

## Medicines Safety Assurance Tool

May 2022

To request this safety tool, or for more information about this tool, to make a comment, or share a safety issue please contact [mlcsu.medicines-safety@nhs.net](mailto:mlcsu.medicines-safety@nhs.net)

### Denosumab 60mg (Prolia): should not be used in patients under 18 years due to the risk of serious hypercalcaemia

18 May 2022

Owing to reports of serious and life-threatening hypercalcaemia with denosumab 60mg (Prolia) in children and adolescents in clinical trials for osteogenesis imperfecta and during off-label use, the MHRA now formally recommend it should not be used in children <18 years.

Proposed action

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



Action taken

Status	Action due date	Date completed

## Risk Minimisation Materials updates

### Amiodarone Patient Alert Card

Patient alert card includes information on the possible side effects of treatment and advises when to contact their doctor immediately, and symptoms for which they should stop treatment immediately and seek medical help.

Proposed action

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



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Midlands and Lancashire  
Commissioning Support Unit

### Summary of Product Characteristics updates

#### Arthrotec (misoprostol, diclofenac sodium) 50 modified-release Tablets

SPC updated to note hydrogenated castor oil as an excipient with known effect and corresponding warning and precaution that this may cause stomach upset and diarrhoea.

#### Cell-based Quadrivalent Influenza Vaccine (Surface Antigen, Inactivated) Seqirus suspension for injection in pre-filled syringe

SPC now notes based on clinical experience this vaccine can be given at the same time as other vaccines (at separate injection sites) including COVID-19 vaccines and pregnancy data added, which demonstrate no evidence of adverse foetal, newborn or pregnancy outcomes.

#### CoAprovel (hydrochlorothiazide, irbesartan) film-coated tablets – all strengths

SPC updated to include adverse effects acute respiratory distress syndrome (very rare) & respiratory distress (including pneumonitis & pulmonary oedema) of unknown frequency with corresponding warning that acute respiratory toxicity can occur from minutes to hours after intake.

#### Dalacin C (clindamycin) Capsules 150 mg

SPC updated to note that in paediatric patients, it should be dosed based on total body weight regardless of obesity, and to include data that show its clearance and volume of distribution normalised by body weight are comparable regardless of obesity.

#### Decapeptyl SR (triptorelin acetate) - 3.0 and 11.25 mg

Information added on: add-back therapy in patients with endometriosis, avoidance of pregnancy on treatment, risk of reduction in bone mineral density, not recommended for patients age <18 years, lactation warning, and pituitary apoplexy as side effect reported in men.

Proposed action

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### Deximune (ciclosporin) – all strengths

SPC cautions the co-administration of ciclosporin and cannabidiol due observed increased blood levels of another calcineurin inhibitor during concomitant use with cannabidiol via inhibition of intestinal P-glycoprotein efflux. Patients should be monitored for adverse events.

### Diprosone (betamethasone dipropionate) & Diprosalic (betamethasone dipropionate/salicylic acid) – all presentations

SPC includes a warning related to topical steroid withdrawal syndrome (frequency not known) whereby a severe form of rebound flare can develop, usually when delicate skin sites such as the face and flexures are treated. Reapplication should be with caution under specialist advice.

### Eliquis (apixaban) tablets

Cutaneous vasculitis has been added as a potential adverse effect of treatment (frequency unknown).

### Elocon (mometasone furoate) – all presentations

SPC includes a warning related to topical steroid withdrawal syndrome (frequency not known) whereby a severe form of rebound flare can develop, usually when delicate skin sites such as the face and flexures are treated. Reapplication should be with caution under specialist advice.

### Flucelvax Tetra (influenza virus surface antigens) vaccine

SPC updated to include data from a US registry study reviewing outcomes from exposure in pregnancy. SPC states inactivated influenza vaccines can be given in any stages of pregnancy as data do not indicate any adverse foetal and maternal outcomes attributable to the vaccine.

### Forxiga (dapagliflozin) film-coated tablets – all strengths

SPC updated to cover new indication of treatment of type 2 diabetes mellitus in children aged 10 years and above and corresponding information for posology and method of administration, safety profile observation of undesirable effects and clinical study results.

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### [Glucophage SR \(metformin\) prolonged release tablets – all strengths](#)

SPC now notes if clinically needed, the use of metformin can be considered during pregnancy and in the periconceptional phase as an addition or an alternative to insulin.

### [Glyxambi \(linagliptin, empagliflozin\) film-coated tablets – all strengths](#)

SPC updated to include constipation as an adverse effect of 'common' frequency and frequency of necrotising fasciitis of the perineum changed from 'not known' to 'rare'.

### [Klaricid \(clarithromycin\) products](#)

Following recent safety review by MHRA, SPC now advises risk vs. benefit needs to be considered when prescribing clarithromycin for any patients taking hydroxychloroquine or chloroquine, due to potential for increased risk of CV events and CV mortality.

### [Kigabeg \(vigabatrin\) soluble tablets- all strengths](#)

Updated to advise that visual field defects reported with use may be characterised by tunnel vision and blindness reported in severe cases, as well as inclusion of reports of cases of intramyelinic oedema, particularly in infants treated for infantile spasms.

