15 November 2022
EMA/890290/2022
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.

Name	EU number	Date of communication	Rationale
Actelsar HCT	All presentations	15/10/2022	To update sections 4.4 and 4.8 of the SmPC and sections 2 of the PL to implement the wording of acute respiratory toxicity agreed by the PRAC following the outcome of the PSUSA/00001662/202101. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (IB/0029), which are available on the Agency's website**
Adenuric	All presentations	15/10/2022	To update section 5.1 of the SmPC to correct a discrepancy between the SmPCs of the two dosages, deleting a sentence which was not removed by mistake following approval of procedure EMEA/H/C/000777/II/0061. In addition, the marketing authorisation holder has taken the opportunity to implement minor editorial changes in the Danish, Spanish and Bulgarian translations of the PI. **Parallel distributors must use the annexes dated 08/08/2022 (IB/0069), which are available on the Agency's website**
Advagraf	All presentations	15/11/2022	Update of sections 4.4, 4.5 and 4.8 of the SmPC to add a warning on the adverse reaction Thrombotic microangiopathy (TMA) based on a cumulative review of fatal cases of TMA during treatment with tacrolimus, requested by the PRAC following the assessment of the PSUR (EMEA/H/C/00002839/202103). Update of section 4.5 of the SmPC to add the drug-drug interaction between tacrolimus and caspofungin based on post-marketing safety report and literature. Update of section 5.2 of the SmPC to add that tacrolimus is metabolized by the cytochrome P450-3A5 (CYP3A5) based on post-marketing safety report and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 06/10/2022 (WS2241/G), which are available on the Agency's website**
Afinitor	All presentations	15/09/2022	Update sections 4.4 and 4.5 of the SmPC, and sections 2 of the PL to implement the signal recommendations on 'interaction with

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			cannabidiol leading to systemic calcineurin inhibitors and mTOR inhibitors serum levels increased and toxicity' (EPITT no 19614)' The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/06/2022 (C/IG1518), which are available on the Agency's website**
Afstyla	All presentations	15/09/2022	Update of section 5.1 of the to assess the safety and efficacy of Afstyla in subjects with severe hemophilia A. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/06/2022 (II/0042), which are available on the Agency's website**
Alecensa	All presentations	15/09/2022	Update of sections 4.2, 4.4 and 4.8 of the SmPC to add a new warning, dose modification advice and description of the known ADR haemolytic anaemia based on an updated drug safety report. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 02/08/2022 (II/0037/G), which are available on the Agency's website**
Aptivus	All presentations	15/09/2022	Update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 28/07/2022 (IAIN/0092), which are available on the Agency's website**
Aripiprazole Accord	All presentations	15/09/2022	Update section 4.8 of the SmPC to add "blood prolactine decreased" in the tabulated list of all adverse reactions in line with the text of reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/07/2022 (IB/0026), which are available on the Agency's website.**

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Aripiprazole Mylan Pharma	All presentations	15/10/2022	Update section 4.8 of the SmPC to add "blood prolactine decreased" in the tabulated list of all adverse reactions in line with the text of reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 12/09/2022 (IB/0021), which are available on the Agency's website.**
Aripiprazole Sandoz	All presentations	15/10/2022	Update section 4.8 of the SmPC to add "blood prolactine decreased" in the tabulated list of all adverse reactions in line with the text of reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/09/2022 (IB/0023), which are available on the Agency's website**
Armisarte	All presentations	15/10/2022	To update Sections 4.4 and 4.6 of the SmPC concerning duration of contraception following the end of treatment with a genotoxic drug. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (IB/0029), which are available on the Agency's website**
Avonex	All presentations	15/11/2022	Update of section 4.4 of the SmPC to add a new warning regarding the risk of injection site necrosis based on post marketing experience. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/09/2022 (II/0192), which are available on the Agency's website.**
Aybintio	All presentations	15/09/2022	To introduce the statement "do not shake" in the Aybintio PI in sections 4.2 and 6.6 of the SmPC, and in the package leaflet. To delete the following manufacturing sites: - FUJIFILM Diosynth, Biotek Alle 1, 3400 Hillerød, Denmark as a site responsible for batch release finished product. To change the ATC Code of bevacizumab from L01XC07 to L01FG01. The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 21/07/2022 (IB/0015/G), which are available on the Agency's website.
Azacitidine Mylan	All presentations	15/09/2022	Update sections 4.4 and 4.8 of the SmPC to add the adverse reaction 'differentiation syndrome' with a frequency "not known" to align the PI with its parent product Vidaza. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/06/2022 (IB/0010), which are available on the Agency's website.**
Azarga	All presentations	15/11/2022	Update the SmPC section 4.4 and 4.8 to include the ADR Stevens-Johnson syndrome /toxic epidermal necrolysis with a frequency "not known" in line with the outcome of EMEA/H/C PSUSA/00000432/202108. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/10/2022 (IB/0048/G), which are available on the Agency's website**
Blitzima	All presentations	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (PSUSA/00002652/202111), which are available on both the Commission the Agency's website.**
Bonviva	All presentations	15/09/2022	Update of section 4.8 of the SmPC to add the ADR hypocalcaemia with a frequency "uncommon". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/07/2022 (PSUSA/00001702/202106), which are available on the Agency's website.**

