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 ask healthcare professionals to report pregnancies exposed to a COVID-19 antiviral to the UK COVID-19 Antivirals Pregnancy Registry. See the article on page 2 for more.

Second, we ask healthcare professionals to carefully consider the benefits and risks before prescribing systemic macrolide antibiotics to patients taking hydroxychloroquine or chloroquine. This advice follows an observational study that showed an increased risk of cardiovascular events and cardiovascular mortality when hydroxychloroquine was used with azithromycin. We also advise prescribers of hydroxychloroquine or chloroquine to be vigilant for psychiatric reactions. See page 5 for more details.

Next, we issue updated advice following cases of serious liver injury reported during Kaftrio–Kalydeco combination treatment for cystic fibrosis. All patients should undergo liver function testing, including for bilirubin, before and during treatment. Caution is required in patients with advanced pre-existing liver disease and these patients should be closely monitored (see page 9).

On page 12 we summarise recent advice relating to COVID-19 vaccines and medicines published since the January 2022 issue of Drug Safety Update. And on page 13 we include recent letters, recalls and notifications sent to healthcare professionals about medicines.

COVID-19 antivirals: reporting to the UK COVID-19 Antivirals Pregnancy Registry

As the safety of COVID-19 antivirals in pregnancy has not been established, please report any pregnancies which occur during use of an antiviral, including paternal use, to the UK COVID-19 Antivirals Pregnancy Registry.

This advice applies to molnupiravir (Lagevrio▼), the combination of PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid▼), and remdesivir (Veklury▼).

Advice for healthcare professionals:

- the UK COVID-19 Antivirals Pregnancy Registry is being operated by the MHRA in collaboration with the UK Teratology Information Service (UKTIS) to collect information about exposures to COVID-19 antivirals in pregnancy and enable follow-up of any reported pregnancies; the registry is also collecting information on outcomes for pregnancies where conception occurred during or shortly after paternal exposure to antiviral treatment
- to report to the registry, telephone: 0344 892 0909 (available 9:00am to 5:00pm, Monday to Friday, excluding bank holidays) – for more information see the UKTIS website
- healthcare professionals in England, Scotland, and Wales (as well as patients and their partners) can report an exposure to a COVID-19 antiviral during pregnancy or around the time of conception, or of partners on a COVID-19 antiviral around the time of conception
- in Northern Ireland, healthcare professionals cannot currently report on behalf of a pregnant women or their partner, but should encourage them to self-report using the same contact details
- since an exposure may occur in very early pregnancy before pregnancy is recognised, we ask healthcare professionals to report (or to encourage patients to self-report), even if some time has passed since the end of their COVID-19 antiviral treatment.

This registry is not relevant to pregnancy exposure or outcomes associated with COVID-19 vaccines. For information about the use of COVID-19 vaccines and pregnancy, see guide on COVID-19 vaccination in pregnancy and breastfeeding.

COVID-19 antiviral medicines

The oral antiviral medicines molnupiravir (Lagevrio▼) and the combination of PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid▼) have been authorised for use in people aged 18 years and older who have mild to moderate COVID-19 and at least one risk factor for developing severe illness. Such risk factors include obesity, older age (older than 60 years), diabetes mellitus, or heart disease. See Summary of Product Characteristics for Lagevrio▼ and Paxlovid▼.

The intravenous antiviral remdesivir (Veklury▼) is authorised for the treatment of COVID-19 in adults and adolescents (aged 12 to 18 years and weighing at least 40 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen or other non-invasive ventilation at start of treatment). It is also authorised for the treatment of COVID-19 in adults who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID-19.

Since the COVID-19 antivirals are new medicines, their safety during pregnancy is not yet understood. Studies of molnupiravir in animals have shown some evidence of reproductive toxicity (harmful effects to the unborn animal); the implications of these data for safety in human pregnancy are not yet known. Animal studies have not shown harm from PF-07321332 or remdesivir, however, human pregnancy data are lacking and a cautious approach to their use is advocated.

Information on effective and safe use, including guidance on contraception, is available in the product information for:

- molnupiravir (Lagevrio▼) – Summary of Product Information and Patient Information Leaflet
- PF-07321332 (nirmatrelvir) plus ritonavir (Paxlovid▼) – Summary of Product Information and Patient Information Leaflet
- remdesivir (Veklury▼) – Summary of Product Information and Patient Information Leaflet

Information for patients about COVID-19 antivirals is also available from other clinical resources or from resources such as UKTIS Bumps and the NHS website.

