



ZHEJIANG HUAHAI PHARMACEUTICAL Co., Ltd.  
Xunqiao, Linhai, Zhejiang 317024, China

## Study Data for Captopril

### Accelerated Stability Study Data for Captopril

Batch No: 5102-11-077

Temperature:  $40 \pm 2^{\circ}\text{C}$

Humidity:  $75 \pm 5\%$

Mfg. Date: 2011.11.16

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Any unknown impurity	Total Impurities
Specs	White or almost white crystalline powder	$-127 \sim -132^{\circ}$	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.10%	1.2%
Initial	White crystalline powder	$-130^{\circ}$	0.1%	100.4%	0.16%	0.12%	N.D	N.D	< LOQ	0.12%
1M	White crystalline powder	$-130^{\circ}$	0.1%	100.3%	0.13%	0.17%	N.D	N.D	N.D	0.17%
2M	White crystalline powder	$-130^{\circ}$	0.1%	99.7%	0.15%	0.21%	N.D	N.D	N.D	0.21%
3M	White crystalline powder	$-130^{\circ}$	0.1%	99.8%	0.11%	0.27%	N.D	N.D	< LOQ	0.27%

As far as Ph. Eur. 7.4 monograph revised in 2012, the tests and acceptance criteria for future stability study is changed according to Ph. Eur. 7.4, the following stability data is stated as follows:

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)					
						Captopril Disulfide	Impurity C	Impurity E	Impurity J	Any unknown impurity	Total Impurities
Specs	White or almost white crystalline powder	$-127 \sim -132^{\circ}$	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.2%	0.10%	1.2%
6M	White crystalline powder	$-130^{\circ}$	0.1%	99.6%	0.12%	0.47%	N.D	N.D	<LOQ	<LOQ	0.47%



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**Accelerated Stability Study Data for Captopril**

Batch No: 5102-11-078

Temperature: 40 ± 2°C

Humidity: 75 ± 5%

Mfg. Date: 2011.11.16

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Any unknown impurity	Total Impurities
Specs	White or almost white crystalline powder	-127~-132 °	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.10%	1.2%
Initial	White crystalline powder	-130 °	0.1%	100.4%	0.13%	0.11%	N.D	N.D	< LOQ	0.11%
1M	White crystalline powder	-130 °	0.1%	100.5%	0.12%	0.16%	N.D	N.D	< LOQ	0.16%
2M	White crystalline powder	-130 °	0.1%	100.0%	0.13%	0.21%	N.D	N.D	N.D	0.21%
3M	White crystalline powder	-130 °	0.1%	99.7%	0.12%	0.26%	N.D	N.D	< LOQ	0.26%

As far as Ph. Eur. 7.4 monograph revised in 2012, the tests and acceptance criteria for future stability study is changed according to Ph. Eur. 7.4, the following stability data is stated as follows:

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Impurity J	Total Impurities
Specs	White or almost white crystalline powder	-127~-132 °	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.2%	0.10%
6M	White crystalline powder	-130 °	0.1%	99.4%	0.10%	0.46%	N.D	N.D	<LOQ	<LOQ



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**Accelerated Stability Study Data for Captopril**

Batch No: 5102-11-079

Temperature: 40 ± 2°C

Humidity: 75 ± 5%

Mfg. Date: 2011.11.17

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Any unknown impurity	Total Impurities
Specs	White or almost white crystalline powder	-127~-132 °	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.10%	1.2%
Initial	White crystalline powder	-130 °	0.1%	100.6%	0.13%	0.12%	N.D	N.D	< LOQ	0.12%
1M	White crystalline powder	-130 °	0.1%	100.5%	0.12%	0.16%	N.D	N.D	< LOQ	0.16%
2M	White crystalline powder	-130 °	0.1%	100.0%	0.13%	0.22%	N.D	N.D	N.D	0.22%
3M	White crystalline powder	-130 °	0.1%	99.5%	0.12%	0.25%	N.D	N.D	< LOQ	0.25%

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Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Impurity J	Any unknown impurity
Specs	White or almost white crystalline powder	-127~-132 °	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.2%	0.10%
6M	White crystalline powder	-130 °	0.1%	99.5%	0.15%	0.49%	N.D	N.D	<LOQ	<LOQ



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**Long Term Stability Study Data for Captopril**

