

Medicines and Healthcare Products Regulatory Agency

CERTIFICATE NUMBER: **UK API 22857 Insp GMP 22857/36790-0007**

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER^{1, 2}

Part 1

Issued following an inspection in accordance with :

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

The competent authority of United Kingdom confirms the following:

The manufacturer: **AESICA PHARMACEUTICALS LIMITED**

Site address: **WINDMILL INDUSTRIAL ESTATE, SHOTTON LANE, CRAMLINGTON, NE23 3JL, United Kingdom**

Has been inspected under the national inspection programme in accordance with Art. 40 of Directive 2001/83/EC .

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

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on **2018-05-23** , it is considered that it complies with :

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/EC³
- The principles of GMP for active substances³ 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.

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

Human Medicinal Products

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

NITISINONE(en)

PAROXETINE HYDROCHLORIDE HEMIHYDRATE(en)

FLUTICASONE PROPIONATE(en)

CANNABIDIOL(en)

S-(+)-FLURBIPROFEN(en)

PAROXETINE HYDROCHLORIDE ANHYDROUS(en)

OXYCODONE HYDROCHLORIDE(en)

OPICAPONE(en)

CODEINE PHOSPHATE(en)

FLURBIPROFEN SODIUM DIHYDRATE(en)

DIIPANONE HYDROCHLORIDE(en)

FLURBIPROFEN(en)

NALOXONE HYDROCHLORIDE(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : NITISINONE

3.1 Manufacture of Active Substance by Chemical Synthesis

3.1.2 Manufacture of crude active substance

3.1.3 Salt formation / Purification steps :

Crystallisation

3.1.1 Manufacture of active substance intermediates

3.5 General Finishing Steps

3.5.1 Physical processing steps :

Drying

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)

3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)

3.6 Quality Control Testing

3.6.1 Physical / Chemical testing

Active Substance : PAROXETINE HYDROCHLORIDE HEMIHYDRATE

3.1 Manufacture of Active Substance by Chemical Synthesis

3.1.1 Manufacture of active substance intermediates

3.1.3 Salt formation / Purification steps :

Crystallisation

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) 3.5.1 Physical processing steps : Conemill, shifter (drying)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : FLUTICASONE PROPIONATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : Crystallisation, sodium salt neutralised and subsequent base crystallised from petrol
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Dried on filter drier and passed through a mill system 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 : CANNABIDIOL	
3.2	Extraction of Active Substance from Natural Sources
	3.2.6 Purification of extracted substance Plant 3.2.1 Extraction of substance from plant source
3.5	General Finishing Steps
	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) 3.5.1 Physical processing steps : Drying 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : S-(+)-FLURBIPROFEN	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance

	3.1.1 Manufacture of active substance intermediates 3.1.3 Salt formation / Purification steps : Crystallisation
3.5	General Finishing Steps
	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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) 3.5.1 Physical processing steps : Filtration, distillation, crystallisation and centrifugation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : PAROXETINE HYDROCHLORIDE ANHYDROUS	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : Crystallisation 3.1.1 Manufacture of active substance intermediates
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying to anhydrous 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 : OXYCODONE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : Salt formation and Crystallisation 3.1.2 Manufacture of crude active substance 3.1.1 Manufacture of active substance intermediates
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) 3.5.1 Physical processing steps : Drying

3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : OPICAPONE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Crystallisation 3.1.1 Manufacture of active substance intermediates
3.5	General Finishing Steps
	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) 3.5.1 Physical processing steps : Dried to anhydrous 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : CODEINE PHOSPHATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation of phosphate salt
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Drying and milling 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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : FLURBIPROFEN SODIUM DIHYDRATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.3 Salt formation / Purification steps : 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)

	3.5.1 Physical processing steps : Dried in Oven 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 : DIPIPANONE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.3 Salt formation / Purification steps : Crystallisation
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) 3.5.1 Physical processing steps : Drying
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : FLURBIPROFEN	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.1 Manufacture of active substance intermediates 3.1.3 Salt formation / Purification steps : Sodium salt neutralised and subsequent base crystallised from petrol
3.5	General Finishing Steps
	3.5.1 Physical processing steps : Dried on filter drier and passed through a mill system 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) 3.5.2 Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : NALOXONE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance

	3.1.3 Salt formation / Purification steps : Salt formation and crystallisation
	3.1.1 Manufacture of active substance intermediates
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)
	3.5.1 Physical processing steps : Drying
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

2018-07-03

Name and signature of the authorised person of the
Competent Authority of United Kingdom

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