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## Medicines Safety Assurance Tool April 2018

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MIDLANDS AND LANCASHIRE  
COMMISSIONING SUPPORT UNIT

### Which medicines require extra care when switching between liquid and tablet/capsule formulations?

*Specialist Pharmacy Services | 16 Apr 2018*

This Q&A considers which medicines may require dose adjustment when switching between oral formulations and presents information on dose adjustment in a summary table.

<https://www.sps.nhs.uk/articles/which-medicines-require-extra-care-when-switching-between-liquid-and-tablet-capsule-formulations/>

Proposed action

Newsletter

Optimise Rx/ScriptSwitch

Practice audit/search

Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

### Gabapentin and pregabalin-are they safe whilst breastfeeding?

*Specialist Pharmacy Services | 17 Apr 2018*

This UKMi Medicines Q & A reviews the evidence available, and makes recommendations, for the use of gabapentin and pregabalin during breastfeeding.

<https://www.sps.nhs.uk/articles/gabapentin-and-pregabalin-are-they-safe-whilst-breastfeeding/>

Proposed action

Newsletter

Optimise Rx/ScriptSwitch

Practice audit/search

Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Risk of mix-ups between insulin Fiasp® (fast-acting insulin aspart) and Tresiba® (basal insulin degludec)

*electronic Medicines Compendium | 20 Apr 2018*

From 1 June 2018, the colour of Fiasp cartridges, pre-filled pens and vials is changing from yellow to red and yellow, following cases where patients have mistakenly injected it instead of Tresiba or vice versa. Patients using both should be alerted to this risk.

<https://www.medicines.org.uk/emc/rmm/1168/Document>

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Valproate contraindicated in women of childbearing potential unless there is a Pregnancy Prevention Programme

*Central Alerting System | 24 Apr 2018*

Following a review of the situation across the EU, valproate is now contraindicated in women of childbearing potential unless they meet the conditions of a Pregnancy Prevention Programme, which will include a risk acknowledgement form to be completed and signed by the specialist prescriber and the patient in a review at least once a year.

[https://www.cas.mhra.gov.uk/ViewAndAcknowledgment/viewAttachment.aspx?Attachment\\_id=103004](https://www.cas.mhra.gov.uk/ViewAndAcknowledgment/viewAttachment.aspx?Attachment_id=103004)

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Obeticholic acid (Ocaliva ▼): risk of serious liver injury in patients with pre-existing moderate or severe hepatic impairment; reminder to adjust dosing according to liver function monitoring

Medicines and Healthcare products Regulatory Agency | 24 Apr 2018

We are aware of reports of serious liver injuries and deaths in patients with primary biliary cholangitis with pre-existing moderate or severe liver impairment who were not adequately dose-adjusted.

<https://www.gov.uk/drug-safety-update/obeticholic-acid-ocaliva-risk-of-serious-liver-injury-in-patients-with-pre-existing-moderate-or-severe-hepatic-impairment-reminder-to-adjust-dosing-according-to-liver-function-monitoring>

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Lamictal (lamotrigine): Drug Safety Communication - Serious Immune System Reaction

US Food and Drug Administration | 26 Apr 2018

FDA is warning that lamotrigine can cause hemophagocytic lymphohistiocytosis, which typically presents as a persistent fever, usually >101°F, and causes severe inflammation throughout the body and lead to hospitalisation and death, especially if not diagnosed and treated quickly.

<https://www.fda.gov/Safety/MedWatch/SafetyInformation/SafetyAlertsforHumanMedicalProducts/ucm605628.htm>

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Oral antiplatelet agents - are they safe in breastfeeding?

Specialist Pharmacy Service | 27 Apr 2018

This updated medicines Q&A provides advice on the safety of oral antiplatelet agents (aspirin, dipyridamole, clopidogrel, prasugrel, and ticagrelor) in breastfeeding mothers.

