15 November 2020
EMA/617621/2020.
Human Medicines 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 notifications of safety update before implementation.

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Name	EU number	Date of communication	Rationale
Abilify	All presentations	15/11/2020	Update of the product information and the Company Core Data Sheet (CCDS) due to new safety data. The applicant used the opportunity to revise the wording for akathisia in the package leaflet for a better differentiation between akathisia and restless leg syndrome The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (II/0136/G), which are available on the Agency's website**
Abilify Maintena	All presentations	15/11/2020	To update the product information with "DRESS" as new identified ADR in section 4.8 of the SmPC and subsequently in section 4 of the package leaflet according to the current CCDS version. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (II/0037), which are available on the Agency's website**
Aimovig	All presentations	15/09/2020	Update of section 4.4 of the SmPC to add information on the characteristics of constipation. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/08/2020 (PSUSA/00010699/201911), which are available on the Agency's website.**
Atripla	All presentations	15/09/2020	Update of sections 4.4, 4.5 and 4.8 of the SmPC regarding the drug-drug interaction with didanosine and of section 4.8 of the SmPC regarding lactic acidosis. Update of section 4.5 of the SmPC to update the wording of the interaction between efavirenz and etonogestrel implants. Update of section 4.5 of the SmPC to state that co-administration of glecaprevir/pibrentasvir with Atripla is not recommended. In addition, the drugs boceprevir, nelfinavir and simeprevir, which have been withdrawn from the European Market, were removed from the PI. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/06/2020 (II/0143/G), which are available on the Agency's website.**
Aubagio	All presentations	15/11/2020	Submission of information in relation to human

Name	EU number	Date of communication	Rationale
			experience of use of teriflunomide during pregnancy from an analysis of the data recorded in the global safety database and available sources (clinical trial cases, registries and cohort studies, literature and post-marketing pregnancy reports) The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (II/0028), which are available on the Agency's website**
Azilect	All presentations	15/11/2020	Section 4.4. of SmPC was updated to amend the information on risk of melanoma associated with the use of rasagiline. The package leaflet is updated in accordingly. **Parallel distributors must use the annexes dated 03/09/2020 (WS/1749), which are available on the Agency's website**
Bavencio	All presentations	15/10/2020	Update of sections 4.2, 4.4 and 4.8 of the SmPC in order to change posology recommendations, amend an existing warning and add new ADRs with frequency uncommon regarding myasthenia gravis and myasthenic syndrome. The update results from an update of the Company Core Data Sheet (CCDS) based on the review of cases of myasthenia gravis/myasthenic syndrome. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (II/0015), which are available on the European Commission website.**
Beovu	All presentations	15/11/2020	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 03/09/2020 (II/0002), which are available on the Agency's website.**
Bexsero	All presentations	15/09/2020	Update of section 4.8 of the SmPC in order to update the safety information and include rash as adverse reaction in adolescents and adults. The package leaflet is updated accordingly

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			Parallel distributors must use the annexes dated 02/07/2020 (II/0091), which are available on the Agency's website
Biktarvy	All presentations	15/11/2020	Update of section 4.8 of the SmPC to amend the wording of suicidal behaviour into suicidal ideation and suicide attempt in the light of the causal relationship between bictegravir / emtricitabine / tenofovir alafenamide and suicidal behaviour, with the frequency remaining uncommon. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 28/10/2020 (II/0029) which are available on the Agency's website**
Constella	All presentations	15/11/2020	Update of section 4.6 of the SmPC based on the final results of Lactation study 1915-7/LIN-PK-01 listed as a category 3 study in the RMP; this is an open-label, multiple-dose, milk-only lactation study in lactating women receiving linaclotide therapeutically. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 04/09/2020 (II/0049) which are available on the Agency's website**
Cosentyx	All presentations	15/10/2020	Update of section 4.8 of the SmPC to add the adverse reaction fatigue, nausea and headache with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/09/2020 (PSUSA/00010341/201912) which are available on the Agency's website**
Cubicin	All presentations	15/09/2020	Update of sections 4.4 and 4.8 of the SmPC in order to include two new terms, tubulointerstitial nephritis (TIN) and drug reaction with eosinophilia and systemic symptoms (DRESS) to the special warnings and precautions of the SmPC. TIN has also been added to the adverse events section, based on a review of the cumulative post-marketing cases associated with the use of daptomycin. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 16/07/2020 (II/0075) which are available on the Agency's website.**

