



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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## Opinions on safety variations/PSURs

Adopted at the CHMP meeting of 16-19 September 2013

Name of medicine	INN	Scope
Advate	octocog alfa	CHMP opinion to update and clarify sections 4.4 and 4.8 of the Summary of Product Characteristics (SmPC) regarding information on hypersensitivity and inhibitor occurrence.
Azilect	rotigotine	PSUR assessment resulting in a CHMP opinion to update sections 4.4 and 4.8 of the SmPC to inform about the risk of impulse control disorders and to include a warning on hypotension, as well as on the risk of exacerbated dopaminergic side effects and worsening of pre-existing dyskinesia when rasagiline is used in combination with levodopa.
Celsentri	maraviroc	CHMP opinion to update sections 4.4 and 4.8 of the SmPC to strengthen the warnings on postural hypotension and include that cases of syncope caused by postural hypotension have been reported.

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Edarbi, Ipreziv	azilsartan medoxomil	CHMP opinion to update sections 4.3, 4.4, 4.5, and 4.8 of the SmPC to include: <ul style="list-style-type: none"> <li>- relevant contraindications and warnings regarding concomitant use of azilsartan medoxomil and aliskiren (section 4.3, 4.4 and 4.5);</li> <li>- the following adverse drug reactions 'rash', 'pruritus', 'nausea' and 'muscle spasm' reported with an 'uncommon' frequency (section 4.8).</li> </ul>
Eviplera	emtricitabine, rilpivirine, tenofovir disoproxil	CHMP opinion to update sections 4.2, 4.3 and 4.5 of the SmPCs regarding rilpivirine-rifabutin interaction. In particular, previous contraindication on the concomitant use of these medicines has been removed.
Edurant	rilpivirine	
Exjade	deferasirox	CHMP opinion to update sections 4.4 and 4.8 of the SmPC with information on Stevens-Johnson syndrome (SJS), in particular that cases of SJS have been reported post-marketing and if SJS is suspected, Exjade should be discontinued immediately and should not be reintroduced.
Kalydeco	ivacaftor	PSUR assessment resulting in a CHMP opinion to update section 4.8 of the SmPC to strengthen the wording for the adverse reactions rash, headache and dizziness, as serious cases of these three adverse reactions have been reported.
Omnitrope	somatropin	CHMP opinion to update section 4.4 of the SmPC to include a new warning regarding the risk of pancreatitis. The updated SmPC and Package Leaflet are now in accordance with the originator's Patient Information Genotropin (UK).
Avastin	bevacizumab	CHMP opinion to update section 4.4 of the SmPC on diabetes as a risk factor for developing arterial thromboembolic events following review of the MAH's safety database.
Caelyx	doxorubicin hydrochloride	CHMP opinion to update sections 4.4 and 4.8 of the SmPC in order to add a warning regarding the incidence of 'secondary oral neoplasms' following review of the MAH's safety database.
Eliquis	apixaban	CHMP opinion to update section 4.4 of the SmPC to include a recommendation that apixaban should not be used in patients with prosthetic heart valves following a routine assessment of the Company Core Data Sheet.

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Enbrel	etanercept	CHMP opinion to update section 4.4 of the SmPC regarding the safety information for Hepatitis B reactivation in patients treated with Enbrel.
Lumigan	bimatoprost	CHMP opinion to update sections 4.3, 4.4 and 4.8 of the SmPC in order to strengthen the existing warning on avoiding allowing the tip of the dispensing container to contact the eye.
Mimpara	cinacalcet	CHMP opinion to update section 4.4 of the SmPC in order to update the safety information regarding life threatening events and fatal outcomes associated with hypocalcaemia reported in adult and paediatric patients treated with Mimpara.
Vitreolis	boceprevir	CHMP opinion to update section 4.4 the SmPC with information on anaemia and neutropenia, resulting from a post hoc analysis of clinical trial data on anaemia and clinical observations on neutropenia and its monitoring by blood counts.
Thymanax, Valdoxan	agomelatine	PSUR assessment resulting in a CHMP opinion to update information related to liver function in the following sections of the SmPC: <ul style="list-style-type: none"> <li>• section 4.2 to state that agomelatine should not be used in patients aged 75 years and older;</li> <li>• section 4.3 to add a contraindication in patients with transaminases exceeding 3X upper limit of normal;</li> <li>• sections 4.4 and 4.8 to include that cases of hepatic failure with fatal outcome or liver transplantation have been reported in patients with hepatic risk factors;</li> <li>• section 4.8 to add restless leg syndrome and tinnitus.</li> </ul>
Bretaris Genuair Eklira Genuair	acclidinium bromide	PSUR assessment resulting in a CHMP opinion to update section 4.2 of the SmPC to state that patients should be instructed on how to administer the product correctly. The instructions for use in this section and in the package leaflet should also be updated to remove some of the repetition which may confuse patients.
Firmagon	degarelix	PSUR assessment resulting in a CHMP opinion to update section 4.4 of the SmPC to add a warning on cardiovascular diseases.
Multaq	dronedarone	PSUR assessment resulting in a CHMP opinion to update section 4.4 of the SmPC to amend the existing warning related to renal failure.

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Revlimid	lenalidomide	PSUR assessment resulting in a CHMP opinion to update sections 4.5 and 4.8 of the SmPC to add the adverse reaction rhabdomyolysis, especially when statins are combined with lenalidomide.
Neulasta	pegfilgratim	PSUR assessment resulting in a CHMP opinion to update section 4.4 of the SmPC with a statement on traceability in line with other products in the class.
Fycompa	perampanel	PSUR assessment resulting in a CHMP opinion to update section 4.4 of the SmPC and section 2 of the Package Leaflet to amend the warning on aggression.
Actos, Glustin	pioglitazone	PSUR assessment resulting in a CHMP opinion to update sections 4.4 and 4.8 of the SmPC to add information on findings from some studies on peripheral oedema and cardiac failure with the concomitant use of non-steroidal anti-inflammatory drugs and on an increased risk of bone fractures in men and to inform about the incidence of heart failure in patients $\geq 65$ years receiving insulin concomitantly.
Tandemact	pioglitazone, glimepiride	
Competact, Glubrava	pioglitazone, metformin	
Prevenar 13	pneumococcal polysaccharide conjugate vaccine (13-valent, adsorbed)	PSUR assessment resulting in a CHMP opinion to update of sections 4.4, 4.5 and 4.8 of the SmPC to add a warning on an increased risk of convulsions and hypotonic hyporesponsive episode with concomitant administration of Prevenar 13 and Infanrix hexa.
Ranexa	ranolazine	PSUR assessment resulting in a CHMP opinion to update section 4.8 of the SmPC (System Organ Class musculoskeletal and connective tissue disorders) to add 'muscular weakness' with frequency 'uncommon'.
Jakavi	ruxolitinib	PSUR assessment resulting in a CHMP opinion to update sections 4.4 and 4.8 of the SmPC in order to warn health care professionals regarding the reported cases of TB and to provide recommendations to evaluate patients for active and inactive TB before starting treatment.
Silodyx Urorec	silodosin	PSUR assessment resulting in a CHMP opinion to update section 4.8 of the SmPC to include swelling of the face, tongue and pharyngeal oedema and additional events of 'hypotension' and 'loss of consciousness'. These ADRs and those currently included under the heading 'adverse

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		reactions from spontaneous reporting' have been included in the table of ADRs with a suitable footnote to explain that these have been reported post-marketing and are included (tachychardia, palpitations, abnormal liver function tests, skin rash, pruritus, urticaria, drug eruption).