

# Drug Safety Update



# MHRA

## 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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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.



MHRA is accredited by NICE to provide Drug Safety Update. Further information can be found on the NICE Evidence Search portal:  
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## Summary

First, we ask healthcare professional to use the new dedicated Yellow Card reporting site to report suspected adverse drug reactions to medicines and incidents with medical devices related to coronavirus (COVID-19). Reporting will enable the MHRA to rapidly identify new and emerging side effects and medical device safety issues, including for medicines taken by patients to manage long-term or pre-existing conditions. For details see page 2.

Next, we make you aware of guidance published to support pregnancy prevention requirements for valproate medicines and for immunomodulatory drugs (thalidomide, lenalidomide, and pomalidomide) during the COVID-19 pandemic (pages 5 and 6)

Finally, see page 7 for recent letters and drug alerts sent to healthcare professionals in the UK, including recalls for 300 microgram and 500 microgram Emerade adrenaline auto-injectors due to an error in one component of the auto-injector believed to cause some pens to fail to activate and deliver adrenaline.

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## Coronavirus (COVID-19): new dedicated Yellow Card reporting site for medicines and medical devices

Reporting to the new site will enable the MHRA to rapidly identify new and emerging side effects and medical device incidents in COVID-19 treatment, including side effects for medicines taken by patients to manage long-term or pre-existing conditions.

### Actions for healthcare professionals:

- be vigilant for any potential safety issues associated with medicines and medical devices used in COVID-19 treatment
- use the [new dedicated COVID-19 Yellow Card reporting site](#) to report:
  - all suspected side effects associated with any medicine used in patients with confirmed or suspected COVID-19, including medicines to manage long-term or pre-existing conditions, and unlicensed medicines or medicines used off-label
  - medical devices incidents related to COVID-19
- reporting of incidents in clinical trials should follow the trial protocol
- for non-COVID related side effects from medicines please continue to report through the standard [Yellow Card website](#), which can also be used for defective or falsified medicines and medical devices (including fake COVID-19 testing kits)
- any medical device incidents should be reported to [Health Facilities Scotland](#) in Scotland and to the [Northern Ireland Adverse Incident centre](#) in Northern Ireland

### Launch of COVID-19 Yellow Card reporting site

The Yellow Card scheme is vital in helping the MHRA monitor the safety of all healthcare products in the UK to ensure they are acceptably safe for patients and users.

The MHRA has launched a dedicated [COVID-19 Yellow Card reporting site](#) for healthcare professionals, patients, and caregivers to report easily:

- suspected side effects associated with any medicine used in patients with confirmed or suspected COVID-19, including
  - medicines to manage long-term or pre-existing conditions
  - unlicensed medicines or medicines used off-label to treat COVID-19
- incidents involving medical devices used in relation to COVID-19, including adverse incidents with equipment, diagnostic testing kits and software/apps

In the future, the dedicated site will enable reporting of suspected side effects associated with new medicines or vaccines authorised to treat and prevent COVID-19.

Report at [coronavirus-yellowcard.mhra.gov.uk](https://coronavirus-yellowcard.mhra.gov.uk)

## **What should I report?**

### ***Medicines COVID-19 reporting***

At present, there are no vaccines and no medicines authorised to prevent or treat COVID-19 in the UK. However, several treatments authorised for other diseases are being used in patients with COVID-19, particularly in clinical trials. If a patient is in a clinical trial, reporting of suspected adverse reactions should follow the trial protocol.

Any suspected side effect to a medicine used in the treatment of COVID-19 can be reported via the COVID-19 Yellow Card reporting site. This includes off-label or unlicensed medicines that healthcare professionals and patients might be using to treat COVID-19.

In addition, please report all suspected side effects associated with any of the medicines being administered to patients in which COVID-19 is suspected or confirmed. This includes any medicines taken by patients to manage long-term or pre-existing conditions. It is also important for any suspected side effects in children and adolescents with confirmed or suspected COVID-19 to be reported via the new site, as for adults.

When reporting, patients and healthcare professionals are encouraged to provide as much information as possible, including whether COVID-19 infection has been confirmed through testing.

Suspected adverse drug reactions for medicines that do not appear in the preselected drop-down list can be reported using the 'Medicines' option at the end of the list.

### ***Medical devices COVID-19 reporting***

This includes medical devices such as ventilators and respiratory support devices, testing kits, certain personal protective equipment that are [classified as medical devices](#), and software/apps.

For medical devices, a description of the incident should be provided, including whether there was an associated injury.

Please note there are different ways for healthcare professionals to report a problem with a medical device in [Scotland](#) or [Northern Ireland](#). For more information see [here](#).

### ***Why report?***

Reporting will enable the MHRA to rapidly identify new and emerging side effects and medical device issues associated with new or repurposed medicines and medical devices (including diagnostic tests) to combat COVID-19.

