Chile

le 10/04/2017

JE SOUSSIGNE
Maître TOUZET
notaire associé à LYON
6ème, 139 rue Vendôme
CERTIFIE la présente copie,
conforme à l'original

COUR D'APPEL DE LYON
LE PROCUREUR GENERAL

TOUZET, Notaire à LYON

COUR D'APPEL

ansm
Agence nationale de sécurité du médicament et des produits de santé

French National Agency for Medicines and Health Products Safety

CERTIFICATE NUMBER: *17MPP007HFR01*

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 France confirms the following:
The manufacturer: ***MERCK SANTE***
Site address: ***5 rue Clément Ader, CALAIS, 62100, France***

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 ***2017-01-27*** , 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.

---

[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.*

143/147 boulevard Anatole France - F-93285 Saint-Denis Cedex - Tél.: +33(0)1 55 87 30 00 - www.ansm.sante.fr

ansm
Agence nationale de sécurité du médicament et des produits de santé

Part 2

Manufacture of active substance. Names of substances subject to inspection :
METFORMINY CHLOROWODOREK(pl) / METFORMÍN HYDROCHLORID(sk) / METFORMINA H IDROCLORURO(es) / METFORMIN HYDROCHLORIDE(en) / METFORMIN HYDROCHLORIDE(bg) / METFORMIINIHYDROKLORIDIA(fi) / METFORMIN HYDROCHLORID(cs) / CHLORHYDRA TE DE METFORMINE.(fr)
ACAMPROSATE CALCIUM(en)
METFORMIN HYDROCHLORIDE AND 0.5% MAGNESIUM STEARATE(en) / METFORMINE (CH LORHYDRATE DE) + 0.5 % DE STEARATE DE MAGNESIUM(fr)

3. MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES

Active Substance : METFORMIN HYDROCHLORIDE AND 0.5% MAGNESIUM STEARATE

3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.2 Manufacture of crude active substance 3.1.3 Salt formation / Purification steps : Crystallization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : 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) 3.5.4 Other : Mixture of metformin HCl and magnesium stearate
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Active Substance : METFORMIN 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 : Crystallization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : 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**

143/147 boulevard Anatole France - F-93285 Saint-Denis Cedex - Tél.: +33(0)1 55 87 30 00 - www.ansm.sante.fr

ansm
Agence nationale de sécurité du médicament et des produits de santé

	3.6.1 Physical / Chemical testing
Active Substance : ACAMPROSATE CALCIUM	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	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)
3.6	**Quality Control Testing**
	3.6.1 Physical / Chemical testing

Clarifying remarks (for public users)

ACAMPROSATE CALCIUM : limited to manufacturing of key intermediate HOMOTAURIN

[redacted]

2017-03-27

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

---

Mr. Jacques Morénas
French National Agency for Medicines and Health Products Safety
Tel: *+33 1 55873911*
Fax *+33 1 55873912*

143/147 boulevard Anatole France - F-93285 Saint-Denis Cedex - Tél.: +33(0)1 55 87 30 00 - **www.ansm.sante.fr**

Référence interne : 17/01533

CHILI

APOSTILLE
(Convention de La Haye du 5 octobre 1961)

1.République française
Le présent acte public
2. a été signé par **Yves TOUZET**
3. agissant en qualité **de notaire**
4. est revêtu du sceau/timbre de **son étude à LYON - COUR D'APPEL**

Attesté

5. à **LYON**
6. le **03 Mai 2017**
7. par le Procureur Général près la Cour d'appel de Lyon
8. sous le n° **3812** - 3 pgs
9. Sceau

10. Signature
Bérengère SINEMIAN

"L'Apostille confirme seulement l'authenticité de la signature, du sceau ou timbre sur le document. Elle ne signifie pas que le contenu du document est correct ou que la République française approuve son contenu."