The UK COVID-19 Antivirals Pregnancy Registry

The UK COVID-19 Antivirals Pregnancy Registry aims to collect information about exposures to COVID-19 antivirals during or shortly before pregnancy. The registry is also collecting information on outcomes for pregnancies where conception occurred during or shortly after paternal exposure to COVID-19 antiviral treatment. It is hoped that the information collected by the registry will allow the MHRA, UKTIS, and healthcare providers to evaluate the outcomes of exposures to COVID-19 antivirals in and around pregnancy.

The route for reporting of relevant exposures into the registry is being supported by the UK Teratology Information Service (UKTIS), on behalf of the MHRA. UKTIS is part of the Newcastle National Poisons Information Service and routinely collect information about medicines in pregnancy to better understand the effects medicines can have on unborn babies.

How to report a pregnancy exposed to a new COVID-19 antiviral

To report an exposed pregnancy to UKTIS, telephone: 0344 892 0909 (available 9:00am to 5:00pm, Monday to Friday, excluding bank holidays).

Patients in the UK (England, Scotland, Wales, and Northern Ireland) can directly report to the registry if they used a COVID-19 antiviral medication when they were pregnant, shortly before pregnancy, or around the time their partner conceived.

Healthcare professionals in England, Scotland, and Wales can report exposures on behalf of pregnant patients or their partners. In Northern Ireland, healthcare professionals cannot currently report on behalf of a patient but should encourage pregnant patients or their partners to self-report to the registry using the same details.

More information is available on the UKTIS Registry website. The website includes details on privacy and follow-up.

Since exposures may occur in very early pregnancy before pregnancy is recognised, we ask healthcare professionals to report (or to encourage patients to self-report), even if some time has passed since the end of their COVID-19 antiviral treatment.

Report suspected adverse drug reactions via a Yellow Card

All other suspected adverse drug reactions should be reported to the Yellow Card scheme.

Report suspected side effects to medicines, vaccines, medical device and test kit incidents used in coronavirus (COVID-19) testing and treatment using the dedicated Coronavirus Yellow Card reporting site or the Yellow Card app. See the MHRA website for the latest information on medicines and vaccines for COVID-19.

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Hydroxychloroquine, chloroquine: increased risk of cardiovascular events when used with macrolide antibiotics; reminder of psychiatric reactions

Carefully consider the benefits and risks before prescribing systemic azithromycin or other systemic macrolide antibiotics (erythromycin or clarithromycin) to patients being treated with hydroxychloroquine or chloroquine. An observational study in patients with rheumatoid arthritis has shown that co-administration of azithromycin with hydroxychloroquine is associated with an increased risk of cardiovascular events and cardiovascular mortality.

Advice for healthcare professionals:

- an observational study has shown that co-administration of azithromycin with hydroxychloroquine in patients with rheumatoid arthritis is associated with an increased risk of cardiovascular events (including angina or chest pain and heart failure) and cardiovascular mortality
- carefully consider the benefits and risks before prescribing systemic azithromycin or other systemic macrolide antibiotics (erythromycin or clarithromycin) to patients being treated with hydroxychloroquine or chloroquine
- if there is a clinical need to prescribe systemic macrolide antibiotics with hydroxychloroquine or chloroquine, use caution in patients with risk factors for cardiac events and follow advice in the product information for each medicine
- be vigilant for psychiatric reactions associated with hydroxychloroquine or chloroquine, especially in the first month of treatment; events have been reported in patients with no prior history of psychiatric disorders
- report suspected adverse drug reactions on a Yellow Card

Advice for healthcare professionals to give to patients and carers:

- some antibiotics (known as macrolides) taken by mouth or given as an injection at the same time as hydroxychloroquine or chloroquine have been associated with an increased risk of side effects that affect the heart
- seek urgent medical help if you have any signs of problems with your heart (for example, palpitations, fainting, chest pain, or unexplained breathlessness)
- some patients have also reported mental health symptoms when they started treatment with hydroxychloroquine or chloroquine
- speak to your doctor as soon as possible if you or your family members or caregivers notice any new or worsening mental health symptoms
- read the patient information leaflet that comes with your medicine (hydroxychloroquine or chloroquine) and keep it handy in case you need to read it again

Hydroxychloroquine and chloroquine indications

Hydroxychloroquine is indicated for treatment of rheumatoid arthritis, systemic lupus erythematosus, and dermatological conditions aggravated by sunlight. Chloroquine is indicated for malaria prophylaxis or treatment, with some products also having indications for treatment of amoebic hepatitis and abscess, rheumatoid arthritis, and discoid or systemic lupus erythematosus.

