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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First, we include advice on new pack size restrictions, revised recommended ages for use, and safety warnings for over-the-counter stimulant laxatives following a national safety review (page 2).

Next, on page 5, we provide advice for situations in which monitoring of blood concentrations of clozapine and other antipsychotics is recommended to reduce the risk of toxicity.

On page 7, we inform prescribers of denosumab 60mg (Prolia) for osteoporosis of an increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment.

On page 9, we communicate new recommendations for the rheumatoid arthritis medicine baricitinib following cases of diverticulitis and gastrointestinal perforation. Caution should be used in patients with diverticular disease and in those concomitantly treated with medications associated with an increased risk of diverticulitis.

On page 11, we remind healthcare professionals of the important risks and precautions to take for isotretinoin while there is an independent review of the risks of psychiatric reactions and sexual dysfunction.

See page 13 for links to new resources to support awareness of the risk of severe and fatal burns with emollient skin products when they dry on to fabric and the fabric is exposed to an ignition source.

drugsafetyupdate@mhra.gov.uk

Stimulant laxatives (bisacodyl, senna and sennosides, sodium picosulfate) available over-the-counter: new measures to support safe use

This article was first published online 18 August 2020.

We have introduced pack size restrictions, revised recommended ages for use, and new safety warnings for over-the-counter stimulant laxatives (orally and rectally administered) following a national safety review. Advise patients that dietary and lifestyle measures should be used first-line for relieving short-term occasional constipation and that stimulant laxatives should only be used if these measures and other laxatives are ineffective.

Advice for healthcare professionals:

Constipation treatment options

- for constipation, manage underlying causes and advise adult patients on appropriate first-line dietary and lifestyle measures, such as increasing dietary fibre, fluid intake, and activity levels
- stimulant laxatives should only be used if other laxatives (bulk-forming and osmotic) are ineffective (as clinical guidance)
- children younger than 12 years should not use stimulant laxatives without advice from a prescriber and clinical guidance should be followed

Changes to availability

- large packs of stimulant laxatives will no longer be available from general sale outlets, such as newsagents and supermarkets — smaller packs will continue to be available in these outlets for short-term, occasional constipation in adults
- pharmacies will continue to hold larger packs of up to 100 tablets for use in adults and children aged 12 years or older, under the supervision of a pharmacist – see Pharmacy Guide produced by the Royal Pharmaceutical Society and MHRA

Advice to provide to patients

- seek support from a doctor, nurse, or pharmacist for ongoing constipation, rather than self-medicating with laxatives in the long-term
- if symptoms of constipation persist after dietary and lifestyle changes and short-term laxative treatment (under the advice of pharmacist), or in case of persistent abdominal pain or passing blood, consult a doctor
- parents and caregivers should seek medical advice about constipation in children – children younger than 12 years should not use stimulant laxatives unless told to do so by their prescriber

Background

Stimulant laxatives are used to treat constipation. Medicines available in the UK over-the-counter are bisacodyl (such as Dulcolax), senna and sennosides (isolated, as calcium salts; such as Senokot), and sodium picosulfate (such as Dulcolax Pico).

The safety of stimulant laxatives has been under close review by the MHRA for many years following concerns relating to misuse and abuse. Previous measures have included the addition of warnings to some products to advise that laxatives do not aid weight loss and that long-term use may be harmful.

National safety review

Following a national safety review, including advice from expert advisory groups and an Expert Working Group, the Commission on Human Medicines (CHM) has recommended the MHRA introduce a package of measures to support the safe use of over-the-counter stimulant laxatives in the UK.

In their in-depth review of the benefits and risks of these medicines, CHM noted that stimulant laxatives have an acceptable safety profile, have been widely used for many years, and are generally used responsibly. However, CHM also considered evidence that stimulant laxatives are subject to misuse and overuse. Such cases mostly concern people with eating disorders, although misuse and overuse are likely to be under-reported (see data in Public Assessment Report). Occasional, serious reports of misuse and overdose have been received, including rare reports of fatalities.

