

# 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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## Contents

<b>Ingenol mebutate gel (Picato ▼): increased incidence of skin tumours seen in some clinical studies</b>	page 2
<b>Nivolumab (Opdivo): reports of cytomegalovirus (CMV) gastrointestinal infection or reactivation</b>	page 4
<b>Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions</b>	page 6
<b>Adrenaline auto-injectors: recent action taken to support safety</b>	page 8
<b>Letters and drug alerts sent to healthcare professionals in September 2019</b>	page 11
<b>Medical Device Alerts issued in September 2019</b>	page 13

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 prescribers of ingenol mebutate gel (Picato ▼) for actinic keratosis that an in-depth review of benefits and risks has started following some studies showing an increased incidence of skin tumours (page 2). Ingenol mebutate gel should be used with caution in patients who have had skin cancer in the past and all patients should be reminded of the need for vigilance for any skin lesions.

Second, we advise prescribers of nivolumab about cases of cytomegalovirus (CMV) gastrointestinal infection or reactivation (page 4). Patients on nivolumab who present with diarrhoea or other symptoms of colitis, and those who do not respond to steroid treatment for immune-related colitis, should be investigated to exclude other causes, including infections such as cytomegalovirus (CMV).

Third, we remind of the importance of using the appropriate estimate of renal function when prescribing medicines in patients with renal impairment. For most patients and most medicines, estimated Glomerular Filtration Rate (eGFR) is an appropriate measure of renal function for determining dosage adjustments in renal impairment. However, in some circumstances, the Cockcroft-Gault formula should be used to calculate creatinine clearance (see page 6).

Finally, see page 8 for a summary of recent advice issued about adrenaline auto-injectors. A drug alert has been issued about activation failures with Emerade adrenaline auto-injectors and letters sent about extension of use-by dates by 4 months for certain batches of EpiPen and Jext adrenaline auto-injectors.

Please continue to report suspected adverse reactions and safety concerns regarding medicines, vaccines, medical devices, and electronic cigarettes to the [Yellow Card Scheme](#). Your report helps the MHRA to protect public health.

[drugsafetyupdate@mhra.gov.uk](mailto:drugsafetyupdate@mhra.gov.uk)

## **Ingenol mebutate gel (Picato ▼): increased incidence of skin tumours seen in some clinical studies**

Advise patients treated with ingenol mebutate gel to be vigilant for new skin lesions and to seek medical advice immediately should any occur. Use with caution in patients with a history of skin cancer.

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

- several clinical studies have shown an increased incidence of benign and malignant skin tumours in patients using ingenol mebutate gel when compared to those using a vehicle only or an alternative treatment
- advise patients using ingenol mebutate gel to be vigilant for the development of any new skin lesions within the treatment area and to seek medical advice immediately should any occur
- use with caution in patients with a history of skin cancer
- report any suspected adverse drug reactions associated with Picato ▼ to the [Yellow Card Scheme](#)

### **Safety review initiated and new warnings added**

Ingenol mebutate gel is indicated for the treatment of non-hyperkeratotic, non-hypertrophic actinic keratosis in adults (ie, when the outer layer of the skin affected is not thickened or raised).

[Letter to healthcare professionals](#)

[European Medicines Agency. Announcement of the start of a review of Picato. 6 Sept 2019.](#)

An in-depth European review into the [safety of ingenol mebutate](#) has begun following data from several studies showing an increased number of skin cancer cases in patients using ingenol mebutate gel.

A warning about the risk of keratoacanthoma was previously included in the product information. Following a separate recent review of safety data, the product information is being updated to include a warning about reports of basal cell carcinoma, Bowen's disease, and squamous cell carcinoma, and to advise that ingenol mebutate gel should be used with caution in patients with a history of skin cancer. A letter has also been sent from the manufacturer of Picato to UK prescribers and dispensers to inform them of this risk.