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Darzalex	All presentations	15/09/2020	Update section 4.8 of the SmPC in order to add sepsis with frequency common as an ADR and incidence data on fatal infections and adverse reactions in the elderly patients based on cross-programmatic review of data. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/07/2020 (II/0038), which are available on the Agency's website**
Dovato	All presentations	15/09/2020	Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir -containing regimens based on the interim analysis from the Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The MAH has taken the opportunity to include a paragraph on section 4 of the PL regarding weight, blood lipid and blood glucose effects too. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (II/0001), which are available on the Agency's website**
DuoPlavin	All presentations	15/09/2020	To update section 4.4 and 4.5 of the SmPC to add drug-drug interaction information for rifampicin and clopidogrel based on a literature review and a review of the MAH pharmacovigilance database. The MAH also took the opportunity to update the product information regarding the standard term for the all-aluminium unit-dose blisters. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (WS/1848), which are available on the Agency's website**
Elebrato Ellipta	All presentations	15/11/2020	Update of section 4.8 of the SmPC to add hypersensitivity reactions including anaphylaxis, angioedema, urticaria and rash

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			with a frequency estimated as rare based on review of the Applicant clinical safety database. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (WS/1814), which are available on the Agency's website**
Erivedge	All presentations	15/11/2020	Update of the educational materials provided as part of the Erivedge Pregnancy Prevention Program, following conclusion of PSUSA/00010140/201901. Annex IID is updated accordingly. Furthermore, section 4.4 of the SmPC is updated to remove the warning on cutaneous squamous cell carcinoma. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 03/09/2020 (II/0046), which are available on the Agency's website**
Evoltra	All presentations	15/10/2020	Update of section 4.2 of the SmPC to add the step of filtration in sub-section "Method of administration". Updated of Annex IIIa, section "Method and route(s) of administration" to include the need of filtration. Addition of a dedicated section in the package leaflet Instructions for use for healthcare professionals was updated on handling clofarabine. Both the **labelling** and **package leaflet** are updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00000805/201912), which are available on the Agency's website**
Eylea	All presentations	15/10/2020	Update of section 4.8 of the SmPC to add the adverse reaction retinal haemorrhage with a very common frequency. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00010020/201911), which are available on the Agency's website**
Fampyra	All presentations	15/09/2020	Update of sections 4.2, 4.3, 4.4, 4.8, 4.9 and 5.2 of the SmPC in order to remove the contraindication for patients with mild renal impairment, add a warning for patients with mild renal impairment, update the frequency of seizure to uncommon, add vertigo with

Name	EU number	Date of communication	Rationale
			frequency common, add dizziness in section 4.9 to reflect safety information based on from final results of study 218MS401 (LIBERATE) listed as category 3 study in the RMP; Study 218MS401 was a Phase IV prospective, noninterventional, multicentre, observational study in MS patients who began Fampyra treatment in the post marketing setting. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/07/2020 (II/0046), which are available on the Agency's website**
Hemangiol	All presentations	15/11/2020	Update of section 4.4 of the SmPC to amend the existing warning on hypoglycaemia and of the package leaflet to amend the existing warnings on hypotension/bradycardia and hypoglycaemia following the completion of a Drug Utilisation Study (DUS)In addition, editorial amendments are made to section 4.4 of the SmPC and to the package leaflet. **Parallel distributors must use the annexes dated 28/11/2019 (II/0019), which are available on the Agency's website.**
Herceptin	All presentations	15/10/2020	Update of section 4.7 of the SmPC in order to add dizziness and somnolence to the recommendations on the effects on the patient's ability to drive and use machines. Update of section 4.8 of the SmPC to remove herpes zoster, erysipelas, cellulitis common, sepsis, thinking abnormal, ataxia, paresis, brain oedema, pericarditis, bradycardia and hepatic failure as adverse drug reactions. An update of the frequencies of adverse reactions is proposed anaphylactic reaction and anaphylactic shock is changed to frequency rare, wheezing is changed to frequency uncommon, pneumonitis is changed to frequency uncommon and palpitation is changed to frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/07/2020 (II/0160), which are available on the Agency's website.**
Humalog	All presentations	15/11/2020	Update sections 4.2, 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement

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			the signal recommendations on "Signal assessment report on cutaneous amyloidosis with insulin human (regular and NPH), insulin degludec, insulin aspart, insulin lispro, insulin detemir, insulin glargine, insulin glulisine and insulin porcine (class effect of insulin containing products) " (EPITT no 19499) **Parallel distributors must use the annexes dated 04/09/2020 (WS/1909), which are available on the Agency's website**
Imbruvica	All presentations	15/09/2020	Update of section 4.4 of the SmPC to add a warning on splenic rupture following discontinuation of ibrutinib treatment. Update of section 4.4 and 4.8 of the SmPC to add the adverse reaction cardiac failure and a warning regarding cardiac failure. Update of section 4.8 of the SmPC to add the adverse reaction neutrophilic dermatoses. Update of section 4.4 of the SmPC to add a warning regarding hemophagocytic lymphohistiocytosis (HLH). Extension of indication in chronic lymphocytic leukaemia (CLL) to add combination with rituximab as follows: In combination with rituximab or obinutuzumab for the treatment of adult patients with previously untreated CLL. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 28/08/2020 (II/0059), which are available on the Agency's website.**
Infanrix hexa	All presentations	15/11/2020	Update of sections 4.8 and 5.1 of the SmPC in relation to the frequency of adverse reactions somnolence and fatigue and to update the safety and immunogenicity information in infants and toddlers born to mothers vaccinated with dTpa during pregnancy; based on data generated from DTPA-048 and DTPA-049; these are phase IV, open-label, non-randomised, multicentre studies aimed to provide immunological responses to Infanrix hexa in terms of seroprotection status for diphtheria (D), tetanus (T), HBs antigen, inactivated poliovirus (IPV) and Haemophilus influenzae type b (Hib) antigens (PRP) and in terms of vaccine or booster responses to the

Name	EU number	Date of communication	Rationale
			pertussis antigens, 1 month after the last dose of the primary vaccination or the booster dose. The MAH took the opportunity to update the posology information as well in the package leaflet to align it with the SmPC. **Parallel distributors must use the annexes dated 03/09/2020 (II/0275), which are available on the Agency's website.**
Iscover	All presentations	15/09/2020	To update section 4.4 and 4.5 of the SmPC to add drug-drug interaction information for rifampicin and clopidogrel based on a literature review and a review of the MAH pharmacovigilance database. The MAH also took the opportunity to update the product information regarding the standard term for the all-aluminium unit-dose blisters. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (WS/1848), which are available on the Agency's website.**
Juluca	All presentations	15/09/2020	Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir -containing regimens based on the interim analysis from the Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (II/0016), which are available on the Agency's website**
Kaletra	All presentations	15/09/2020	Update of section 4.5 of the SmPCs in order to add information on drug-drug interactions with fostamatinib. Update of section 4.8 of the SmPC in order to update the safety information for nephrolithiasis as an adverse reaction following an update to company core data sheets (CCDS 0220) In addition, the MAH/SOH

