

Italian Medicines Agency

CERTIFICATE NUMBER: **IT-API/93/H/2016**

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 Italy confirms the following:

The manufacturer: **CORDEN PHARMA BERGAMO SPA**

Site address: **VIA BERGAMO, 121, TREVIGLIO, 24047, Italy**

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 **2016-03-18** , it is considered that it complies with :

- 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 :

MICONAZOLO NITRATO(it) / MICONAZOLE NITRATE(en)
CLOTRIMAZOLO(it) / CLOTRIMAZOLE(en)
DICLOFENAC(it) / DICLOFENAC(en)
METAXALONE(it) / METAXALONE(en)
MESALAZINA(it) / MESALAZINE(en)
SODIO CLODRONATO TETRAIDRATO(it) / SODIUM CLODRONATE TETRAHYDRATE(en)
BETANECOLO CLORURO(it) / BETHANECHOL CHLORIDE(en)
CIMETIDINA(it) / CIMETIDINE(en)
LANTANIO CARBONATO(it) / LANTANIUM CARBONATE(en)
OPIPRAMOLO DICLORIDRATO(it) / OPIPRAMOL HYDROCHLORIDE(en)
ACIDO RITALINICO(it) / RITALINIC ACID(en)
BENSERAZIDE CLORIDRATO GREZZO(it) / BENSERAZIDE HYDROCHLORIDE CRUDE(en)
CIMETIDINA CLORIDRATO(it) / CIMETIDINE HYDROCHLORIDE(en)
TRIMEBUTINA MALEATO(it) / TRIMEBUTINE MALEATE(en)
SECNIDAZOLO(it) / SECNIDAZOLE(en)
DISULFIRAM(it) / DISULFIRAM(en)
DOXILAMINA SUCCINATO(it) / DOXYLAMINE SUCCINATE(en)
NAPROSSENE(it) / NAPROXEN(en)
TRIMEBUTINA(it) / TRIMEBUTINE(en)
BENZOIL PEROSSIDO IDRATO(it) / BENZOYL PEROXIDE HYDRATE(en)
METRONIDAZOLO(it) / METRONIDAZOLE(en)
METRONIDAZOLO BENZOATO(it) / METRONIDAZOLE BENZOATE(en)
IMIPRAMINA CLORIDRATO(it) / IMIPRAMINE HYDROCHLORIDE(en)
MESALAZINA H.D.(it) / MESALAZINE HIGH DENSITY(en)
OLSALAZINA SODICA(it) / OLSALAZINE SODIUM(en)
SERINHYDRAZIDE HYDROCHLORIDE(it) / SERINHYDRAZIDE HYDROCHLORIDE(en)
SULFASALAZINA(it) / SULFASALAZINE(en)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : MICONAZOLE NITRATE

3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance
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 :

	drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : CLOTRIMAZOLE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : DICLOFENAC	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : METAXALONE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : MESALAZINE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : purification 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) 3.5.2 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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : SODIUM CLODRONATE TETRAHYDRATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : BETHANECHOL CHLORIDE	
3.5	General Finishing Steps

	3.5.4 Other : batch certification
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : CIMETIDINE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : LANTANIUM CARBONATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation 3.1.2 Manufacture of crude active substance
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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : OPIPRAMOL HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation 3.1.2 Manufacture of crude active substance

	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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : RITALINIC ACID	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : BENSERAZIDE HYDROCHLORIDE CRUDE	
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
3.5	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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

Active Substance : CIMETIDINE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : TRIMEBUTINE MALEATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : SECNIDAZOLE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance
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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : DISULFIRAM	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance
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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : DOXYLAMINE SUCCINATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : NAPROXEN	
3.1	Manufacture of Active Substance by Chemical Synthesis

	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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : TRIMEBUTINE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance 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) 3.5.2 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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : BENZOYL PEROXIDE HYDRATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : precipitation
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)
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : METRONIDAZOLE	
3.1	Manufacture of Active Substance by Chemical Synthesis

	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : METRONIDAZOLE BENZOATE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
	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)
	3.5.2 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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : IMIPRAMINE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : salt formation
	3.1.2 Manufacture of crude active substance
	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)
	3.5.2 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 :

	drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : MESALAZINE HIGH DENSITY	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : purification
	3.1.2 Manufacture of crude active substance
	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)
	3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : OLSALAZINE SODIUM	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
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 : drying,sieving,micronisation
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : SERINHYDRAZIDE HYDROCHLORIDE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation
	3.1.2 Manufacture of crude active substance
	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) 3.5.2 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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing
Active Substance : SULFASALAZINE	
3.1	Manufacture of Active Substance by Chemical Synthesis
	3.1.3 Salt formation / Purification steps : crystallisation 3.1.2 Manufacture of crude active substance
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 : drying,sieving
3.6	Quality Control Testing
	3.6.1 Physical / Chemical testing

4. Other Activities - Active Substances :

Importation of: NAPROXEN CRUDE (confidential)

Clarifying remarks (for public users)

Imported active substances marked as confidential undergo further processing within the importing site. The Inspectorate adopted a risk-based approach for planning of inspections, therefore the validity of the GMP certificate for this manufacturing site is not more than 42 months from the last general GMP inspection, which was conducted on 18/03/2016. It will still be AIFA's right to re-evaluate the validity of the GMP certificate based on risk profile changes.

2016-11-10

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

Confidential
Italian Medicines Agency
Tel: ***Confidential***
Fax: ***Confidential***