Patients should be made aware of this risk and be provided with the current [patient information leaflet for Picato](#), which already includes information about the need for patients to be vigilant for new or changing lesions. Patients should be alert for changes to the treatment area and immediately talk to their doctor if any new scaly red patches, open sores, or elevated or warty growths occur.

### **Studies of skin cancer risk**

The potential for ingenol mebutate gel to induce skin cancer was considered during the initial licence application, based on the purported mechanism of action and findings from an animal study. Overall, the potential for tumour promotion was considered low but the manufacturer was requested to carry out a 3-year safety study, [LP0041-63](#), to assess the risk of skin cancer, including squamous cell carcinoma.

In 2017, as a result of data from a phase 2 trial ([LP0105-1020](#)) comparing ingenol mebutate gel to vehicle only (gel without the active ingredient), the product information for Picato was updated to reflect an excess of benign skin tumours (keratoacanthoma) seen in the ingenol mebutate arm.

The preliminary results of the ongoing 3-year safety study ([LP0041-63](#)) showed an increased incidence of squamous cell carcinoma with ingenol mebutate versus a comparator treatment (imiquimod cream).

in addition, a meta-analysis of 4 studies of the related substance ingenol disoxate (a non-licensed treatment investigated for actinic keratosis) showed a statistically significant increase in skin cancer at 14 months in the active treatment group compared to vehicle gel when analysing the incidence for all tumour types together, including basal cell carcinoma, Bowen's disease, and squamous cell carcinoma.

Other studies have not shown an increased incidence of skin tumours with ingenol mebutate. The [review by the European Medicines Agency](#) will consider all relevant data for the risk of skin cancer, including from ongoing studies, and the implications for the balance of benefits and risks of ingenol mebutate.

### **UK reports of skin cancers during use of ingenol mebutate gel**

In the past year, approximately 32,450 packs of ingenol mebutate gel were dispensed in the UK.<sup>1</sup> Since 2013 and up to August 2019, we have received reports of 9 cases of skin malignancies in the UK associated with ingenol mebutate, including cutaneous squamous cell carcinoma (including 1 metastatic case), atypical fibroxanthoma, neuroendocrine carcinoma of the skin, Bowen's disease, and basosquamous carcinoma. These reports were received in both clinical trial and post-marketing settings.

1. Data derived from IQVIA MIDAS Q3 2018 to Q2 2019, by the MHRA, September 2019.

### **Report any suspected adverse drug reaction**

Picato is subject to additional monitoring. Healthcare professionals are asked to report any suspected adverse drug reactions (ADRs) to drugs under additional monitoring to the Yellow Card Scheme.

It is easiest and quickest to report ADRs online 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.

*Article citation: Drug Safety Update volume 13, issue 3: October 2019: 1.*

## **Nivolumab (Opdivo): reports of cytomegalovirus (CMV) gastrointestinal infection or reactivation**

Patients on nivolumab who present with diarrhoea or other symptoms of colitis, and those who do not respond to steroid treatment for immune-related colitis, should be investigated to exclude other causes, including infections such as cytomegalovirus (CMV).

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

- colitis is known to occur commonly in patients treated with nivolumab; advise patients to contact their healthcare professional immediately at the onset of symptoms of colitis (including diarrhoea, blood in stools, or abdominal pain)
- if patients on nivolumab present with diarrhoea or colitis, investigate possible causes, including infections; perform a stool infection work-up and screen for cytomegalovirus (CMV)
- for patients with immune-related colitis that is corticosteroid refractory, use of an additional immunosuppressive agent should only be considered if other causes are excluded using appropriate laboratory tests and additional examinations (including screening for CMV using viral PCR on biopsy, and for other viral, bacterial, and parasitic causes)
- report suspected adverse drug reactions associated with nivolumab to the [Yellow Card Scheme](#)

