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Inspections, Human Medicines Pharmacovigilance & Committees Division

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
Abilify	All presentations	15/01/2018	<p>Update of sections 4.4 and 4.8 of the SmPC with further information about the risk of impulse control disorders, and section 4.8 of the SmPC to include the new ADRs 'impulse control disorders', 'binge eating', 'compulsive shopping' and 'poriomania' and to delete the ADR 'hyperglycaemia'. The package leaflet is updated accordingly. Further, the MAH has implemented minor editorial changes in section 6.1 of the SmPC, section 6 of the package leaflet and module 3.2.P.1 to include lactose as one of the components of the excipient vanilla flavour for Abilify orodispersible tablets.</p> <p>Parallel distributors must use the annexes dated 26/10/2017 (II/0127), which are available on the Agency's website</p>



Abilify Maintena	All presentations	15/01/2018	<p>Update of sections 4.4 and 4.8 of the SmPC with further information about the risk of impulse control disorders, and section 4.8 of the SmPC to include the new ADRs 'impulse control disorders', 'binge eating', 'compulsive shopping' and 'poriomania'. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 26/10/2017 (II/0023), which are available on the Agency's website</p>
Aptivus	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/2973/201612), which are available on the Agency's website</p>
CellCept	All presentations	15/02/2018	<p>Update of sections 4.4 and 4.5 of the SmPC of all pharmaceutical forms, in order to update information regarding potential interactions with antibiotics and other drugs interfering with glucuronidation pathway, based on a review of published literature. The package leaflet is updated accordingly. In addition, update of section 6.6 of the SmPC and section 3 of the package leaflet to improve the recommendations regarding safe handling of the powder for oral suspension formulation as well as other minor editorial changes.</p> <p>Parallel distributors must use the annexes dated 23/11/2017 (II/0136), which are available on the Agency's website</p>
Cimzia	All presentations	15/02/2018	<p>Update of section 4.8 of the SmPC to add the adverse reaction "worsening of symptoms of dermatomyositis" and to add the TNF-antagonist class adverse reactions: "Stevens-Johnson syndrome" and "erythema multiform » with a frequency "rare". The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/01/2018 (PSUSA/624/201703), which are available on the European Commission website</p>

Dexdor	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add polyuria with a frequency unknown. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/998/201703), which are available on the Agency's website</p>
Esmya	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add the adverse reactions of drug hypersensitivity with a frequency uncommon and of angioedema with a frequency not known. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/00009325/201702), which are available on the Agency's website</p>
Exviera	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/10393/201702), which are available on the European Commission website</p>
Gilenya	All presentations	15/01/2018	<p>Update of section 4.3 of the SmPC to include contra-indication for patients with underlying cardiac conditions, update of section 4.4 to add a warning on immunosuppressive effects and amend the existing warnings on infections and cutaneous neoplasms and update of section 4.8 of the SmPC to add the adverse reactions squamous cell carcinoma, Merkel cell carcinoma and to change the frequency of Kaposi's sarcoma from not known to very rare.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/10363/201701), which are available on the European Commission website</p>
Humira	All presentations	11/12/2017	<p>Update of section 2 of the PL to add a clarifying statement that allergic reactions with Humira in rare cases can be life-threatening.</p> <p>Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/57/201612), which are available on the European Commission website</p>

Hycamtin	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 28/09/2017 (II/0074), which are available on the Agency's website</p>
Iclusig	All presentations	15/02/2018	<p>Update of section 4.8 of the SmPC in order to include a paragraph regarding severe cutaneous adverse reactions (SCARs) reported in the post-marketing setting. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 07/12/2017 (II/0041), which are available on the Agency's website</p>
Imbruvica	All presentations	15/02/2018	<p>Update of section 4.8 of the SmPC to add: 'panniculitis' with frequency 'uncommon'. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 09/02/2018 (PSUSA/10301/201705), which are available on the European Commission website</p>
Ixiaro	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add the adverse reaction 'Syncope' with a frequency 'rare'. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/01/2018 (PSUSA/00001801/201703), which are available on the Agency's website</p>
Jakavi	All presentations	15/01/2018	<p>Update of section 4.4 of the SmPC to extend the existing warning on tuberculosis also to polycythaemia vera patients and of section 4.8 of the SmPC to add the adverse reaction pneumonia with a frequency common in myelofibrosis (MF) patients. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 01/12/2017 (PSUSA/10015/201702), which are available on the European Commission website</p>

Keytruda	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add pneumonia as an adverse drug reaction with a frequency uncommon. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/ 10403/201703), which are available on the European Commission website</p>
Kyprolis	All presentations	15/12/2017	<p>Update of section 4.8 of the SmPC to add the adverse reaction tinnitus with a frequency common. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 15/11/2017 (PSUSA/10448/201701), which are available on the European Commission website</p>
Lemtrada	All presentations	15/01/2018	<p>Update of section 4.3, 4.4 and 4.8 of the SmPC to add a contraindication on patients with severe active infection until resolution, the adverse reaction listeria meningitis with a frequency of not known; to add the adverse reaction pneumonitis with a frequency uncommon; to add a warning on pneumonitis, and to revise an existing warning on listeriosis. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/10055/201703), which are available on the European Commission website</p>
Moventig	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add the adverse reaction Hypersensitivity with a frequency not known. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/00010317/201703), which are available on the Agency's website</p>