Understanding of the COVID-19 virus is limited, including possible interactions with medicines patients might be taking. By reporting suspected side effects of any medicines used in the context of COVID-19, healthcare professionals and patients can provide valuable evidence to inform decisions on the safe and effective use of medicines as the pandemic evolves.

## **What happens to my report?**

Yellow Card reports submitted in relation to medicines or medical devices used in COVID-19 treatment are used alongside other scientific safety information such as clinical trials, scientific literature, other safety databases, and studies. The MHRA are closely monitoring any new or emerging safety signals in relation to medicines or medical devices used in or for patients with COVID-19. Where necessary, the MHRA can take appropriate regulatory action and communicate any associated risks.

All information provided will be kept secure and confidential – see the [privacy policy online](#).

## **Support for reporting Yellow Cards – please continue to report all adverse incidents for medicines and medical devices**

We appreciate healthcare professionals are under pressure at this challenging time, but reporting remains essential both to understand the impact of COVID-19 on existing medicines and medical devices, and to identify new safety issues.

Non-COVID-19 related suspected side effects to medicines or concerns about medical devices (in England), defective or falsified products (including fake COVID-19 testing kits), and e-cigarettes should still be reported to the standard [Yellow Card website](#). Please note, any medical device incidents should be reported to Health Facilities Scotland in Scotland and to the Northern Ireland Adverse Incident Centre in Northern Ireland.

During the pandemic, Yellow Card reporting for suspected side effects has decreased, especially from healthcare professionals. The Yellow Card scheme continues to operate as usual and safety concerns should still be reported to the MHRA. Further information on Yellow Card reporting or guidance for healthcare professionals during the pandemic please see our [website](#).

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## Valproate Pregnancy Prevention Programme: temporary advice for management during coronavirus (COVID-19)

[Guidance](#) has been published to support initiation of valproate in female patients and for annual review and pregnancy testing during the coronavirus pandemic.

### Temporary guidance for specialists

Valproate is harmful if used in pregnancy. Children exposed to valproate in utero have a very high risk for congenital malformations (10% risk) and neurodevelopmental disorders (30–40% risk). Valproate medicines (for any indication) are therefore contraindicated in girls and women of childbearing potential unless the conditions of the [Pregnancy Prevention Programme \(PPP\)](#) are fulfilled.

On 6 May we published [guidance for specialists](#) to support adherence to the pregnancy prevention requirements for girls (of any age) and women of childbearing potential taking valproate during the pandemic, particularly patients who are shielding due to other health conditions.

**See MHRA guidance at [gov.uk/guidance/valproate-pregnancy-prevention-programme-temporary-advice-for-management-during-coronavirus-covid-19](https://www.gov.uk/guidance/valproate-pregnancy-prevention-programme-temporary-advice-for-management-during-coronavirus-covid-19)**

The valproate PPP states that patients on valproate who have experienced menarche must have a review at least annually with the prescribing specialist to reassess the need for valproate therapy and consider alternative treatment options. Annual reviews should not be delayed due to the pandemic.

No woman or girl should stop taking valproate without first discussing it with their doctor.

Guidance will be updated once these temporary recommendations are no longer considered necessary.

### Call for reporting

Valproate medicines are black triangle medicines and all suspected adverse drug reactions should be reported to the MHRA.

Healthcare professionals, patients, and caregivers are asked to submit all suspected side effect reports using 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](#)
- through some clinical IT systems (EMIS/SystmOne/Vision/MiDatabank)

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## Immunomodulatory drugs and pregnancy prevention: temporary advice for management during coronavirus (COVID-19)

[Guidance](#) has been published about thalidomide, lenalidomide, and pomalidomide and the use of remote consultations and home pregnancy testing for patients taking them during COVID-19.

### Temporary guidance

Thalidomide (Thalidomide Celgene), lenalidomide (Revlimid) and pomalidomide (Imnovid) are teratogenic immunomodulatory drugs with a pregnancy prevention programme.

To enable the shielding of patients who are receiving these medicines during the coronavirus (COVID-19) pandemic, the manufacturer (Celgene) has issued a [letter to healthcare professionals](#) informing them of temporary modifications to the pregnancy prevention programmes to facilitate remote consultations, where clinically appropriate.