[https://www.sps.nhs.uk/wp-content/uploads/2015/12/QA286\\_4\\_AntiplateletsOralBM\\_FINAL.docx](https://www.sps.nhs.uk/wp-content/uploads/2015/12/QA286_4_AntiplateletsOralBM_FINAL.docx)

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

## Summary of Product Characteristics Update

electronic Medicines Compendium | Apr 2018

### Abstral (fentanyl citrate) Sublingual Tablets

SPC now adds detail that fentanyl is metabolised by CYP3A4 and that caution should be used when prescribing for patients taking CYP3A4 inducers (e.g. phenytoin) and inhibitors (e.g. itraconazole).

<https://www.medicines.org.uk/emc/product/6432/smpc>

### Adenuric (febuxostat) tablets

Agranulocytosis has been added as a potential adverse effect of treatment (frequency –rare)

<https://www.medicines.org.uk/emc/product/487/smpc>

### Alzhok (memantine) 5 mg, 10 mg, 15 mg, 20 mg Soluble Tablets initiation pack

Information about sodium levels contained in the different strength tablets has been added. Section 4.2 now advises the soluble tablets are best taken dissolved in half a glass of water, and a minimum volume of approximately 10ml of water is sufficient for complete dissolution.

<https://www.medicines.org.uk/emc/product/788/smpc>

Proposed action

- Newsletter  Optimise Rx/ScriptSwitch  
 Practice audit/search  Other (please specify)

Action taken

Status

Unassigned ▼

Action due date

Date completed

**Apidra (insulin glulisine) cartridge and Apidra Solostar pen**

The SPC notes that Apidra 100 Units/ml in cartridges and Apidra SoloStar 100 units/ml in pre-filled pen is only suitable for subcutaneous injections from a reusable pen. If administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used.

<https://www.medicines.org.uk/emc/product/2499/smpc>

**Atripla (efavirenz/emtricitabine/tenofovir) 600 mg/200 mg/245 mg film-coated tablets**

SPC has been updated to warn of catatonia as an uncommon adverse effect noted in post-marketing reports.

<https://www.medicines.org.uk/emc/product/6173/smpc>

**Dymista (azelastine hydrochloride fluticasone propionate) nasal spray**

Nasal ulcers has been added as a potential adverse effect of treatment (frequency unknown).

<https://www.medicines.org.uk/emc/product/3036/smpc>

**EpiPen (adrenaline)**

A number of risk minimisation materials are available to support the safe prescribing and use of EpiPen® devices, including for example a checklist for prescribers, and a patient carry card describing how EpiPen® should be administered in case of emergency.

<http://www.medicinesresources.nhs.uk/en/Medicines-Awareness/Safety-Alerts/Safety-alerts/Risk-minimisation-materials-for-EpiPen-adrenaline/>

**Fiasp (insulin aspart) 100 units/mL solution for injection in cartridge (Penfill)**

The SPC now advises that pre-filled pen is only suitable for subcutaneous injections; and if administration by syringe, intravenous injection or infusion pump is necessary, a vial should be used.

<https://www.medicines.org.uk/emc/product/8108/smpc>

**Fostair (beclometasone dipropionate/formoterol fumarate dehydrate) 100/6 inhalation solution**

Sections 4.4, 4.5, 4.8 and 6.3 have been updated. It is advised that beclometasone is less dependent on CYP3A metabolism compared to other corticosteroids, but possibility of systemic effects with concomitant use of CYP3A inhibitors (eg ritonavir, cobicistat) cannot be excluded.

<https://www.medicines.org.uk/emc/product/6318/smpc>

**Fucithalmic / Fusidic Acid 1% Viscous Eye Drops**

The SPC now notes that contact lenses should be kept out until all symptoms of the infection have gone; and that due to negligible systemic exposure, systemic interactions are unlikely, and they can be used during pregnancy. Further information on side-effects has been added.

