Medicines and Healthcare Products Regulatory Agency

Report No: ***Insp GMP 46177/14316169-0001 NCR***

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 United Kingdom confirms the following:
The manufacturer: ***AKUMS DRUGS & PHARMACEUTICALS LIMITED***
Site address: ***Plant IV, Sector - 6A, IIE, SIDCUL, HARIDWAR, UTTRAKHAND, 249403, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2016-04-13*** , it is considered that **it does not comply with the Good Manufacturing Practice** requirements referred to in

- The principles and guidelines of Good Manufacturing Practice laid down in Directive 2003/94/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

Human Medicinal Products

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;	
1.1	**Sterile products**
	1.1.2 Terminally Sterilised (processing operations for the following dosage forms) 1.1.2.3 Small volume liquids
1.4	**Other products or manufacturing activity**
	1.4.2 Sterilisation of active substance/ excipients/ finished product 1.4.2.2 Dry heat
1.5	**Packaging**
	1.5.2 Secondary packing
	1.5.1 Primary Packing 1.5.1.6 Liquids for internal use
1.6	**Quality control testing**
	1.6.1 Microbiological: sterility *1.6.2 Microbiological: non-sterility* *1.6.3 Chemical/Physical*

Clarifying remarks (for public users)

This statement of non-compliance refers to the manufacture of injectable products in Plant IV only. The other plants at the site do not manufacture for EEA markets. This inspection was specifically for a terminally sterilised oily injection (Progesterone 50mg/ml) and no aseptic products are known to be manufactured for the EEA.

Part 3

1. Nature of non-compliance:
One critical and 3 major deficiencies were raised at this inspection: The critical deficiency was for lack of sterility assurance as there was insufficient evidence during validation to confirm that all ampoules in the load met the sterilising conditions of 160oC for 2 hours, a weak sterility sampling plan and lack of qualification of the leak test cycle. The major deficiencies were for inadequate control and validation of sterilisation, deficiencies across all aspects of the quality management system and lack of a robust environmental monitoring programme. 13 other deficiencies covering all aspects of GMP were recorded but not formally reported so as not to distract from the critical and major deficiencies.
Action taken/proposed by the NCA

Requested Variation of the marketing authorisation(s)
The inspection was in response to a variation to PL 05827/0012 - Progesterone injection 50mg/ml Ampoules (Gestone); Nordic Pharma Limited.

Recall of batches already released
The site currently manufactures some unlicensed Progesterone injection which is supplied to the UK and Eire. 4 batches will be recalled although there is little stock expected on the market. A notification to healthcare practitioners has been issued which recommends to healthcare professionals: • Do not start treatment for new patients • Only continue use for existing patients where the patient's clinician judges that there is no suitable alternative treatment. Additional monitoring should be considered.

Prohibition of supply
The variation to add Akums as a manufacturing site to the marketing authorisation has been put on hold.

Others
As this was the first inspection of the site so no manufacturing authorisation has been issued.

Products manufactured at site, if known	Products	Dosage Form	Reference Member State, National or EMA
Human Medicinal Products	Progesterone Injection 50mg/ml	Ampoule for injection	NATIONAL

2016-06-10

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

---

Confidential
Medicines and Healthcare Products Regulatory Agency
Tel: ***Confidential***
Fax: ***Confidential***