

## 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 14 Issue 7 February 2021

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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.



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First, we inform of new advice for ulipristal acetate 5mg for uterine fibroids. Although the temporary suspension of this medicine has been lifted, further restrictions have been introduced due to the risk of serious liver injury and liver failure, with some cases requiring liver transplantation. See page 2 for the new restricted indication and advice following a safety review.

Second, we make prescribers aware that the pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without the presence of concomitant opioid medicines. Adjustments in dose or dosing regimen may be necessary in patients at increased risk (page 6).

Third, we inform of the need for vigilance when children with adrenal insufficiency are switched from hydrocortisone tablets to Alkindi hydrocortisone granules. Parents or carers should be advised to carefully observe children for symptoms of adrenal insufficiency in the first week after switching and seek medical advice if they occur (page 9).

On page 11 we inform of a new initiative from the MHRA and 16 partner organisations to ensure pregnant and breastfeeding women can make informed decisions about their healthcare, particularly relating to the medicines they take. We also provide information about the new report on optimising data on medicines used during pregnancy.

Finally, on page 13 we include recent updates on MHRA advice relating to COVID-19 vaccines and medicines up to 16 February 2021.

## Ulipristal acetate 5mg (Esmya): further restrictions due to risk of serious liver injury

The indication of ulipristal acetate 5mg for uterine fibroids has been further restricted due to the risk of serious liver injury and liver failure, with some cases requiring liver transplantation.

Although the temporary suspension has been lifted, this medicine should only be used for intermittent treatment of moderate to severe symptoms of uterine fibroids before menopause and when surgical procedures (including uterine fibroid embolisation) are not suitable or have failed.

### Advice for healthcare professionals:

- ulipristal acetate 5mg for uterine fibroids has been associated with cases of serious liver injury and liver failure (requiring transplantation in some cases); the licence was temporarily suspended in March 2020 to allow a further review of these risks
- although the temporary suspension has been lifted, the indication for ulipristal acetate 5mg has been further restricted
  - it should be used only for intermittent therapy of moderate to severe uterine fibroid symptoms before menopause and when surgical procedures (including uterine fibroid embolisation) are not suitable or failed
- ulipristal acetate 5mg should no longer be prescribed for controlling symptoms of uterine fibroids while waiting for surgical treatment
- if ulipristal acetate 5mg is felt to be an appropriate therapy, talk about the risks and benefits with patients before prescribing so they can make an informed decision about treatment options; this conversation should include discussion of:
  - all available treatment options for moderate to severe symptoms of uterine fibroids, and the advantages and risks of these depending on personal situation
  - the potential risk of liver injury and liver failure with ulipristal acetate 5mg, which in rare cases has led to liver transplantation
  - signs and symptoms of liver injury and what to do if they occur
- do not use ulipristal acetate 5mg in patients with an underlying liver disorder
- continue to follow advice to monitor liver function according to the recommended schedule of liver function tests before, during, and after treatment courses (see reminder below)
- report suspected adverse drug reactions associated with ulipristal acetate 5mg on a [Yellow Card](#)

### **Advice to give to patients:**

- infrequent but serious cases of liver damage (with some cases requiring a liver transplant) have been reported in association with ulipristal acetate 5mg for uterine fibroids
- ulipristal acetate 5mg can only be used for intermittent treatment of moderate to severe symptoms of uterine fibroids if:
  - you have not experienced menopause; and
  - an operation or embolisation procedure for uterine fibroids is not suitable for you or these procedures have not worked
- blood tests are needed before treatment is started, during treatment, and 2–4 weeks after treatment to check your liver is functioning normally
- stop taking your ulipristal acetate tablets and speak with your doctor immediately if you get any signs of liver damage such as yellowing of the skin or eyes, dark urine, or nausea or vomiting
- carefully read the patient card included in the package and the leaflet that accompanies your medicines and keep it safe in case you need to read it again

### **Risk of serious liver injury**

#### ***Background to the risks and measures previously taken***

Ulipristal acetate 5mg (Esmya and generics) was first authorised in 2012 for intermittent or pre-operative treatment of moderate to severe symptoms of uterine fibroids in women of reproductive age.