Furthermore, CHM noted that current clinical guidance recommends that stimulant laxatives should not be used first-line for short-term constipation. CHM concluded that stimulant laxatives could continue to be available to patients to purchase, subject to a range of proportionate measures to reduce the risk of misuse and support correct use.

Changes to stimulant laxatives to support safety

Pack size restrictions

Smaller packs will continue to be available for general sale for the treatment of short-term, occasional constipation for use in adults only. Products available for general sale will be limited to a pack size of two short treatment courses (up to 20 standard-strength tablets, 10 maximum-strength tablets or 100ml solution/syrup). This limit is to reflect that these medicines should be used for only short-term, occasional constipation.

Revised recommended ages for use

Stimulant laxatives on general sale (in shops and supermarkets) will be recommended for use only in people 18 years or older. Stimulant laxatives should no longer be used in children under 12 years without advice from a prescriber, while products for children aged 12 to 17 years can be supplied under the supervision of a pharmacist.

Harmonisation of indications and new safety warnings

The indications for all stimulant laxative products available over-the-counter have been made consistent and any uses not appropriate for the self-care setting have been removed. Where stimulant laxatives are required regularly for longer-term use in chronic constipation or for indications not appropriate for the self-care setting, such as bowel clearance before surgery, they will be available as prescription-only products.

Warnings in the patient information leaflets that accompany these medicines will be made consistent and advise patients that overuse of stimulant laxatives may be harmful due to the risk of fluid and electrolyte disturbances and potential disruption of intestinal function. Warnings are also being added to packaging to support awareness. The product information will also include the new age recommendations.

We have worked with the Royal Pharmaceutical Society to produce a Pharmacy Guide for pharmacists and those working in pharmacies to support these changes, see Dealing with over-the-counter stimulant laxatives in community pharmacy.

General advice about constipation

Constipation is a common condition and affects people of all ages, although it is more common in older people. There may be many factors involved, including not eating enough fibre, not drinking enough fluids, not moving enough or exercising, changes to diet or daily routine, adverse effects of medicines, stress, anxiety or depression or, rarely, an underlying medical condition.

Constipation can usually be treated at home with simple changes to diet and lifestyle. If these measures do not work, a pharmacist can provide advice on an appropriate laxative.

Usually a bulk-forming laxative (such as ispaghula husk [Fybogel and Ispagel]) or methylcellulose [Celevac] or sterculia [Normacol]) would be used first, followed by an osmotic laxative (such as lactulose [Duphalac] or macrogols [Movicol, CosmoCol and Laxido]) in addition to, or instead of, a bulk-forming laxative. If these are not effective, then a stimulant laxative may be added in addition to a bulk-forming laxative. All of these laxatives are available as over-the-counter medicines and should only be taken occasionally.

Availability of updated packs

Updated stimulant laxative products have already begun to become available in general sale outlets and pharmacies. Existing packs may continue to be available for sale until early Autumn of 2020.

We ask for pharmacists to provide parents and caregivers with the most up-to-date instructions (provided in Pharmacy Guide or updated Patient Information Leaflets) with purchase of existing packs without the safety changes during the transition.

Report suspected adverse drug reactions

Suspected adverse drug reactions to stimulant laxatives should be reported via the Yellow Card Scheme. Healthcare professionals, patients, and caregivers can report suspected side effects via the Yellow Card website or via the Yellow Card app.

Download the app via iTunes Yellow Card for iOS devices or via PlayStore Yellow Card for Android devices. You can also view recent alerts from the MHRA and read Drug Safety Updates through the App newsfeed.

Article citation: Drug Safety Update volume 14, issue 1: August 2020: 1.

Clozapine and other antipsychotics: monitoring blood concentrations for toxicity

Monitoring blood concentrations of clozapine (Clozaril, Denzapine, Zaponex) for toxicity is now advised in certain clinical situations. Blood level monitoring of other antipsychotics for toxicity may also be helpful in certain circumstances, where testing and reference values are available.