**See MHRA guidance (21 May 2020) at [gov.uk/guidance/immunomodulatory-drugs-temporary-pregnancy-prevention-guidance-during-coronavirus-covid-19](https://www.gov.uk/guidance/immunomodulatory-drugs-temporary-pregnancy-prevention-guidance-during-coronavirus-covid-19)**

### Call for reporting

Healthcare professionals, patients, and caregivers are asked to submit all suspected side effect reports using 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](#)
- through some clinical IT systems (EMIS/SystemOne/Vision/MiDatabank)

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# Letters and drug alerts sent to healthcare professionals in April 2020

## **Emerade: recall of 300 and 500 microgram adrenaline auto-injectors**

- [Class 2 Medicines Recall: Emerade 300 micrograms solution for injection in pre-filled syringe, PL 33616/0014 \(EL\(20\)A/20\)](#) – issued 7 April 2020
- [Class 2 Medicines Recall: Emerade 500 micrograms solution for injection in pre-filled syringe, PL 33616/0014 \(EL\(20\)A/20\)](#) – issued 18 May 2020

Pharmaswiss Česká republika s.r.o. (an affiliate of Bausch & Lomb UK Limited) is recalling all unexpired batches of Emerade 300 and 500 microgram auto-injectors (also referred to as pens) from patients due to an error in one component of the auto-injector believed to cause some pens to fail to activate and deliver adrenaline. These alerts follow the recall for Emerade 150 microgram auto-injectors on 4 March 2020.

A patient letter is provided with the alert to be provided to all patients and carers, as appropriate, who have been prescribed Emerade auto-injectors.

While Emerade remains unavailable, alternative devices should be considered for patients. There is evidence to suggest that a single EpiPen (300 microgram) or Jext (300 microgram) pen will be a suitable replacement for a single Emerade 500 microgram pen. This is based on recently available results from a study which compared blood levels of adrenaline following injection of Emerade 500 microgram pens with those following EpiPen 300 microgram or Jext 300 microgram pens.

## **Safety letters**

In April 2020, the following letters were sent or provided to relevant healthcare professionals about medicines safety issues:

- [ReQuip \(ropinorole hydrochloride\) tablets: important changes to the colour of carton and blister packs](#)
- [Cyproterone acetate: restrictions in use of due to risk of meningioma](#)
- [Temporary modifications to the Pregnancy Prevention Programmes for thalidomide \(Thalidomide Celgene\), lenalidomide \(Revlimid ▼\) and pomalidomide \(Imnovid ▼\)](#) – see article on page 6

## **Supply-related letters – April 2020**

In April 2020, the following letters were sent or provided to relevant healthcare professionals to support the supply of medicines in the UK:

- [Noradrenaline \(Norepinephrine\) 4mg/4ml concentrate for solution for infusion: temporary supply of a different presentation in market and changes to the instructions](#)
- [Suxamethonium: temporary foreign label product - Label and patient information leaflet \(PIL\) is in Portuguese](#)

- [Diprivan emulsion \(Aspen propofol\): Interim supply to Mitigate Supply Disruption of 10mg/ml \(1%\) Panamanian Stock; 20mg/ml \(2%\) Brazilian stock; 10mg/ml \(1%\) stock with Chinese tray label](#)
- [Propofol 10mg/ml \(1%\) Emulsion for Injection/Infusion Interim Supply of Sweden Stock to Mitigate Supply Disruption](#)
- [Midazolam 1mg/ml Solution for Injection or Infusion \(Midazolam\): supply disruption](#)
- [Esmeron \(rocuronium bromide\) 10mg/ml solution for injection: supply of some packs originally for Australia](#)
- [Ioversol \(Optiray\) 300 mg Iodine/ml: 100ml syringe and bottle shortage](#)
- [Polivy ▼ \(polatuzumab vedotin\): 140mg powder for concentrate for solution for injection: temporary plastic vial flip-off cap colour](#)
- [Adoport \(tacrolimus\): limited number of packs with Italian foil - for 0.75mg and 5mg capsules and for 1 mg capsules](#)

#### **Supply-related letters – May 2020**

In May 2020 (up to 15 May), the following letters were sent or provided to relevant healthcare professionals to support the supply of medicines in the UK:

- [Ativan 4mg/ml Solution for Injection \(Lorazepam\): Temporary supply of a different presentation and changes to the instructions - US product](#)
- [Calrencia, 100mmol/l, solution for infusion \(calcium chloride\): Interim Supply of stock from the below countries to Mitigate Supply Disruption](#)
- [Sirturo ▼ 100 mg \(bedaquiline\): Interim Supply of Irish Stock to Mitigate Supply Disruption](#)
- [Pancuronium bromide 2mg/ml: Temporary supply of alternative US product 10mg/10ml \(1mg/ml\) multiple-dose fliptop glass vials](#)

#### **Other drug alerts issued in April 2020**

[Class 4 Medicines Defect Information: Glaxosmithkline Consumer Healthcare \(UK\) Trading Limited, various products, EL\(20\)A/22](#). Issued 20 April 2020. Due to a

machinery defect with the printing line, a small number of packs may not have the batch number and expiry date printed on the outer carton

[Class 4 Medicines Defect Information: Levofloxacin 500mg Tablets, PL 00289/1047 EL \(20\)A/21](#). Issued 16 April 2020. The Product Code/GTIN (PC) number found on the listed batches is incorrect

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