EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 December 2017
EMA/815228/2017
Committees and Inspections

List of centrally authorised products requiring a notification of a change for update of annexes

Parallel distributors are only required to inform the EMA of changes to the labelling or leaflet related to any update of the annexes of marketing authorisation once a year in their annual update application, except in cases related to safety or quality issues. The following table lists the centrally authorised products for which the EMA requires a notification of change before implementation.

Name	EU number	Date of communication	Rationale
Aptivus	All presentations	11/12/2017	Update of section 4.3 and 4.5 of the SmPC to add the contraindication to use concomitantly lurasidone. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/2973/201612), which are available on the Agency's website**
Aranesp	All presentations	15/11/2017	Update of section of section 4.2 and 4.8 of the SmPC in order to add information that Aranesp may be administered by the patient or carer after being trained by a doctor and a warning on injection site bruise and haemorrhage with frequency unknown. The package leaflet is updated to provide additional instructions on the use of the device. **Parallel distributors must use the annexes dated 14/09/2017 (II/143), which are available on the Agency's website**.

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Elonva	All presentations	15/11/2017	Update of section 4.5 of the SmPC to add information pertaining to potential hCG cross-reactivity resulting in a false positive pregnancy test. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/09/2017 (II/0034), which are available on the Agency's website**
Emend	All presentations	15/11/2017	Update of sections 4.2 of the SmPC in order to replace the nomogram for the paediatric formulation provided in ml/kg with purely weight-based dosing instructions (in mg/kg) This is based on data that were already submitted as part of the paediatric application X/49. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/10/2017 (II/0055), which are available on the Agency's website**
Exviera	All presentations	11/12/2017	Update of section 4.4 of the SmPC to add a warning on depression, suicidal ideation and suicide attempt. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/10363/201701), which are available on the European Commission website**
Humalog	All presentations	15/11/2017	Update of sections 4.2 and 4.4 of the SmPC of the already authorised 100 U/ml Humalog and Liprolog presentations to indicate in section 4.2 that it can be used in paediatric population instead of in section 4.4, where the text that states that the product should only be used in children in preference to soluble insulin, when a fast action of insulin might be beneficial, is deleted. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/10/2017 (WS/1158/G), which are available on the European Commission website**
Humira	All presentations	11/12/2017	Update of section 2 of the PL to add a clarifying statement that allergic reactions with Humira in rare cases can be life-threatening. **Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/57/201612), which are available on the European Commission website**

Hycamtin	All presentations	11/12/2017	To update the section 4.8 (undesirable effects) of the SmPC in order to add two new identified ADRs: GI perforation and mucosal inflammation, which have been identified for Hycamtin in the post-marketing experience. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 28/09/2017 (II/0074), which are available on the Agency's website**
Kyprolis	All presentations	11/12/2017	Update of section 4.8 of the SmPC to add the adverse reaction tinnitus with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2017 (PSUSA/10448/201701), which are available on the European Commission website**
Lynparza	All presentations	15/10/2017	Update of section 4.8 of the SmPC to add the adverse reaction rash with a frequency common and hypersensitivity and dermatitis with a frequency uncommon. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 18/09/2017 (PSUSA/10322/201612), which are available on the European Commission website**
Nulojix	All presentations	15/11/2017	Update of sections 4.4 and 4.8 of the SmPC in order to add a warning and update the safety information on the risk of venous thrombosis of the renal allograft when anti-thymocyte globulin (ATG) and belatacept are coadministered (at the same or nearly the same time) in patients with other predisposing risk factors for thrombosis. Update section 6.6 "Special precautions for disposal and other handling" of the SmPC and the "Information for healthcare professionals (HCPs)"in the package leaflet (PL) with additional safety instructions for the co-administration of belatacept. **Parallel distributors must use the annexes dated 01/09/2017 (II/0045), which are available on the Agency's website**

Plegridy	All presentations	11/12/2017	Update of section 4.8 of the SmPC to add “alopecia” with a frequency “common”. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/00010275/201701), which are available on the Agency’s website**.
Prolia	All presentations	15/11/2017	Update of section 4.8 of the SmPC in order to remove cataracts from the list of adverse reaction associated with denosumab therapy based on final data from study 20080560, a category 3 study in the RMP (multicentre, randomized, double blind, placebo-controlled study in men with non-metastatic prostate cancer receiving androgen deprivation therapy cataract development and progression study using a slit-lamp-based evaluation system (Lens Opacities Classification System III (LOCS III).) The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 18/09/2017 (X/0059/G), which are available on the Agency’s website**.
Revlimid	All presentations	15/10/2017	Update of sections 4.2, 4.4 and 4.8 of the SmPC to introduce dose modifications in case of drug reaction with eosinophilia and systemic symptoms (DRESS), to add a relevant warning and to include DRESS in the list of adverse reactions with a frequency unknown. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 18/09/2017 (PSUSA/ 00001838/201612), which are available on the Agency’s website**
Reyataz	All presentations	15/11/2017	Update of sections 4.4 and 4.8 of the SmPC to add a warning on chronic kidney disease observed in HIV infected patients during treatment with atazanavir (with or without ritonavir). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/09/2017 (II/0111), which are available on the Agency’s website**

