STABILITY DATA ON STELBAT TABLETS, 20 MG

1. DETAILS OF THE BATCHES TESTED

Full details of the batches under examination are given in Table 1.

The batches of product were manufactured using the proposed commercial composition and manufacturing process.

The product was packaged in 100 cc HDPE bottles, containing 2 g desiccant. This pack is of identical composition and volume to that proposed for the commercial product.

Table 1 Details of Stability Batches of Stelbat Tablets, 20 mg

Product Strength	20 mg	20 mg	20 mg
Stability Protocol Number	ABC1234	ABC1234	ABC1234
Drug Product Batch Number	33445	33446	33447
Input Drug Substance Batch Number	CAT1	CAT2	CAT3
Site of Drug Substance Manufacture	AAA Molybdenum Products, Inc.	AAA Molybdenum Products, Inc.	AAA Molybdenum Products, Inc.
Batch Size (Tablets)	100,100	100,050	100,125
Scale	Production	Production	Production
Site of Manufacture	AAA Pharmaceutical, Inc., Lumberton	AAA Pharmaceutical, Inc., Lumberton	AAA Pharmaceutical, Inc., Lumberton
Date of Manufacture	June, 2020	June 2020	July 2020
Site of Packaging	MySite	MySite	MySite
Date of Packaging	August, 2020	August, 2020	August, 2020
Pack	100 cc HDPE Bottle 2 g desiccant	100 cc HDPE Bottle 2 g desiccant	100 cc HDPE Bottle 2 g desiccant
Date Stability Started	December, 2020	December, 2020	December, 2020
Data Presented (Months)	18	18	18

2. STABILITY TEST PROTOCOLS

The stability test protocol for accelerated and long-term storage of Stelbat Tablets, 20 mg is given in Table 2.

Table 2 Stability Test Protocol for Long-term and Accelerated Storage of Stelbat Tablets, 20 mg

Storage Test Type	Storage Condition	Storage Time (Months)							
		Initial	3	6	9	12	18	24	36
Long-term	25°C/60% RH	XYZ	X	X	X	XY	XY	XY	(XY)
Accelerated	40°C/75% RH		X	X	–	–	–	–	–

Notes:
RH Relative Humidity.
( ) Denotes optional testing.
– Denotes testing not scheduled at these time points.

Key to Tests:

X Indicates that the following tests will be performed:
Description
Assay
Degradation Products
Dissolution
Water Content

Y Indicates that the following tests will be performed:
Microbiological Quality

Z Indicates that the following tests will be performed:
Identification
Uniformity of dosage units (by weight)

3. RESULTS AND DISCUSSION

Results are available following storage for up to 18 months at 25°C/60% RH and 6 months at 40°C/75% RH. The stability data are presented in Section 4.

Description

No significant change in description was observed for Stelbat Tablets 20 mg after storage at 25°C/60% RH up to 18 months and 40°C/75%RH up to 6 months. All results complied with the proposed specification.

Identification

The test for identification was only conducted at initial time point, because this parameter is not required by the protocol as considered not stability relevant. The results comply with the proposed specification.

Assay by HPLC

A decrease in API content is observed for Stelbat Tablets 20 mg after storage at 25°C/60% RH up to 18 months (see Figure 1), but results remain within the proposed specification.

An out of specification result was observed at the 12 month time point for batch 33446 stored at 25°C/65% RH. An associated investigation did not find a root cause; however, the data at 18 months is within the proposed specification, therefore this is not indicative of a stability trend.

Degradation Products

Significant changes were observed for Impurity 1, Impurity 2, Impurity 3 and Total Degradation Impurities for Stelbat Tablets 20 mg after storage at 25°C/60% RH up to 18 months and 40°C/75%RH up to 6 months. An increase in these impurities was observed which is related to the increase water content observed as discussed in P5.4 Justification of Specification.

All results complied with the proposed specification.

Dissolution

No significant change in dissolution was observed for Stelbat Tablets 20 mg after storage at 25°C/60% RH up to 18 months and 40°C/75%RH up to 6 months. All results complied with the proposed specification.

Uniformity of dosage units

The test for uniformity of dosage units (by weight) was only conducted at initial time point, because this parameter is not required by the protocol as considered not stability relevant. The results comply with the proposed specification.

Microbiological quality

Microbiological quality is tested annual, and also at the 18 month timepoint. The results comply with the proposed specification.