In 2018, a European safety review was conducted due to 4 cases reported worldwide of severe liver injury resulting in liver transplantation. Several measures were introduced in 2018 to minimise the risk of severe liver injury. See [Drug Safety Update, August 2018](#).

#### ***Latest review and new advice***

In 2020, a fifth case of severe liver injury resulting in liver transplantation was reported, prompting a further European review. While this further review was conducted, the licences for all ulipristal acetate 5mg medicines were temporarily suspended ([March 2020, Drug Safety Update](#)). Esmya 5mg tablets were [recalled](#) from patients, pharmacies and wholesalers in the UK on 18 March 2020.

The temporary suspension has now been lifted, but the indication for ulipristal acetate 5mg has been further restricted. The review recommended that the risk of severe liver injury does not justify its use for the pre-operative treatment of uterine fibroids. However, the review considered that the benefits of ulipristal acetate 5mg in controlling fibroids may outweigh this risk in women who have no other treatment options (see [public assessment report](#) from the European Medicines Agency).

As such, Esmya can be used for:

- intermittent treatment of moderate to severe symptoms of uterine fibroids in adult women who have not reached menopause and when surgical procedures (including uterine fibroid embolisation) are not suitable or have failed.

The [Commission on Human Medicines' Medicines in Women's Health Expert Advisory Group \(MWHEAG\)](#) has considered the safety data and advised that physicians should carefully consider if ulipristal acetate 5mg is an appropriate option for their patient, and accurately and thoroughly discuss the benefits and risks of ulipristal acetate 5mg with them before prescribing. This conversation should include the risk of liver injury and liver failure, including rare cases requiring liver transplantation associated with ulipristal acetate 5mg.

[NICE guidance NG88 Heavy Menstrual Bleeding](#) should be considered for clinical guidance on appropriate therapies for symptoms of uterine fibroids. All available treatment options for symptoms of uterine fibroids should be discussed with patients, including the advantages and risks of these depending on their personal situation. Surgical procedures and uterine fibroid embolisation (if available) should be considered, taking into account the patient's preferences and plans for fertility.

The product information for medicines containing ulipristal acetate 5mg has been amended and a [letter](#) sent to healthcare professionals to inform them of the latest safety advice. The prescribing guide for physicians and the patient card will also be updated.

The frequency of occurrence of liver failure with ulipristal acetate 5mg is unknown and no patient risk factors could be identified from the available data. Since authorisation and to date, we have received 20 suspected adverse drug reaction reports of liver disorders with the use of Esmya in the UK. None report liver transplant or death. In the UK, Esmya has been suspended since March 2020.

### **Reminder of liver function monitoring**

Ulipristal acetate 5mg is contraindicated in patients with an underlying hepatic disorder.

Liver function tests must be performed before starting treatment with ulipristal acetate 5mg. Treatment must not be initiated if transaminases (alanine transaminase (ALT) or aspartate aminotransferase (AST)) exceed 2-times the upper limit of normal (ULN).

During treatment, liver function tests must be performed monthly during the first 2 treatment courses. For further treatment courses, liver function must be tested once before each new treatment course and when clinically indicated.

If a patient shows signs or symptoms compatible with liver injury (fatigue, asthenia, nausea, vomiting, right hypochondrial pain, anorexia, jaundice), treatment should be stopped, and the patient investigated immediately. Liver function tests should be performed urgently.

Stop treatment if transaminase levels (ALT or AST) are greater than 3-times the ULN and closely monitor patients. The need for specialist hepatology referral should be considered. Liver function tests should also be performed 2–4 weeks after treatment has stopped.

