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CMDh confirms that methylprednisolone injections containing lactose must not be given to patients allergic to cow's milk proteins

Current formulations containing lactose will be replaced with lactose-free formulations

The CMDh[1] has endorsed the recommendation of EMA's Pharmacovigilance Risk Assessment Committee (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.

CMDh further confirmed that patients being treated with methylprednisolone for an allergic reaction should have their treatment stopped if their symptoms worsen or they develop new symptoms.

Methylprednisolone injections are used to treat the symptoms of severe allergic reactions and other inflammatory conditions. The review of these medicines was triggered following reports of serious allergic reactions such as bronchospasm (excessive contraction of the airway muscles causing breathing difficulty) and anaphylaxis (sudden severe allergic reaction) with these medicines in patients allergic to cow's milk proteins. The review found that methylprednisolone injections containing lactose derived from cow's milk may also contain traces of cow's milk proteins which can trigger allergic reactions. This is of particular concern in patients already being treated for an allergic reaction as they are more prone to developing new allergic reactions. In this case it may be difficult to determine whether the patient's symptoms are due to a new allergic reaction caused by methylprednisolone products containing lactose or due to a worsening of the original condition. This may lead to additional doses being given which will further worsen the patient's condition.

CMDh agreed with the PRAC's conclusion that there is no level of cow's milk proteins that can be considered safe for these medicines when used to treat severe allergic reactions. Considering that methylprednisolone is used for the treatment of severe allergic reactions in an emergency setting where details of the patients' allergies may not always be known, the CMDh confirmed that the most effective way of minimising any risks is to remove cow's milk proteins from the preparation. Companies have been asked to provide data allowing the replacement of formulations containing lactose from cow's milk; this data should be provided by the middle of 2019.

[1] The Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh) is a medicines regulatory body representing the European Union (EU) Member States, as well as Iceland, Liechtenstein and Norway.

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In the meantime, the product information will be revised to reflect that methylprednisolone injections containing lactose must not be given to patients allergic to cow's milk proteins. In addition, the vial and packaging of these medicines will be clearly marked with a warning against use in patients with cow's milk allergy.

Information for patients

- If you are allergic or suspected to be allergic to the proteins in cow's milk, you must not receive methylprednisolone injections containing lactose. This is because these products could contain traces of cow's milk proteins, which can cause serious allergic reactions in patients allergic to cow's milk.
- If you are being treated for an allergic reaction with these products and your symptoms worsen, your doctor will stop your treatment.
- If you are allergic to cow's milk proteins and you require methylprednisolone, your doctor will use a methylprednisolone medicine that does not contain lactose or use an alternative medicine.
- Allergy to cow's milk proteins affects a small percentage of the population (up to 3 people in 100) and is different from lactose intolerance where the body cannot easily digest lactose.
- Tell your doctor if you have or suspect you have an allergy to cow's milk proteins.
- If you have any questions or concerns, speak with your doctor or pharmacist.

Information for healthcare professionals

- Methylprednisolone injections containing lactose of bovine origin are now contraindicated in patients known or suspected to be allergic to cow's milk proteins.
- Lactose of bovine origin is used as an excipient in some injectable methylprednisolone-containing products. These products may also contain trace amounts of milk proteins, which can trigger an allergic reaction in patients allergic to cow's milk proteins.
- Serious allergic reactions, including bronchospasm and anaphylaxis, were reported in patients allergic to cow's milk proteins who were treated for acute allergic conditions with these medicines.
- Patients being treated for an allergic reaction with these products should have their treatment stopped if their symptoms worsen or they develop new symptoms as these could be signs of an allergic reaction to cow's milk proteins.
- Allergy to cow's milk proteins affects a small percentage of the population (up to 3 people in 100) and should not be confused with lactose intolerance which is a separate condition.
- For patients allergic to cow's milk protein who require methylprednisolone, consider preparations that do not contain lactose or use alternative treatments.
- Companies have been asked to take steps by 2019 to replace current formulations containing lactose with lactose-free formulations.

The above recommendations are based on analyses of spontaneous reports of suspected adverse effects and a review of published literature. Most cases of allergic reactions occurred in patients under 12 years of age. In some of the reported cases the adverse reaction was misinterpreted as a lack of therapeutic effect, leading to re-administration of methylprednisolone and subsequent worsening of the patient's clinical condition. It is considered that allergic conditions, such as asthma exacerbation, may

increase susceptibility to allergic reactions to cow's milk proteins in methylprednisolone products containing lactose of bovine origin.

More about the medicine

The review covered certain injectable medicines which contain the corticosteroid methylprednisolone and are used to treat the symptoms of severe allergic reactions and other inflammatory conditions. Specifically, the review covered the strengths of injections that contain lactose (milk sugar) derived from cows' milk and hence can contain traces of cows' milk proteins. Methylprednisolone-containing medicines have been authorised by national procedures for use by injection into a vein or muscle and have been available for many years in the EU under a variety of brand names including Solu-Medrol.

Corticosteroids are anti-inflammatory medicines used to control the immune system (the body's natural defences) when it is overactive, as in allergic conditions.

More about the procedure

The review of injectable medicines for acute allergic reaction that contain lactose from cows' milk was initiated on 1 December 2016 at the request of Croatia, under Article 31 of Directive 2001/83/EC.

The review was first carried out by the Pharmacovigilance Risk Assessment Committee (PRAC), the Committee responsible for the evaluation of safety issues for human medicines, which made a set of recommendations. The PRAC recommendations were sent to Co-ordination Group for Mutual Recognition and Decentralised Procedures – Human (CMDh), which adopted a position. The CMDh is a body representing EU Member States as well as Iceland, Liechtenstein and Norway. It is responsible for ensuring harmonised safety standards for medicines authorised via national procedures across the EU.

On 31 July 2017 the CMDh adopted its position by consensus, so the measures recommended by the PRAC will be directly implemented by the Member States where the medicines are authorised, according to an agreed timetable.