Water Content

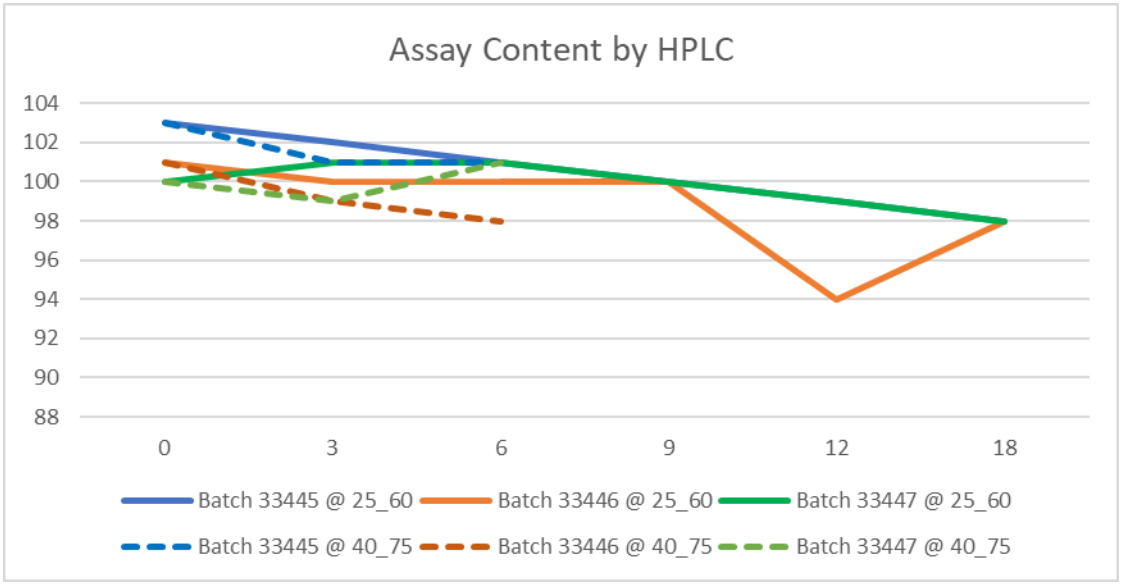
An increase in water content is observed for Stelbat Tablets 20 mg after storage at 25°C/60% RH up to 18 months (see Figure 2), but results remain within the proposed specification.

Conclusion

All the results, with exception of the assay content result at the 12 month time point for Batch 33446 stored at 25°C/65% RH, for Stelbat Tablets 20 mg are within the proposed specification.

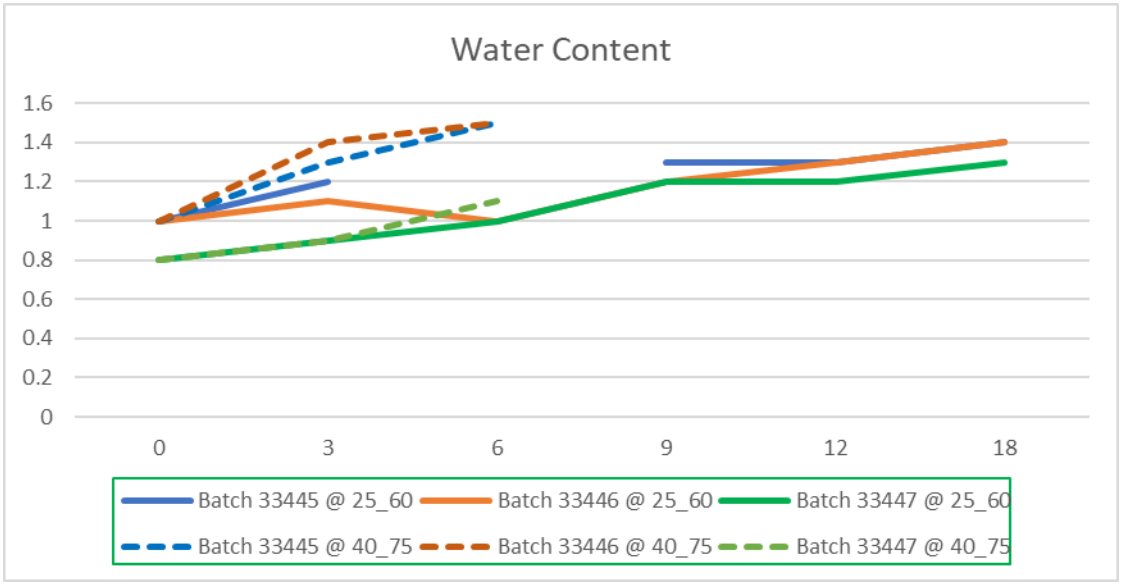
P.8.3. Stability Data

Figure 1 Effect of Storage at Long-term Storage Condition/Accelerated Storage Condition on Assay Content (% Label Claim) for Stelbat Tablets, 20 mg



Key:
25_60 = 25°C/60% RH.
40_75 = 40°C/75% RH.

