Drug Safety Update

Latest advice for medicines users

The monthly newsletter from the Medicines and Healthcare products Regulatory Agency and its independent advisor the Commission on Human Medicines

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Contents

The Medicines and Healthcare products Regulatory Agency (MHRA) is the government agency responsible for ensuring that medicines and medical devices work and are acceptably safe.

The Commission on Human Medicines gives independent advice to ministers about the safety, quality, and efficacy of medicines. The Commission is supported in its work by Expert Advisory Groups that cover various therapeutic areas of medicine.

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In our issue this month, we inform that the addition of a polyethylene glycol (PEG)-based laxative to a liquid that has been thickened with a starch-based thickener may counteract the thickening action, placing patients with dysphagia at a greater risk of aspiration (page 2). Avoid directly mixing together PEG laxatives and starch-based thickeners, especially in patients with swallowing difficulties, such as elderly people and people with disabilities that affect swallowing.

On page 4, we include a summary of recent MHRA advice relating to COVID-19 vaccines up to 21 April 2021. And on page 5 we include letters and medicines recalls and notifications sent to healthcare professionals in March 2021.

Polyethylene glycol (PEG) laxatives and starch-based thickeners: potential interactive effect when mixed, leading to an increased risk of aspiration

Addition of a polyethylene glycol (PEG)-based laxative to a liquid that has been thickened with a starch-based thickener may counteract the thickening action, placing patients with dysphagia at a greater risk of aspiration.

Advice for healthcare professionals:

- there have been reports of a possible potential harmful interaction between polyethylene glycol (PEG) laxatives and starch-based thickeners when they are mixed together
- combining the two compounds can counteract the thickening action and result in a thin watery liquid – patients with swallowing difficulties (dysphagia) are potentially at a greater risk of aspiration of the thinner liquid
- avoid directly mixing together PEG laxatives and starch-based thickeners, especially in patients with dysphagia who are considered at risk of aspiration such as elderly people and people with disabilities that affect swallowing
- report suspected adverse drug reactions (ADRs) to the Yellow Card Scheme

About polyethylene glycol (PEG) laxatives

Polyethylene glycol (PEG) laxative products treat constipation through an osmotic effect. They are indicated mostly for adults with some formulations also indicated for use in children. Some PEG laxative products such as Movicol, Macrogol 3350, and Moviprep are available in the form of a powder, which must be dissolved in liquid before administration.

About starch-based thickeners

Thickened liquids are usually taken by patients with dysphagia, including people who are elderly or have disabilities that affect swallowing. Thickening the liquid before swallowing improves bolus control and reduces the risk of aspiration, which can be life-threatening.

There are two main types of thickening agents – a starch-based (for example, corn-starch) or a gum-based (xanthan gum). Most thickeners are classified as foods for special medicinal purposes and are used to thicken both liquids and foods to various consistencies. There are many different brands of thickeners available and they can be in the form of powder or a liquid.

The recommendation to use a thickener should be based on the patient's degree of dysphagia (and potential risk of aspiration), the desired consistency required, the texture required, palatability, and other clinical considerations (see guidance from the Specialist Pharmacist Service).

Reports of a potentially harmful interactive effect

The Institute for Safe Medication Practices (ISMP) Canada issued a Safety Bulletin discussing the possible potential harmful interaction between PEG laxative and starch-based thickeners. One case report was identified where a patient was switched to a thickened diet for dysphagia. PEG-3350 was mixed with a starch-based pre-thickened juice. On day 2 of administration the patient showed possible signs of aspiration after swallowing the dose. The patient died a few hours later. Although the cause of death was difficult to establish due to the patients underlying medical conditions, aspiration was thought to have been a contributing factor.

Addition of a PEG laxative to a liquid that has been thickened with a starch-based thickener can produce a mixture that is thin and watery – undoing the intended act of thickening. Patients with dysphagia who swallow the thinner liquid are potentially at greater risk of aspiration.

Constipation and dysphagia coexist more commonly in the elderly and in people with disabilities that affect swallowing. Therefore, these populations may be of particular risk if a PEG laxative is added to liquid thickened with starch. The MHRA is currently not aware of any case reports of this potential interaction in the UK.

We have requested that the manufacturers of UK PEG laxative products add information about the potential interactive effect to the Summary of Product Characteristics and the Patient Information Leaflet.

Report any suspected adverse drug reactions

Please continue to report any suspected adverse drug reactions via the Yellow Card Scheme. Your report will help us safeguard public health.

Healthcare professionals, patients, and caregivers are asked to submit reports using the Yellow Card scheme electronically using:

- the Yellow Card website
- the Yellow Card app; download from the Apple App Store or Google Play Store
- some clinical IT systems for healthcare professionals (EMIS, SystmOne, Vision, MiDatabank, and Ulysses)

When reporting please provide as much information as possible, including information about batch numbers, medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

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COVID-19 vaccines: updates for April 2021

A summary of advice recently issued by the MHRA relating to coronavirus (COVID-19), up to 21 April 2021.