Selincro	All presentations	11/12/2017	Update of section 4.4 of the SmPC to add a warning about the risk of suicidality in the target population. Update of section 4.8 of the SmPC to add the adverse drug reaction myalgia with frequency “unknown”. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/11/2017 (R/0022), which are available on the Agency’s website**
Stayveer	All presentations	15/10/2017	Update of section 4.5 of the SmPC to add the interaction between bosentan and tadalafil. In addition, the following interactions which could have clinical relevance and which are already mentioned in bosentan SmPC should be added to the package leaflet: warfarin, simvastatin, ketoconazole and sildenafil. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/09/2017 (PSUSA/425/201611), which are available on the Agency’s website**
Stelara	All presentations	11/12/2017	Update of section 4.8 of the SmPC in order to include lower respiratory tract infection as an adverse drug reaction based on a comprehensive evaluation of safety information from the Stelara clinical studies database and post-marketing database, as well as available literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/09/2017 (II/0058), which are available on the Agency’s website**
Taxotere	All presentations	15/11/2017	Update of sections 4.4 and 4.8 of the SmPC to add information about ventricular arrhythmia including ventricular tachycardia based on review of the MAH’s global pharmacovigilance database and scientific literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/09/2017 (WS/1203/G), which are available on the Agency’s website**

Teysuno	All presentations	11/12/2017	Update of sections 4.4 and 4.8 of the SmPC to add Hepatitis B reactivation as an adverse reaction with a frequency of rare/ very rare .The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/00002875/201701), which are available on the Agency's website**
Tracleer	All presentations	15/10/2017	Update of section 4.5 of the SmPC to add the interaction between bosentan and tadalafil. In addition, the following interactions which could have clinical relevance and which are already mentioned in bosentan SmPC should be added to the package leaflet: warfarin, simvastatin, ketoconazole and sildenafil. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/09/2017 (PSUSA/425/201611), which are available on the Agency's website**
Vargatef	All presentations	15/11/2017	Update of section 4.8 of the SmPC in order to add 'weight decreased' as a new adverse drug reaction based on a safety review of clinical trials and post-marketing data. Update of section 4.4 of the SmPC to amend the current warning on hepatic function to include that drug liver induced injury was associated with nintendanib administration, to include low body weight, Asian origin, female sex and age as factors of increased risk of liver enzymes elevations. Update of section 4.8 of the SmPC to add 'drug-induced liver injury' (DILI) as new ADR with an 'uncommon' frequency. Update of section 5.2 of the SmPC to amend the current information related to the mean exposure to nintedanib by race, based on a review of clinical trials and post-marketing data on DILI and on the exposure safety relationship between nintedanib plasma exposure and liver enzyme elevations. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/09/2017 (II/0017), which are available on the Agency's website**.

Viekirax	All presentations	11/12/2017	Update of section 4.4 of the SmPC to add a warning on depression, suicidal ideation and suicide attempt. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/11/2017 (PSUSA/00010367/201701), which are available on the Agency's website**
Visudyne	All presentations	11/12/2017	Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning with information on localised skin necrosis upon extravasation and to add injection site necrosis as a new adverse drug reaction with frequency unknown. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 12/10/2017 (II/0095), which are available on the Agency's website**
Xyrem	All presentations	15/11/2017	Update of section 4.8 of the SmPC in order to add the adverse reactions "increased libido" and "seborrhea" with an unknown frequency. Update of section 4.6 of the SmPC in order to amend the information about breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/09/2017 (II/0067/G), which are available on the Agency's website**.
Zydelig	All presentations	11/12/2017	To update section 4.4 of SmPC with hepatotoxicity data and to update section 5.1 of SmPC with drug induced lymphocytosis, section 4.8 has been updated with hepatocellular injury as common adverse reaction and lymphocytosis as very common adverse reaction. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/11/2017 (PSUSA/10303-201701), which are available on the European Commission website**

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