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Braftovi	All presentations	15/09/2022	Update of section 4.2 of the SmPC to introduce a new scheme of encorafenib dose reduction recommendations for the treatment of adult patients with unresectable or metastatic melanoma with a BRAF V600 mutation, by replacing the second dose reduction level of 200 mg once daily by 225 mg once daily; based on results from simulation report (ARRA-CSC-104). In addition, the MAH took the opportunity to introduce an update of the user instructions in the package leaflet for increased clarity. **Parallel distributors must use the annexes dated 25/07/2022 (II/0026), which are available on both the Commission the Agency's website.**
Bydureon	All presentations	15/09/2022	Update of section 4.8 of the SmPC in order to add cholelithiasis and cholecystitis to the list of adverse drug reactions (ADRs) with frequency "unknown" based on the cumulative review of pre-clinical and clinical study data, post-marketing data, medical/scientific literature and signal searches in internal and external databases on 'Gallbladder-related disorders' and exenatide. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/07/2022 (II/0074), which are available on the Agency's website**
Byetta	All presentations	15/09/2022	Update of section 4.8 of the SmPC in order to add cholelithiasis and cholecystitis to the list of adverse drug reactions (ADRs) with frequency "unknown" based on the cumulative review of pre-clinical and clinical study data, post-marketing data, medical/scientific literature and signal searches in internal and external databases on 'Gallbladder-related disorders' and exenatide. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/07/2022 (II/0078), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Cablivi	All presentations	15/09/2022	Update of sections 4.4 and 4.8 of the SmPC to amend an existing warning on increased risk of bleeding and add blood and lymphatic system disorders to the list of adverse drug reactions (ADRs) with frequency "not known" based on a safety evaluation report. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/06/2022 (II/0035), which are available on the Agency's website**
Cabometyx	All presentations	15/10/2022	Update of section 4.8 of the SmPC to add cutaneous vasculitis and pneumothorax as adverse reactions under SOC Skin and subcutaneous tissue disorders with a frequency "not known" and SOC Respiratory, thoracic and mediastinal disorders with frequency "uncommon", respectively. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 29/09/2022 (PSUSA/00010180/202111), which are available on the European Commission website.**
Celsentri	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 19/08/2022 (IG1531), which are available on the Agency's website**
Clopidogrel Zentiva	All presentations	15/09/2022	To update section 4.5 of the SmPC to add rosuvastatin which use lower your cholesterol level to align the PI with reference product Plavix. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/06/2022 (IB/0081), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Combivir	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 11/08/2022 (IG1532), which are available on the Agency's website.**
Cometriq	All presentations	15/11/2022	Update of section 4.8 of the SmPC to add cutaneous vasculitis and pneumothorax as adverse reactions under SOC Skin and subcutaneous tissue disorders with a frequency not known and SOC Respiratory, thoracic and mediastinal disorders with frequency uncommon, respectively. In addition, only for Cabometix medicinal product containing cabozantinib: update of section 4.4 of the SmPC to update the warning on hypertension. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/09/2022 (PSUSA/00010180/202111), which are available on both the European Commission and the Agency's website**
Crysvita	All presentation	15/10/2022	Update of sections 4.8 and 5.1 of the SmPC to update the frequency of the adverse drug reactions, to split immunogenicity data into paediatric and adult populations and to update clinical efficacy in paediatric patients, upon request by the CHMP following the assessment of PAM procedures P46/006 and P46/007 and type II variations II/04 and II/10/G, based on the final results from studies UX023-CL201, UX023-CL205 and UX023-CL301. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/09/2022 (II/0028), which are available on the European Commission website**