### [Lenzetto \(estradiol\) 1.53 mg/spray, transdermal spray, solution](#)

The warnings and precautions section includes a new section discussing ALT elevations and a new section to note that exogenous oestrogens may induce or exacerbate symptoms of hereditary angioedema.

### [Librium \(chlordiazepoxide\) capsules](#)

Owing to genotoxic potential, women of childbearing potential should use effective contraceptive during, and for 7 months after treatment. Men should use effective contraceptive and not father a child during, and for 4 months after treatment.

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### MOVICOL – all formulations adult and paediatric

SPC now notes Movicol may result in a potential interactive effect if used with starch-based food thickeners. The Macrogol ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

### Moviprep (Macrogol 3350) – all formulations

SPC now notes Moviprep may result in a potential interactive effect if used with starch-based food thickeners. The macrogol ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

### Nimenrix (meningococcal groups A, C, W-135 and Y conjugate vaccine) powder and solvent for solution for injection in pre-filled syringe

SPC updated to include long-term immunogenicity data in toddlers from study MenACWY-TT-104.

### Oxyargin (oxycodone/naloxone) prolonged-release tablets – all strengths

SPC updated to include central sleep apnoea (CSA) as an adverse effect of unknown frequency with corresponding warning that opioid use increases risk of CSA in a dose-dependent fashion and advises to consider decreasing the total opioid dosage in patients who present with CSA.

### PecFent (fentanyl citrate) 400 micrograms/spray nasal spray, solution

SPC updated to warn that concomitant use of central nervous system depressants such as gabapentinoids (gabapentin and pregabalin) may produce additive depressant effects.

### Plenvu (Macrogol 3350) powder for oral solution

SPC now notes Plenvu may result in a potential interactive effect if used with starch-based food thickeners. The macrogol ingredient counteracts the thickening effect of starch, effectively liquefying preparations that need to remain thick for people with swallowing problems.

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### [Priorix \(MMR live vaccine\) powder and solvent for solution for injection in a pre-filled syringe](#)

SPC updated to note the vaccine contains para-aminobenzoic acid (6.5 nanograms per dose), which may cause allergic reactions, and phenylalanine (334 micrograms per dose), which may be harmful for individuals with phenylketonuria.

### [Progynova \(estradiol hemihydrate\) TS 50 and 100 micrograms/24 hours Transdermal Patch](#)

SPC updated with caution on co-administration with the combination drug regimen ombitasvir/paritaprevir/ritonavir with or without dasabuvir and also the regimen glecaprevir/pibrentasvir, due to risk of ALT elevations observed in women using another oestrogen, ethinylestradiol.

### [Prolia \(denosumab\) 60 mg solution for injection in pre-filled syringe](#)

SPC advises that denosumab should not be used in children aged <18 years because of safety concerns of serious hypercalcaemia, and potential inhibition of bone growth and lack of tooth eruption. Some clinical trial cases were complicated by acute renal injury.

### [Prostap \(leuporelin acetate\) SR DCS powder and solvent for prolonged-release suspension for injection in pre-filled syringe – all strengths](#)

SPC updated to include adverse effect idiopathic intracranial hypertension (ICH) of unknown frequency & now advises patients should be warned for signs & symptoms of ICH, including severe/recurrent headache, vision disturbances & tinnitus. Consider discontinuation if ICH occurs.

### [Qlaira \(estradiol valerate/dienogest\) tablets](#)

SPC advises caution with co-administration with hepatitis C virus treatments eg ombitasvir/paritaprevir/ritonavir with and without dasabuvir and glecaprevir/pibrentasvir, owing to increased risk of significant ALT elevations.

### [Revatio \(sildenafil\) preparations](#)

SPC notes that caution should be exercised when sildenafil is initiated in patients treated with sacubitril/valsartan as pharmacokinetic studies suggest it may be associated with significantly greater blood pressure reduction compared to sacubitril/valsartan alone.

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### Tacrolimus (all formulations)

The potential for tacrolimus to interact with medicines that inhibit P-glycoprotein has been added to the SPC. Cannabidiol has been highlighted as a specific example of a medicine to be aware of.

### Trandate (labetalol) film-coated tablets – all strengths

SPC updated to include 'Nipple pain' and 'Raynaud's phenomenon of the nipple' as adverse effects of unknown frequency.

### Welldorm Elixir (chloral hydrate)

SPC updated to include warnings related to the following excipients: liquid glucose, sodium benzoate, glycerol and propylene glycol.

### Yemex (fentanyl) Transdermal Patch- all strengths

Gabapentinoids (gabapentin, pregabalin) have been added to list of central nervous system depressants that may disproportionately increase CNS depressant effects such as respiratory depression, hypotension, profound sedation, coma or death, when used concomitantly with fentanyl.

### Zamadol (tramadol) 50 mg Capsules

SPC updated to include hyponatraemia as an adverse effect of unknown frequency.

## About this document

MLCSU collates and shares the latest current awareness and evidence-based medicines information from NICE and UKMi relating to medicines safety each month.

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