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Richiamo lotti difettosi

4495
Ospedale Sant'Andrea
Direttore farmacia
La Spezia
Fax n° +39 (0187) 53 39 05

Prodotto: Thiopental VUAB inj plv sol 1.0 g 1 vial
Lotto: SC170130

Attenzione!!! Comunicare immediatamente il numero di confezioni in giacenza presso i vostri magazzini inviando copia della presente al n° +41 91 985 62 22.

Unipharma SA
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6917 Barbengo-Lugano
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Cert. N°23997

RICHIAMO LOTTI

Thiopental VUAB sol inj

Prodotto:	Thiopental VUAB sol inj
Fabbricante:	VUAB Pharma
Paese di origine:	Repubblica Ceca
Forma galenica:	soluzione iniettabile
Dosaggi:	Tutti
N° lotti difettosi:	Tutti
Data di scadenza:	Tutti
Ente regolatorio:	SUKL (State Institute for Drug Control) – Praga
Motivo del richiamo:	Il produttore del principio attivo Lampugnani farmaceutica SpA con sede a Nerviano (MI) non ha superato l'ispezione GMP effettuata da AIFA in data 24.05.2018. Sono state riscontrate gravi carenze nel monitoraggio delle aree di contaminazione controllata e durante le operazioni di produzione asettica nelle aree di produzione. A seguito del riscontro di tale non conformità, le autorità della Repubblica Ceca hanno deciso il ritiro di tutti i lotti del prodotto finito.
Note di Unipharma:	Si fa presente che al momento risultano carenti sul mercato europeo tutti i prodotti a base di tiopentale. Alla parte 3 del documento EudraGMP sono riportate motivazioni e raccomandazioni di AIFA relativamente al principio attivo.

Comunicare al numero fax 004191 985 6222 entro 24 ore dal ricevimento della presente comunicazione il numero di confezioni giacenti presso codesta struttura utilizzando il modulo allegato.

Barbengo, 26 luglio 2018

Italian Medicines Agency

Report No: *IT/NCR/APV/1/2018*

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 Italy confirms the following:
The manufacturer: ***LAMPUGNANI FARMACEUTICI SPA***
Site address: ***Via Gramsci, 4, via Ticino, NERVIANO, 20014, Italy***

From the knowledge gained during inspection of this manufacturer, the latest of which was conducted on ***2018-05-24*** , 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**
	1.4.3 Other: manufacture of active substances(en)

Manufacture of active substance. Names of substances subject to non-compliant:
DEFEROXAMINA MESILATO STERILE(it) / DEFEROXAMINE MESILATE STERILE(en)
ERITROMICINA GLUCOEPTONATO STERILE(it) / ERYTHROMYCIN GLUCEPTATE STERILE(en)
FRAMICETINA SOLFATO STERILE(it) / FRAMYCETIN SULFATE STERILE(en)
IDROCORTISONE SODIO FOSFATO STERILE(it) / HYDROCORTISONE SODIUM PHOSPHATE STERILE(en)
IDROCORTISONE SODIO SUCCINATO STERILE(it) / HYDROCORTISONE SODIUM SUCCINATE STERILE(en)
KANAMICINA SOLFATO ACIDO STERILE(it) / KANAMYCIN ACID SULFATE STERILE(en)
STREPTOMICINA SOLFATO STERILE(it) / STREPTOMYCIN SULFATE STERILE(en)
TEICOPLANINA STERILE(it) / TEICOPLANIN STERILE(en)
TIOPENTALE SODICO E SODIO CARBONATO STERILE(it) / THIOPENTAL SODIUM AND SODIUM CARBONATE STERILE(en)
VANCOMICINA CLORIDRATO STERILE(it) / VANCOMYCIN HYDROCHLORIDE STERILE(en)
DIIDROSTREPTOMICINA SOLFATO STERILE(it) / DIHYDROSTREPTOMYCIN SULFATE STERILE(en)
ERITROMICINA LATTOBIONATO STERILE(it) / ERYTHROMYCIN LACTOBIONATE STERILE(en)
FRUTTOSIO 1.6 DIFOSFATO SALE SODICO STERILE(it) / FRUCTOSE 1,6-BISPHOSPHATE SODIUM SALT STERILE(en)
GLUTATIONE SODICO STERILE(it) / GLUTATHIONE SODIUM STERILE(en)