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Review of cardiovascular safety after observational trial

An observational retrospective study[1] published in August 2020 compared records of adverse events in patients initiated on hydroxychloroquine alone with those in patients initiated on sulfasalazine alone for rheumatoid arthritis. The same study compared severe adverse events associated with use of hydroxychloroquine plus azithromycin with those associated with use of hydroxychloroquine plus amoxicillin.

The study showed that in a short-term period (up to 30 days) after first use of hydroxychloroquine treatment in combination with azithromycin there was an increased risk of angina or chest pain, heart failure, and cardiovascular mortality compared with the combination of hydroxychloroquine and amoxicillin.

No excess risk of severe adverse events was identified in the short-term period of hydroxychloroquine alone (compared with sulfasalazine), but longer-term use past 30 days was associated with increased cardiovascular mortality.

Although the mechanism of the observed effects was not examined in detail by the study, it has been proposed that events could be caused by cumulative effects of hydroxychloroquine and azithromycin on the QT interval, potentiating arrythmias and cardiac death, or through other additive cardiotoxic effects more generally.

A national review of safety data by the Pharmacovigilance Expert Advisory Group of the Commission on Human Medicines considered these data. We have published a Public Assessment Report of this assessment.

The review recommended that the product information for hydroxychloroquine and systemic azithromycin medicines should be amended to include new warnings and advice on these risks. Due to the similar safety profiles, the risks seen with concurrent use of hydroxychloroquine and azithromycin are considered to apply to concurrent use of hydroxychloroquine and other systemic macrolide antibiotics (clarithromycin or erythromycin) and to use of chloroquine with systemic macrolide antibiotics. As such, the review recommended that similar warnings should also be added to the product information for chloroquine and for systemic clarithromycin or erythromycin.

These warnings are not being introduced for topical macrolide products (which are indicated for conjunctivitis or acne), as these products are used at lower doses and with very limited potential for systemic exposure, and do not list cardiovascular events as potential adverse effects associated with their use.

Reminder of existing cardiac warnings

The product information for hydroxychloroquine and chloroquine already contains warnings about cases of cardiomyopathy resulting in cardiac failure, in some cases with fatal outcome. Clinical monitoring for signs and symptoms of cardiomyopathy is advised for patients taking hydroxychloroquine or long-term chloroquine. If signs and symptoms of cardiomyopathy occur during treatment with either hydroxychloroquine or chloroquine, then treatment should be stopped.

Evidence suggests both hydroxychloroquine and chloroquine can prolong the QT interval, especially in overdose or when used in combination with other medicines with the potential to induce cardiac arrhythmias. Warnings are also in place across the product information for azithromycin, clarithromycin, and erythromycin to use caution in patients with a history of QT interval prolongation or in patients receiving a medicine known to cause QT prolongation.

Characteristics of psychiatric reactions

Hydroxychloroquine and chloroquine have been previously associated with psychiatric reactions, including reports of depression, anxiety, hallucinations, and psychosis.

In November 2020, a European safety review recommended updates to the warnings for hydroxychloroquine and chloroquine medicines to include a range of reported psychiatric reactions, including rare cases of suicidal behaviour. The review noted that when psychiatric events occurred, they were typically within the first month of treatment. Events have been reported in patients with no previous history of psychiatric disorders.

Information about these reactions have been added to the Summary of Product Characteristics and Patient Information Leaflets for hydroxychloroquine and chloroquine.

Advise patients taking hydroxychloroquine or chloroquine medicines to contact a doctor immediately if they experience new or worsening mental health problems (such as irrational thoughts, anxiety, hallucinations, and feeling confused or feeling depressed, including thoughts of self-harm or suicide). Family members or caregivers may also be advised to be vigilant for these reactions and the need to seek medical advice if they occur.

