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

Volume 16 Issue 12 July 2023

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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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First, we inform healthcare professionals that there have been a small number of reports of serious and life-threatening anticholinergic side effects associated with hyoscine hydrobromide patches, particularly when used outside the licence. Healthcare professionals, patients, parents and carers should be aware of the signs and symptoms of serious side effects and the need to seek medical help if they occur.

Second, we inform about the launch of a public consultation on the reclassification of codeine linctus to a prescription-only medicine in response to multiple reports that codeine linctus is being used recreationally for its opioid effects, rather than for its intended use as a cough suppressant.

We also provide a summary of recent letters and notifications sent to healthcare professionals about medicines and medical devices. If you have been forwarded this issue of Drug Safety Update, subscribe directly via our website.

Hyoscine hydrobromide patches (Scopoderm 1.5mg Patch or Scopoderm TTS Patch): risk of anticholinergic side effects, including hyperthermia

There have been a small number of reports of serious and life-threatening anticholinergic side effects associated with hyoscine hydrobromide patches, particularly when used outside the licence. Healthcare professionals, patients, parents and carers should be aware of the signs and symptoms of serious side effects and the need to seek medical help if they occur.

Advice for healthcare professionals:

- be alert to the potential for anticholinergic side effects in patients who are prescribed hyoscine hydrobromide patches, particularly if used outside the licence
- usage outside the licence includes: use for indications other than motion or travel sickness, use in children younger than 10 years of age, cutting patches, application of more than one patch at a time, continuous use of patches without a break, and long-term use
- children and elderly patients are more susceptible to anticholinergic toxicity
- serious anticholinergic side effects can include hyperthermia, urinary retention, delirium, hallucinations, seizures, coma, and respiratory paralysis
- if used in hospital or residential care settings, monitor patients for signs and symptoms of anticholinergic side effects and manage these promptly if they occur
- if used at home, counsel patients, parents and carers on side effects to be aware of and what to do if they occur
- report suspected adverse drug reactions associated with hyoscine hydrobromide to the Yellow Card scheme

Advice for healthcare professionals to provide to patients, parents and carers:

- hyoscine hydrobromide patches are used commonly without any problems
- all medicines can cause unwanted side effects, and while not everybody gets them, some side effects can be serious and even life-threatening
- it is important to be aware of the signs and symptoms of serious side effects that could be associated with hyoscine hydrobromide patches – these include high temperature, inability to urinate, confusion, disorientation, seeing or hearing things that are not there, fits or convulsions, reduced consciousness, and breathing difficulties
- if these symptoms occur seek medical help and remove the patch immediately
- if there is a high temperature, take immediate action to reduce body heat in addition to seeking medical help and removing the patch

Use of hyoscine hydrobromide patches

The licensed indication of a hyoscine hydrobromide patch (Scopoderm 1.5 mg Patchor Scopoderm TTS Patch) is for the prevention of motion or travel sickness symptoms (for example nausea, vomiting and vertigo) in adults and children aged 10 years of age or older. Each patch should be used for 72 hours.

There is widespread use of hyoscine hydrobromide patches outside the licence. Usage outside the licence includes:

- indications other than motion or travel sickness
- use in children younger than 10 years of age
- cutting patches (this may adversely affect the bioavailability of the drug)
- application of more than one patch at a time
- continuous use without a break
- long-term use

Hyoscine hydrobromide patches are often recommended in clinical guidance for indications other than motion or travel sickness. These indications (which are outside the licence) include:

- the management of hypersecretion or hypersalivation in diverse clinical populations; for example, in patients with complex multiple disabilities or cerebral palsy, patients on ventilation, patients with Parkinson's disease, patients requiring palliative care, and patients with drug-induced hypersalivation
- the management of nausea and vomiting; for example, in patients after surgery or in patients with cancer

Reports of serious or life-threatening anticholinergic side effects

Hyoscine hydrobromide is a muscarinic acetylcholine receptor antagonist. Since it crosses the blood–brain barrier it has both central and peripheral actions, causing a range of anticholinergic side-effects including hyperthermia, urinary retention, dry mouth, disturbances of visual accommodation (blurred vision), mydriasis, skin irritation, generalised rash, somnolence, dizziness, memory impairment, disturbances in attention, restlessness, disorientation, confusion, hallucinations, delirium, seizures, coma, and respiratory paralysis.

After removal of the patch, hyoscine in the skin continues to enter the blood stream. Side effects may therefore persist for up to 24 hours or longer after patch removal. Children and elderly people are more susceptible to anticholinergic toxicity. Other specific risk factors for developing side effects have not been identified and there is no robust data available to give an estimate of frequency.