### **Review of reports of CMV associated with nivolumab**

Nivolumab ([Opdivo](#) ▼) is an immune checkpoint inhibitor used in the treatment of various cancers. It is indicated as monotherapy or in combination with ipilimumab. Ipilimumab (Yervoy) has also been associated with CMV gastrointestinal infection or reactivation – see [January 2019, Drug Safety Update](#). As of July 2019, the worldwide cumulative patient exposure to nivolumab as monotherapy or combination therapy is estimated to be 430,000 patients.<sup>1</sup>

A European review of spontaneous and clinical trial reports received up to 31 August 2018, identified 20 serious cases worldwide suggestive of cytomegalovirus (CMV) infection or reactivation with nivolumab monotherapy. A further 8 cases were reported of either CMV infection or CMV hepatitis associated with nivolumab and ipilimumab combination therapy. Of the total 28 serious cases with nivolumab and nivolumab plus ipilimumab, 18 were suspected to be gastrointestinal CMV infection (10 cases for nivolumab and 8 cases for nivolumab plus ipilimumab).

The 20 serious cases of CMV infection or reactivation with nivolumab monotherapy described patients who experienced CMV infection (n=12), CMV enterocolitis (n=3), CMV test positive (n=3), and CMV colitis (n=2). Most cases were in men (n=17) and age of patients ranged from 40 years to 81 years (median age 67 years). The time to onset, where stated, from the first dose of nivolumab ranged from 15 to 205 days (median onset 114 days; based on 12 reports).

1. Provided to the MHRA by Bristol-Myers Squibb. Data on File, Aug 2019.

Where reported, the outcomes were fatal in 4 reports (3 deaths listed CMV infection and one listed CMV colitis), recovered in 6 reports, and 1 report each of recovered with sequelae and recovering (it is unknown whether the drug was stopped in the reported cases). Of the 4 fatal reports, 1 report of fatal CMV-induced colitis and haemorrhage associated with nivolumab was received in the UK. The patient was being treated with nivolumab for classical Hodgkin's lymphoma. The patient had a past medical history of colitis, rectal cancer, and large bowel removal.

### **Risk of severe diarrhoea and colitis with nivolumab**

Diarrhoea is a very common adverse drug reaction associated with nivolumab. In clinical trials of nivolumab monotherapy, 13% of patients had diarrhoea, colitis, or frequent bowel movements. Most cases were mild to moderate (grade 1 or 2), but severe (grade 3) cases were reported in 21% of these patients. No life-threatening or fatal cases (grade 4 or 5) were reported in these studies.

Median time to onset of diarrhoea was 1.8 months (range 0–26.6). Cases resolved in nearly all patients (88%) with a median time to resolution of 2 weeks (advice on management of colitis was included in the study protocol). Gastrointestinal reactions can also occur when nivolumab is used in combination with ipilimumab, see the [Summary of Product Characteristics](#).

Management recommendations for diarrhoea or colitis are provided in the [Summary of Product Characteristics](#) and are based on severity of symptoms. Diarrhoea or colitis occurring after initiation of nivolumab must be promptly evaluated to exclude infectious or other alternate causes. For severe or life-threatening (grade 3 and 4) diarrhoea and immune-related colitis, nivolumab should be permanently discontinued and systemic high-dose intravenous corticosteroid therapy initiated.

In patients with immune-related colitis who are refractory to corticosteroids, the addition of an immunosuppressive agent should only be considered if other causes have been excluded, including CMV infection or reactivation.

### **Report any suspected adverse drug reactions**

Please continue to report any suspected adverse reactions to nivolumab via the [Yellow Card Scheme](#). Your report will help us safeguard public health.

*Article citation: Drug Safety Update volume 13, issue 3: October 2019: 2.*

## Prescribing medicines in renal impairment: using the appropriate estimate of renal function to avoid the risk of adverse drug reactions

For most patients and most medicines, estimated Glomerular Filtration Rate (eGFR) is an appropriate measure of renal function for determining dosage adjustments in renal impairment; however, in some circumstances, the Cockcroft-Gault formula should be used to calculate creatinine clearance (CrCl).