Figure 2 Effect of Storage at Long-term Storage Condition/Accelerated Storage Condition on Water Content (% w/w) for Stelbat Tablets, 20 mg



Key:
25_60 = 25°C/60% RH.
40_75 = 40°C/75% RH.

4. TABULATED STABILITY DATA FOR STELBAT TABLETS, 20 MG

Table 3 Stability Data for Stelbat Tablets, 20 mg

Protocol Number: ABC1234 Batch Number: 33445 **Testing Ongoing**

Storage Condition	Time (Months)	Description	Assay Content by HPLC (% label claim) (Mean)	Degradation Products by HPLC (% w/w)				
				Impurity 1	Impurity 2	Impurity 3	Any Unspecified Degradation Impurity	Total Degradation Impurities
Specification		Note 1	95 to 105	NMT 0.8	NMT 0.4	NMT 0.4	NMT 0.2	NMT 2.3
Initial	0	Complies	103	0.1	0.2	0.2	< 0.1	0.8
25°C/60% RH	3	Complies	102	0.1	0.2	0.2	< 0.1	0.9
	6	Complies	101	0.3	0.2	0.2	0.1	0.8
	9	Complies	100	0.3	0.2	0.2	0.1	1.2
	12	Complies	99	0.6	0.3	0.3	0.1	1.4
	18	Complies	98	0.6	0.3	0.3	0.1	1.6
40°C/75% RH	3	Complies	101	0.3	0.2	0.2	0.1	1.2
	6	Complies	101	0.6	0.3	0.3	0.1	1.6

Note:
1. An orange film-coated tablet, debossed with 175 on one side

NMT Not More Than.

Table 3 Stability Data for Stelbat Tablets, 20 mg (Cont'd)

Protocol Number: ABC1234 Batch Number: 33445 **Testing Ongoing**

Storage Condition	Time (Months)	Dissolution (Mean)			Microbiological quality	Water Content (% w/w) (Mean)
		% API Released after 15 minutes	% API Released after 30 minutes	% API Released after 45 minutes		
Specification		-	Q=80% at 30 minutes	-	Complies with PhEur	NMT 2.0
Initial	0	65	83	93	Complies	1.0
25°C/60% RH	3	62	85	95	-	1.2
	6	66	84	94	-	NA
	9	68	85	95	-	1.3
	12	64	85	95	Complies	1.3
	18	66	86	93	Complies	1.4
40°C/75% RH	3	66	85	95	-	1.3
	6	67	87	94	-	1.5

Note:
- Not required by the protocol.
NA Result Not Available due to analytical error during testing.
NMT Not More Than

P.8.3. Stability Data

Table 4 Stability Data for Stelbat Tablets, 20 mg

Protocol Number: ABC1234 Batch Number: 33446 **Testing Ongoing**

Storage Condition	Time (Months)	Description	Assay Content by HPLC (% label claim) (Mean)	Degradation Products by HPLC (% w/w)				
				Impurity 1	Impurity 2	Impurity 3	Any Unspecified Degradation Impurity	Total Degradation Impurities
Specification		Note 1	95 to 105	NMT 0.8	NMT 0.4	NMT 0.4	NMT 0.2	NMT 2.3
Initial	0	Complies	101	0.1	0.2	0.2	< 0.1	0.8
25°C/60% RH	3	Complies	100	0.1	0.2	0.2	< 0.1	0.9
	6	Complies	100	0.2	0.4	0.1	0.1	1.0
	9	Complies	100	0.3	0.2	0.2	0.1	1.2
	12	Complies	94	0.4	0.3	0.2	0.1	1.3
	18	Complies	98	0.6	0.3	0.3	0.1	1.7
40°C/75% RH	3	Complies	99	0.3	0.2	0.2	0.1	1.2
	6	Complies	98	0.4	0.3	0.3	0.1	1.7

Note:
1. An orange film-coated tablet, debossed with 175 on one side

NMT Not More Than.

