Medicines & Healthcare products Regulatory Agency

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.

NICE accredited
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NICE has accredited the process used by the MHRA to produce Drug Safety Update guidance. More information on accreditation can be viewed on the NICE website.

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In our first article we inform healthcare professionals of the potential risk of pulmonary aspiration in patients using GLP-1 or dual GIP/GLP-1 receptor agonists who undergo surgery or procedures with general anaesthesia or deep sedation.

Our second article provides a summary of recent letters and notifications sent to healthcare professionals about medicines and medical devices.

Windsor Framework Announcement

Drug Safety Update subscribers should also note that the Windsor Framework (WF) arrangements for medicines came into effect on 1 January 2025, introducing UK-wide licensing. This means that medicines approved and licensed on a UK-wide basis by the MHRA will be supplied in the same packs across the whole UK.

Guidance is available in our WF Hub, including information that healthcare professionals, particularly pharmacists and prescribers, need to be aware of.

If you have been forwarded this issue of the Drug Safety Update, you can subscribe directly via our website.

GLP-1 and dual GIP/GLP-1 receptor agonists: potential risk of pulmonary aspiration during general anaesthesia or deep sedation

Healthcare professionals should be aware of the potential risk of pulmonary aspiration in patients using GLP-1 or dual GIP/GLP-1 receptor agonists who undergo surgery or procedures with general anaesthesia or deep sedation. GLP-1 and dual GIP/GLP-1 receptor agonists are known to cause delayed gastric emptying, which may increase the risk of residual gastric contents despite preoperative fasting.

Advice for healthcare professionals:

- glucagon-like peptide-1 (GLP-1) and dual glucose-dependent insulinotropic polypeptide (GIP)/GLP-1 receptor agonists, such as the dual agonist tirzepatide, are known to slow gastric emptying, which is a recognised side effect of these medicines
- consider that patients taking these medicines who are undergoing surgeries or procedures with general anaesthesia or deep sedation may have residual gastric contents despite preoperative fasting
- anaesthetists should consider the potential risk of aspiration within their risk assessment of patients being treated with GLP-1 or dual GIP/GLP-1 receptor agonists for all indications and manage the aspiration risk, in line with usual anaesthetic practice
- anaesthetists should provide an individualised assessment of the aspiration risk. Within the risk assessment, consider the following points:
    - that patients taking GLP-1 or dual GIP/GLP-1 receptor agonists who have underlying diabetic gastroparesis, as well as other comorbidities such as obesity or gastroesophageal reflux disease, and symptoms of delayed gastric emptying (such as nausea, vomiting, and abdominal pain) may be at higher risk of aspiration
    - patients should be asked about whether they are taking GLP-1 or dual GIP/GLP-1 receptor agonists. Consider the possibility that patients may have purchased GLP-1 or dual GIP/GLP-1 receptor agonists for aesthetic weight loss and may not readily disclose this information unless directly asked. Be aware that private prescriptions may not always be included in the patient's medical notes or drug history
- healthcare professionals should identify the increased risk of aspiration as early as possible before surgery and specifically at pre-assessment clinic before surgery
- remind patients to inform their healthcare teams and anaesthetists if they are on GLP-1 or dual GIP/GLP-1 receptor agonists
- report suspected adverse drug reactions associated with GLP-1 and dual GIP/GLP-1 receptor agonists, aspiration and other surgical complications on a Yellow Card

Advice for healthcare professionals to provide to patients:

- if you are taking a GLP-1 or dual GIP/GLP-1 receptor agonist, make sure you inform your healthcare team including the anaesthetist about this prior to your surgical procedure
- this medicine slows the emptying of your stomach, increasing the risk that stomach contents (e.g. food and drink) could enter into your airways and lungs during surgery or procedures whilst you are under general anaesthesia or deep sedation. This means that a modification to the pre-procedure instruction and anaesthetic technique may be required
- take your prescribed medicine(s) as usual and do not stop your treatment without first discussing this with your doctor