### Advice for healthcare professionals:

- MHRA has received reports and queries related to the choice of renal function estimate used when prescribing medicines for patients with renal impairment
- for most drugs and for most adult patients of average build and height, estimated Glomerular Filtration Rate (eGFR) should be used to determine dosage adjustments
- creatinine clearance (CrCl) should be calculated using the Cockcroft-Gault formula (see below) to determine dosage adjustments for:
  - direct-acting oral anticoagulants (DOACs)
  - patients taking nephrotoxic drugs (examples include vancomycin and amphotericin B)
  - elderly patients (aged 75 years and older)
  - patients at extremes of muscle mass (BMI <18 kg/m<sup>2</sup> or >40 kg/m<sup>2</sup>)
  - patients taking medicines that are largely renally excreted and have a narrow therapeutic index, such as digoxin and sotalol
- when dose adjustment based on CrCl is important and no advice is provided in the relevant BNF monograph, consult the Summary of Product Characteristics
- reassess renal function and drug dosing in situations where eGFR and/or CrCl change rapidly, such as in patients with acute kidney injury (AKI)

### Background

Estimated glomerular filtration rate (eGFR) and creatinine clearance (CrCl) are two estimates of renal function available to prescribers. Clinical laboratories routinely report renal function in adults based on eGFR normalised to a body surface area of 1.73 m<sup>2</sup>.

[The Renal Association: About eGFR](#)

For most drugs and most situations, eGFR is an acceptable estimate of renal function. However, eGFR can overestimate renal function compared with CrCl in some patient groups or clinical situations. This overestimation can result in patients receiving higher than recommended doses of their medicine in relation to their renal function.

### When to use estimated creatinine clearance

[BNF guidance on prescribing in renal impairment](#)

Existing [guidance from the BNF](#) advises prescribers to use calculated CrCl rather than eGFR when initiating or adjusting dose in people taking nephrotoxic drugs, elderly patients, and patients at extremes of muscle mass.

CrCl should also be considered for dosage adjustment of medicines that are substantially renally excreted and have a narrow therapeutic index.

In particular, CrCl should always be used to guide dose adjustment for direct-acting oral anticoagulants (DOACs; apixaban, dabigatran etexilate, edoxaban ▼, and rivaroxaban ▼). Use of eGFR for dosing of DOACs is known to increase risk of bleeding events as a consequence of overestimating renal function.

Other medicines that are largely renally excreted and have a narrow therapeutic index include digoxin and sotalolol.

### Calculation of creatinine clearance

It is normal to calculate CrCl based on the Cockcroft-Gault formula rather than measuring it via 24-hour urine collection. Applications such as [MDCalc](#) provide the ability to use adjusted body weight, ideal body weight, or actual bodyweight as appropriate when calculating the Cockcroft-Gault CrCl value.

### Examples of harm related to incorrect renal impairment calculations

MHRA has received reports and queries concerning suspected adverse drug reactions related to the use of eGFR rather than calculated CrCl when prescribing in patients with renal impairment. For example, we have received a Yellow Card report that provided sufficient detail to outline that the initial dosing of a DOAC in an elderly patient was based on eGFR values. The suspected adverse drug reaction was a significant bleeding event. Retrospective review of the renal function in terms of CrCl identified that the dose initiated was too high for the patient.

In addition, a recent cross-sectional study of data from 80 general practices in the UK<sup>1</sup> reviewed the application of prescribing recommendations in older people with reduced kidney function. Prescribing of drugs outside recommendations for use in patients with reduced kidney function was widespread for the 8 drugs analysed. The prescribed dose was too high for kidney function in up to 40% of people aged 65 years and older, and up to 80% of people aged 85 years and older. Use of eGFR overestimated kidney function for up to 28% of those aged 65 years and older, and up to 58% of those aged 85 years and older.