<https://www.medicines.org.uk/emc/product/5188/smpc>

**Fycompa (perampanel) film-coated tablets**

SPC now warns that severe cutaneous adverse reactions including drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported in association with perampanel treatment. Patients should be advised of signs and symptoms and monitored closely for skin reactions

<https://www.medicines.org.uk/emc/product/7879/smpc>

**Infanrix hexa, (Diphtheria, tetanus, pertussis, hepatitis B, poliomyelitis and Haemophilus influenzae type b conjugate vaccine) injection**

SPC states that Infanrix hexa can be given concomitantly with pneumococcal, meningococcal serogroup C, meningococcal serogroups A, C, W-135 and Y conjugate vaccines, meningococcal serogroup B vaccine, oral rotavirus vaccine and the measles-mumps-rubella-varicella vaccine.

<https://www.medicines.org.uk/emc/product/2586/smpc>

**Insuman Comb (human insulin)**

The SPC notes that Insuman Comb cartridges are only suitable for subcutaneous injections from a reusable pen. If administration by syringe is necessary, a vial should be used.

<https://www.medicines.org.uk/emc/product/4101/smpc>

**Jaydess (levonorgestrel) intrauterine system**

Information on how to differentiate between the physical appearances of Jaydess (levonorgestrel) and Mirena (levonorgestrel) and the risks of ectopic pregnancy in women using Jaydess is available for healthcare professionals.

<https://www.medicines.org.uk/emc/product/5297/rmms>

**Jinarc (tolvaptan) tablets**

Existing warning regarding co-administration of tolvaptan with CYP3A inhibitors has been modified based on data from a completed study investigating the effect of oral fluconazole, a moderate CYP3A4 inhibitor, on tolvaptan kinetics in healthy adult subjects.

<https://www.medicines.org.uk/emc/product/6854/smpc>

**Marvelon (desogestrel/ethinylestradiol)**

SPC has been updated with information on hepatitis C virus (HCV) and risk of elevated ALT due to HCV combination regimens co-administered with ethinylestradiol products. Concomitant use with ombitasvir/paritaprevir/ritonavir and dasabuvir is contraindicated.

<https://www.medicines.org.uk/emc/product/1359/smpc>

**Mercilon (Desogestrel and Ethinylestradiol)**

SPC now highlights that this product is contraindicated for concomitant use with medicinal products containing ombitasvir/paritaprevir/ritonavir and dasabuvir.

<https://www.medicines.org.uk/emc/product/1360/smpc>

**Methotrexate injectable and oral formulations**

Alveolar haemorrhage (which may be associated with vasculitis and other co-morbidities) has been added as a rare potential adverse effect of treatment. Prompt investigations should be considered when pulmonary alveolar haemorrhage is suspected to confirm the diagnosis.

<https://www.medicines.org.uk/emc/product/1404/smpc>

**Microgynon 30 (levonorgestrel; ethinylestradiol)**

Concomitant use with medicines containing ombitasvir/paritaprevir/ritonavir and dasabuvir is contraindicated, as in clinical trials of these medicines ALT elevations >5 times the upper limit of normal were seen more frequently in women using ethinylestradiol-containing medicines.

<https://www.medicines.org.uk/emc/product/1130/smpc>

**Mydrilate (cyclopentolate) 0.5 and 1.0% Eye Drops**

SPC has been revised to advise that prior to first opening, remove from refrigerator and store at room temperature for 30 minutes; after first opening, do not store above 25°C, do not refrigerate; and discard 28 days after opening.

<https://www.medicines.org.uk/emc/product/1724/smpc>

**Neulasta (pegfilgrastim) on body injector patient alert card**

The Patient Alert Card contains information regarding the importance of actively monitoring the on body injector device, how to recognize a failure of the device, and actions to take if patients have issues with the device or symptoms of infection.

<https://www.medicines.org.uk/emc/product/6770/rmms>

**NovoMix 30 Penfill and FlexPen (100 units/ml)**

Section 4.2 of the SPCs has been updated to note that NovoMix 30 Penfill and NovoMix 30 FlexPen are only suitable for subcutaneous injections from a reusable pen. If administration by syringe is necessary, a vial should be used.