## **ellaOne (ulipristal acetate 30mg)**

The emergency contraceptive ellaOne also contains ulipristal acetate in a single dose of 30mg. No concern has been raised about serious liver injury with ellaOne and there are no changes to its use.

### **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, treatment dates, and product brand name.

Report suspected side effects to medicines, vaccines or medical device and diagnostic adverse incidents used in coronavirus (COVID-19) 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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## Pregabalin (Lyrica): reports of severe respiratory depression

Pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without the presence of concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment; those using concomitant central nervous system (CNS) depressants; and people older than 65 years might be at higher risk of experiencing these events and adjustments in dose or dosing regimen may be necessary.

### Advice for healthcare professionals:

- pregabalin has been associated with reports of respiratory depression, in some cases without concomitant opioid treatment
- consider whether adjustments in dose or dosing regimen are necessary for patients at higher risk of respiratory depression, this includes people:
  - with compromised respiratory function, respiratory or neurological disease, or renal impairment
  - taking other CNS depressants (including opioid-containing medicines)
  - aged older than 65 years
- report suspected adverse drug reactions associated with use of pregabalin on a [Yellow Card](#) (see reporting section)

### Advice to give to patients and carers:

- some patients have experienced breathing difficulties when taking pregabalin – certain people may need a lower dose to reduce the risks of these issues
- contact your doctor if you notice new or increased trouble breathing or you experience shallow breathing after taking pregabalin; a noticeable change in breathing might be associated with sleepiness
- read the leaflet that comes with your medicine and talk to your doctor or pharmacist if you are worried about the other prescribed medicines you are taking with pregabalin
- avoid drinking alcohol during pregabalin treatment

### Risk of respiratory depression

Pregabalin is indicated in adults for the treatment of peripheral and central neuropathic pain, as adjunctive therapy in adults with partial seizures with or without secondary generalisation, and for generalised anxiety disorder in adults.

Use of pregabalin with opioid medicines or other central nervous system (CNS) depressant medicines has been previously associated with reports of respiratory failure, coma, and deaths. Studies show use of high doses of pregabalin (over 300mg a day) alongside opioid medicines to be particularly associated with an increased risk of opioid-related death.<sup>1</sup>

A recent European review of safety data considered reports of severe respiratory depression thought to be related to the action of pregabalin alone on the CNS. Given the available data on this risk, including spontaneous reports, and the plausible mechanism of action, the product information for medicines available in the UK will be amended to include new warnings for respiratory depression.

<sup>1</sup> [Gomes T and others.](#)  
Ann Intern  
Med. 2018;  
169: 732–34.

The review identified a small number of worldwide cases of respiratory depression without an alternative cause or underlying medical conditions. In these cases, respiratory depression had a temporal relationship with the initiation of pregabalin or dose increase. Other cases were noted in patients with risk factors or underlying medical history. The majority of cases reviewed were reported in elderly patients.

Similar warnings are already in place for gabapentin (Neurotonin), the other gabapentinoid medicine available in the UK – see [Drug Safety Update, October 2017](#).

### **Patients at increased risk**

Adjustments in dose or dosing regimen might be necessary in patients at increased risk of experiencing this severe adverse reaction, including patients:

- with compromised respiratory function or respiratory disease
- with neurological disease
- with renal impairment
- using concomitant CNS depressants
- older than 65 years

The patient information leaflet that accompanies pregabalin is being updated to include warnings about breathing problems. The leaflet advises patients to seek medical help if they experience any trouble breathing or are taking shallow breaths related to their medicine. Pregabalin clearance is directly proportional to creatinine clearance, and dose reductions in patients with compromised renal function should be individualised – see [the posology section of the Summary of Product Characteristics](#).

### **UK Yellow Card Reports**

In the UK, from January 2014 to 31 December 2020, we have received 122 reports of respiratory depression or dyspnoea associated with pregabalin to the Yellow Card scheme. 80 of 122 cases report a CNS depressant as either a co-suspect or concomitant medicine alongside pregabalin. Co-administered CNS depressant medicines include opioids, benzodiazepines, and gabapentin.