### Report suspected adverse drug reactions on a Yellow Card

Please continue to report relevant 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 via [iTunes Yellow Card](#) for iOS devices or via [PlayStore Yellow Card](#) for Android devices.

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## Adrenaline auto-injectors: recent action taken to support safety

Healthcare professionals should be aware of alerts and letters issued about adrenaline auto-injectors in September and October 2019. This article provides a summary of recent advice issued to healthcare professionals, including information to provide to patients, to support safe use of adrenaline auto-injectors.

### Advice for healthcare professionals:

#### Emerade – activation failure

- some Emerade pens have failed to activate, which could lead to an injection of adrenaline not being administered in cases of anaphylaxis
- contact patients (and their caregivers if necessary) in possession of Emerade adrenaline auto-injectors to advise them:
  - when an Emerade pen is used, it should be pressed very firmly against the thigh
  - if administration does not result in activation (see pictures of an activated vs in-activated pen in [letter for patients](#)), a second pen should be immediately used
  - If there is no improvement in a patient's condition and a further dose of adrenaline is needed, additional attempts should be made to administer a pen that has failed to activate, while awaiting the arrival of the emergency services
- any suspected defective adrenaline auto-injectors should be retained for investigation (see advice on reporting defects on page 9)

#### EpiPen and Jext – extended use beyond labelled expiry date

- to support adequate supply of adrenaline auto-injectors in the UK, an extension by 4 months of the use-by dates has been approved for:
  - [specific lots](#) of EpiPen 300 microgram adrenaline auto-injectors
  - [specific lots](#) of Jext 150 and 300 microgram adrenaline auto-injectors
- if patients are in possession of a device with an extended use-by date, advise them or their caregivers that it will continue to work safely within this extended period, but that a new auto-injector will need to be obtained at the end of the period stated
- advise patients to continue to check periodically the viewing window in the label of their device to ensure the liquid inside is clear and colourless; it should not be used if the liquid is discoloured

#### All adrenaline auto-injectors

- patients should continue to follow existing advice to carry 2 in-date pens with them at all times
- different brands of adrenaline auto-injector are not used in exactly the same way so specific training and advice for patients and carers is required before using each of the devices
- show patients and caregivers where to find the lot numbers on their device (on the end-flap of the box and if necessary, on the device label itself) and encourage them to sign up for the Expiry Alert Service of their specific adrenaline auto-injector on the manufacturer's website

See [Class 4 Medicines Defect Information – 3 October 2019](#)

[EpiPen. Letter for healthcare professionals.](#)

[Jext. Letter for healthcare professionals.](#)

### **Emerade: activation issue**

Emerade adrenaline auto-injectors are one of 3 brands available for emergency treatment of anaphylaxis. MHRA has notified Bausch and Lomb UK of reports that Emerade pens have failed to activate. An activation failure means that the needle is not released from the device and therefore the injection is not administered. Bausch and Lomb UK is conducting extensive investigations. It has been confirmed that some Emerade pens did not activate when normal force was applied, however the rate of occurrence could not be accurately estimated at the time the drug alert was issued.

See [Class 4 Medicines Defect Information alert](#) for more information.

MHRA advice, endorsed by the [UK Commission on Human Medicines](#), is that in the interests of patient safety it is important to allow patients to keep their Emerade pens, so they still have access to adrenaline.

Most Emerade pens in circulation will activate and deliver adrenaline as expected. However, it is important for patients to be aware of the possibility of activation failure so they can take measures to ensure they always have 2 pens with them and to be aware how to check that a pen has activated successfully. A [letter for healthcare professionals to provide to patients](#) is provided in the Drug Alert, issued 3 October 2019.

### **Emerade: update on previous alert on needle blockage**

On 11 July 2019, a [Class 4 Medicines Defect Information alert](#) was issued related to a risk of needle blockage. This issue is not related to the activation issue described above and is expected to be resolved in batches of Emerade released from July 2019, however, in the meantime affected devices will remain on the market and in patients' possession. There is a very small risk of inadvertent injection of small particles from the blocked needle into the bloodstream, or of a minor localised inflammatory response from injection of particles into muscle or subcutaneous tissue.