<https://www.medicines.org.uk/emc/product/7915/smpc>

**Ocaliva (obeticholic acid) 5mg and 10mg film-coated tablets**

Sections 4.2 and 4.4 have been updated to include advice on specific dosing recommendations for patients with hepatic impairment (Child-Pugh Classes A, B, and C), and management and dose adjustment for severe pruritus in patients with hepatic impairment.

<https://www.medicines.org.uk/emc/product/7630/smpc>

**Renvela 2.4g (sevelamer carbonate) powder for oral suspension**

SPC now highlights that as an alternative to water the powder may be pre-mixed with a small amount of beverage or food (e.g. 100g/120mL) and consumed within 30 minutes. Do not heat the powder (e.g. microwave) or add to heated food or beverages.

<https://www.medicines.org.uk/emc/product/473/smpc>

**Soolantra (ivermectin) 10mg/g cream**

The SPC includes a new adverse event - swelling of the face (frequency not known).

<https://www.medicines.org.uk/emc/product/6819/smpc>



**Spiriva Respimat (tiotropium) 2.5 microgram, inhalation solution**

Spiriva Respimat is now licensed as add-on maintenance bronchodilator treatment in patients aged 6 years and older with severe asthma who experienced one or more severe asthma exacerbations in the preceding year.

<https://www.medicines.org.uk/emc/product/407/smpc>

**Suprax (cefixime) tablets**

The SPC warns that beta-lactams, including cefixime, predispose the patient to encephalopathy risk (which may include convulsions, confusion, impairment of consciousness, movement disorders), particularly in case of overdose or renal impairment.

<https://www.medicines.org.uk/emc/product/5534/smpc>

**Targretin (bexarotene) Capsules**

The SPC now notes that psychiatric disorders (depression, depression aggravated, anxiety, and mood alterations) have been reported in patients treated with systemic retinoids, including bexarotene. Particular care should be taken in patients with a history of depression.

<https://www.medicines.org.uk/emc/product/4161/smpc>

**Tecfidera (dimethyl fumarate.) capsules**

SPC now advises that a short course of acetylsalicylic acid that may be beneficial in patients affected by intolerable flushing from dimethyl fumarate. Information relating to the use of dimethyl fumarate with live and non-live vaccines has also been updated.

<https://www.medicines.org.uk/emc/product/5256/smpc>

**Tetralysal (lymecycline) 300**

SPC now advises to take with glass of water to reduce risk of oesophageal irritation/ulceration. Concomitant use of oral retinoids should be avoided. Warnings also added about renal/hepatic impairment/hepatotoxicity/antibiotic resistance/phototoxicity and use of expired medication.

<https://www.medicines.org.uk/emc/product/926/smpc>

**Topiramate Accord SPC (all strengths)**

Updated to include warnings about oligohydrosis, metabolic disorder, impairment of cognitive function, hyperammonemia and encephalopathy (additional risk if used with valproate). Also cautions use in patients with impaired renal function (CLCR).

<https://www.medicines.org.uk/emc/product/5307/smpc>

**Venclyxto (venetoclax) film-coated tablets**

SPC has been updated with data on interactions with azithromycin (decreased venetoclax [VC] C<sub>max</sub> by 25% and AUC<sub>∞</sub> by 35% in study in 12 healthy subjects) and digoxin [DG], a P-gp substrate (increased DG C<sub>max</sub> by 35% and AUC<sub>∞</sub> by 9% in study of single 100mg dose of VC with 0.5mg DG).

<https://www.medicines.org.uk/emc/product/2267>

**Zyclara (imiquimod) 3.75% cream**

SPC has been updated with inclusion of benzyl alcohol as an excipient and warning that it may cause allergic reactions or mild local irritation. Abdominal pain has been added as an uncommon possible adverse reaction.

<https://www.medicines.org.uk/emc/product/2929/smpc>