P.8.3. Stability Data

Table 4 Stability Data for Stelbat Tablets, 20 mg (Cont'd)

Protocol Number: ABC1234 Batch Number: 33446 **Testing Ongoing**

Storage Condition	Time (Months)	Dissolution (Mean)			Microbiological quality	Water Content (% w/w) (Mean)
		% API Released after 15 minutes	% API Released after 30 minutes	% API Released after 45 minutes		
Specification		-	Q=80% at 30 minutes	-	Complies with PhEur	NMT 2.0
Initial	0	66	82	95	Complies	1.0
25°C/60% RH	3	63	84	96	-	1.1
	6	67	86	94	-	1.0
	9	66	85	95	-	1.2
	12	65	85	95	Complies	1.3
	18	66	84	92	Complies	1.4
40°C/75% RH	3	66	84	95	-	1.4
	6	67	87	94	-	1.5

Note:
- Not required by the protocol.
NMT Not More Than

P.8.3. Stability Data

Table 5 Stability Data for Stelbat Tablets, 20 mg

Protocol Number: ABC1234 Batch Number: 33447 **Testing Ongoing**

Storage Condition	Time (Months)	Description	Assay Content by HPLC (% label claim) (Mean)	Degradation Products by HPLC (% w/w)				
				Impurity 1	Impurity 2	Impurity 3	Any Unspecified Degradation Impurity	Total Degradation Impurities
Specification		Note 1	95 to 105	NMT 0.8	NMT 0.4	NMT 0.4	NMT 0.2	NMT 2.3
Initial	0	Complies	100	0.1	0.2	0.2	< 0.1	0.7
25°C/60% RH	3	Complies	101	0.1	0.2	0.2	< 0.1	0.8
	6	Complies	101	0.2	0.2	0.2	0.1	0.8
	9	Complies	100	0.2	0.2	0.3	0.1	1.1
	12	Complies	99	0.4	0.3	0.3	0.1	1.3
	18	Complies	98	0.4	0.3	0.3	0.1	1.5
40°C/75% RH	3	Complies	99	0.3	0.2	0.2	0.1	1.2
	6	Complies	101	0.5	0.3	0.3	0.1	1.6

Note:
1. An orange film-coated tablet, debossed with 175 on one side

NMT Not More Than.

P.8.3. Stability Data

Table 5 Stability Data for Stelbat Tablets, 20 mg (Cont'd)

Protocol Number: ABC1234 Batch Number: 33447 **Testing Ongoing**

Storage Condition	Time (Months)	Dissolution (Mean)			Microbiological quality	Water Content (% w/w) (Mean)
		% API Released after 15 minutes	% API Released after 30 minutes	% API Released after 45 minutes		
Specification		-	Q=80% at 30 minutes	-	Complies with PhEur	NMT 2.0
Initial	0	60	82	95	Complies	0.8
25°C/60% RH	3	63	85	94	-	0.9
	6	64	84	95	-	1.0
	9	67	85	95	-	1.2
	12	65	85	95	Complies	1.2
	18	66	86	94	Complies	1.3
40°C/75% RH	3	65	85	95	-	0.9
	6	67	87	94	-	1.1

Note:
- Not required by the protocol.
NMT Not More Than

5. STATISTICAL EVALUATION OF STABILITY DATA FOR STELBAT TABLETS, 20 MG

Statistical analyses of Stelbat Tablets, 20 mg was performed on 18 months of stability data after storage at 25°C/60% RH. For each batch of Stelbat Tablets, 20 mg the critical responses for Degradation Products by HPLC Impurity 1, Impurity 2 and Impurity 3 were analyzed.

A summary of the predicted shelf-life, together with the statistical model used to represent the stability data, is given in Table 6.

Table 6 Statistics Summary for Shelf-Life Prediction for Primary Stability Batches of Stelbat Tablets, 20 mg

Storage Condition	Test	Model	Least Favorable Batch	Predicted Expiry
25°C/60% RH	Degradation Products by HPLC Impurity 1	Pooled	33447	26 months
25°C/60% RH	Degradation Products by HPLC Impurity 2	Pooled	33445	22 months
25°C/60% RH	Degradation Products by HPLC Impurity 3	Pooled	33447	27 months