27 February 2013
EMA/CHMP/109950/2013
Press Office

Opinions on safety variations

Adopted at the CHMP meeting of 18-21 February 2013

Name of medicine	INN	Marketing authorisation holder	Scope
Abilify	aripiprazole	Otsuka Pharmaceutical Europe Ltd	CHMP opinion to update section 4.8 of the SmPC to add serotonin syndrome and hepatic failure as new adverse reactions. This information is included following assessment of PSUR data. Additional information is also included regarding excretion of aripiprazole in human breast milk (section 4.6) and potential drug interaction associated with serotonin syndrome (section 4.5). The Package Leaflet is amended accordingly.
Aloxi	palonosetron	Helsinn Birex Pharmaceuticals Ltd.	CHMP opinion to update section 4.4 of the SmPC to clarify the risk factors for developing QT prolongation which is a recognised safety concern for the class and is classified as a potential risk in the Risk Minimisation Plan for Aloxi.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8669
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Name of medicine	INN	Marketing authorisation holder	Scope
			The Package Leaflet is amended accordingly. This information is included following assessment of PSUR data. Additionally in section 4.8 of the SmPC information on the adverse reaction 'anaphylaxis, anaphylactic/ anaphylactoid reactions and shock' with a frequency 'very rare' is introduced, following evidence submitted by the marketing authorisation holder.
Celsentri	maraviroc	ViiV Healthcare UK Limited	CHMP opinion to update sections 4.4 and 4.8 of the SmPC with a warning on reported severe skin and hypersensitivity reactions.
Doribax	doripenem	Janssen-Cilag International N.V.	CHMP opinion to update section 4.4 of the SmPC to include the risk of seizures in patients with pre-existing central nervous system disorders, compromised renal function and at doses higher than 500 mg. In section 4.8 information on seizures as an adverse drug reaction is added. The Package Leaflet is amended accordingly.
Erbitux	cetuximab	Merck KGaA	CHMP opinion to update sections 4.4 and 4.8 of the SmPC to add warnings that necrotizing fasciitis may develop in the course of Erbitux treatment. These changes follow a review of relevant cases by the marketing authorisation holder after a similar variation (and a Direct Healthcare Professional Communication) was finalised for Vectibix (panitumumab), another medicinal product in the same class (anti-EGFR monoclonal antibodies).
Mozobil	plerixafor	Genzyme Europe B.V.	CHMP opinion to update sections 4.4 and 4.8 of the SmPC to add a warning regarding post-marketing reports of anaphylactic reactions. These changes follow a review of the marketing authorisation holder's safety database which indicated that 3 spontaneous reports of anaphylactic reaction were received post-marketing between 15 December 2008 and 30 April

Name of medicine	INN	Marketing authorisation holder	Scope
			2012. All patients recovered without sequelae.
Nulojix	belatacept	Bristol-Myers Squibb Pharma EEIG	CHMP opinion to update sections 4.2 and 4.4 of the SmPC in order to add a warning that corticosteroid tapering in patients taking belatacept should be implemented cautiously, particularly in patients at high immunologic risk, such as those with 4 to 6 human leukocyte antigen (HLA) mismatches. Section 5.1 of the SmPC has been updated to reflect the corticosteroid doses used during the first 6 months post-transplant in Phase III studies. These changes follow an increased rate of acute graft rejection reported with Nulojix when the corticosteroid regimen has been tapered rapidly in patients with one or more risk factors for acute rejection. The CHMP endorsed a Direct Healthcare Professional Communication (DHPC) informing healthcare professionals of the revised recommendations.
Taxotere/ Docetaxel Winthrop	docetaxel	Aventis Pharma S.A.	CHMP opinion to update sections 4.4 and 4.8 of the SmPC in order to add a warning related to respiratory disorders and include interstitial pneumonitis, interstitial lung disease and pulmonary fibrosis as new adverse reactions observed in the post-marketing setting following a relevant cumulative review of the MAH's safety database.
Thalidomide Celgene	thalidomide	Celgene Europe Ltd.	CHMP opinion to update sections 4.4 and 4.8 of the SPC to include a warning of the risk of developing second primary malignancies (acute myeloid leukaemia or myelodysplastic syndromes). These changes follow an observation in an ongoing clinical trial of increased risk of these malignancies in patients with previously untreated multiple myeloma given a regimen of melphalan, prednisone, and thalidomide (MPT) compared with patients treated with lenalidomide plus dexamethasone. The CHMP endorsed a Direct Healthcare Professional Communication (DHPC)

Name of medicine	INN	Marketing authorisation holder	Scope
			informing healthcare professionals of the revised recommendations.
Thymanax/ Valdoxan	agomelatine	Servier (Ireland) Industries Ltd./ Les Laboratoires Servier	CHMP opinion to update sections 4.2, 4.4, 5.1 and 5.2 of the SmPC in order to add information on the safety and efficacy of agomelatine in patients < 75 years of age, and to add a new warning to prevent its use in patients ≥75 years of age, as requested by the CHMP further to the assessment of a phase III study in elderly patients.