### **Reporting non-activated devices**

It is important to report all suspected adverse reactions or product quality defects to the [Yellow Card Scheme](#). For adrenaline auto-injectors, details of the strength and batch number should also be included to assist monitoring.

Any suspected non-activated or otherwise defective pens should be retained for investigation and the marketing authorisation holder contacted for advice (see [alert for contact details](#)).

### **Other available adrenaline auto-injectors in the UK**

In the UK there are 3 adrenaline auto-injector devices on the market, Emerade, manufactured by Pharmaswiss Česka republika s.r.o. (an affiliate of Bausch & Lomb UK); EpiPen, manufactured by Mylan; and Jext, manufactured by ALK-Abello. These different brands of adrenaline auto-injector are not used in exactly the same way and specific training and advice for patients and carers should be provided as appropriate. Training devices can be ordered via the websites of each brand.

There is also [an MHRA fact sheet with advice on the use of adrenaline auto-injectors](#), which patients or carers are encouraged to read. This advice is relevant to all 3 adrenaline auto-injectors available on the UK market.

### **Extended use beyond labelled expiry date**

Adrenaline auto-injectors are in short supply around the world, not only in the UK. The overall market supply of adrenaline auto-injectors is being monitored by the Department of Health and Social Care.

To ensure patients have access to adrenaline, MHRA has given permission for the manufacturers of EpiPen and Jext to extend the use-by dates of certain batches of medicines for 4 months after the listed expiry date. Letters with this information (for [EpiPen](#) and [Jext](#)) have been sent to allergists and allergy clinics, and information has been issued to patients registered for such alerts including via the Expiry Reminder Service. Further information may also be found on the UK websites of [EpiPen](#) and [Jext](#).

[EpiPen. Letter for healthcare professionals.](#)

[Jext. Letter for healthcare professionals.](#)

Not all batches are included in this extension. Patients must continue to adhere to the labelled expiry date on any auto-injector not covered by the lot numbers noted in the letter or on the websites.

Patients should be advised to seek a new adrenaline auto-injector before the end of the month stated in the extension (for example, if a pen lists expiry of December 2019, and the use-by date has been extended to April 2020, they can use the pen up to 30 April 2020).

Advise patients to continue to check periodically the viewing window in the label of their device to ensure the liquid inside is clear and colourless. Patients should not use the device if the liquid is discoloured and should return the device for replacement.

*Article citation: Drug Safety Update volume 13, issue 3: October 2019: 4.*

## Letters and drug alerts sent to healthcare professionals in September 2019

### Letters

#### ***Parenteral nutrition products for neonates and children below 2 years of age: protect from light***

In September 2019, [a letter about parenteral nutrition products](#) was sent to healthcare professionals and compounding centres.

A European review identified that light exposure may lead to increased peroxides and other degradation products in parenteral nutrition products containing amino acid and/or lipids, particularly those containing vitamins and trace elements. These particles can lead to severe adverse effects, especially in premature neonates who are at high risk of oxidative stress related to multiple factors including oxygen therapy, phototherapy, weak immune systems and inflammatory response with reduced oxidant defence. See [letter](#) for more information.

For administration to neonates and children below 2 years of age, parenteral nutrition products containing amino acids and/or lipids should be protected from light (containers and administration sets). This recommendation is already present in European paediatric parenteral nutrition guidelines by the European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and the European Society for Clinical Nutrition and Metabolism (ESPEN).