### **Gabapentinoids: reminder of advice for dependence and addiction**

As of 1 April 2019, pregabalin and gabapentin are controlled under the Misuse of Drugs Act 1971 as Class C substances and scheduled under the Misuse of Drugs Regulations 2001 as Schedule 3 – see [Drug Safety Update, April 2019](#).

Existing advice asks healthcare professionals to evaluate patients carefully for a history of drug abuse before prescribing pregabalin and gabapentin and to observe patients for development of signs of abuse and dependence.

As for all medicines, patients should be given information on the expected benefits and potential risks of pregabalin and gabapentin, including through provision of the Patient Information Leaflet at dispensing. Prescribers should be aware of all medicines (including any over-the-counter products or illicit drugs) patients are taking to minimise or avoid drug interactions.

## 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, SystemOne, Vision, MiDatabank, and Ulysses)

If a patient experiences any side effect related to dependence to a medicine or is recognised by the prescriber to be dependent, we encourage prescribers, patients, or carers to report this to the MHRA with the term 'dependence'. Use of this specific term will assist the MHRA to monitor the rates reported in the UK and therefore to further protect public health.

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 or medical device and diagnostic adverse incidents used in coronavirus (COVID-19) 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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## **Alkindi (hydrocortisone granules): risk of acute adrenal insufficiency in children when switching from hydrocortisone tablet formulations to granules**

When children receiving replacement therapy for adrenal insufficiency are being switched from hydrocortisone tablets to Alkindi granules, parents or carers should be informed of the need to be extra vigilant for symptoms of adrenal insufficiency.

### **Advice for healthcare professionals:**

- adrenal crisis has been reported in an infant who was switched from hydrocortisone soluble tablets to Alkindi (hydrocortisone granules)
- acute adrenal insufficiency could also occur when switching from crushed hydrocortisone tablets to Alkindi granules due to a potential risk of inaccurate dosing
- if the child is switching to Alkindi granules, parents or carers should be advised to carefully observe the child during the first week for symptoms of adrenal insufficiency, such as tiredness, floppiness, unstable temperature, headache and vomiting
- counsel parents or carers on what to do if the child develops symptoms of adrenal insufficiency, including the need to seek immediate medical advice and administer extra doses of Alkindi if appropriate
- if a child requires additional doses during the first week after switching to Alkindi, a long-term increase in the daily dose of Alkindi should be considered
- report suspected adverse drug reactions associated with hydrocortisone medicines on a [Yellow Card](#)

### **Case of severe adrenal insufficiency**

[Alkindi hydrocortisone granules](#) are indicated for replacement therapy of adrenal insufficiency in infants, children and adolescents (from birth to age 18 years).

A single case has been reported of an infant developing severe adrenal insufficiency when switched from hydrocortisone soluble tablets to Alkindi granules. The child experienced an adrenal crisis approximately 48 hours after starting Alkindi. The child had no evidence of transient illness such as severe infection and there was no indication that Alkindi had been administered incorrectly, nor any symptoms of malabsorption.

Due to the low solubility of hydrocortisone, preparing hydrocortisone soluble tablets not in accordance with the manufacturer's instructions may risk variable dosing and make conversion to other forms of hydrocortisone in younger children difficult.

Similarly, variable dosing could also potentially occur with the use of crushed hydrocortisone tablets in younger children, resulting in the starting dose of Alkindi not corresponding to the actual dose of hydrocortisone previously being taken.

## **New safety advice to parents or carers**

When converting children from oral hydrocortisone formulations, such as soluble or crushed tablets, to Alkindi granules, parents or carers should be advised to observe the child carefully in the first week after the switch. This is especially important in younger children less able to communicate symptoms of adrenal insufficiency.

