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Worldwide Biopharmaceutical Businesses

Direct healthcare professional communication

November 2020

Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection.

Change from lactose-containing to a *lactose-free* formulation: risk of serious allergic reactions if formulations are confused.

Dear Healthcare Professional,

Pfizer Limited in agreement with the Medicines and Healthcare Products Regulatory Agency (MHRA) would like to inform you of the following:

Summary

- Pfizer Limited has reformulated Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection to a lactose-free formulation in which the lactose is replaced by sucrose. We plan to initiate transition to the lactose free formulation on WC Monday 7th December 2020, Pfizer will stop distributing the lactose-containing product from 9th December 2020.

- Currently marketed Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection presentation include lactose monohydrate produced from cow's milk as an excipient. Serious allergic reactions have been reported in patients allergic to cow's milk proteins who were treated intravenously or intramuscularly with this product.

- There is a risk of serious allergic reactions if the new lactose-free formation is confused with the lactose-containing formulation on the market and all healthcare professionals should be alert to the risk of medication error. **It is important that patients who have been treated with the new (lactose-free) formulation DO NOT inadvertently receive a lactose-containing formulation.**

- Ensure that healthcare professionals in your practice are fully aware of the transition to the lactose-free formulation of this product, and that they should also be vigilant for the 'New Formulation' markings on the packaging and/or vial labels when administering this product to patients who are allergic to cow's milk.

- Prescribers are instructed to ensure patients who are allergic to cow's milk and who require the new lactose-free formulation are prescribed 'Solu-Medrone injection 40 mg **lactose free**' or'methylprednisolone injection 40 mg **lactose free**.'

Registered in England: No 526209
Registered Office: Ramsgate Road
Sandwich, Kent CT13 9NJ, UK

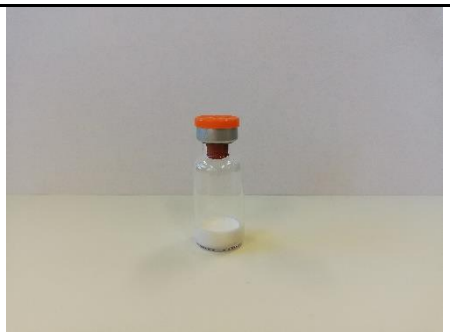
- Pfizer Limited has taken the following precautionary measures, which will be implemented in order to help clearly distinguish and differentiate between the old (lactose-containing) and new (lactose-free) formulations and to help avoid potential medication errors:
    - a clarifying statement ("New Formulation") on both the outer carton and vial labels to denote that these are lactose free formulations,
    - a change of the vial flip cap colour for Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution from "grey" back to "orange" for the new formulation (lactose-free),
    - a change of colour of both the outer carton artwork and the vial label artwork,
    - updated Product Information.

Detailed description of the precautionary measures to be implemented:

1) The new formulation of Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection will feature a revised outer carton and vial label which includes a clarifying statement with the following wording (see reproduction below):

NEW FORMULATION	This labelling provides a clear distinction between the two current formulations (lactose containing and lactose free)

2) The new formulation of Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection will have an orange cap for the powder vial to differentiate from the current formulation (grey cap).

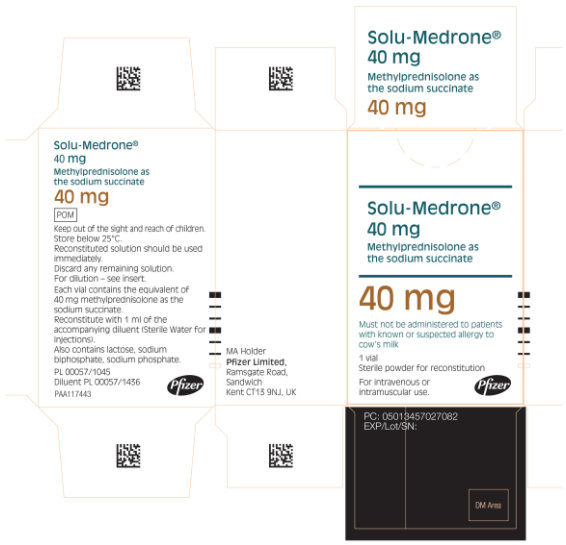
Current formulation (lactose containing)	**New formulation (lactose free)**
	

3) The new formulation of Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection will be packaged in a carton with revised labelling. Vial labels will also be revised. Please see below for a comparison of the current (lactose-containing) and new (lactose free) carton and vial labels.