Name	EU number	Date of communication	Rationale
Cyramza	All presentation	15/09/2022	Update of section 4.4 and 4.8 of the SmPC to add a new warning on heart failure following a detailed cumulative review of post-marketing data. In addition, the MAH took the opportunity to update the package leaflet to include hypothyroidism as a common side effect. **Parallel distributors must use the annexes dated 25/07/2022 (II/0043), which are available on both the European Commission the Agency's website**
Dasatinib Accord	All presentation	15/09/2022	To update Sections 4.4 and 4.8 of SmPC to add warning on and to include the adverse reaction to chylothorax with the frequency "uncommon" following the same update for the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/06/2022 (IB/0001), which are available on the Agency's website**
Delstrigo	All presentations	15/11/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding **Parallel distributors must use the annexes dated 10/10/2022 (IG1535), which are available on the Agency's website**
Dovato	All presentations	15/09/2022	Update sections 4.4 and 4.6 of the SmPC to delete the information related to sexual transmission and update of the text regarding HIV transmission in breastfeeding women following the CHMP recommendation in January. To update section 4.8 of the SmPC and section 4 of the PL to include the ADR weight increased with a frequency "common". **Parallel distributors must use the annexes dated 01/09/2022 (WS2268 which also includes the II/0029 safety scopes too), which are available on the Agency's website**.

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Dynastat	All presentations	15/09/2022	Update of section 4.9 of the SmPC to amend it with the current medical guidance for acute NSAIDs poisoning/overdose. In addition, the MAH took the opportunity to introduce a minor editorial change to the PI and to update the list of local representatives in the package leaflet. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/06/2022 (II/0085), which are available on the Agency's website**
Edurant	All presentations	15/11/2022	To update section 4.4 and 4.6 of the SmPC and section 2 of the PL, to delete the information related to sexual transmission and update of the text regarding HIV transmission in breast-feeding women. **Parallel distributors must use the annexes dated 28/10/2022 (IB/0041), which are available on the Agency's website**
Efavirenz/Emtricitabine/Tenofovir disoproxil Mylan	All presentations	15/10/2022	To update section 4.5 of the SmPC with the drug-drug interaction between praziquantel and efavirenz. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/08/2022 (IB/0020), which are available on the Agency's website**
Emgality	All presentations	15/09/2022	Update of section 4.4 of the SmPC to add information that serious hypersensitivity reactions may occur more than 1 day to four weeks after administration and be prolonged in duration. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/07/2022 (PSUSA/00010733/202103), which are available on both the Agency and the European Commission website**
Envarsus	All presentations	15/09/2022	To update sections 4.4 and 4.5 of the SmPC and section 2 of the PL, to implement the signal recommendation on drug interaction with cannabidiol leading to systemic calcineurin

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			inhibitors and mTOR inhibitors serum levels increased and toxicity (EPITT 19614). Update of sections 4.4, and 4.5 of the SmPC on the interaction with CYP3A4 based on a comprehensive review of available data. Section 4.5 of the SmPC is also updated to include impact of direct acting antiviral therapy. In addition, to update section 4.8 of the SmPC to add posterior reversible encephalopathy syndrome as an adverse reaction and update the SOC for febrile neutropenia from 'General disorders and administration site conditions' to 'Blood and lymphatic system disorders', following assessment of the same changes for Advagraf). Furthermore, the marketing authorisation holder has taken the opportunity to align the PI to the latest QRD template (v.10.2). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/07/2022 (IB/0028/G), which are available on the Agency's website**
Epivir	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 11/08/2022 (IG1532), which are available on the Agency's website**
Esperoct	All presentations	15/11/2022	Update of sections 4.4 and 4.8 of the SmPC to add a new warning and update the list of ADRs based on a validated safety signal concerning a lack of factor VIII activity in patients switching from a similar factor VIII product to Esperoct. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/07/2022 (II/0010), which are available on the Agency's website**

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Eucreas	All presentations	15/11/2022	Update of section 4.8 of the SmPC in order to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). Update of section 4.8 of the SmPC in order to add the new ADRs 'cutaneous vasculitis' with the frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/07/2022 (WS2253), which are available on the Agency's website**
Evra	All presentations	15/09/2022	To correct the inconsistent information related to the pharmacodynamic drug-drug interaction between ethinyl estradiol and Maviret (glecaprevir/pibrentasvir) in section(s) 4.3, 4.4 and 4.5 of the SmPC and in section 2 of the package leaflet. To update SmPC section 4.4 and 4.8 on ethinyl estradiol containing products regarding angioedema. **Parallel distributors must use the annexes dated 13/06/2022 (IB/0051/G), which are available on the Agency's website**
Ferriprox	All presentations	15/11/2022	To update the SmPC section 4.6 following the recommendations from SWP regarding the contraception and genotoxicity. The package leaflet and patient alert card have been updated accordingly **Parallel distributors must use the annexes dated 30/09/2022 (IB/0158), which are available on the Agency's website**
Flixabi	All presentations	15/09/2022	To update Section 4.4, 4.5 and 4.6 of the SmPC regarding administration of live vaccine to infants exposed to infliximab during pregnancy, following assessment of the same changes adopted for the reference product Remicade. Patient reminder card and section 2 of the package leaflet are amended accordingly. **Parallel distributors must use the annexes dated 07/06/2022 (IB/0074), which are available on the Agency's website**