Advice for healthcare professionals:

- monitoring blood clozapine levels for toxicity is now advised in certain clinical situations such as when:
  - a patient stops smoking or switches to an e-cigarette
  - concomitant medicines may interact to increase blood clozapine levels
  - a patient has pneumonia or other serious infection
  - poor (reduced) clozapine metabolism is suspected
  - toxicity is suspected
- if blood clozapine level monitoring is carried out, this should be in addition to the required blood tests to manage the risk of agranulocytosis
- for other antipsychotics, where assays and suggested reference values are available (see list below), blood level monitoring for toxicity may be helpful in certain circumstances, for example in the event of symptoms suggestive of toxicity or when concomitant medicines may interact to increase antipsychotic drug levels
- refer to the full Summaries of Product Characteristics for other important warnings, interactions, and recommendations for clozapine and other individual antipsychotics

Reviews of monitoring advice for toxicity

Clozapine and other antipsychotic medicines are used for indications related to psychosis, including schizophrenic disorders and some forms of bipolar disorder.

It is recognised that blood level monitoring of these medicines can be beneficial in the care and management of patients, particularly those with treatment-resistant conditions.[1] For example, monitoring of blood clozapine levels may be useful when a patient starts (or restarts) smoking as this may lead to a decrease in blood clozapine levels and dose adjustment may be necessary. However, the advice below focuses on drug blood level monitoring for toxicity of clozapine and other antipsychotics.

1. Maudsley Prescribing Guidelines. 13th edition. May 2018

The MHRA has received two separate reports from Coroners raising concerns regarding the need for monitoring of clozapine blood levels in one report and monitoring antipsychotic blood levels during long-term high-dose antipsychotic use in the other. In the first report, the individual's death was determined to have been caused by clozapine toxicity, pneumonia, and treatment-resistant schizophrenia. In the second report, the death of a patient on long-term high-dose antipsychotic treatment was determined to have been caused by coronary artery atherosclerosis and amisulpride toxicity. In both Coroner's reports the MHRA was asked to take action to prevent further deaths.

Expert Advisory Groups of the Commission on Human Medicines considered safety data for clozapine and other antipsychotic drugs and advised that blood concentrations of clozapine should be monitored for toxicity in certain clinical situations.

The Groups also advised that, where assays and suggested reference values are available, blood level monitoring of other antipsychotic drugs may be helpful in certain circumstances. See ‘Advice for healthcare professionals’ above for further details.

At the time of publication, assays and suggested reference values for therapeutic blood concentrations are known to be available for amisulpride, aripiprazole, olanzapine, quetiapine, risperidone and sulpiride, although availability of testing may vary locally.

Report suspected adverse drug reactions on a Yellow Card

Please continue to report suspected adverse drug reactions (ADRs) on a Yellow Card. Reporting suspected ADRs, even those known to occur in association with the medicine, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines.

Healthcare professionals, patients, and caregivers can report suspected ADRs via the Yellow Card website or via the Yellow Card app. Download the app today via iTunes Yellow Card for iOS devices or via PlayStore Yellow Card for Android devices. You can also view recent alerts from the MHRA and read Drug Safety Updates through the App newsfeed.

Article citation: Drug Safety Update volume 14, issue 1: August 2020: 2.

Denosumab 60mg (Prolia): increased risk of multiple vertebral fractures after stopping or delaying ongoing treatment

Evaluate a patient's individual factors for benefits and risks before initiating treatment with denosumab 60mg, particularly in those with previous vertebral fracture. Patients should not stop denosumab without specialist review.

Advice for healthcare professionals:

- an increased risk of multiple vertebral fractures has been reported in patients within 18 months of stopping or delaying ongoing denosumab 60mg treatment for osteoporosis; cases have been reported in patients in the UK
- patients with a previous vertebral fracture may be at highest risk
- evaluate a patient's individual factors for benefits and risks before initiating treatment with denosumab, particularly in patients at increased risk of vertebral fractures for example those with previous vertebral fracture
- patients should not stop denosumab without specialist review
- the optimal duration of denosumab treatment for osteoporosis has not been established; re-evaluate the need for continued treatment periodically based on the expected benefits and potential risks of denosumab on an individual patient basis, particularly after 5 or more years of use
- risks of long-term treatment with denosumab include rare cases of osteonecrosis of the jaw and atypical femoral fractures; osteonecrosis of the external auditory canal has also been reported in association with denosumab
- NICE rapid guidance (30 April 2020) advises not to postpone ongoing treatment with denosumab during the coronavirus (COVID-19) pandemic
- report suspected adverse drug reactions to denosumab on a Yellow Card