### ***Other letters***

The following letters were sent to healthcare professionals in September 2019:

- [Lucentis \(ranibizumab\) 10 mg/ml pre-filled syringe: plunger on syringe too stiff](#)
- [Picato ▼ \(ingenol mebutate\): Use with caution in patients with a history of skin cancer](#)
- [Jext 150 and 300 microgram adrenaline auto-injectors: extended use beyond labelled expiry date for selected lots](#)
- [EpiPen 0.3 mg adrenaline auto-injectors: extended use beyond labelled expiry date for specific lots](#)
- [Emerade 150/300/500 micrograms solution for injection in pre-filled pen: complaints of initial failure to activate](#)
- [Gilenya ▼ \(fingolimod\): contraindication in pregnant women and in women of childbearing potential not using effective contraception](#)

For more information on fingolimod see [September 2019 Drug Safety Update](#)

## Alerts

### **Ranitidine**

**[Class 2 Medicines recall: Zantac \(ranitidine\) Injection 50mg/2ml, Zantac Syrup 150mg/10ml, Zantac Tablets 150mg, Zantac Tablets 300mg \(EL \(19\)A 24\)](#)**. Issued 8 October 2019. GlaxoSmithKline is recalling all unexpired stock of Zantac (ranitidine hydrochloride) prescription-only medicines (POM) from pharmacies as a precautionary measure due to possible contamination with an impurity N-nitrosodimethylamine (NDMA), which has genotoxic and carcinogenic potential.

**[Class 2 Medicines recall: Ranitidine Effervescent Tablets 150mg, Ranitidine Effervescent Tablets 300mg \(EL \(19\)A/27\)](#)**. Issued 17 October 2019. Teva UK Ltd is recalling all unexpired stock of the listed products from pharmacies as a precautionary measure due to possible contamination with an impurity N-nitrosodimethylamine (NDMA), which has genotoxic and carcinogenic potential.

### **Other alerts**

**[Class 2 Medicines Recall: Aripiprazole 1mg/ml oral solution EL \(19\)A/21](#)**. Issued 12 September 2019. Dr Reddy's Laboratories (UK) is recalling batch number 050618 due to the potential for small particles of aripiprazole active material to be present, which may affect the efficacy of the product. Quarantine all remaining stock of the listed batch and return it to your supplier.

**[Class 2 Medicines Recall: Bisacodyl 10mg Suppositories EL \(19\)A/22](#)**. Issued 23 September 2019. Martindale Pharmaceuticals is recalling the batch number BUK901 due to an issue with homogeneity, which may result in individual suppositories containing too little or too much active substance. Quarantine all remaining stock of the listed batch and return it to your supplier.

*Article citation: Drug Safety Update volume 13, issue 3: October 2019: 5.*

## Medical Device Alerts issued in September 2019

In this monthly update, we highlight selected Medical Device Alerts 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](#).

### **All models of T34 ambulatory syringe pumps – updated cleaning advice and maintenance requirements due to the risk of fluid ingress (MDA/2019/030).**

Issued 18 September 2019. Manufactured by CME (a BD company). Function may be affected by fluid getting into the pump and building up over time because of specific cleaning and disinfection practices. Updated guidance is given in the [alert](#) for cleaning and maintenance.

### **Deltec Gripper non-coring needles and PORT-A-CATH trays containing Gripper needles – recall due to risk of needle occlusion.**

Issued 12 September 2019. Manufactured by Smiths Medical. Due to a manufacturing process failure, needles may be occluded, potentially causing a delay to treatment. Affected devices should be identified and quarantined and returned to the manufacturer.

### **Johnson & Johnson Vision 1-day Acuvue Moist for Astigmatism contact lenses.**

Issued 26 September 2019. Certain lots of contact lenses have been recalled following a limited number of reports of foreign matter on the lens or in the lens blister solution. The [Field Safety Notice](#) asks opticians or optometrists to review their inventory and stop use of affected products. Patients who may have received any of the affected contact lenses should be contacted and if they have affected batches, instructed to discontinue use immediately and return the product for replacement.

*Article citation: Drug Safety Update volume 13, issue 3: October 2019: 6.*

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