The prescriber should instruct parents and carers what to do if the child develops any symptoms of adrenal insufficiency such as tiredness, floppiness, temperature instability, headache, or vomiting. This could include giving the child extra doses of Alkindi, in accordance with the recommendations in the [Summary of Product Characteristics](#). In addition, carers and patients should be advised to seek immediate medical advice if such symptoms occur.

If a child requires additional dosing during the first week after transferring from oral hydrocortisone formulations, such as crushed or soluble tablets, to Alkindi, an increase in the daily dose of Alkindi should be considered.

These risks have been considered by a European safety review and the product information for Alkindi will be updated with appropriate advice. A letter has been sent to healthcare professionals.

## **Report on a Yellow Card**

Suspected adverse drug reactions associated with hydrocortisone should be reported to us on a Yellow Card.

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, treatment dates, and product brand name.

Report suspected side effects to medicines, vaccines or medical device and diagnostic adverse incidents used in coronavirus (COVID-19) 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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## **Medicines in pregnancy and breastfeeding: new initiative for consistent guidance; report on optimising data for medicines used during pregnancy**

Information on the newly launched Safer Medicines in Pregnancy and Breastfeeding Consortium and a new report on optimising data on medicines used during pregnancy.

### **New Safer Medicines in Pregnancy and Breastfeeding Consortium**

On 11 January 2021, the MHRA and partner organisations launched a major new initiative to ensure pregnant and breastfeeding women can make informed decisions about their healthcare, particularly relating to the medicines they take.

The [Safer Medicines in Pregnancy and Breastfeeding Consortium](#) is a partnership of 16 leading organisations working together to improve the health information available to women who are thinking about becoming pregnant, are pregnant, or are breastfeeding. The partnership includes the NHS, regulators, and leading third sector and charitable organisations.

To support this work, we ask healthcare professionals to report important inconsistencies in UK advice on use of individual or classes of medicines used in pregnancy or breastfeeding via the address on the [consortium's webpage](#).

For more information on the consortium and its information strategy see the [Guidance page](#). We also have a new guidance page to assist users in finding MHRA [information and projects related to medicines use in pregnancy and breastfeeding](#).

### **Optimising data on medicines used during pregnancy**

The launch of the consortium coincides with the publication of a [Report of the Commission on Human Medicines Expert Working Group on Optimising Data on Medicines used During Pregnancy](#).

The report provides recommendations on ways in which data on medicines used in pregnancy and breastfeeding can be better collected and made available for analysis. This will enable more robust evidence to be generated through research and will be important in helping to develop clear and consistent advice about medicines used during pregnancy and breastfeeding.

Recommendations of the report include the better capture and linking of existing data, exploring new ways to collect relevant information on exposure to medicines during pregnancy and breastfeeding, and improving access to and quality of data to further enable research.

### **Report on a Yellow Card**

Please continue to report any suspected adverse drug reactions (ADRs) associated with [medicines taken during pregnancy or breastfeeding](#) experienced by the woman and any suspected effects on the baby or child.

All patients, caregivers, and healthcare professionals can report a Yellow Card when they suspect a medication used during pregnancy has caused an adverse reaction or adverse pregnancy outcome.

When reporting ADRs related to medicines used in pregnancy, the following information is particularly valuable for our assessment of the report:

- Timings of when the medicine was taken during the pregnancy
- The outcome of the pregnancy (when known)
- Details of any relevant family history, including any obstetric history
- Detailed clinical descriptions and the results of any imaging (for example, scans), or laboratory tests

Please include any other relevant information; including other medications or substances taken during the pregnancy, as well as folic acid intake.

Report Yellow Cards 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, treatment dates, and product brand name.

Report suspected side effects to medicines, vaccines or medical device and diagnostic adverse incidents used in coronavirus (COVID-19) 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](#).

*Article citation: Drug Safety Update volume 14, issue 7: February 2021: 4.*

## COVID-19 vaccines and medicines: updates for February 2021

In January 2021, we included the latest advice for the [Pfizer/BioNTech and COVID-19 Vaccine AstraZeneca](#). Here we include a summary of key MHRA advice issued since the publication of the January 2021 edition of Drug Safety Update and up to 16 February 2021.