Advice to give to patients:

- there have been reports of increased risk of multiple fractures in the spine after stopping or delaying ongoing treatment with denosumab 60mg (Prolia) treatment
- do not stop denosumab treatment without talking to your doctor to discuss your individual risk factors
- if you miss a prescribed dose of denosumab, the missed injection should be administered as soon as possible. After this, your next injection will be scheduled 6 months from the date of your last injection
- continue to regularly review your treatments for osteoporosis with your doctor

Increased risk of vertebral fractures

Denosumab 60mg (Prolia) is indicated for the treatment of osteoporosis and bone loss, see background section for full indication.

The Commission on Human Medicines' Pharmacovigilance Expert Advisory Group has considered EU and worldwide safety data, together with data submitted by the manufacturer, suggesting an increased risk of multiple vertebral fractures after stopping denosumab for osteoporosis, alongside national and international clinical guidance advising of the potential risk on treatment cessation.[1,2]

1 NOGG 2017 Clinical Guidance. Updated July 2019.

2 *Bone* 105; 2017, 11–17.

Given the reports and guidance in the UK (see later section), we make healthcare professionals aware of this risk and advice for patients not to stop denosumab without specialist review.

UK reports of vertebral fractures after stopping denosumab

Between 1 January 2015 and 31 December 2019, approximately 396,000 denosumab 60mg pre-filled syringes were dispensed in the UK, making the estimated UK exposure in this time about 197,000 patient-years.[3]

3 Data derived from IQVIA MIDAS, January to December 2019, and analysed by the MHRA, March 2020.

Since 2015 and up to and including June 2020, 44 cases of vertebral fracture, including multiple fractures, have been reported in the UK in post-marketing settings in patients after stopping or delaying ongoing treatment with denosumab (Prolia). Where reported, these fractures occurred within 18 months of stopping or delaying denosumab treatment, with some in the first 9 months. These fractures were described as life-changing in some cases.

Patient information and support regarding the use of denosumab in osteoporosis is available from the Royal Osteoporosis Society.

Background

Denosumab 60mg (Prolia) is indicated for treatment of:

- Osteoporosis in postmenopausal women and in men at increased risk of fractures. In postmenopausal women Prolia significantly reduces the risk of vertebral, non-vertebral and hip fractures.
- Bone loss associated with hormone ablation in men with prostate cancer at increased risk of fractures. In men with prostate cancer receiving hormone ablation, Prolia significantly reduces the risk of vertebral fractures
- Treatment of bone loss associated with long-term systemic glucocorticoid therapy in adult patients at increased risk of fracture

Denosumab is also available as a 120mg dose (Xgeva) for the prevention of skeletal related events in adults with advanced malignancies involving bone and for the treatment of adults and skeletally mature adolescents with giant cell tumour of bone that is unresectable or where surgical resection is likely to result in severe morbidity. Although data for risk of multiple vertebral fractures after stopping treatment is insufficient for similar advice to be issued for the 120mg dose at the present time, the risks will be kept under review.

Report suspected adverse drug reactions on a Yellow Card

Please continue to report suspected adverse drug reactions (ADRs) on a Yellow Card. Reporting suspected ADRs, even those known to occur in association with the medicine, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines.

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Article citation: Drug Safety Update volume 14, issue 1: August 2020: 3

Baricitinib (Olumiant▼): increased risk of diverticulitis, particularly in patients with risk factors

Use baricitinib with caution in patients with diverticular disease and in those concomitantly treated with medications associated with an increased risk of diverticulitis.