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Forxiga	All presentations	15/09/2022	Update of sections 4.8 of the SmPC to add the adverse reaction tubulointerstitial nephritis with a frequency "very rare", and 4.5 of the SmPC to add an interaction between dapagliflozin and lithium. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/07/2022 (PSUSA/00010029/202110), which are available on both the Agency and the European Commission website**
Fycompa	All presentations	15/10/2022	To update the warning information for sorbitol, and to include the warning and quantitative information for both sodium benzoate and benzoic acid to align with the excipient guidance for the oral solution. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (IB/0063), which are available on the Agency's website**.
Galvus	All presentations	15/11/2022	Update of section 4.8 of the SmPC to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). Update of section 4.8 of the SmPC to add the new ADRs 'cutaneous vasculitis' with the frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/07/2022 (WS/2253), which are available on the Agency's website**.
Genvoya	All presentations	15/11/2022	Extension application to introduce a new strength (90 mg/90 mg/120 mg/6 mg film-coated tablets). The extension application is grouped with a type II variation (C.I.6.a) to include treatment of human immunodeficiency virus 1 (HIV 1) infection without any known mutations associated with resistance to the integrase inhibitor class, emtricitabine or tenofovir in paediatric patients aged from 2 years and with body weight at least 14 kg. Sections 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC and the package leaflet are updated to support

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			the extended indication. The RMP (version 5.1) is updated in accordance. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 03/10/2022 (X/0079/G), which are available on both the Agency and the European Commission website**
Granpidam	All presentations	15/09/2022	To update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and entresto to align the PI with its parent product Revation. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/07/2022 (IB/0013), which are available on the Agency's website**
Grepid	All presentations	15/09/2022	To update section 4.5 of the SmPC to add the drug-drug interaction between clopidogrel and rosuvastatin to align the PI with its parent product Plavix. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/07/2022 (IB/0053), which are available on the Agency's website**
HBVaxPro	All presentations	15/09/2022	Update of section 5.1 of the SmPC in relation to study V419-013, following procedure EMEA/H/C/000373/P46/061. The sentence "As with other hepatitis B vaccines, the duration of the protective effect in healthy vaccinees is unknown at present" was revised to "The duration of the protective effect in healthy vaccinees is unknown". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/08/2022 (IG1524/G which includes the II/0076 safety scopes) which are available on the Agency's website.**
Hepcludex	All presentations	15/09/2022	Update of section 4.4 of the SmPC in order to move the warnings for the ADRs 'Increase of bile salts' and 'Administration site reactions' to section 4.8 of the SmPC as additional

Name	EU number	Date of communication	Rationale
			describing information to the listed PTs , together with the addition of a new ADR: hypersensitivity reactions (including anaphylactic reaction). Further to a safety review based on pooled data from clinical trials and post-marketing experience, editing of existing ADRs in Section 4.8 was also carried out. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/07/2022 (II/0011), which are available on the Agency's website**
Icandra	All presentations	15/11/2022	Update of section 4.8 of the SmPC in order to add the new ADRs 'cutaneous vasculitis' with the frequency "not known". Update of section 4.8 of the SmPC in order to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/10/2022 (WS2224), which are available on the Agency's website.** This is the latest version, **not** the YU on the EC website
Incruse Ellipta	All presentations	15/11/2022	Update of section 4.8 of the SmPC to add the adverse reaction anaphylaxis, in the existing wording for hypersensitivity reactions. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2022 (PSUSA/00010263/202112), which are available on the Agency's website**
Instanyl	All presentations	15/11/2022	To update the instructions of use on the PIL for the nasal spray. **Parallel distributors must use the annexes dated 16/09/2022 (IB/0070/G), which are available on the Agency's website**
Invirase	All presentations	15/11/2022	To implement CHMP recommendations to update product information of all HIV products approved in the EU with regards to removal of the disease information relating to sexual transmission of HIV (section 4.4 of the SmPC