Hyoscine hydrobromide patches are used widely, however there have been a small number of serious and life-threatening anticholinergic side effects reported, particularly in use outside the licence. This includes the unexpected death of a child from hyperthermia caused by the hyoscine hydrobromide patch.

Following advice from the Paediatric Medicines Expert Advisory Group (PMEAG) of the Commission on Human Medicines, we have requested that Marketing Authorisation Holders (MAHs) for hyoscine hydrobromide patches add hyperthermia to both the list of side effects in section 4.8 (undesirable effects) of the Summary of Product Characteristic (SmPC) and to the Patient Information Leaflet (PIL). This is consistent with current warnings in the tablet formulation. We have also requested that the MAHs include information in the PIL regarding actions to take if hyperthermia occurs. This is consistent with information in Section 4.9 (overdose) of the SmPC.

The PMEAG also noted that underreporting of anticholinergic side effects is likely and encouraged the reporting of adverse reactions through the Yellow Card scheme.

Report suspected reactions on a Yellow Card

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.

Article citation: Drug Safety Update volume 16, issue 12: July 2023: 1.

Codeine linctus: public consultation on the proposal to reclassify to a prescription-only medicine

We have launched a public consultation on the proposal to reclassify codeine linctus to a prescription-only medicine.

If, following consultation between the patient and a healthcare professional, use of a systemic NSAID after week 20 of pregnancy is considered necessary, it should be prescribed for the lowest dose for the shortest time and additional neonatal monitoring considered if used for longer than several days. This is in addition to giving advice to discontinue use of any NSAID in the last trimester of pregnancy.

About the consultation:

- we are consulting on the reclassification of codeine linctus to a prescription-only medicine – access the consultation here
- codeine linctus is an oral solution or syrup with the active ingredient codeine phosphate and is used to stop an unproductive or dry cough.
- the consultation has been launched in response to multiple Yellow Card reports that codeine linctus is being used recreationally for its opioid effects, rather than for its intended use as a cough suppressant.
- this medication is currently licensed as a pharmacy medicine, meaning that it is available to purchase over the counter in pharmacies. If reclassified as a prescription-only medicine, all strengths of codeine linctus will only be available upon presentation of a prescription

Responding to the consultation

Healthcare professionals and all members of the public are asked their views on whether cough medicines containing the opioid codeine should become a prescription-only medicine or should remain available to purchase over the counter in pharmacies. Your views will help us to gather important information on your experiences and make an informed decision on the best way to minimise risks associated with misuse.

The codeine linctus consultation is open until 15 August 2023 – access the consultation here.

Read more in our press release.

Article citation: Drug Safety Update volume 16, issue 12: July 2023: 2.

Letters and medicine recalls sent to healthcare professionals in June 2023

Letters

In June 2023, the following letters were sent or provided to relevant healthcare professionals:

- Tresiba FlexTouch 100 units/mL solution for injection (insulin degludec): Supply Shortage in the UK
- Gavreto▼(pralsetinib): Increased risk for tuberculosis and measures to minimise this risk
- Menopur Powder and solvent for solution for injection (menotropin) Interim supply of Irish packs to mitigate supply disruptions in UK (letters for 75 IU dose, 600 IU dose, 1200 IU dose)
- NovoMix 30 FlexPen (insulin aspart) 100units/1ml suspension for injection in pre-filled pen – GB Pack provided to Northern Ireland

Medicine Recalls and Notifications

In June 2023, recalls and notifications for medicines were issued on:

Class 3 Medicines Recall: Tricodent Limited (supplier), Medical Oxygen B.P (MEDIGAS OXYGEN B.P), EL (23)A/20. Issued 6 June 2023. The MHRA has been made aware that falsified medical oxygen has been provided to several dental practices across the UK. The source of the supply has been identified as batches provided by Tricodent Limited. Stop using the product immediately and quarantine all remaining stock. Authorised and licensed suppliers can offer advice regarding disposal of falsified cylinders, do not return cylinders to Tricodent Limited.

National Patient Safety Alert: Potential risk of underdosing with calcium gluconate in severe hyperkalemia (NatPSA/2023/007/MHRA)

On 27 June 2023, we issued a National Patient Safety Alert to support organisations to update local policies and guidelines for the treatment of severe hyperkalaemia in adults.

We also published a Drug Safety Update article in June 2023 with further information.

Article citation: Drug Safety Update volume 16, issue 12: July 2023: 3.