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			takes the opportunity to make additional changes in the PI in order to comply with the current QRD template and provide clarity to instructions contained in the PL. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/07/2020 (WS/1845), which are available on the Agency's website**
Keppra	All presentations	15/10/2020	Update of section 4.4 of the SmPC: special warnings and precautions for use was updated as follows: - Addition of warning: seizure worsening Section 4.8 Undesirable effects was updated as follows: - Addition of ADR: seizures aggravated The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (WS/1827), which are available on the Agency's website**
Kisqali	All presentations	15/11/2020	Update of sections 4.2, 4.4, 4.8, 5.1, 5.2 of the SmPC to include updated information about the use of Kisqali in patients with mild, moderate or severe renal impairment based on the results of Study CLEE011A2116 Part II and additional data from breast cancer patients with mild or moderate renal impairment. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/10/2020 (II/0018), which are available on the Agency's website.**
Liprolog	All presentations	15/11/2020	Update sections 4.2, 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement the signal recommendations on "Signal assessment report on cutaneous amyloidosis with insulin human (regular and NPH), insulin degludec, insulin aspart, insulin lispro, insulin detemir, insulin glargine, insulin glulisine and insulin porcine (class effect of insulin containing products) "" (EPITT no 19499) In addition, the MAH took the opportunity to make some corrections to the pictures in the Liprolog instructions information for use .The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 04/09/2020 (WS/1909), which are available on the Agency's website**

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Lynparza	All presentations	15/10/2020	Update of section 4.8 of the SmPC to add erythema nodosum and angioedema with a frequency rare and uncommon respectively. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00010322/201912), which are available on the Agency's website**
Ninlaro	All presentations	15/09/2020	Update of section 4.4 of the SmPC to add a warning on thrombotic microangiopathy and update of section 4.8 of the SmPC to add the adverse reaction thrombotic microangiopathy with a frequency rare. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/08/2020 (PSUSA/00010535/201911), which are available on the Agency's website.**
Norvir	All presentations	15/09/2020	Update of section 4.5 of the SmPC in order to add information on drug-drug interactions with fostamatinib. Update of section 4.8 of the SmPC in order to update the safety information for nephrolithiasis as an adverse reaction following an update to company core data sheets. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/07/2020 (WS/1845), which are available on the Agency's website**
Orkambi	All presentations	15/09/2020	Update of section 4.8 of the SmPC with safety data in children from the Phase 3, open-label, multicentre rollover study for Study 115 Part B, designed to evaluate long-term safety of Orkambi treatment for 96 weeks in patients with cystic fibrosis, 2 years of age and older, homozygous for F508del. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 09/07/2020 (II/0049), which are available on the Agency's website.**
Ozempic	All presentations	15/10/2020	Update of sections 4.8 of the SmPC to introduce the grouped term hypersensitivity, covering adverse events related to hypersensitivity, rash and urticaria, to the list of adverse drug reactions with a frequency