Name	EU number	Date of communication	Rationale
			and section 2 of the Package Leaflet) and amendment of the sections relating to breastfeeding (section 4.6 of the SmPC). In addition, the MAH took the opportunity to make the following editorial changes: - Addition of sentence "Invirase contains lactose" in line with EMA guidelines on SmPC, QRD template, Excipients & stylistic matters The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/10/2022 (IB/0138), which are available on the Agency's website**
Irbesartan/Hydrochlorothiazide Teva	All presentations	15/10/2022	Update sections 4.4 and 4.8 of the SmPC to implement the wording agreed by the PRAC following the outcome of the PSUSA/00001662/202101. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/08/2022 (IB/0058), which are available on the Agency's website**
Imatinib Accord	All presentations	15/09/2022	To update section 4.8 of the SmPC to add panniculitis (including erythema nodosum) and additional information has been required regarding frequency calculation. To update section 4.8 of the SmPC to add pemphigus with frequency" rare" and osteonecrosis with frequency "uncommon" to the list of adverse drug reactions based on an analysis of pre-clinical data, scientific literature, clinical trial datasets, Novartis pharmacovigilance database, EVDAS and other safety database with the already approved ADR section of the SmPC as a number of ADRs is not reflected accurately to align the PI with its parent product Glivec. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/06/2022 (IB/0035/G), which are available on the Agency's website**
Imatinib Teva	All presentations	15/09/2022	To update section 4.8 of the SmPC to add panniculitis (including erythema nodosum) and additional information has been required regarding frequency calculation. To update

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			section 4.8 of the SmPC to add pemphigus with frequency "rare" and osteonecrosis with frequency "uncommon" to the list of adverse drug reactions based on an analysis of pre-clinical data, scientific literature, clinical trial datasets, Novartis pharmacovigilance database, EVDAS and other safety database with the already approved ADR section of the SmPC as a number of ADRs is not reflected accurately to align the PI with its parent product Glivec. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/06/2022 (IB/0051/G), which are available on the Agency's website**
Imbruvica	All presentations	15/09/2022	Update of the SmPC section 4.4. to include information on fatal and serious cardiac arrythmias and cardiac failure, relevant warnings and periodical monitoring of patients and update of the SmPC Section 4.8 to include cardiac arrest as an ADR following a safety assessment for increased risk of sudden death/cardiac death with the use of ibrutinib. Section 2 of the PL has been updated accordingly. Update of section 4.2, 4.8, 5.1, and 5.2 of the SmPC in order to update the information related to Paediatrics. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (II/0074), which are available on the European Commission website**
Imfinzi	All presentations	15/09/2022	An update of section 4.8 of the SmPC to add the adverse reaction psoriasis with a frequency "uncommon". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/08/2022 (PSUSA/00010723/202110), which are available on both the Agency and the European Commission website.**

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Incruse Ellipta	All presentations	15/10/2022	To update to the lactose statement in Section 2 of SmPC. in addition, some of the handling instructions in the SmPC and PL. The MAH also to remove the undesirable effect "rash" with the frequency of rare" from SmPC section 4.8. Furthermore, the instruction to not shake was included in the labelling that also include a warning to not swallow desiccant. The package leaflet and **labelling** are updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (IB/0036), which are available on the Agency's website**
Isentress	All presentations	15/11/2022	To update the Product Information (section 4.4 and 4.6 of the SmPC) to be in line with EMA request regarding HIV sexual and breastfeeding transmission. The Package Leaflet is updated accordingly (section 2). In addition, the applicant took the opportunity to correct a spelling mistake in section 4.5: "disaproxil" was stated in place of "disoproxil"; - add the tradename of Isentress 25 mg and 100 mg (section 6, PIL); - add the dosage of Isentress 400 mg, in section "6. Contents of the pack and other information", for more clarity. **Parallel distributors must use the annexes dated 17/10/2022 (IB/0103), which are available on the Agency's website**
Jardiance	All presentations	15/09/2022	To update section 4.4 of the SmPC to clarify that the medicinal product should not be used in patients with type I diabetes. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/07/2022 (II/0062/G which includes the IB/0069 safety scopes) which are available on the Agency's website.**
Jemperli	All presentations	15/09/2022	Update of sections 4.2, 4.4 and 4.8 of the SmPC to update dose modifications recommendations in immune related adverse reactions, amend existing warnings, and add further immune-related ADRs to the list of adverse drug reactions (ADRs), with different