Revised Outer Carton and Vial Labelling for Solu-Medrone (methylprednisolone sodium succinate) 40 mg powder and solvent for solution for injection:

Current formulation (lactose containing)

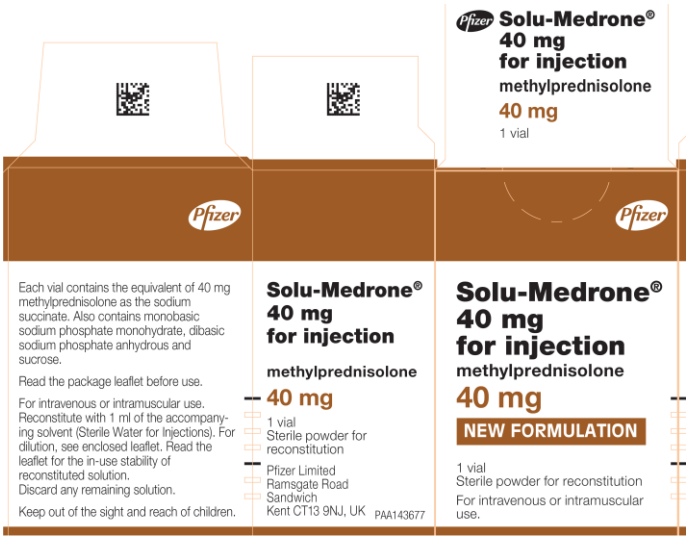
Outer carton



Vial Label

New formulation (lactose free)

Outer Carton



Vial Label

It is important that patients who are allergic to lactose and require the new (lactose-free) formulation **DO NOT** inadvertently receive a lactose-containing formulation.

Further information on recommendations to healthcare professionals

- Pfizer Limited also markets Solu-Medrone (methylprednisolone as sodium succinate) 125 mg, 500 mg, 1000 mg and 2000 mg powder and solvent for solution for injection and these presentations do not contain lactose.

- Pfizer Limited also markets Depo-Medrone (methylprednisolone as acetate) and Solu-Cortef (hydrocortisone as sodium succinate) injection products and these also do not contain lactose.

Background on the safety concern

Pfizer Limited has reformulated Solu-Medrone (methylprednisolone as sodium succinate) 40 mg powder and solvent for solution for injection to a lactose-free formulation and plans to initiate transition to the lactose-free formulation.

The reformulation was a requirement by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) following reports of serious allergic reactions in patients allergic to cow's milk proteins who were treated intravenously or intramuscularly with 40 mg presentations of methylprednisolone products containing bovine lactose and is applicable to all Marketing Authorization Holders of such products. As part of the transition to a lactose-free formulation, the product information (i.e. Summary of Product Characteristics, Patient Information Leaflet and labels) in the EU will also be updated accordingly, to remove the contraindication and warning relating to cow's milk protein, and a Dear Healthcare Professionals letter was disseminated to all EU markets following PRACs recommendation. The product information in the EU for formulations of Solu-Medrone containing bovine lactose had been revised as an interim measure to provide clear guidance on use in patients who may be allergic to cow's milk proteins until reformulated product was available. The revisions for interim labelling included:

A contraindication specifying that methylprednisolone injections containing lactose must not be given to patients known or suspected to be allergic to cow's milk proteins, as it may contain traces of milk ingredients.

A warning specifying that allergic reactions to cow's milk proteins should be considered in patients receiving Solu-Medrone 40 mg powder and solvent for solution for injection for the treatment of acute allergic conditions in whom symptoms worsen or who are presenting new allergic symptoms. In these patients, administration of Solu-Medrone 40 mg powder and solvent for solution for injection should be stopped, and the patient's condition should be treated accordingly.

These changes are no longer applicable and have been removed from the product information for the new lactose-free formulation.

Cow's milk allergy (CMA) is an adverse reaction of an immunological nature induced by cow's milk proteins. Estimates of prevalence of CMA vary from 0% to 3%. Most children outgrow their CMA in early childhood and only a smaller proportion of patients remain allergic in adulthood. CMA should be clearly distinguished from lactose intolerance, which is a non-immunologically mediated reaction to milk caused by a lack of the enzyme lactase in the small intestines, that breaks down lactose from milk into glucose and galactose.

Call for reporting

Healthcare professionals are requested to report any suspected adverse events associated with the use of Solu-Medrone via the Yellow Card Scheme at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play or Apple App Store.

Adverse events should also be reported to Pfizer Medical Information on 01304 616161.

Company contact point

Further information is available on request from Medical Information Department at Pfizer Limited, Walton Oaks, Dorking Road, Tadworth, Surrey, KT20 7NS, UK.

Annexes:

Link to CMDh endorsement on the recommendation of EMA's PRAC that methylprednisolone injections containing lactose (milk sugar), which potentially contain traces of cow's milk proteins, must not be used in patients with a known or suspected allergy to the proteins in cow's milk:

https://www.ema.europa.eu/en/medicines/human/referrals/medicinal-products-containing-lactose-bovine-origin-ivim-use-acute-allergic-reactions

Yours faithfully

Seema Patel
UK Medical Director
Hospital Business Unit
Pfizer Ltd