Name	EU number	Date of communication	Rationale
			uncommon. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 30/09/2020 (PSUSA/00010671/201911), which are available on the European Commission website**
Plavix	All presentations	15/09/2020	To update section 4.4 and 4.5 of the SmPC to add drug-drug interaction information for rifampicin and clopidogrel based on a literature review and a review of the MAH pharmacovigilance database. The MAH also took the opportunity to update the product information regarding the standard term for the all-aluminium unit-dose blisters. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 12/07/2020 (WS/1848), which are available on the Agency's website**
Prezista	All presentations	15/11/2020	Update of section 4.5 of the SmPC for Prezista, Rezolsta and Symtuza in order to include information on the interaction with Clopidogrel. The MAH also takes the opportunity to make several editorial changes in the SmPC to include the sodium-free statement in section 4.4 and remove simeprevir, boceprevir and nelfinavir from section 4.5 from the list of interactions, as they are no longer marketed. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 03/09/2020 (WS/1883), which are available on the Agency's website.**
Protopic	All presentations	15/09/2020	Update of sections 4.4, 4.8, 5.1, 5.2 and 5.3 of the SmPC following results from two non-interventional post-authorisation safety studies: JOELLE study (Joint European Longitudinal Lymphoma and skin cancer Evaluation, category 3) and APPLES study (a prospective paediatric longitudinal evaluation to assess the long-term safety of tacrolimus ointment for the treatment of atopic dermatitis, category 3. The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 23/07/2020 (II/0083/G), which are available on the Agency's website.
Qutenza	All presentations	15/09/2020	Update of section 4.8 of the SmPC in order to update the safety information on adverse reactions frequencies based on latest clinical data pooling. The package leaflet is updated accordingly**.** **Parallel distributors must use the annexes dated 16/07/2020 (II/0049), which are available on the Agency's website.**
Rasagiline ratiopharm	All presentations	15/11/2020	Section 4.4. of SmPC was updated to amend the information on risk of melanoma associated with the use of rasagiline. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 03/09/2020 (WS/1749), which are available on the Agency's website**
Rezolsta	All presentations	15/11/2020	Update of section 4.5 of the SmPC for Prezista, Rezolsta and Symtuza in order to include information on the interaction with Clopidogrel. The MAH also takes the opportunity to make several editorial changes in the SmPC to include the sodium-free statement in section 4.4 and remove simeprevir, boceprevir and nelfinavir from section 4.5 from the list of interactions, as they are no longer marketed. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 03/09/2020 (WS/1883), which are available on the Agency's website.**
Reyataz	All presentations	15/09/2020	Update of sections 4.3 and 4.5 of the SmPC to add a new contraindication and a new drug-drug interaction related to co-administration with lomitapide, based on recommendations already approved for lomitapide; update of section 4.5 of the SmPC to add new drug-drug interactions related to co-administration with the direct oral anticoagulants (DOACs) apixaban, dabigatran, edoxaban and rivaroxaban, to align with wording approved for DOACs; the package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 28/08/2020 (II/0129/G), which are available on the Agency's website
Revlimid	All presentations	15/11/2020	Update of section 4.4 and 4.8 of the SmPC to add the adverse reaction pulmonary hypertension with a frequency uncommon for all grades and rare for grade 3-4, and a warning on the risk of pulmonary hypertension. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00001838/201912), which are available on the Agency's website**
RotaTeq	All presentations	15/09/2020	Update of section 4.4. of the SmPC to add a warning on the use of the vaccine in children who have been in utero exposed to immunosuppressive treatment. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 25/08/2020 (PSUSA/00002666/201911), which are available on the Agency's website**
Saxenda	All presentations	15/11/2020	Update of section 4.9 of the SmPC to inform HCP's that hypoglycaemia has occurred in cases of liraglutide overdose. The package Leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00001892/201912), which are available on the European Commission website**
Siklos	All presentations	15/09/2020	Update of sections 4.2, 4.4, 4.5, 4.6, 4.8, 4.9 and 5.1 of the SmPC because of the final study results of the non-interventional cohort study ESCORT-HU (European Sickle Cell Disease Cohort – Hydroxyurea) and harmonisation with other HU products. In addition, Annex II is amended to revise the information on the physician information pack and to add that pharmacists should receive targeted communication on the risk of medication error due to the confusion between the two strengths where both are available. The package leaflet is updated accordingly