Name	EU number	Date of communication	Rationale
			frequencies, based on data from company sponsored trials and literature. In addition, the MAH took the opportunity to remove information on Polysorbate 80 and update the list of local representatives The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 13/09/2022 (II/0007), which are available on the European Commission website**
Jinarc	All presentations	15/11/2022	Submission of an updated RMP version 15.0 in order to reflect the outcome of the substantial amendment to the protocol of the category 1 PASS study (156-12-299) as concluded in (PSA/S/0078.1). The Annex II is updated accordingly. In addition, the MAH took the opportunity to correct an oversight/editorial error in the package leaflet relevant to (II/0033/G). **Parallel distributors must use the annexes dated 01/09/2022 (II/0036), which are available on the Agency's website**
Juluca	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. To update section 4.8 of the SmPC and section 4 of the PL to include the ADR "weight increased" with a frequency "common" **Parallel distributors must use the annexes dated 01/09/2022 (WS2323/0045 which includes the WS/2268 and IG/1531 safety scopes), which are available on the Agency's website**
Jyseleca	All presentations	15/11/2022	Update of sections 4.4, 4.6 and 5.1 of the SmPC in order to update information on fertility based on interim results from studies GLPG0634-CL-227 (MANTA Ray) and GS-US-418-4279 (MANTA) listed as a category 3 study

Name	EU number	Date of communication	Rationale
			in the RMP. The package leaflet and Annex II are updated accordingly. **Parallel distributors must use the annexes dated 29/09/2022 (II/0018) which are available on the Agency's website.**
Kaletra	All presentations	15/11/2022	The updates section 4.4 and section 4.6 of the SmPC and section 2 of the package leaflet to remove information related to sexual transmission and update the text regarding HIV transmission in breast-feeding women. In addition, the MAH has taken the opportunity to add the wording on sodium in compliance with the EC excipients guideline in the SmPCs and the package leaflets. **Parallel distributors must use the annexes dated 15/09/2022 (IB/0194) which are available on the Agency's website.**
Keytruda	All presentations	15/09/2022	Update of sections 4.4 and 4.8 of the SmPC to add a new warning for 'Hypoparathyroidism' and to add it to the list of adverse drug reactions (ADRs) with frequency "rare" based on literature references; the package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/06/2022 (II/0122) which are available on the Agency's website.**
Kisqali	All presentations	15/09/2022	Update of sections 4.4, 4.8 and 5.1 of the SmPC based on the final Overall Survival (OS) analysis from Study A2301 (MONALEESA-2); a Phase III, randomized, double-blind, placebo-controlled, multicenter study of ribociclib in combination with letrozole in postmenopausal women with HR+, HER2–, locoregionally recurrent or metastatic breast cancer who had not received previous systemic therapy for advanced disease, and based on an updated pooled safety dataset (including the studies MONALEESA-2, MONALEESA-3 and MONALEESA-7). The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 26/07/2022 (II/0035) which are available on the Agency's website.
Kinzalkomb	All presentations	15/10/2022	To update sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement the wording provided by PRAC assessment Report on the PSUR for hydrochlorothiazide/spironolactone regarding the adverse event Acute Respiratory Distress Syndrome (ARDS) affecting the medicinal products that contain hydrochlorothiazide (PSUSA/00001662/202101) **Parallel distributors must use the annexes dated 24/08/2022 (IG1549) which are available on the Agency's website**
Kivexa	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 19/08/2022 (IG1531) which are available on the Agency's website**
Kovaltry	All presentations	15/09/2022	Update of the SmPC sections 4.8 and 5.1 to include data from the LEOPOLD Kids Part B (previously submitted as Art 46; an addendum on biomarker data is included in this submission) and Extension study results included as part of this submission. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 10/06/2022 (II/0038) which are available on the Agency's website.**
Laventair Ellipta	All presentations	15/11/2022	Update of section 4.8 of the SmPC to add the adverse reaction muscle spasms with a frequency "uncommon". Update of section 4.8 of the SmPC to add the adverse reaction Eye pain. The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 09/11/2022 (PSUSA/00010264/202112), which are available on the European Commission website
Levetiracetam Actavis	All presentations	15/09/2022	To update section 4.8 of the SmPC to include predisposition of the Japanese population to neuroleptic malignant syndrome (NMS) following assessment of the same changes adopted for the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 29/06/2022 (IB/0035) which are available on the Agency's website**
Levetiracetam Actavis Group	All presentations	15/09/2022	To update section 4.8 of the SmPC to include predisposition of the Japanese population to neuroleptic malignant syndrome (NMS), following assessment of the same changes adopted for the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 29/06/2022 (IB/0026) which are available on the Agency's website**
Levetiracetam ratiopharm	All presentations	15/09/2022	To update section 4.8 of the SmPC to include predisposition of the Japanese population to neuroleptic malignant syndrome (NMS), following assessment of the same changes adopted for the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/06/2022 (IB/0035) which are available on the Agency's website**
Levetiracetam Sun	All presentations	15/09/2022	To update section 4.8 of the SmPC to include predisposition of the Japanese population to neuroleptic malignant syndrome (NMS), following assessment of the same changes adopted for the reference product. The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 23/06/2022 (IB/0028) which are available on the Agency's website
Levetiracetam Teva	All presentations	15/09/2022	To update section 4.8 of the SmPC to include predisposition of the Japanese population to neuroleptic malignant syndrome (NMS), following assessment of the same changes adopted for the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 06/07/2022 (IB/0036) which are available on the Agency's website**
Lokelma	All presentations	15/09/2022	Update of section 4.5 of the SmPC to add drug-drug interaction information based on final report for interventional study D9480C00012, "A Two-Cohort, Randomised Sequence, Crossover, Open-label Study to Assess the Effect of a Single Dose of Sodium Zirconium Cyclosilicate (SZC) on the Pharmacokinetics of Tacrolimus and Cyclosporin in Healthy Subjects". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/07/2022 (II/0025) which are available on the Agency's website**
Lucentis	All presentations	15/11/2022	Update of section 4.6 of the SmPC to update information on breastfeeding following the PRAC Recommendation (EMEA/H/C/PSUSA/00002609/202010) based on a cumulative assessment of pre-clinical studies, pharmacokinetic data, published literature and post-marketing spontaneous reports. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/09/2022 (YU which includes the II/0098 safety scope), which are available on the European Commission website.**
Luveris	All presentations	15/09/2022	Update of sections 4.1, 4.2, 5.1 and 5.2 of the SmPC in order to update details regarding the definition of severe LH and FSH deficiency, to

