

Health and Youth Care Inspectorate - Pharmaceutical Products

CERTIFICATE NUMBER: NL/H 17/1013229V1

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with:

Art. 111(5) of Directive 2001/83/EC as amended

The competent authority of Netherlands confirms the following:

The manufacturer: Katwijk Chemie B.V.

Site address: Snijderstraat 6, KATWIJK ZH, 2222BA, Netherlands

Is an active substance manufacturer that has been inspected in accordance with Art. 111(1) of Directive 2001/83/EC transposed in the following national legislation:

Art. 100 of the Medicines Act

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 2017-02-02, it is considered that it complies with:

• The principles of GMP for active substances ³ referred to in Article 47 of Directive 2001/83/EC.

This certificate reflects the status of the manufacturing site at the time of the inspection noted above and should not be relied upon to reflect the compliance status if more than three years have elapsed since the date of that inspection. However, this period of validity may be reduced or extended using regulatory risk management principles by an entry in the Restrictions or Clarifying remarks field. This certificate is valid only when presented with all pages and both Parts 1 and 2. The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

Signatory: Ing. Mos van Berlo

¹ The certificate referred to in paragraph 111(5) of Directive 2001/83/EC and 80(5) of Directive 2001/82/EC, shall also be required for imports coming from third countries into a Member State.

² Guidance on the interpretation of this template can be found in the Help menu of EudraGMDP database.

³ These requirements fulfil the GMP recommendations of WHO.



Part 2

Manufacture of active substance. Names of substances subject to inspection:

Calcium Valproate(en)

Deferiprone(en)

Divalproex Sodium(en)

Ethosuximide(en)

Magnesium Pemoline(en)

Magnesium Valproate(en)

Oxaprozin(en)

Pemoline(en)

Phenylethylacetylurea(en)

Phenytoin(en)

Phenytoin Calcium(en)

Phenytoin Sodium(en)

Phthalylsulfacetamide(en)

Sodium Valproate(en)

Sulfacetamide(en)

Sulfacetamide Sodium(en)

Valdisoval(en)

Valproic Acid(en)

Valpromide(en)

XANTHOPTERIN(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation
	3.1.4 Other:
	Drying
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

Active Substance : Deferiprone

3.1 Manufacture of Active Substance by Chemical Synthesis
3.1.1 Manufacture of active substance intermediates

72885
3.1.2 Manufacture of crude active subs
3.1.3 Salt formation / Purification steps:
Crystallisation
3.1.4 Other:
Drying General Finishing Steps
3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
which is in direct contact with the substance)
3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
Quality Control Testing
3.6.1 Physical / Chemical testing
Substance : Divalproex Sodium
Manufacture of Active Substance by Chemical Synthesis
3.1.1 Manufacture of active substance intermediates
3.1.2 Manufacture of crude active substance
3.1.3 Salt formation / Purification steps:
Salt formation
General Finishing Steps
3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
which is in direct contact with the substance)
3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
material or container. This also includes any labelling of the material which could be used for
identification or traceability (lot numbering) of the active substance)
Quality Control Testing
3.6.1 Physical / Chemical testing
Substance : Ethosuximide
Manufacture of Active Substance by Chemical Synthesis
3.1.1 Manufacture of active substance intermediates
3.1.2 Manufacture of crude active substance
3.1.3 Salt formation / Purification steps:
Distillation
General Finishing Steps
3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
which is in direct contact with the substance)
3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
material or container. This also includes any labelling of the material which could be used for
identification or traceability (lot numbering) of the active substance)
Quality Control Testing
3.6.1 Physical / Chemical testing

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Active	e Substance : Magnesium Pemoline
3.1	Manufacture of Active Substance by Chemical Synthesis
1436	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation
	3.1.4 Other:
3.5	Drying General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
	C. L. J. M. J. W. Welmerte
	e Substance : Magnesium Valproate
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation
	3.1.4 Other:
3.5	Drying General Finishing Steps
3.5	
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Activ	e Substance : Oxaprozin
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallisation
	3.1.4 Other:
	Drying
3.5	General Finishing Steps