Batch No: 5102-11-077

Temperature: 25 ± 2°C

Relative Humidity: 60 ± 5%

Mfg. Date: 2011.11.16

Test time	Appearance	Specific Optical Rotation	Loss on Drying	Assay	Impurity F (by GC)	Impurities (by HPLC)				
						Captopril Disulfide	Impurity C	Impurity E	Any unknown impurity	Total Impurities
Specs	White or almost white crystalline powder	-127~-132°	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.10%	1.2%
Initial	White crystalline powder	-130°	0.1%	100.4%	0.16%	0.12%	N.D	N.D	< LOQ	0.12%
3M	White crystalline powder	-130°	0.1%	99.9%	0.12%	0.12%	N.D	N.D	< LOQ	0.12%

As far as Ph. Eur. 7.4 monograph revised in 2012, the tests and acceptance criteria for future stability study is changed according to Ph. Eur. 7.4, the following stability data is stated as follows:

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Specs	White or almost white crystalline powder	-127~-132°	1.0%	98.0~101.5%	0.2%	1.0%	0.15%	0.15%	0.2%	0.10%	1.2%
6M	White crystalline powder	-130°	0.1%	99.9%	0.10%	0.12%	N.D	N.D	<LOQ	<LOD	0.12%
9M	White crystalline powder	-130°	0.1%	100.6%	0.10%	0.13%	N.D	N.D	<LOD	<LOQ	0.13%
12M	White crystalline powder	-130°	0.1%	99.8%	0.10%	0.14%	N.D	N.D	<LOD	<LOD	0.14%
18M	White crystalline powder	-130°	0.1%	100.6%	0.09%	0.13%	N.D	N.D	<LOD	<LOD	0.13%
24M	White crystalline powder	-130°	0.1%	100.0%	0.12%	0.14%	N.D	N.D	<LOQ	<LOQ	0.14%
36M	White crystalline powder	-130°	0.1%	99.9%	0.12%	0.16%	N.D	N.D	<0.05%	0.05%	0.21%
48M	White crystalline powder	-129°	0.2%	99.4%	0.12%	0.15%	N.D	N.D	<LOD	<LOQ	0.15%
60M	White crystalline powder	-130°	0.1%	100.0%	0.12%	0.26%	N.D	N.D	<LOD	<LOQ	0.26%



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Initial	White crystalline powder	-130 °	0.1%	100.4%	0.13%	0.11%	N.D	N.D	< LOQ	0.11%
3M	White crystalline powder	-130 °	0.1%	99.5%	0.11%	0.12%	N.D	N.D	< LOQ	0.12%

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6M	White crystalline powder	-130 °	0.1%	99.7%	0.10%	0.12%	N.D	N.D	<LOQ	<LOD	0.12%
9M	White crystalline powder	-130 °	0.1%	100.3%	0.10%	0.13%	N.D	N.D	<LOD	<LOQ	0.13%
12M	White crystalline powder	-130 °	0.1%	99.7%	0.09%	0.13%	N.D	N.D	<LOD	<LOD	0.13%
18M	White crystalline powder	-130 °	0.1%	100.6%	0.09%	0.13%	N.D	N.D	<LOD	<LOD	0.13%
24M	White crystalline powder	-129 °	0.1%	99.9%	0.10%	0.14%	N.D	N.D	<LOD	<LOQ	0.14%
36M	White crystalline powder	-130 °	0.1%	100.4%	0.11%	0.17%	N.D	N.D	<LOD	0.06%	0.23%
48M	White crystalline powder	-130 °	0.1%	99.7%	0.12%	0.19%	N.D	N.D	<LOD	<LOD	0.19%
60M	White crystalline powder	-130 °	0.1%	100.1%	0.12%	0.19%	N.D	N.D	<LOD	<LOD	0.19%



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3M	White crystalline powder	-130 °	0.1%	99.8%	0.12%	0.13%	N.D	N.D	< LOQ	0.13%

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9M	White crystalline powder	-130 °	0.1%	100.2%	0.11%	0.13%	N.D	N.D	<LOD	<LOQ	0.13%
12M	White crystalline powder	-130 °	0.1%	100.1%	0.09%	0.14%	N.D	N.D	<LOQ	<LOD	0.14%
18M	White crystalline powder	-130 °	0.1%	99.9%	0.10%	0.13%	N.D	N.D	<LOQ	<LOD	0.13%
24M	White crystalline powder	-130 °	0.1%	99.5%	0.11%	0.15%	N.D	N.D	<LOQ	<LOQ	0.15%
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60M	White crystalline powder	-130 °	0.1%	99.8%	0.12%	0.26%	N.D	N.D	<LOD	<LOQ	0.26%