Name	EU number	Date of communication	Rationale
			clarify follicular development as the treatment target and selection of the most adequate medically assisted reproduction procedure for healthcare providers and to clarify the pharmacokinetic and pharmacodynamic properties of the two gonadotropins, in alignment with the variation EMEA/H/C/000714/II/0075 for Pergoveris, based on a systematic literature search and review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/06/2022 (II/0091) which are available on the Agency's website**
Lynparza	All presentations	15/09/2022	Extension of indication to include adjuvant treatment of breast cancer for Lynparza (for tablets); therefore, sections 4.1, 4.2, 4.5, 4.8 and 5.1 of the SmPC are updated. In addition, sections 4.8 of the SmPC for Lynparza hard capsules are revised based on the updated safety data analysis. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 01/09/2022 (II/0056/G which includes the II/0051/G safety scopes) which are available on the Agency's website.**
Lyrica	All presentations	15/09/2022	To update SmPC sections 4.4 and 4.8 to reflect new data on suicidal ideation following the review of the data provided in LEG 007 and 054. To update SmPC sections 4.4 and 4.8 with a warning regarding severe cutaneous adverse reactions (SJS and TEN). To update sections 4.4 and 4.8 of the SmPC and sections 2, 3 and 4 of the PL, to implement the wording related to the cases of abuse and dependence in patients without a history of substance disorder. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 29/07/2022 (N/0120 which includes the WS2261, WS2168, WS2293**

Name	EU number	Date of communication	Rationale
			safety scopes) which are available on the Agency's website.
Lyxumia	All presentations	15/11/2022	To update section 4.8 of the SmPC and section 4 of the PL to implement the wording agreed by the PRAC following the outcome of the PSUSA procedure for Suliqua, EMEA/H/C/PSUSA/00010577/202111. **Parallel distributors must use the annexes dated 22/09/2022 (IAIN/0036) which are available on the Agency's website**
MabThera	All presentations	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (PSUSA/00002652/202111), which are available on both the Agency and the European Commission website.**
Matever	All presentations	15/09/2022	To update section 4.8 of the SmPC to add predisposition of the Japanese population to neuroleptic malignant syndrome (NMS) to align the PI with its parent product Keppra. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/06/2022 (IB/0042) which are available on the Agency's website**
Mayzent	All presentations	15/09/2022	Update of the sections 4.4 and 4.8 of the SmPC to add squamous cell carcinoma with a frequency "uncommon". The package leaflet section 4 and the Patient/Caregiver guide (Annex IID) are updated accordingly. Update of section 4.4 of the SmPC to include a warning about herpes viral infection and an amendment of subsection "Description of selected adverse reactions" in the section 4.8. The package leaflet section 2, Physician's checklist and the Patient/Caregiver guide (Annex IID) are updated accordingly. Update of section 4.4 of the SmPC to amend the warning about

