French National Agency for Medicines and Health Products Safety

Report No: ***18MPP079NCR01***

STATEMENT OF NON-COMPLIANCE WITH GMP

Exchange of information between National Competent Authorities (NCAs) of the EEA following the discovery of serious GMP non-compliance at a manufacturer [1]

Part 1

Issued following an inspection in accordance with :
Art. 111(7) of Directive 2001/83/EC as amended

The competent authority of France confirms the following:
The manufacturer: ***KORES (INDIA) LIMITED***
Site address: ***Plot Nos. 58/1, 58/2, 59A, 65A, 65B, 65C & 66A, M.I.D.C. Industrial Area Dhatav, Roha, Maharashtra, 402 116, India***
DUNS Number: ***67-760-4350***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-10-31*** , it is considered that **it does not comply 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 .

[1] *The statement of non-compliance referred to in paragraph 111(7) of Directive 2001/83/EC and 80(7) of Directive 2001/82/EC, as amended, shall also be required for imports coming from third countries into a Member State.*

Part 2

1 NON-COMPLIANT MANUFACTURING OPERATIONS	
Include total and partial manufacturing (including various processes of dividing up, packaging or presentation), batch release and certification, storage and distribution of specified dosage forms unless informed to the contrary;	
1.4	**Other products or manufacturing activity**
	1.4.1 Manufacture of 1.4.1.4 Other: active substances(en)

Manufacture of active substance. Names of substances subject to non-compliant :
AMBROXOL HYDROCHLORIDE PH. EUR.(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES	
Active Substance : AMBROXOL HYDROCHLORIDE PH. EUR.	
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 : filtration and crystallization
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : drying, milling and 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 3.6.2 Microbiological testing excluding sterility testing

Part 3

1. Nature of non-compliance:
5 Major deficiencies were found in the following areas: Data integrity (1), risks of contamination and/or cross-contamination related to production Equipment (2), risks of contamination related to reusable material containers (1), computerised systems validation (1). It should be noted that the site was already declared non compliant (see NCR report number IT/NCR/API/1/2017 issued by italian authorities) after a first EDQM inspection, conducted from 2 to 4 March 2017 and the corresponding CEPs were suspended.
Action taken/proposed by the NCA **Prohibition of supply** After issuance of the non-compliance report and as long as it remains active, the site should not be named in any new Marketing Authorisations (MAs) or used in drug compounding activities. **Suspension or voiding of CEP (action to be taken by EDQM)**

EDQM to consider the withdrawal of the CEPs n°2013-115 Ambroxol HCl, n°2015-012 Ambroxol HCl and n°2015-224 Glimepiride.
Additional comments This inspection was performed in the framework of the CEP dossier for the manufacture of Ambroxol hydrochloride. The deficiencies found could affect the other APIs manufactured at the site listed below: Doxofylline, Etofylline, Acefylline, Glimepiride, 3-Methylxanthine, 2-Amino-3,5-dibromobenzaldehyde, 8-ChloroTheophylline,8-Benzyl Theophylline, Theobromine, Acebrophylline, Theophylline, Piperazine/Acepifylline, Pamabrom, Ivabradine HCl, Dorzolamide Hydrochloride.

2018-12-19

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

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