Context of clinical studies

This article concerns regulatory action taken based on safety data from the use of these medicines in their authorised indications. Other safety studies on hydroxychloroquine alone or with azithromycin have been conducted in the context of COVID-19 treatment.

Hydroxychloroquine and chloroquine are not authorised to treat symptoms related to COVID-19 or to prevent infection. MHRA advice since March 2020 is that these products should only be used for COVID-19 within a clinical trial. However, there are currently no ongoing clinical trials in this indication, since recruitment to the hydroxychloroquine arm of the RECOVERY trial was suspended after results showed no benefit of hydroxychloroquine in patients hospitalised with COVID-19.

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 medical history, any concomitant medication, onset timing, treatment dates, and product brand name.

Report suspected side effects to medicines, vaccines or medical device and test kit incidents used in coronavirus (COVID-19) testing and treatment using the dedicated Coronavirus Yellow Card reporting site or the Yellow Card app.

Footnotes

1. Lane JCE and others. Risk of hydroxychloroquine alone and in combination with azithromycin in the treatment of rheumatoid arthritis: a multinational, retrospective study. Lancet Rheumatol 2020: volume 2, pages e698-e711.

Article citation: Drug Safety Update volume 15, issue 7: February 2022: 2.

Ivacaftor, tezacaftor, elexacaftor (Kaftrio▼) in combination with ivacaftor (Kalydeco): risk of serious liver injury; updated advice on liver function testing

Cases of serious liver injury with elevated transaminases and bilirubin have been reported during treatment with Kaftrio–Kalydeco combination therapy. In all patients, measure alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin levels before starting treatment, every 3 months during the first year of treatment, and annually thereafter.

Advice for healthcare professionals:

- cases of serious liver injury characterised by concomitant elevations in alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin have been reported with ivacaftor/tezacaftor/elexacaftor (Kaftrio) in combination with ivacaftor (Kalydeco)
- one case of serious liver injury in a patient with pre-existing cirrhosis and portal hypertension resulted in liver failure requiring liver transplantation
- measure total bilirubin levels in addition to ALT and AST levels before initiating treatment, every 3 months during the first year of treatment, and annually thereafter; consider more frequent monitoring for patients with a history of liver disease or a history of transaminase elevations
- use with caution in patients with advanced pre-existing liver disease (for example, cirrhosis or portal hypertension) and only if the benefits are expected to outweigh the risks; if used, these patients should be closely monitored
- perform prompt clinical evaluation and measure liver function in patients who report symptoms that may indicate liver injury
- discontinue treatment in the event of significant elevation of liver enzymes (see criteria on page 11) or clinical signs and symptoms of liver injury; following resolution of liver abnormalities, consider the benefits and risks before resuming treatment
- report any suspected adverse reactions associated with Kaftrio▼ in combination with ivacaftor (Kalydeco) to the Yellow Card scheme

Advice for healthcare professionals to provide to patients and carers:

- Kaftrio and Kalydeco are medicines used in cystic fibrosis to help breathing by improving lung function
- these medicines can affect the liver in some patients; a few patients on Kaftrio and Kalydeco combination therapy have developed severe liver problems – in isolated cases, a liver transplant could be needed
- blood tests to check your liver function are needed before your treatment starts, every 3 months for the first year, and then once a year after this; you might need more frequent tests if you have had liver problems or high liver enzymes in the past
- talk to your doctor straight away if you have signs of liver problems, such as pain in the upper right area of your stomach, yellowing of your skin or the white part of your eyes, loss of appetite, nausea or vomiting, or dark urine

Kaftrio–Kalydeco combination therapy and liver injury

Ivacaftor/elexacaftor/tezacaftor (Kaftrio▼) is indicated in a combination regimen with ivacaftor (Kalydeco) for the treatment of cystic fibrosis in patients aged 6 years and older who have at least one F508del mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

Cystic fibrosis can lead to liver fibrosis and liver cirrhosis, and elevations in ALT and AST are common. Elevated transaminases have also been observed in patients treated with Kaftrio–Kalydeco combination therapy. Regular monitoring of liver function, including transaminases, has been advised since authorisation.