Advice for healthcare professionals:

- cases of diverticulitis and gastrointestinal perforation have been reported in patients taking baricitinib
- most, but not all, cases of diverticulitis occurred in patients who were concomitantly taking medicines associated with an increased risk of diverticulitis
- use caution in patients with pre-existing diverticular disease and in patients on long-term concomitant medications associated with an increased risk of diverticulitis such as non-steroidal anti-inflammatory drugs (NSAIDs), corticosteroids, and opioids
- advise patients on baricitinib to seek immediate medical care if they experience severe abdominal pain especially accompanied with fever, nausea and vomiting or other symptoms of diverticulitis
- ensure prompt evaluation of any patients on baricitinib who present with new-onset abdominal signs and symptoms to identify early diverticulitis or gastrointestinal perforation
- report any suspected adverse drug reactions to black triangle medicines to the Yellow Card scheme

Review of increased risk of diverticulitis

Baricitinib (Olumiant▼) is a Janus kinase (JAK) inhibitor drug first authorised in the EU in February 2017. It is authorised for the treatment of moderate to severe active rheumatoid arthritis in adults who have responded inadequately to, or who are intolerant to one or more disease-modifying anti-rheumatic drugs.

A European review has assessed cases of diverticulitis associated with baricitinib reported in clinical trials and in clinical (post-marketing) use worldwide. The risk of diverticulitis has been added to the product information for baricitinib with an uncommon frequency and healthcare professionals are asked to use caution in patients at risk of this condition.

Diverticulitis is also a potential side effect of tofacitinib (Xeljanz▼), another JAK inhibitor indicated for rheumatoid arthritis, psoriatic arthritis, and ulcerative colitis. Prescribers of tofacitinib should exercise the same caution in patients with risk factors for diverticulitis.

Cases in clinical trials

In clinical trials of baricitinib to treat rheumatoid arthritis, there were 21 cases of diverticulitis (including 3 [14%] with a complication of gastrointestinal perforation) in 3770 patients across 13,380 patient-years of observation (incidence rate 0.16 per 100 patient-years [95% CI 0.10–0.24]).

Of the 21 patients, 7 (33%) had diverticulosis or diverticulitis noted in their medical history. For concomitant medicines, 13 (62%) of the 21 patients were on chronic corticosteroid treatment, 9 patients were chronically treated with NSAIDs, and 4 patients with acetylsalicylic acid (aspirin) medications.

Cases of diverticulitis and diverticulosis were also reported in clinical trials of baricitinib for other conditions not authorised in the UK. Overall, the observed frequency of diverticulitis in baricitinib use in clinical trials was 0.43% (uncommon).

Cases in post-marketing use

For post-marketing use of baricitinib outside of clinical trials, 35 spontaneous cases of diverticulitis have been reported worldwide up to 31 December 2019. Of these, 25 (71%) cases specifically included a medical history of diverticulitis and/or chronic use of NSAIDs, corticosteroids or opioids, which are known important risk factors for diverticulitis. However, 10 cases had no pre-existing conditions or use of concomitant medications as confounding factors. Gastrointestinal perforation as a complication of diverticulitis was reported in 5 (14%) cases. None of the cases were fatal.

The time to onset of clinical trial and post-marketing cases ranged from 6 days to 6 years. The majority of cases occurred after more than 90 days of treatment.

Report any suspected adverse drug reactions

Baricitinib (Olumiant ▼) is a black triangle medicine and any suspected adverse drug reactions (ADRs) should be reported to the Yellow Card scheme.

Reporting suspected ADRs, even those known to occur, adds to knowledge about the frequency and severity of these reactions and can be used to identify patients who are most at risk. Your report helps the safer use of medicines.

Article citation: Drug Safety Update volume 14, issue 1: August 2020: 4.

Isotretinoin (Roaccutane▼): reminder of important risks and precautions

We remind healthcare professionals that isotretinoin should only be used for severe forms of acne resistant to adequate courses of standard therapy with systemic antibacterials and topical therapy. Prescription of isotretinoin should be supervised by specialist dermatologists with a full understanding of the potential risks and monitoring requirements.