Here we include a summary of key MHRA advice issued up to 21 April 2021 and since the publication of the March 2021 edition of Drug Safety Update.

We continue to publish the summaries of the Yellow Card reporting for the COVID-19 vaccines being used in the UK. This report is being updated weekly. The report summarises information received via the Yellow Card scheme and will be published regularly to include other safety investigations carried out by the MHRA under the COVID-19 Vaccine Surveillance Strategy.

The MHRA encourages anyone to report any suspicion or concern they have beyond the known, mild side effects on the Coronavirus Yellow Card reporting site.

We have also recently:

- Issued new advice concluding there is a possible link between COVID-19 Vaccine AstraZeneca and extremely rare and unlikely to occur blood clots (7 April 2021)
- Revised the COVID-19 Vaccine AstraZeneca product information for healthcare professionals, including further clarification on specific pre-existing medical conditions where the vaccine should not be given, and those pre-existing conditions where particular caution is needed; the information for UK vaccine recipients has also been updated (15 April 2021)

See the MHRA website for the latest information on medicines and vaccines for COVID-19, including after publication of this article.

We previously included a summary of latest advice in the January 2021, February 2021 and March 2021 issues of Drug Safety Update.

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Letters and medicine recalls sent to healthcare professionals in March 2021

Letters

In March 2021, the following letters were sent or provided to relevant healthcare professionals:

- Zolgensma▼ (onasemnogene abeparvovec): Risk for thrombotic microangiopathy
- Xeljanz▼ (tofacitinib): Initial clinical trial results of increased risk of major adverse cardiovascular events and malignancies (excluding NMSC) with use of tofacitinib relative to TNF-alpha inhibitors
- Tecentriq (atezolizumab): risk of severe cutaneous adverse reactions (SCARs)
- Sublimaze Solution for injection, 50µg/ml (Fentanyl citrate): Interim Supply of Ireland Stock to Mitigate Supply Disruption
- Finomel Emulsion for Infusion (1435ml - 1101320): Interim Supply of Belgian Stock to Mitigate Supply Disruption
- Choledíam, kit for the preparation of technetium [99mTc] mebrofenin injection (Mebrofenin): Interim Supply of French Stock to Mitigate Supply Disruption

We are also aware of the following letter, sent to relevant healthcare professionals in February 2021:

- Lojuxta (lomitapide): Reminder to monitor the liver function of patients and to avoid use in pregnancy

Medicines Recalls and Notifications

Class 3 Medicines Recall: Easyhaler Salbutamol Sulfate 100 micrograms per actuation/200 micrograms per actuation inhalation powder, EL (21)A/06. Issued 1 March 2021. Defects have been identified in two batches of Easyhaler Salbutamol Sulfate 100 micrograms and 200 micrograms per actuation inhalation powder. A hole in the bulk chamber where inhalation powder is stored has potential for a minor loss of inhalation powder. As a precautionary measure, the product is being recalled. Stop supplying the batch immediately, quarantine all remaining stock and return to supplier.

Class 4 Medicines Defect Information, Accord Diazepam 2mg/5ml Oral Solution Sugar Free (EL (21)A/07) (PL 0142/0103). Issued 9 March 2021. Batches of Accord's Diazepam 2mg/5ml oral solution have been identified with incomplete product information. The products have outdated sorbitol wording and are missing important excipient safety wording on propylene glycol. Accord will provide hard copies of updated leaflets to pharmacies. When prescribing, healthcare professionals are asked to inform patients and provide updated product leaflets from the supplier when dispensing the product.

Class 3 Medicines Recall: Thame Laboratories, Itraconazole 10mg/ml Oral Solution, EL (21)A/08. Issued 15 March 2021. Two batches of Itraconazole 10mg/ml oral solution are being recalled due to defective child-resistant container closures which are difficult to open. Stop supplying the batch immediately, quarantine all remaining stock and return to supplier.

Class 4 Medicines Defect Information, Caffeine Citrate 10mg/ml Solution for Injection, (PL 01883/0344), EL (21)A/09. Issued 18 March 2021. A batch of Caffeine Citrate 10mg/ml Solution for Injection has been identified with an incorrect EAN barcode on the outer carton. Scanning the barcode will show the batch as Methylthionium Chloride Injection 1%. There is no risk to product quality, and all other packaging components are correct. Healthcare professionals are advised not to use barcode scanning for any activities related to this batch and to use caution when supplying or dispensing this item, as the barcode may show incorrectly on automated pharmacy inventory systems.

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