A recent European review of safety data identified a case of liver failure leading to liver transplantation in a patient taking Kaftrio–Kalydeco combination. This case was reported post-marketing in an adult patient with pre-existing cirrhosis and portal hypertension. The review also identified 2 other cases of serious liver injury in adult patients with no prior history of liver disease. These patients had elevations in transaminases and total bilirubin, and the patients were hospitalised with jaundice.

It is not possible to estimate the frequency of reports of serious liver injury or bilirubin elevations. The mechanism underlying liver injury following treatment is also unknown.

In the UK, from October 2020 and up to 12 December 2021, the Yellow Card scheme has received 22 reports of serious liver disorders and 54 reports of abnormal liver test results (6 with concomitant bilirubin elevations) associated with Kaftrio–Kalydeco combination therapy.[1]

As for all medicines, the MHRA will keep reports of suspected serious adverse drug reactions under close review.

New advice to minimise risk of liver injury

Following the findings of the European review, existing warnings on hepatotoxicity in the product information for Kaftrio and Kalydeco have been strengthened to include the risk of clinically relevant drug-induced liver injury with Kaftrio–Kalydeco combination therapy.

The recommendations for liver function monitoring before and during treatment, which already included regular assessment of ALT and AST, have been strengthened to include advice to measure total bilirubin concomitantly. The advice that more frequent monitoring should be considered in patients with a history of transaminase elevations has been extended to include also patents with pre-existing liver disease.

In patients with pre-existing advanced liver disease (for example, cirrhosis, portal hypertension) Kaftrio–Kalydeco combination therapy should be used with caution and only if the benefits are expected to outweigh the risks. If these patients receive combination therapy, they should be closely monitored after the initiation of treatment.

Advice in cases of significant liver enzyme abnormalities

If aminotransferases are more than 5-times upper limit of normal (ULN) without bilirubin elevation or more than 3-times ULN with bilirubin more than 2-times ULN:

- interrupt treatment dosing
- monitor aminotransferases and bilirubin until within normal limits
- following resolution, consider the benefits and risks of resuming treatment

Reminder of advice for hepatic impairment

Ivacaftor, tezacaftor, and elexacaftor are extensively metabolised by the cytochrome P450 system in the liver. For patients with moderate hepatic impairment (Child-Pugh Class B), the use of Kaftrio–Kalydeco combination therapy should only be considered when there is a clear medical need and the benefits are expected to outweigh the risks. If this is the case, the combination should be used with caution at a reduced dose as advised in the Summary of Product Characteristics. Studies have not been conducted in patients with severe hepatic impairment (Child-Pugh Class C), but the exposure is expected to be higher than in patients with moderate hepatic impairment. It is recommended that patients with severe hepatic impairment should not be treated with Kaftrio.

Report suspected reactions on a Yellow Card

Kaftrio is a black triangle medicine and all suspected adverse drug reactions should be reported to the Yellow Card scheme. Report 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.

Report suspected side effects to medicines, vaccines, medical device and test kit incidents used in coronavirus (COVID-19) testing and treatment using the dedicated Coronavirus Yellow Card reporting site or the Yellow Card app. See the MHRA website for the latest information on medicines and vaccines for COVID-19.

Footnotes

1. In interpreting these data, caution should be exercised as the data may not be complete, and the reporting rates and the information provided within the reports can be influenced by many factors. Reporters are asked to submit Yellow Card reports even if they only have a suspicion that the medicine may have caused the adverse drug reaction.

Article citation: Drug Safety Update volume 15, issue 7: February 2022: 3.

COVID-19 vaccines and medicines: updates for February 2022

Approval of Novavax COVID-19 vaccine: Nuvaxovid

We have approved Nuvaxovid, the COVID-19 Vaccine developed by Novavax. This follows a rigorous review of the safety, quality and effectiveness of this vaccine, and expert advice from the government's independent scientific advisory body, the Commission on Human Medicines (CHM). For more information, please see the Decision page on our website which includes the Summary of Product Characteristics and Product Information Leaflet.

Summaries of Yellow Card reporting and other recent MHRA publications

We continue to publish the summaries of the Yellow Card reporting for the COVID-19 vaccines being used in the UK. 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.

We have also recently:

- updated the product information for Vaxzevria (previously COVID-19 Vaccine AstraZeneca) to include extremely rare cases of transverse myelitis. A further dose of Vaxzevria should not be given to those who have experienced symptoms of transverse myelitis after a previous dose of this vaccine
- published the Public Assessment Report and a summary of the Public Assessment Report for Paxlovid antiviral treatment for COVID-19

We previously included summaries of latest COVID-19 information, including in the November 2021, December 2021 and January 2022 issues of Drug Safety Update. See guidance on COVID-19 for all our latest information, including after publication of this article.

