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Press office

Opinions on safety variations/PSURs

Adopted at the CHMP meeting of 21-24 September 2015

Name of medicine	INN	Scope
Alimta	pemetrexed	CHMP opinion to update the section 4.8 of the SmPC to specify the type of haemolytic anaemia (immune-mediated) which has been reported in patients treated with pemetrexed.
Aluvia	lopinavir/ritonavir	CHMP opinion to update of section 4.4 of the SmPC with information that combination of bedaquiline with lopinavir/ritonavir should be avoided. However, if the benefit outweighs the risk, co-administration of bedaquiline with lopinavir/ritonavir must be done with caution. More frequent electrocardiogram monitoring and monitoring of transaminases are recommended.
Bosulif	bosutinib	PSUR assessment resulting in a variation to update section 4.8 of the SmPC to add the adverse reaction hypertension with the frequency "common" under the system organ class "vascular disorders".
Carbaglu	carglumic acid	PSUR assessment resulting in a variation to update section 4.2 of the SmPC to add a warning highlighting the correct route of administration, and section 4.8 to add the adverse reaction "rash".



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Cystadane	betaine anhydrous	PSUR assessment resulting in a variation to update sections 4.4 and 4.8 of the SmPC to clarify that only patients with cystathionine beta-synthase (CBS) deficiency are affected by brain oedema.
Exelon, Prometax, Rivastigmine 1A Pharma, Rivastigmine Hexal, Rivastigmine Sandoz	rivastigmine	PSUR assessment resulting in a variation to update sections 4.4 and 4.8 of the SmPC to add the adverse reaction "nightmares" and to add a warning on cardiac arrhythmia.
Fosavance, Adroavance, Vantavo	alendronic acid	CHMP opinion to update of section 4.4 of the SmPC to add "angiogenesis inhibitors" as example of a risk factor for osteonecrosis of the jaw (ONJ).
Gilenya	fingolimod	PSUR assessment resulting in a variation to update sections 4.4 and 4.8 of the SmPC to include information on skin cancers, risk of infection including opportunistic infections, hypersensitivity, lymphoma, T-wave inversion, peripheral oedema and nausea; a small modification in an existing contraindication in section 4.3 of the SmPC was also introduced.
Imnovid	pomalidomide	PSUR assessment resulting in a variation to update section 4.4 of the SmPC to specify that the arterial thrombotic events of myocardial infarction and cerebrovascular accidents can occur with pomalidomide in combination with dexamethasone. In addition, the tabulated list of adverse reactions in section 4.8 of the SmPC has been updated with these events.
Krystexxa	pegloticase	CHMP opinion to update of section 4.2 of the SmPC to: 1. add further amendments that close monitoring is required for at least 2 hours instead of 1 hour after the end of infusion to avoid the risk of anaphylaxis, and that delayed-type hypersensitivity reactions have also been reported. 2. add an amendment relating to the the importance of not taking oral urate-lowering medication before monitoring the serum acid levels, in order to avoid masking the rise of serum uric acid associated with the loss of response (therapeutic efficacy), and place patients at greater risk of infusion reactions and anaphylaxis. The revised order of the two corresponding paragraphs is to emphasize the correlation between concomitant medication with urate lowering products and serum uric acid measurement.

Name of medicine	INN	Scope
Mirvaso	brimonidine	PSUR assessment resulting in a variation to update section 4.8 of the SmPC to add the adverse reactions "hypotension" and "angioedema" both with a frequency rare.
NovoNorm, Prandin	repaglinide	PSUR assessment resulting in a variation to update section 4.5 of the SmPC to add information on interaction with clopidogrel.
Optimark	gadoversetamide	PSUR assessment resulting in a variation to update section 4.8 of the SmPC to add a footnote to the adverse reactions table to reflect the published cases of gadolinium associated skin plaques.
Teysono	tegafur / gimeracil / oteracil	CHMP opinion to update section 4.6 of the SmPC to reflect that there have been some cases reports of foetal abnormalities.
Thymanax/ Valdoxan	agomelatine	PSUR assessment resulting in a variation to update section 4.8 of the SmPC to add the adverse reaction "confusional state" with a frequency uncommon.
Xalkori	crizotinib	PSUR assessment resulting in a variation to update sections 4.4 and 4.8 of the SmPC to add the adverse reaction "cardiac failure" with a frequency "common". The package leaflet is updated accordingly.
Xenical, Alli	orlistat	PSUR assessment resulting in a variation to update section 4.5 of the SmPC to add warning on the possible interactions with benzodiazepines, antidepressants, antipsychotics and lithium.
Xiapex	collagenase clostridium histolyticum	PSUR assessment resulting in a variation to update section 4.4 of the SmPC to add a warning on the consequences following on rupture of the penis (e.g. need for surgical intervention).
Xtandi	enzalutamide	CHMP opinion to update of section 4.8 of the SmPC to add the adverse reaction "thrombocytopenia" and "diarrhea".
Zelboraf	vemurafenib	According to CHMP opinion sections 4.4, 4.5 and 4.8 of the SmPC are being amended to update information on the risk of potentiation of radiation toxicity and to update the risk of progression of cancers with RAS mutations with information on progression of pre-existing pancreatic adenocarcinoma with KRAS mutation.
Ranexa	ranolazine	CHMP opinion to update section 4.8 of the SmPC and PL, respectively to reflect that hyponatremia can occur rarely during the treatment with Ranexa.

Name of medicine	INN	Scope
Sycrest	Asenapine	CHMP opinion to update section 4.2 of the SmPC in order to change the starting therapeutic dose to 5mg BID based on the results of an exploratory dose finding study (P05691) conducted to establish the optimal dosing regimen for manic episodes in bipolar disorder. Section 5.1 of the SmpC is updated to reflect the results of the study and minor consequential changes are introduced in sections 4.8 and 5.1 of the SmPC.