Reminder for healthcare professionals:

- isotretinoin has important risks (including teratogenicity) requiring specialist oversight and therefore must not be used outside of the authorised terms of use
- isotretinoin should only be prescribed for the treatment of severe acne by or under the supervision of physicians with expertise in the use of systemic retinoids and a full understanding of the risks of isotretinoin therapy and monitoring requirements (including for signs of depression)
- isotretinoin is a powerful teratogen associated with a high frequency of severe and life-threatening birth defects if there is exposure in utero; women of childbearing potential must be under a Pregnancy Prevention Programme
- only use isotretinoin for severe forms of acne (such as nodular or conglobate acne or acne at risk of permanent scarring) that are resistant to adequate courses of standard therapy with systemic antibacterials and topical therapies
- counsel patients fully on the potential risks of isotretinoin, including what to do if they feel their mental health is affected or worsening
- be vigilant for serious side effects such as sexual dysfunction in patients taking isotretinoin
- report any suspected adverse drug reactions to retinoid medicines to the Yellow Card scheme

New national independent safety review

Isotretinoin (Roaccutane▼, Reticutan▼, and Rizuderm▼) is indicated for severe acne that is resistant to adequate courses of standard antibacterial or topical therapy. Although an effective treatment for severe acne, isotretinoin has significant risks that require specialist oversight, including teratogenic effects if pregnancies are exposed (see section on the Pregnancy Prevention Programme) and the potential for psychiatric reactions and sexual dysfunction. Isotretinoin should therefore be prescribed only by a consultant dermatologist-led team.

The MHRA regularly reviews the safety of isotretinoin, as for all medicines, to ensure that the benefits of use in UK patients continue to outweigh the risks. Following concerns raised by patients and patient representatives about the nature and severity of some adverse effects, the Commission on Human Medicines (CHM) has endorsed an independent review of the available evidence by the Isotretinoin Expert Working Group.

The review aims to examine the available evidence for the possible risks of psychiatric adverse reactions and sexual dysfunction, including whether they can persist for some time after discontinuation, and to advise the CHM whether further action is needed to minimise or to raise awareness of these risks in the UK. The Expert Working Group may also consider that other aspects of the safety of isotretinoin need to be reviewed based on the available evidence.

While the review is ongoing, we remind healthcare professionals of the important risks and precautions to take when prescribing or dispensing isotretinoin.

Risks of psychiatric reactions and sexual dysfunction

Depression, anxiety, and psychotic symptoms have been reported in patients treated with isotretinoin. Very rarely, suicidal thoughts, or suicide attempts, and suicide have been reported.

Patients prescribed isotretinoin should be advised of what to do if they feel their mental health is affected or is worsening. Patients taking isotretinoin are also recommended to ask family and friends to help watch out for potential symptoms of psychiatric disorders. The patient information leaflet provided with isotretinoin medicines is a good basis for this discussion. All patients taking isotretinoin should be monitored for signs of depression by their prescriber and referred for appropriate treatment if necessary. Particular care is needed in patients with a history or family history of depression. Any concerns about possible psychiatric symptoms should be discussed with the prescriber and treatment may be stopped. However, it is important to remember that psychiatric symptoms may not be fully alleviated after discontinuation and further psychiatric or psychological evaluation may be necessary. The Expert Working Group will consider whether further action is needed to minimise these risks and/or ensure awareness of these risks.

Isotretinoin has also been associated with reports of sexual dysfunction, predominantly involving erectile dysfunction and decreased libido as well as vaginal dryness. The exact incidence of these adverse reactions is unknown but they are currently thought to be rare. The Expert Working Group review will also explore the risks of these reactions and other symptoms of sexual dysfunction, their possible persistence after treatment cessation, and the impact reported by affected patients.

Reminder of pregnancy prevention advice

Isotretinoin, as all oral retinoids, is a powerful teratogen associated with a high frequency of severe and life-threatening birth defects if there is exposure in utero. Isotretinoin is contraindicated in women of childbearing potential unless all the conditions of the Pregnancy Prevention Programme are met. Following a detailed review, in 2019 pregnancy prevention educational materials for healthcare professionals and women were revised and simplified.

