Agenzia Italiana del Farmaco

AIFA

Certificate No: IT-API/14/H/2017

CERTIFICATE OF GMP COMPLIANCE OF A MANUFACTURER

Part 1

Issued following an inspection in accordance with Art. 111(5) of Directive 2001/83/EC

The competent authority of Italy confirms the following:
The manufacturer BIDACHEM S.P.A.
Site address S.S. 11 (Padana Superiore), 8 - 24040 FORNOVO SAN GIOVANNI (BG)

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: **D.L. n. 219 of 24th April 2006 art. 53**

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on 2016/07/29, it is considered that it complies with the Good Manufacturing Practice requirements referred to in the principles of GMP for active substances 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.
The authenticity of this certificate may be verified in EudraGMDP. If it does not appear, please contact the issuing authority.

AIFA - Italian Medicines Agency
GMP Inspections and Manufacturing Authorizations of APIs Office
Via del Tritone, n° 181 - 00187 ROMA (ITALY)
Tel.+390659784409 Fax +390659784617
website: www.agenziafarmaco.it
SIS : 7101

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Part 2

Name and address of the site:

BIDACHEM S.P.A. - S.S. 11 (Padana Superiore), 8, 24040 FORNOVO SAN GIOVANNI (BG)

Name of the active Substances manufactured or imported:

NICOTINIC ACID BUTOXYETHYL ESTER
AMBROXOL HYDROCHLORIDE
BROMHEXINE HYDROCHLORIDE
CARBOCISTEINE LYSINE SALT
CIMETROPIUM BROMIDE
CROTAMITON
DABIGATRAN ETEXILATE MESILATE
DROPROPIZINE
EMPAGLIFLOZIN
FLIBANSERIN
KETOPROFEN
KETOPROFEN LYSINE SALT
LEVODROPROPIZINE
MELOXICAM
NITROFURANTOIN
NONIVAMIDE
ORCIPRENALINE SULFATE
RIBAVIRIN
SODIUM PICOSULFATE

3 - Manufacturing Operations - Active Substances

NICOTINIC ACID BUTOXYETHYL ESTER

3.1	Manufacture of Active Substance by Chemical Synthesis

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	3.1.2. Manufacture of crude active substance **3.1.3.** Salt formation / Purification steps: distillation
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

3 - Manufacturing Operations - Active Substances

AMBROXOL 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: crystallisation,salt formation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,sieving **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

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3 - Manufacturing Operations - Active Substances

BISACODYL

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

3 - Manufacturing Operations - Active Substances

BROMHEXINE 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:

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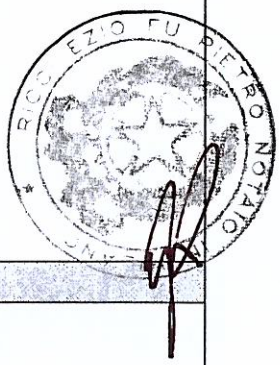
	crystallisation,salt formation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,sieving **3.5.2.** Primary Packaging (enclosing / sealing the active substance within a packaging material which is in direct contact with the substance) **3.5.3.** Secondary Packaging (placing the 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

3 - Manufacturing Operations - Active Substances

CARBOCISTEINE LYSINE SALT



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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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**
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3 - Manufacturing Operations - Active Substances

CIMETROPIUM BROMIDE

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

3 - Manufacturing Operations - Active Substances

CROTAMITON

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

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

3 - Manufacturing Operations - Active Substances

DABIGATRAN ETEXILATE MESILATE

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,salt formation
3.5	**General Finishing Steps**
	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) **3.5.3.** 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

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3 - Manufacturing Operations - Active Substances

DROPROPIZINE

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

3 - Manufacturing Operations - Active Substances

EMPAGLIFLOZIN

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
3.5	**General Finishing Steps**

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	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) **3.5.3.** 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

3 - Manufacturing Operations - Active Substances

FLIBANSERIN

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
3.5	**General Finishing Steps**
	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) **3.5.3.** 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

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3 - Manufacturing Operations - Active Substances

KETOPROFEN

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

3 - Manufacturing Operations - Active Substances

KETOPROFEN LYSINE SALT

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,salt formation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps

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	drying,milling **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

3 - Manufacturing Operations - Active Substances

LEVODROPROPIZINE

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

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3 - Manufacturing Operations - Active Substances

MELOXICAM

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling **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

3 - Manufacturing Operations - Active Substances

NITROFURANTOIN

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3. Salt formation / Purification steps: crystallisation
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,sieving **3.5.2.** Primary Packaging (enclosing / sealing the active substance within a

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	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

3 - Manufacturing Operations - Active Substances

NONIVAMIDE

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

3 - Manufacturing Operations - Active Substances

ORCIPRENALINE SULFATE

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,crystallisation
3.5	**General Finishing Steps**
	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) **3.5.3.** 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

3 - Manufacturing Operations - Active Substances

RIBAVIRIN

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
3.5	**General Finishing Steps**
	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)

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	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

3 - Manufacturing Operations - Active Substances

SODIUM PICOSULFATE

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
3.5	**General Finishing Steps**
	3.5.1. Physical processing steps drying,milling,sieving **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

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Restrictions or clarifying remarks:

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 2016/07/29. It will still be AIFA's right to re-evaluate the validity of the GMP certificate based on risk profile changes.

Rome, 2017/02/02

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

Dott.ssa Isabella Marta
AIFA - GMP Inspections and Manufacturing Authorizations of APIs Office

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Certifico io sottoscritto dr. Ezio Ricci, Notaio in Milano e iscritto al Collegio Notarile di Milano che la presente copia fotostatica composta da 16 (sedici) pagine è conforme all'originale documento.
Milano, 30 marzo 2017

Dr. Ezio Ricci Notaio
Piazza San Babila, n. 3 - MILANO
Tel. 02 - 6597205 - Fax. 02-654339

005860

APOSTILLE

(Convention de la Haye du 5 octobre 1961)

1. Paese: ITALIA

Il presente atto pubblico

2. è stato sottoscritto da E. Rocco

3. agente in qualità di Ispettore

4. è segnato dal contrassegno/timbro di

Attestato

5. a Milano 6. il - 5 APR. 2017

7. dall'ufficio del pubblico ministero

8. sotto il numero 1586

9. contrassegno timbro 10. firma

IL SOST. PROCURATORE DELLA REPUBBLICA
Dr. Paolo Nicola Filippini

PROCURA DELLA REPUBBLICA PRESSO IL TRIBUNALE MILANO