Mysimba	All presentations	15/02/2018	<p>Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the dosage recommendation and safety information for patients with moderate renal impairment. The proposed update removes the contraindication for patients with severe renal impairment, provides new information on the posology and additional warning that the maximum recommended daily dose for naltrexone / bupropion should be reduced for this patient population. The package leaflet is updated accordingly</p> <p>Parallel distributors must use the annexes dated 26/01/2018 (II/0023), which are available on the Agency's website</p>
NeoRecormon	All presentations	15/02/2018	<p>To update sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the package leaflet to implement the signal recommendations on 'Darbepoetin alfa; epoetin alfa; epoetin beta; epoetin theta; epoetin zeta; methoxy polyethylene glycol-epoetin beta – Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)</p> <p>Parallel distributors must use the annexes dated 24/11/2017 (IAIN/0097), which are available on the Agency's website</p>
Neupro	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add the adverse reaction "diarrhoea" with a frequency not known. To replace the secondary packaging of the finished product: a folding cardboard carton is being replaced with a solid plastic box for Neupro EU/1/05/331/001-012 and EU/1/05/331/014. To change the time that time transdermal patch requires to be pressed against the skin from 20 s to 30 s.</p> <p>The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 09/11/2017 (WS/1238/G), which are available on the Agency's website</p>
Plegridy	All presentations	15/12/2017	<p>Update of section 4.8 of the SmPC to add "alopecia" with a frequency "common". The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/00010275/201701), which are available on the Agency's website.</p>

Revatio	All presentations	15/01/2018	<p>Update of section 4.6 of the SmPC in order to revise the statement concerning the detection of sildenafil and its active metabolite in human milk and the potential for impact on the breastfed infant. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 26/10/2017 (II/0077), which are available on the Agency's website. The yearly update on EC website doesn't include this variation.</p>
Reyataz	All presentations	15/01/2018	<p>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.</p> <p>Parallel distributors must use the annexes dated 11/12/2017 (WS/1193), which are available on the Agency's website</p>
Selincro	All presentations	15/02/2018	<p>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.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA/10120/201702), which are available on the Agency's website</p>
Soliris	All presentations	15/02/2018	<p>Update of sections 4.6 and 5.3 of the SmPC in order to update the safety information related to pregnancy, lactation and fertility following the review of data in PSUR 13 and 14. Annex II and the package leaflet are updated accordingly.</p> <p>Parallel distributors must use the annexes dated 14/12/2017 (II/98), which are available on the Agency's website</p>

Stelara	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 14/09/2017 (II/0058), which are available on the Agency's website</p>
Taltz	All presentations	15/01/2018	<p>Update of section 4.8 of the SmPC to add the adverse reaction "anaphylaxis" with a frequency rare and to modify the existing hypersensitivity warning in section 4.4. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/12/2017 (PSUSA /10493/201703), which are available on the European Commission website</p>
Teysono	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 10/11/2017 (PSUSA/00002875/201701), which are available on the Agency's website</p>
Toujeo	All presentations	15/02/2018	<p>Update of sections 4.2, 4.4 and 6.6 of the SmPC in order to add a warning on the risk for medication error associated with pre-filled pens and cartridges presentations following the evaluation of a signal (EPITT 18893). The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 26/10/2017 (II/0100), which are available on the Agency's website</p>
Velphoro	All presentations	15/02/2018	<p>Update of section 4.4 of the SmPC in order to remove a warning related to allergy to gluten. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 16/11/2017 (II/0012), which are available on the Agency's website</p>

Viekirax	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 15/11/2017 (PSUSA/00010367/201701), which are available on the Agency's website</p>
Visudyne	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 12/10/2017 (II/0095), which are available on the Agency's website</p>
Xalkori	All presentation	15/02/2018	<p>Update of sections 4.2, 4.3, 4.4, 4.8 and 5.2 of the SmPC in order to update the information about hepatic impairment based on the results of study A8081012 which evaluated the effect of hepatic impairment on the pharmacokinetics and safety of crizotinib in advanced cancer patients. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 14/12/2017 (II/0050), which are available on the Agency's website</p>
Yervoy	All presentation	15/01/2018	<p>Update of section 4.4 of the SmPC to add a warning on histiocytosis haematophagic and of section 4.8 of the SmPC to add 'pemphigoid' and 'histtiocytosis haematophagic' as new adverse drug reactions with a 'not known' frequency. The package leaflet is updated accordingly. In addition the MAH took the opportunity to include in section 4 of the package leaflet the standard statement about contacting your doctor in case of side effects to ensure consistency with the other frequency categories.</p> <p>Parallel distributors must use the annexes dated 08/01/2018 (PSUSA/00009200/201703), which are available on the Agency's website</p>

Zonegran	All presentations	15/02/2018	<p>Update of section 4.4 and 4.6 to add information from a registry study on the risk of low birth weight and small for gestational age in infants exposed to zonisamide in utero and to update information regarding the need to counsel women of child-bearing potential on the risk of anti-epileptic drugs in pregnancy. The package leaflet is updated accordingly.</p> <p>Parallel distributors must use the annexes dated 08/01/2018 (PSUSA/3152/201703), which are available on the Agency's website</p>
Zydelig	All presentations	15/12/2017	<p>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.</p> <p>Parallel distributors must use the annexes dated 16/11/2017 (PSUSA/10303/201701), which are available on the European Commission website</p>

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