See Guidance from the MHRA on key principles to achieve compliance with a pregnancy prevention programmes for medicines during the COVID-19 pandemic (updated 19 May 2020).

Call for reporting

Isotretinoin is a black triangle medicine and all suspected adverse reactions, including any sexual and psychiatric adverse reactions, should be reported via the Yellow Card scheme.

Reports can be made of suspected reactions experienced at any time, including historic adverse experiences with medicines. Please include in the report as much detail as possible, particularly if a side effect continued or started after treatment was stopped.

Report to the Yellow Card scheme electronically using:

- the Yellow Card website
- the Yellow Card app; download now from the Apple App Store or Google Play Store
- some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank)

Article citation: Drug Safety Update volume 14, issue 1: August 2020: 5.

Emollients and risk of severe and fatal burns: new resources available

We inform healthcare professionals of the recent campaign to promote awareness of the risk and new resources available to support safe use following previous advice to health and care professionals.

There is a risk of severe and fatal burns with all emollients – see the Drug Safety Update from December 2018.

Emollients can transfer from the skin onto clothing, bedding, dressings, and other fabric. Once there, they can dry onto the fabric and build up over time. In the presence of a naked flame, fabric with emollient dried on is easily ignited.

Although emollients are not flammable in themselves or when on the skin, when dried on to fabric they act as an accelerant, increasing the speed of ignition and intensity of the fire. This accelerant effect significantly reduces the time available to act to put out a clothing or bedding fire before serious and fatal burns are sustained.

This applies to all emollients, whether they contain paraffin or not.

On 29 July 2020, MHRA in partnership with the National Fire Chiefs Council, charities, and organisations from across health and social care launched a campaign to raise awareness of this important risk. A toolkit of resources is now available for health and social care professionals to support the safe use of emollients.

The resources are freely available for download from https://www.gov.uk/guidance/safe-use-of-emollient-skin-creams-to-treat-dry-skin-conditions and include:

- MHRA and NFCC emollients leaflet A5
- MHRA and NFCC emollients poster with text A3
- MHRA and NFCC emollients poster background A3
- MHRA and NFCC emollients alert sticker
- MHRA and NFCC emollients toolkit presentation pack

How you can support the safe use of emollients:

- use the materials to inform patients and caregivers of the risks with emollient products
- encourage dialogue and learning between colleagues about the safe use of emollients
- report suspected adverse drug reactions or adverse incidents involving emollients, including fires and burns, to the Yellow Card scheme – your report improves the safety of medicines and medical devices

Article citation: Drug Safety Update volume 14, issue 1: August 2020: 6.

Letters and drug alerts sent to healthcare professionals in July 2020

Leuprorelin-containing depot products

Leuprorelin-containing medicines are used to treat prostate cancer, breast cancer and conditions that affect the female reproductive system (endometriosis, uterine fibroids) and early puberty. Cases of handling errors, potentially resulting in lack of efficacy, have been reported with depot formulations. See letter for more information.

Following a European review, the marketing authorisation holders of leuprorelin-containing depot products (Prostap, Staladex, Lutrate) have written to UK healthcare professionals to inform them that:

- handling errors have been reported with leuprorelin-containing depot medicinal products, potentially resulting in lack of efficacy
- the risk of handling errors is increased when there are multiple steps in the product reconstitution and administration process
- products should be prepared, reconstituted (if applicable), and administered only by healthcare professionals who are familiar with these procedures
- instructions for reconstitution and administration in the product information must be followed

Other letters

Keppra 100 mg/ml Oral Solution (levetiracetam): interim supply of Ireland stock to mitigate supply disruption

Wockhardt UK's Amoxicillin Sodium 250mg, 500mg and 1g Powder for Solution for Injection - Healthcare professionals should also be aware of a letter issued 24 August 2020 to inform of caution and monitoring requirements when using Wockhardt UK's Amoxicillin Sodium 250mg, 500mg and 1g Powder for Solution for Injection. This product can now be used with caution in neonates and infants, following the update of the previous MHRA advice not to use due reports of extravasation and injections site reactions. See updated drug alert for more information.