### Yellow Card reporting data confirms safety of vaccines

In February 2021 we published the first summaries of the [Yellow Card reporting for the COVID-19 vaccines](#) being used in the UK. The data confirms that the vast majority of reported side effects are mild and short-lasting, reflecting a normal immune response to vaccines – including a sore arm and fatigue.

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 take every report of a suspected adverse reaction seriously and encourage everyone to report through the [Coronavirus Yellow Card reporting site](#).

### Pfizer/BioNTech vaccine: advice on six doses

On 26 January 2021, information for the Pfizer vaccine was amended from containing five doses to six doses when the [latest guidance for Healthcare Professionals](#) is followed.

### Moderna vaccine authorised for use

On 8 January 2021, the [COVID-19 Vaccine Moderna](#) was approved for use by the MHRA after meeting required safety, quality, and effectiveness standards. This followed a rigorous, detailed scientific review by the MHRA's expert scientists and clinicians and on the basis of the advice of its scientific, independent advisory body, the [Commission on Human Medicines \(CHM\)](#).

See [Information for Healthcare Professionals](#) and [Information for UK Recipients](#), which also includes subsequent updates to information on the quantity of doses in the vials.

### Update on conditions of regulatory authorisation

The MHRA has updated the 'Conditions' for the three vaccines ([Pfizer/BioNTech](#), [AstraZeneca](#), [Moderna](#)) authorised under Regulation 174 to clarify how the approval interacts with the broader regulatory context.

### COVID-19 Therapeutic Alerts

On 1 February 2021, the Chief Medical Officer (CMO) issued a COVID-19 Therapeutic Alert to recommend that NHS trusts/health boards consider prescribing either [tocilizumab](#) or [sarilumab](#) to hospitalised patients with COVID-19 pneumonia. Please see the [Central Alerting System website for more information and subsequent alerts](#).

On 28 January 2021, the CMO issued a COVID-19 Therapeutic Alert to inform that antimicrobials (azithromycin and doxycycline) were not beneficial in the management of COVID-19 patients. Please see the [Central Alerting System website for more information](#).

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# Letters and drug alerts sent to healthcare professionals in January 2021

## Letters

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

- [Voriconazole 200 mg powder for solution for infusion: Interim supply arrangements to mitigate supply disruption](#)
- [Esmya \(ulipristal acetate\) 5mg: Indications for uterine fibroids restricted due to concerns of severe liver injury](#)
- [Accord Thalidomide 50mg hard capsules: Pregnancy Prevention Programme to minimise the risk of teratogenicity](#)

Thalidomide is a powerful human teratogen that can cause severe and life-threatening birth defects and must not be used during pregnancy. All thalidomide medicines must be used within a pregnancy prevention programme (PPP). To facilitate the implementation of the PPP during the coronavirus (COVID-19) pandemic, we have published [temporary guidance](#).

For letters relating to medicines with a centralised European license with respect to Northern Ireland, see [the European Medicines Agency website](#).

## Drug alerts

[Company led medicines recall: Instanyl 100mcg nasal spray solution \(EU/1/09/531/015\)](#).

Issued 18 January 2021. A single batch of Instanyl 100mcg nasal spray solution is being recalled due to cracked vials identified during bulk inspection and release testing. There is a low potential for cracking of the glass vials and consequent microbial contamination and the batch is being recalled as a precautionary measure. Remaining stock of these batches should be quarantined and returned for replacement stock where available.

[Company led medicines recall: Respreeza 1,000 mg powder and solvent for solution for infusion \(EU/1/15/1006/001\)](#).

Issued 20 January 2021. Specific batches of Respreeza 1,000mg powder and solvent for infusion have been identified to be at risk of microbial contamination due to failure of HEPA filters at the manufacturing site. All remaining stock should be quarantined and returned.

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