	3.5.2 Primary Packaging (enclosing / sective substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : Pemoline
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallisation
	3.1.4 Other:
	Drying
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
STIMILES	
	3.6.1 Physical / Chemical testing
Active	e Substance : Phenylethylacetylurea
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallisation
	3.1.4 Other:
	Drying
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
-355 11 - 11	3.6.1 Physical / Chemical testing
I	
Active	e Substance : Phenytoin
3.1	Manufacture of Active Substance by Chemical Synthesis
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	3.1.1 Manufacture of active substance liates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
3.5	Crystallisation General Finishing Steps
0.0	
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : Phenytoin Calcium
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps :
	Saltformation
	3.1.4 Other:
3.5	Drying General Finishing Steps
0.0	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
7	3.6.1 Physical / Chemical testing
Activ	e Substance : Phenytoin Sodium
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation
-	3.1.4 Other: Drying
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)

T	
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : Phthalylsulfacetamide
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallisation
	3.1.4 Other:
2.5	Drying
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
3.0	
	3.6.1 Physical / Chemical testing
A =41==	- Culestanaa , Cadiyya Walanasta
	e Substance : Sodium Valproate
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation
	3.1.4 Other:
3.5	3.1.4 Other: Drying
3.5	3.1.4 Other: Drying General Finishing Steps
3.5	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
3.5	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.5	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
3.5	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
3.5	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing
	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
3.6	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing
3.6	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing
3.6	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance: Sulfacetamide Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates
3.6	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance: Sulfacetamide Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates 3.1.2 Manufacture of crude active substance
3.6	3.1.4 Other: Drying General Finishing Steps 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance) Quality Control Testing 3.6.1 Physical / Chemical testing e Substance: Sulfacetamide Manufacture of Active Substance by Chemical Synthesis 3.1.1 Manufacture of active substance intermediates

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	3.1.4 Other:
3.5	Orying General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Activ	e Substance : Sulfacetamide Sodium
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Salt formation and crystallisation
	3.1.4 Other:
3.5	Drying General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
ĺ	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
	material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active	e Substance : Valdisoval
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
ĺ	3.1.3 Salt formation / Purification steps:
2 =	Salt formation
3.5	General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance) 3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging)
1	5 8 G B the states primary packaging
	material or container. This also includes any labelling of the material which could be used for identification or traceability (lot numbering) of the active substance)
- 1	
3.6	Quality Control Testing
3.6	Quality Control Testing 3.6.1 Physical / Chemical testing

3.1	TATE OF THE PARTY
3.1	Synthesis
İ	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
3.5	Distillisation General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
	1
Activ	ve Substance : Valpromide
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates
	3.1.2 Manufacture of crude active substance
	3.1.3 Salt formation / Purification steps:
	Crystallisation
	3.1.4 Other:
3.5	Orying General Finishing Steps
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer realist
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging material or container. This also includes any labelling of the material which could be used for
	identification or traceability (lot numbering) of the active substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Activ	e Substance : XANTHOPTERIN
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance
3.5	General Finishing Steps
	3.5.1 Physical processing steps :
	crystallisation, drying
	3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material
	which is in direct contact with the substance)
	3.5.3 Secondary Packaging (placing the sealed primary package within an outer packaging
}	material or container. This also includes any labelling of the material which could be used for identification or tracechility (let much in). Set
3.6	identification or traceability (lot numbering) of the active substance) Quality Control Testing
	Canada Control resting

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3.6.1 Physical / Chemical testing

Clarifying remarks (for public users)

Following a risk-based review of GMP compliance information conducted on 24 October 2019, the validity period of this certificate is extended to 2 February 2021.

2019-10-24

Name and signature of the authorised person of the Competent Authority of Netherlands

Ing. Mos van Berlo

Health and Youth Care Inspectorate - Pharmaceutical

Products

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APOSTILLE

(Convention de La Haye du 5 octobre 1961)

- Country: THE NETHERLANDS
 This public document
- 2. has been signed by ing. M. van Berlo
- acting in the capacity of Inspector for Medical Technology of the Ministry of Public Health, Welfare and Sports
- 4. bears the seal/stamp of aforesaid Ministery

Certified

- 5. in Den Haag
- 6. on 10-01-2020
- by the registrar of the district court of Den Haag
- 8. no. 2020-314
- 9. Seal/stamp:



S.P.C. Mee wesen