Drug Alerts from July 2020

Class 2 Medicines Recall: Mepacrine Hydrochloride 100 mg Tablets (Batch 85641), EL (20)A/27. Issued 2 July 2020. A specific batch of mepacrine 100mg tablets has been recalled due to a number of foreign body particulates found in the containers of the Active Pharmaceutical Ingredient (API) used in manufacturing. Patients who have been supplied with the affected batch should be contacted and asked to stop using these tablets and to return any unused medicine to their pharmacy.

Class 2 Medicines Recall: Nitrofurantoin 50 mg Tablets, PL 08553/0087, EL (20)A/28. Issued 15 July 2020. A specific batch of nitrofurantoin 50mg tablets has been recalled from pharmacies and wholesalers as a precautionary measure due to out of specification results for dissolution during routine stability testing.

Class 2 Medicines Recall: Ferring Pharmaceuticals Limited, desmopressin nasal spray (all strengths), PL 03194/0024, PL 03194/0090, PL 03194/0056, EL (20)A/29. Issued 15 July 2020. All unexpired stock of the products listed has been recalled from pharmacies and wholesalers as a precautionary measure due to a lower volume of solution being observed in the bottles, and out-of-specification results for the content of the desmopressin acetate (active substance) and benzalkonium chloride (excipient).

Class 2 Medicines Recall: Kyowa Kirin Limited, Abstral 200 microgram sublingual tablets, EL (20)A/34. Issued 29 July 2020. A specific batch has been recalled as a precautionary measure due to the reports of double tablets in a single blister pocket.

Class 3 Medicines Recall: Accord Healthcare Limited, Irinotecan Hydrochloride Concentrate for Solution for Infusion 20mg/ml (5ml vial), EL (20)A/33. Issued 23 July 2020. A specific batch has been recalled as a precautionary measure due to the observation of precipitation in the solution in the same batch marketed in another country (Malta).

Class 4 Medicines Defect Information: Pfizer Limited, Ecalta 100mg powder for concentrate for solution for infusion, EL (20)A/32. Issued 23 July 2020. Pfizer Limited has informed us that the packs for the affected batches below have not been packaged with the current version of the Patient Information Leaflet (PIL) containing updated storage instructions. The infusion solution must not be frozen.

Class 4 Medicines Defect Information: Ennogen Pharma Limited, Trimogal 100mg and 200mg Tablets, EL (20)A/31. Issued 20 July 2020. The Patient Information Leaflets within the packs for the affected batches contain an error with regard to the dosage instruction for children younger than 6 years. The correct PIL is available from the electronic medicines compendium (EMC) website and the MHRA website, and should be used when dispensing packs from the affected batches.

Class 4 Medicines Defect Information: Aspar Pharmaceuticals Limited, Ibuprofen 200mg and 400mg tablets packaged in various liveries, EL (20)A/30. Issued 20 July 2020. The Patient Information Leaflets (PILs) within the ibuprofen packs listed are missing some information identified from post-marketing experience that should be documented in Section 3 (How To Take The Tablets) and Section 4 (Possible Side Effects) of the PIL. Please ensure that patients are aware of the missing information and know to seek immediate medical advice in the situations described in the updates.

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Medical Device Alerts issued in July 2020

In this monthly update, we highlight selected Medical Device Alerts and notices that have been issued recently by MHRA. Please note, this is not an exhaustive list of medical device alerts. For all Medical Device Alerts from MHRA, see Alerts and recalls for drugs and medical devices.

Masks: type IIR from Cardinal Health – destroy affected lots (MDA/2020/021). Issued 20 July 2020. The foam strip on the mask can flake and enter the wearer's airway or mouth; ties and/or stitching may detach from the mask.

Field safety notice: Eltrombopag interference for VITROS Chemistry Products TBIL Slides and BuBc Slides and VITROS XT Chemistry Products TBIL-ALKP Slides. Issued July 2020. Eltrombopag is a bone marrow stimulant used to treat thrombocytopenia and severe aplastic anaemia. See July 2018 Drug Safety Update for potential for reports of interference with bilirubin and creatinine test results with eltrombopag.

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