3. NON-COMPLIANT MANUFACTURING OPERATIONS - ACTIVE SUBSTANCES Active Substance : DEFEROXAMINE MESILATE STERILE	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.4 Other : Dissolution
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : lyophilisation, 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

	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 3.6.3 Microbiological testing including sterility testing
Active Substance : GLUTATHIONE SODIUM STERILE	
3.1	**Manufacture of Active Substance by Chemical Synthesis**
	3.1.3 Salt formation / Purification steps : salt formation 3.1.4 Other : Dissolution
3.4	**Manufacture of sterile Active Substance**
	3.4.1 Aseptically prepared
3.5	**General Finishing Steps**
	3.5.1 Physical processing steps : lyophilisation, 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 3.6.3 Microbiological testing including sterility testing

Part 3

1. Nature of non-compliance:
Major deficiencies were found in the following areas: Premises/equipment (9): Deficiencies found in monitoring the controlled contamination areas and Deficiencies found in the status of Premises/Equipment and personnel/material flows. Production (1): Deficiencies were observed during the aseptic manufacturing operations in the production areas. Microbiological quality control testing (2) Personnel (1) Deviation management (1) These major deficiencies are mainly referring to the aseptic production and quality control which constitutes a critical risk for public health due to the lack of sterility assurance of the drug substances.
Action taken/proposed by the NCA **Recall of batches already released** If there are alternative suppliers and there is no risk of shortage, recall of medicinal products manufactured using APIs aseptically lyophilised by Lampugnani should be evaluated by involved NCAs' following assessment conducted in conjunction with MAHs. **Prohibition of supply** Prohibition of supply of APIs aseptically lyophilized by Lampugnani is recommended. Lack of alternative suppliers

and risk of shortage should be assessed case by case.

Suspension or voiding of CEP (action to be taken by EDQM)
Since Lampugnani Farmaceutici is a contract manufacturer carrying out the lyophilisation in aseptic conditions of APIs manufactured by other Companies, information about the CEP are not currently available.

Others
The Company holds authorization for manufacturing sterile APIs and registration for non sterile APIs. The Company holds also a MIA for finished dosage operations (storage, quality control testing: chemical/physical and microbiological testing, excluding sterility testing). Proposed actions: 1. Authorization for production of sterile APIs to be suspended 2. Registration for production of non-sterile APIs to be maintained as the Statement of non-compliance does not impact the non-sterile APIs manufactured at the site. 3. MIA for finished dosage forms (storage, quality control testing: chemical/physical and microbiological testing - sterility testing excluded) to be maintained as the GMP-non compliance statement does not have an impact on non-sterile products GMP certificate related to APIs for human use will be updated removing all sterile APIs. No impact on the GMP certificate related to finished dosage forms and non sterile APIs. This Contract manufacturer for aseptic lyophilisation should not be approved in any new/ongoing applications until appropriate corrective actions will be implemented and GMP compliance will be resumed. The CAPA plan provided by the Company was evaluated by AIFA, all the responses were considered acceptable; however, due to the seriousness of the deficiencies, AIFA is planning a follow-up inspection in a short timeframe, for an on-site evaluation of the implementation and suitability of the CAPA and, in case of positive outcome, the withdrawal of the statement of GMP non compliance with re-issuance of the GMP certificate covering also the sterile APIs; currently, AIFA is going to issue the GMP certificate only for Drug products (for storage and quality control testing, excluding sterility testing) and non sterile APIs.

Additional comments
The Statement of non-compliance also impacts on the active substances for veterinary use:
DIHYDROSTREPTOMYCIN SULFATE STERILE and CHLORAMYCETIN SULFATE STERILE.

2018-07-17

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

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Confidential
Italian Medicines Agency
Tel: ***Confidential***
Fax: ***Confidential***