Medicines and Healthcare Products Regulatory Agency

Report No: ***UK GMP 19826 Insp GMP 19826/39398-0003 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: ***MARKSANS PHARMA LIMITED***
Site address: ***PLOT NO L-82, L-83, VERNA INDUSTRIAL ESTATE, VERNA, GOA, IN-403 722, India***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2015-11-25*** , 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;

1.2	**Non-sterile products**
	1.2.1 Non-sterile products (processing operations for the following dosage forms) 1.2.1.1 Capsules, hard shell 1.2.1.2 Capsules, soft shell 1.2.1.13 Tablets
1.5	**Packaging**
	1.5.2 Secondary packing
1.6	**Quality control testing**
	1.6.2 Microbiological: non-sterility *1.6.3 Chemical/Physical*

Part 3

1. Nature of non-compliance:
A prior inspection in March 2015 identified several serious Major deficiencies in the operation of the Pharmaceutical Quality System. These included systems to ensure Data integrity, Deviations and CAPA management, Change Controls, PQRs and Self-Inspection. A November 2015 re-inspection was carried out to assess the remediation plan from the company. There was a lack of evidence to demonstrate the effectiveness of resultant CAPAs taken and a lack of interim assurances to ensure that the on-going operations remain in compliance with GMP, including failures to carry out effective investigations. The November inspection identified a critical deficiency relating to systems to ensure Data Integrity in the following respects: o Evidence of destruction of multiple parts of records of prime data o Overall Data Integrity management and oversight o Investigations into Missing and deleted data within the laboratory incomplete o Procedures controlling Data Integrity within the laboratory not in place

Action taken/proposed by the NCA

Withdrawal, of current valid GMP certificate No. UK GMP 19826 Insp GMP 19826/39398-0003
Withdrawal of previous GMP Certificate No: UK GMP 19826 Insp GMP 19826/39398-0003

Requested Variation of the marketing authorisation(s)
No further MA should be approved naming the site as manufacturer. Current pending MA applications should be held or refusal to grant stated whilst this statement of non-compliance remains in force.

Recall of batches already released
There is no evidence of defective product currently on the market. Recall of products is not considered necessary.

Prohibition of supply
No further batches of medicinal products considered non-critical to public health to be supplied to the market whilst this statement on non-compliance remains in force

Additional comments
National competent authorities should evaluate the criticality of products supplied from this site and enact measures to ensure continued supply. Marketing authorisation holders are requested to contact the relevant National Competent Authority to verify whether their products are considered medically critical, and therefore outside the scope of this non-compliance statement.

Products manufactured at site, if known	Products	Dosage Form	Reference Member State, National or EMA
Human Medicinal Products	SIMVASTATIN 10 MG	Tablets	National
	SIMVASTATIN 20MG	Tablets	National
	SIMVASTATIN 40MG	Tablets	National
	PROPRANOLOL 40MG	Tablets	National
	PROPRANOLOL 80MG	Tablets	National
	DOMPERIDONE 10MG	Tablets	National
	SILDENAFIL TEVA 25 MG	Tablets	MR; Netherlands = RMS
	SILDENAFIL TEVA 50 MG	Tablets	MR; Netherlands = RMS
	SILDENAFIL TEVA 100 MG	Tablets	MR; Netherlands = RMS
	PARACETAMOL 500MG	Tablets	National
	IBUPROFEN 200MG	Tablets	National
	IBUPROFEN 200MG	Capsules	National
	METFORMIN 500MG	Tablets	National
	METFORMIN 850MG	Tablets	National
	TEVA MOCLOBEMIDE 150MG	Tablets	MR; UK = RMS
	TEVA MOCLOBEMIDE 300MG	Tablets	MR; UK = RMS
	ASPIRIN 75MG GASTRO-RESISTANT	Tablets	National
	ENPRIN	Tablets	National
	FLUOXETINE 20MG	Capsules	National
	RANITIDINE 150MG	Tablets	National
	RANITIDINE 300MG	Tablets	National
	LISINOPRIL 2.5MG	Tablets	National
	LISINOPRIL 5MG	Tablets	National
	LISINOPRIL 10MG	Tablets	National
	LISINOPRIL 20MG	Tablets	National
	BISOPROLOL 5MG	Tablets	National
	BISOPROLOL 10MG	Tablets	National
	PROPRANOLOL 10MG BP	Tablets	National
	PROPRANOLOL 80MG	Tablets	National

BP		
RELOSORB XL 60MG	Tablets	National
MIRTAZAPINE 30MG	Tablets	National
TERBINAFINE 250MG	Tablets	National
GLICLAZIDE 80MG	Tablets	National
TRAMADOL 50MG	Capsules	MR; UK = RMS
HAYLIEF HAYFEVER & ALLERGY 10MG	Tablets	National
LORATADINE 10MG	Tablets	National
TESCO ONE A DAY HAYFEVER & ALLERGY 10MG	Tablets	National
VANTAGE ALLERGY RELIEF 10 MG	Tablets	National
RANITIDINE 75MG	Tablets	National
IBUPROFEN 400MG	Tablets	National
PARACETAMOL 500MG	Capsules	National
PROPRANALOL 40 MG	Tablets	National
ALEXANDER'S HAYFEVER & ALLERGY 10MG	Tablets	National
BELL'S HEALTHCARE HAYFEVER & ALLERGY 10MG	Tablets	National
ESSENTIAL WAITROSE HAYFEVER & ALLERGY 10MG	Tablets	National
PEACH HAYFEVER & ALLERGY 10MG	Tablets	National
RELONCHEM HAYFEVER AND ALLERGY 10MG	Tablets	National
IBUPROFEN 200MG	Tablets	National
MIRTAZAPINE 15MG	Tablets	MR; UK = RMS
MIRTAZAPINE 45MG	Tablets	MR; UK = RMS
BELL'S HEALTHCARE ALLERGY RELIEF 10MG	Tablets	MR; UK = RMS
CETIRIZINE	Tablets	MR; UK = RMS

	HYDROCHLORIDE 10MG		
	FOLIC ACID 5MG	Tablets	National
	SOLOC 10MG	Tablets	National
	INDAPAMIDE HEMIHYDRATE 2.5MG	Tablets	National
	NATRAMID/OPUMIDE	Tablets	National
	PHENYTOIN SODIUM NRIM 100MG	Capsules	MR; UK = RMS
	OMEPRAZOLE 20 MG	Capsules	National
	IBUPROFEN 600 MG	Tablets	National
	INDAPAMIDE 2.5MG	Tablets	National
	IBUPROFEN BP 200MG	Tablets	National
	IBUPROFEN BP 400MG	Tablets	National
	IBUPROFEN BP 600MG	Tablets	National
	DOANS 500MG	Capsules	National
	ACTAVIS PARACETAMOL 500MG	Caplets	National
	PARACETAMOL 500MG	Caplets	National
	PARACETAMOL BP 500MG	Tablets	National
CIMETIDINE 200MG	Tablets	National	
CIMETIDINE 400MG	Tablets	National	

2016-03-17

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

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