Reporting Yellow Cards

Report suspected side effects to medicines, vaccines, medical device and test kit incidents used in coronavirus (COVID-19) testing and treatment using the dedicated Coronavirus Yellow Card reporting site or the Yellow Card app. As these products are under additional monitoring, this includes all suspected adverse reactions associated with these vaccines. This will allow quick identification of new safety information.

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

You may be contacted following submission of a Yellow Card report so that we can gather additional relevant information for the assessment of the report. These contributions form an important part of our understanding of suspected adverse events.

Article citation: Drug Safety Update volume 15, issue 7: February 2022: 4.

Letters and medicine recalls sent to healthcare professionals in January 2022

Letters

In January 2022, the following letters were sent or provided to relevant healthcare professionals:

- Nulojix (belatacept): Further extension of the temporary restriction in supply up until 3Q 2022 in the United Kingdom (Great Britain & Northern Ireland)
- Ronapreve▼ (casirivimab and imdevimab) 120 mg/ml solution for injection or infusion: Important information for healthcare professionals about the expiry date of the 6ml vial packs and the 20ml vial packs
- Prismasol 4 mmol/L Potassium Solutions for haemodialysis/haemofiltration: supply of non-UK labelled batches during the Covid-19 Pandemic
- Hemosol B0 Solutions for haemodialysis/haemofiltration: supply of non-UK labelled batches during the Covid-19 Pandemic
- Phoxilium 1.2mmol/l phosphate Solutions for haemodialysis/haemofiltration: supply of non-UK labelled batches during the Covid-19 Pandemic

Gina 10 microgram vaginal tablets (estradiol): consultation on proposal to make available from pharmacies

Gina 10 microgram vaginal tablets are a low dose local hormone replacement therapy, authorised for the treatment of vaginal atrophy due to oestrogen deficiency in postmenopausal women. Gina is currently available as a prescription only medicine (POM) and we are considering a proposal to make it available in pharmacies.

The MHRA has launched a public consultation which will be open for comments until midday on 23 February 2022. We are seeking views on reclassifying Gina as a pharmacy medicine and ask healthcare professionals to see the consultation page for more information.

Medicine Recalls and Notifications

In January 2022, recalls and notifications for medicines were issued on:

Class 2 Medicines Recall: SANTEN Oy (trading as Santen UK Limited) IKERVIS 1 mg/mL eye drops, emulsion, EL (22)A/01. Issued 19 January 2022. A batch of Ikervis (ciclosporin) 1 mg/mL eye drops emulsion are being recalled as particles or crystals of ciclosporin have been identified during stability monitoring. This is a precautionary recall; the Marketing Authorisation Holder's investigation has not confirmed that adverse reactions have been caused by the presence of particles. Stop supplying the batch immediately, quarantine all remaining stock and return to supplier.

Class 4 Medicines Defect Information: Fresenius Kabi Limited, Kabiven Emulsion for Infusion, EL (22)A/02. Issued 25 January 2022. Batches of Kabiven emulsion for infusion, 2053 ml 3-chamber infusion bags have been identified that incorrectly state the amount of glucose monohydrate as 110g. The correct amount of 200g as glucose anhydrous stated on the infusion bag in the energy content section as carbohydrates, on the outer carton and in the Summary of Product Characteristics. Healthcare professionals are advised to exercise caution when administering this product, particularly when calculating patient nutritional requirements.

Class 4 Medicines Defect Information: Antibiotice SA, Piperacillin / Tazobactam 4g/0.5 g, powder for solution for infusion, EL (22)A/03. Issued 31 January 2022. Batches of Piperacillin 4g and Tazobactam 0.5g powder for solution for infusion have been identified with Patient Information Leaflets that incorrectly state sodium content as 9.39mmol (108mg). The correct sodium content is 9.39mmol (216mg) per product. There are no product quality issues and the batches are not being recalled. Healthcare professionals are advised to calculate sodium content using the correct values when administering this product to patients on sodium restricted diets.

See Alerts, recalls and safety information for all recent notices.

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