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			Parallel distributors must use the annexes dated 09/07/2020 (II/0045), which are available on the Agency's website.
Skilarence	All presentations	15/11/2020	Update section 4.8 of the SmPC with herpes zoster under SOC Infections and infestations and shingles included in section 4. Possible side effects, under frequency not known: The package leaflet is updated accordingly**.** **Parallel distributors must use the annexes dated 09/10/2020 (PSUSA/00010647/201912), which are available on the Agency's website**
Stocrin	All presentations	15/11/2020	Update of sections 4.4 and 4.8 of the SmPC in order to add new warnings regarding late-onset neurotoxicity, including ataxia and encephalopathy, based on reviews of the published literature and MAH safety database. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 13/10/2020 (IB/0124 which includes the II/0123 safety variation), which are available on the Agency's website**
Symtuza	All presentations	15/11/2020	Update of section 4.5 of the SmPC for Prezista, Rezolsta and Symtuza in order to include information on the interaction with Clopidogrel. The MAH also takes the opportunity to make several editorial changes in the SmPC to include the sodium-free statement in section 4.4 and remove simeprevir, boceprevir and nelfinavir from section 4.5 from the list of interactions, as they are no longer marketed. The package leaflet is updated accordingly**.** **Parallel distributors must use the annexes dated 03/09/2020 (WS/1883), which are available on the Agency's website**
Tecentriq	All presentations	15/11/2020	Update of section 4.8 of the SmPC in order to add headache, dry skin and blood creatinine increased to the list of adverse drug reactions (ADRs) for atezolizumab given as monotherapy identified in study WO29636. The MAH has taken this opportunity to update the frequencies of existing ADRs in section 4.8 subsections 'Summary of the safety profile' and 'Description of selected adverse reactions' to

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			reflect the updated pool of patients for atezolizumab monotherapy The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 27/10/2020 (II/0039 which includes the II/0047 safety variation scopes), which are available on the European Commission website**
Tivicay	All presentations	15/09/2020	Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir -containing regimens based on the interim analysis from the Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020(II/0052) which are available on the Agency's website.**
Trelegy Ellipta	All presentations	15/11/2020	Update of section 4.8 of the SmPC to add hypersensitivity reactions including anaphylaxis, angioedema, urticaria and rash with a frequency estimated as rare based on review of the Applicant clinical safety database. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (WS/1814), which are available on the Agency's website**
Triumeq	All presentations	15/09/2020	Update of section 4.6 of the SmPC in order to update the safety information regarding the occurrence of neural tube defects with the dolutegravir -containing regimens based on the interim analysis from the Tsepamo study. This is a birth outcomes surveillance study being conducted in Botswana that was designed to evaluate adverse birth outcomes by HIV status and antiretroviral regimen, and to determine if there is an increased risk of neural tube defects

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			among infants exposed to efavirenz at conception. This surveillance system captures all antiretroviral exposure including dolutegravir. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (II/0069), which are available on the Agency's website.**
Vfend	All presentations	15/11/2020	Update of Section 4.5 of the SmPC in order to include additional text regarding interactions between voriconazole and letermovir & tolvaptan in the interaction table. Update section 4.4 of the SmPC in order to add a new warning on adrenal events, along with editorial changes to the paragraph and the abbreviation of severe cutaneous adverse reactions (SCARs). Update section 4.5. of the SmPC in order to add drug-drug interaction information with naloxegol, ivacaftor and corticosteroids; update of the French "Medical Interaction Thesaurus" (May 2018), where voriconazole is classified as a strong CYP3A4 inhibitor. In addition, the MAH has taken the opportunity to update the information in the SmPC in line with the EU excipient guidance from October 2017 (SANTE-2017-11668) for sodium and cyclodextrin, to introduce a correction to the amount of sodium per vial for the IV presentations in sections 2. QUALITATIVE AND QUANTITATIVE COMPOSITION and 4.4 Special warnings and precautions for use of the SmPC. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/09/2020 (II/0137/G) which are available on the Agency's website**
Vemlidy	All presentations	15/09/2020	Update of the section 4.4 Special warnings and precautions for use of the SmPC, and corresponding section in the PL, are warranted to integrate the existing warning on nephrotoxicity. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/08/2020 (25/08/2020), which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Victoza	All presentations	15/10/2020	Update of Section 4.5 of the SmPC in order to include additional text regarding interactions between voriconazole and letermovir and tolvaptan in the interaction table. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/09/2020 (PSUSA/00001892/201912) which are available on the European Commission website**
Zejula	All presentations	15/09/2020	Update of section 4.8 of the SmPC in order to add hypersensitivity, confusional state, and pneumonitis to the list of adverse drug reactions (ADRs) with the frequency common, and uncommon respectively based on safety evaluations. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/07/2020 (II/0020) which are available on the Agency's website.**

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