Review of the risk of aspiration associated with GLP-1 and dual GIP/GLP-1 receptor treatment

GLP-1 and dual GIP/GLP-1 receptor agonists are a class of medications that are used to treat type II diabetes mellitus and/or obesity. The GLP-1 and dual GIP/GLP-1 receptor agonists available in the UK include dulaglutide, exenatide, liraglutide, lixisenatide, semaglutide. Tirzepatide is a GLP-1 receptor agonist combined with glucose-dependent insulinotropic polypeptide (GIP) receptor agonist. Semaglutide is also approved to reduce the risk of cardiovascular events in patients with established cardiovascular disease.

Some of the GLP-1 and dual GIP/GLP-1 receptor agonists have more than one brand name and more than one indication. Please refer to Annex 1 for the GLP-1 and dual GIP/GLP-1 receptor agonist products currently authorised in the UK with their brand names and indications.

Residual gastric content is a risk factor for aspiration in patients who undergo surgery or procedures with general anaesthesia or deep sedation. All GLP-1 and dual GIP/GLP-1 receptor agonists slow down gastric emptying, therefore patients taking these medicines may have a higher risk of pulmonary aspiration due to retained gastric contents. This can potentially lead to severe complications, such as aspiration pneumonia. Cases have been reported in the literature as well as through Yellow Card reports.

A recent European review of the available evidence for all GLP-1 and dual GIP/GLP-1 receptor agonists concluded that the data supports an association between GLP-1 or dual GIP/GLP-1 receptor agonists and the potential risk of pulmonary aspiration during anaesthesia or deep sedation because of the delayed gastric emptying associated with these medicines. The findings of this review were considered by the Pharmacovigilance Expert Advisory Committee (PEAG) of the Commission on Human Medicines (CHM), which agreed with the recommendations. The product information of all GLP-1 and dual GIP/GLP-1 receptor agonists has been updated to include the potential risk of pulmonary aspiration under general anaesthesia or deep sedation.

The PEAG recommended that the MHRA inform healthcare professionals and patients of the possibility of aspiration in patients using GLP-1 or dual GIP/GLP-1

receptor agonists who undergo surgery or procedures requiring general anaesthesia or deep sedation.

The European assessment evaluated whether a specific time to pause the use of a GLP-1 or dual GIP/GLP-1 receptor agonist prior to anaesthesia could be recommended, as well recommending new fasting guidelines or an appropriate medical procedure to confirm an empty stomach. The evidence to support further recommendations was limited and it was concluded that anaesthetists should retain the flexibility to provide individualised assessment.

Product information update

New warnings have been added to the Summaries of Product Characteristics (SmPC) and Patient Information Leaflets. The new advice aims to raise awareness of the risk of pulmonary aspiration amongst healthcare professionals and patients. Anaesthetists are warned that residual gastric contents may remain despite routine recommended fasting in patients taking a GLP-1 or dual GIP/GLP-1 receptor agonists. This should be considered within the preoperative risk assessment, with subsequent management in preventing or minimising the risk.

UK Yellow Cards

As of 12 December 2024, the MHRA has received a very small number of reports of aspiration during a surgical procedure associated with GLP-1 or dual GIP/GLP-1 receptor agonists, including one case that resulted in aspiration pneumonia.

Clinical Guidelines

In January 2025, the Association of Anaesthetists published a multidisciplinary consensus statement on 'Elective peri-operative management of adults taking glucagon-like peptide-1 receptor agonists (GLP-1) | Association of Anaesthetists' which advises taking the GLP-1 or dual GIP/GLP-1 receptor agonist as normal (irrespective of dosing schedule i.e. daily or weekly).

The UK SmPCs for all GLP-1 and dual GIP/GLP-1 receptor agonist products does not provide guidance on withholding these medications before surgery or procedures requiring general anaesthesia or deep sedation.

