Medicines and Healthcare Products Regulatory Agency

Report No: ***Insp GMP/IMP 41521/16682-0030 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
Art. 80(7) of Directive 2001/82/EC as amended
Art. 15 of Directive 2001/20/EC

The competent authority of United Kingdom confirms the following:
The manufacturer: ***RECIPHARM LIMITED***
Site address: ***VALE OF BARDSLEY, ASHTON-UNDER-LYNE, OL7 9RR, United Kingdom***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-08-24*** , 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
- The principles and guidelines of Good Manufacturing Practice laid down in Directive 91/412/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
Veterinary Medicinal Products
Human Investigational 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) 1.2.1.5 Liquids for external use 1.2.1.6 Liquids for internal use 1.2.1.8 Other solid dosage forms 1.2.1.13 Tablets 1.2.1.17 Other

Clarifying remarks (for public users)

The scope of this statement of non-compliance is limited to the manufacture with associated primary packaging of medicinal products considered to be potent products and that are non-critical to public health. Where manufacture is continued for critical potent products, this should be supported by a documented risk assessment containing sufficient information to support activity on a risk management basis. The restriction does not apply to the manufacture of non-potent products or to QC testing or to batch certification of sterile products. National competent authorities should evaluate the criticality of products being supplied by this manufacturing site and enact measures to ensure continued supplies where appropriate. Marketing authorisation holders are requested to contact the relevant national authority to verify whether their products are considered medically critical to public health in their territory and therefore outside the scope of the non-compliance statement.

Part 3

1. Nature of non-compliance:
The measures to prevent and detect cross-contamination were deficient and presented a risk that cross contamination between products could occur and would not be detected. The site operates separate manufacturing areas for products considered potent and non-potent. In particular, the potential for cross-contamination with highly potent products poses a risk to public health and the National Competent Authority therefore believes that it is necessary in the interests of patient safety to immediately restrict the manufacture of non-critical potent products until the issues are satisfactorily resolved.
Action taken/proposed by the NCA **Suspension of the manufacturing authorisation No. UK MIA 41521 in Part** Partially suspend MIA 41521, MS 41521 and MIA(IMP) 41521 to restrict the manufacture of potent products to critical products only.

Prohibition of supply
No batches of non-critical potent product to be supplied to EU markets whilst this statement of non-compliance remains in force. Supply of non-potent product is permitted.

Suspension of clinical trials
The statement of non-compliance also applies to manufacture of all potent investigational medicinal products (IMPs) manufactured at the site and the manufacture and supply of these products should cease. The only exemption to this is where a trial sponsor can demonstrate that the benefit risk ratio remains positive and supports the continuation of the particular trial. The site is required to carry out a risk assessment, in conjunction with the sponsor of each trial for which they manufacture IMP, to discuss such continuation of supply on the batch by batch basis.

Additional comments
It is noted that the manufacture and release of potent products has been voluntarily stopped until corrective actions have been completed. However, for the avoidance of doubt, the National Competent Authority considers that it is necessary to formalise this commitment by restricting that part of the certificate until such time that it is satisfied that potent product manufacture is in a position to return to compliance with the principles of GMP. It is acknowledged that the site may need to manufacture non-critical potent products as part of cleaning trials to return into compliance and this will be permitted provided that it is supported by a documented risk assessment containing sufficient information to support the activity on a risk management basis. However, these products may not be released to market whilst the restriction is in place. The following list of products are known to be manufactured in the potent area.

Products manufactured at site, if known	Products	Dosage Form	Reference Member State, National or EMA
Human Medicinal Products	ESTRACE	Tablets 0.5 mg	N/A – supplied to Canada
	ESTRACE	Tablets 1 mg	N/A – supplied to Canada
	ESTRACE	Tablets 2 mg	N/A – supplied to Canada
	ESTROVAL	Tablets 1 mg Bulk Pack	N/A - supplied to South Africa, Botswana, Namibia
	ESTROVAL	Tablets 2 mg Bulk Pack	N/A - supplied to South Africa, Botswana, Namibia
	CLIMACTOL	Tablets 1+1 mg Bulk Pack	N/A – supplied to South Africa, Botswana, Namibia
	LOESTRIN 20	Tablets	National
	LOESTRIN 30	Tablets	National
	NARDIL	Tablets 15mg	National
	NARDELZINE	Tablets	Belgium
	Cloral Betaine (Welldorm)	Tablets	National
	Elleste Solo	Tablets 1 mg	Mutual Rec. UK RMS
	Elleste Solo	Tablets 2 mg	Mutual Rec. UK RMS
	Elleste Duet Conti	Tablets	Mutual Rec. UK RMS
	Ellest Duet	Tablets 1mg	Mutual Rec. UK RMS
	BETAMETHASONE SOL	Tablets 500MCG 100	National
	COLCHICINE	Tablets 500MCG	National
	COLCHIMEX	Tablets 500MCG 100 DK	Denmark
	LEVOTHYROXINE	Tablets 25MCG	National
	PREDNISOLONE	Liquid - 20MG/100ML RECTAL SOLUTION	National
	ETHINYLESTRADIOL	Tablets 2MCG	N/A - Special
	ETHINYLESTRADIOL	Tablets 50MCG	National
	ETHINYLESTRADIOL	Tablets 10MCG	National
	ETHINYLESTRADIOL	Tablets 1 mg	National
	Special : Kidmel(melantonin)	Liquid	N/A - Special
	Special : Kidnaps	Liquid	N/A – Special Under tech transfer, not currently supplied

	DEXAMETHASONE	Tablets 0.5 mg	N/A – not currently marketed (process val)
	DEXAMETHASONE	Tablets 2 mg	N/A – not currently marketed (process val)
	HYDROCORTISONE	Tablets 10 mg	Decentral. UK RMS (Pending)
	HYDROCORTISONE	Tablets 20mg	Decentral. UK RMS (Pending)
Veterinary Medicinal Products	Perlutex	Tablets 5 mg	N/A - not currently marketed (recently approved)

Products manufactured at site, if known	**Products**	**EudraCT nos**
Investigational Medicinal Products	LEVOTHYROXINE TABLETS 25MCG	
	DEXAMETHASONE TABLETS 0.5MG	
	DEXAMETHASONE TABLETS 2MG	
	HYDROCORTISONE TABLETS 10MG	
	HYDROCORTISONE TABLETS 20MG	

2018-10-03

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

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