦0.6%	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.			
	Impurity C≦0.4%	N.D.	N.D.	N.D.	N.D.	N.D.	N.D.			
	Unspecified impurities≦0.10%	<0.05%	<0.05%	<0.05%	<0.05%	<0.05%	<0.05%			
	Total impurities≦1.0%	0.11%	0.12%	0.12%	0.14%	0.12%	0.12%			
Related compound	≦1.0%	0.19%	0.22%	0.21%	0.18%	0.18%	0.23%			
Loss on drying	≦1.0%	0.08%	0.10%	0.10%	0.12%	0.10%	0.12%			
Assay	98.0% ~ 102.0%	99.6%	99.5%	99.6%	99.5%	99.2%	99.3%			

* Remark: N. D. = Not Detected

Tabulated Long Term Study Data for Thiamine Mononitrate -3

Batch No. TN19012001 | Date of initial test: Jan 2, 2019 | 30±2 °C, 65±5%RH

Test	Specification, Ph. Eur.	Duration, month								
		0	3	6	9	12	18	24	36	48
Appearance	White crystals or crystalline powder, usually having a slight, characteristic odor.	White crystalline powder			On-going					
pH	6.0 ~ 7.5	6.9	7.2	7.1						
Related substances	Impurity A≤0.15%	0.13%	0.14%	0.13%						
	Impurity B≤0.6%	N.D.	N.D.	N.D.						
	Impurity C≤0.4%	N.D.	N.D.	N.D.						
	Unspecified impurities≤0.10%	<0.05%	<0.05%	<0.05%						
	Total impurities≤1.0%	0.13%	0.14%	0.13%						
Related compound	≤1.0%	0.18%	0.28%	0.28%						
Loss on drying	≤1.0%	0.14%	0.14%	0.14%						
Assay	98.0% ~ 102.0%	99.2%	99.2%	99.2%						

* Remark: N. D. = Not Detected