Reporting Advice

Please continue to report suspected adverse drug reactions to the Yellow Card scheme. 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

For queries or more information, please contact info@mhra.gov.uk

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Letters and medicine recalls sent to healthcare professionals in December 2024

A summary of recent letters and notifications sent to healthcare professionals about medicines and medical devices.

Letters

In December 2024, the following letters were sent or provided to relevant healthcare professionals:

- Medikinet XL▼10mg capsules and Medikinet® XL▼20mg capsules (methylphenidate hydrochloride) - Voluntary Notification Defective Medicine
- Xevudy® (sotrovimab) 500 mg concentrate for solution for infusion: Important information for healthcare professionals about the expiry date of all packs
- Hydroxocobalamin - Cyanokit® 5 g powder for solution for infusion: – Important information regarding batch 2404 in a product shortage context.
- Fucithalmic 1% w/w Viscous Eye Drops/ Fusidic acid 1% w/w Viscous Eye Drops - Interim supply of Chinese stock to Mitigate supply disruption
- Movymia 20 micrograms/80 microliters solution for injection▼ (teriparatide): Interim Supply of Italian Stock to Mitigate Supply Disruption
- Ocrevus® (ocrelizumab) 920 mg solution for injection: Significant update to premedication administration timing for patients on Ocrevus in Northern Ireland (NI) to align with the UK Summary of Product Characteristics (SmPC) from 1st January 2025, as a result of the Windsor Framework Agreement.
- COLUMVI®▼ (glofitamab): Significant Update on Patient Monitoring Requirements for New and Existing Patients on COLUMVI in Northern Ireland (NI) to align with the UK Summary of Product Characteristics (SmPC) and Patient Information Leaflet (PIL) from 1st January 2025
- Abrysvo ®▼ powder and solvent for solution for injection (respiratory syncytial virus vaccine (bivalent, recombinant)): Change of Marketing authority from EMA to MHRA in effect from 1st January 2025 resulting in change to Posology for pregnant individuals

Medicine Recalls and Notifications

In December 2024, recalls and notifications for medicines were issued on:

Class 2 Medicines Recall: Wockhardt UK Limited, WockAIR 160 microgram/4.5 microgram, inhalation powder, EL(24)A/62. Issued 9 December 2024. Wockhardt UK Limited is recalling this batch as a precautionary measure following the identification of a low number of units which may have a defect in the 'top case' resulting in a dose not being able to be dispensed.

Class 3 Medicines Recall: Kent Pharma UK, Phenoxymethylpenicillin 250mg/5ml Oral Solution Sugar Free, EL (24)A/60. Issued 3 December 2024. Kent Pharma UK is recalling a batch of phenoxymethylpenicillin 250mg/5mL oral solution sugar free due to a low phenoxymethylpenicillin assay.

Class 4 Medicines Defect Information: Rosemont Pharmaceuticals Limited, Mycophenolate Mofetil 1g/5ml Oral Suspension, EL(24)A/59. Issued 2 December 2024. Rosemont Pharmaceuticals Limited has informed the MHRA that the Press-In-Bottle-Adaptor (PIBA) supplied with the batches listed above may cause the medicine to leak when attempting to withdraw a dose.

Class 4 Medicines Defect Information: Brillpharma Limited, Oxybutynin hydrochloride Brillpharma 2.5 mg/5 ml Oral Solution, EL(24)A/61. Issued 4 December 2024. L M Manufacturing Limited has informed the MHRA that the patient information leaflet (PIL) in the cartons for the batch listed for Oxybutynin hydrochloride Brillpharma 2.5 mg/5 ml Oral Solution include an out of date PIL, dated July 2021.

Class 4 Medicines Notification: Argenx BV, Vyvgart 1000 mg solution for injection, EL (24)A/63. Issued 19 December 2024. Argenx BV have informed MHRA that the Patient Information Leaflet (PIL) in the affected packs incorrectly contains reference to two subcutaneous injection sites. Only subcutaneous injection to the abdomen is permitted.

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