Name	EU number	Date of communication	Rationale
			cryptococcal meningitis and section 4.8 to include this ADR in the tabulated list of adverse reactions. The package leaflet section 4, Physician's checklist and the Patient/Caregiver guide (Annex IID) are updated accordingly. **Parallel distributors must use the annexes dated 18/07/2022 (PSUSA/00010818/202109), which are available on both the Agency and the European Commission website.**
MicardisPlus	All presentations	15/10/2022	To update sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement the wording provided by PRAC assessment Report on the PSUR for hydrochlorothiazide/spironolactone regarding the adverse event Acute Respiratory Distress Syndrome (ARDS) affecting the medicinal products that contain hydrochlorothiazide (PSUSA/00001662/202101). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (IG1549) which are available on the Agency's website**
Modigraf	All presentations	15/11/2022	Update of sections 4.4, 4.5 and 4.8 of the SmPC to add a warning on the adverse reaction thrombotic microangiopathy (TMA) based on a cumulative review of fatal cases of TMA during treatment with tacrolimus, requested by the PRAC following the assessment of the PSUR (EMEA/H/C/00002839/202103). Update of section 4.5 of the SmPC to add the drug-drug interaction between tacrolimus and caspofungin based on post-marketing safety report and literature. Update of section 5.2 of the SmPC to add that tacrolimus is metabolized by the cytochrome P450-3A5 (CYP3A5) based on post-marketing safety report and literature. The package leaflet is updated accordingly. In addition, the MAH took the opportunity to implement some editorial changes.)

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 06/10/2022 (WS2241/G) which are available on the Agency's website
Mvasi	All presentations	15/09/2022	Update of section 4.2 and 6.6 of the SmPC and section 3 of the package leaflet by adding "Do not shake the vial". **Parallel distributors must use the annexes dated 12/07/2022 (IB/0028) which are available on the Agency's website**
Myclausen	All presentations	15/10/2022	Update section 5.1 of the SmPC based on a literature review on mycophenolate mechanism of action. Update section 5.2 of the SmPC to add new information to the Distribution and Elimination subsections based on a literature review. Update of sections 4.5 and 5.2 of the SmPC to amend the existing information on patients taking oral contraceptives based on study Roche Report N-181041/ BP 15543. Update section 2 of the package leaflet to align the wording of the text with the SmPC section 4.4. C.I.2.a Update Sections 4.2, 4.4, 4.6 and 4.8 of the SmPC and Sections 1, 2 and 3 of the package leaflet to be in line with the PI of the reference product. **Parallel distributors must use the annexes dated 01/08/2022 (IB/0054/G) which are available on the Agency's website**
Mysimba	All presentations	15/09/2022	Update section 5.1 of the SmPC based on a literature review on mycophenolate mechanism of Action. Update section 5.2 of the SmPC to add new information to the Distribution and Elimination subsections based on a literature review. Update of sections 4.5 and 5.2 of the SmPC to amend the existing information on patients taking oral contraceptives based on study Roche Report N-181041/ BP 15543. Update section 2 of the package leaflet to align the wording of the text with the SmPC section 4.4 and update section 6 of the package leaflet to add the quantity of the active substance, mycophenolate based on recommendations from NCA (Ireland) and EMA respectively.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 23/06/2022 (IB/0048/G) which are available on the Agency's website
Mylotarg	All presentations	15/09/2022	Update of sections 4.8, 5.1, and 5.2 of the SmPC based on the final results from study B176103; this is a single-arm, open-label, phase 4 study evaluating the QT interval, pharmacokinetics, and safety of gemtuzumab ozogamicin as a single-agent regimen in patients with relapsed or refractory CD33-positive Acute Myeloid Leukemia. **Parallel distributors must use the annexes dated 23/06/2022 (II/0024) which are available on the Agency's website**
Myozyme	All presentations	15/11/2022	Update of section 4.8 of the SmPC in order to add palpitations, asthenia, malaise, feeling cold and blood pressure decreased to the list of adverse drug reactions (ADRs) with frequency "not-known" following the Final Assessment Report for the Post-Authorisation Measure MEAs 024.13 and 0.25.13 (the 2019 Pompe Disease Registry Annual Report) In addition, section 4.9 of the SmPC was updated to include further guidance with regards to overdose. Update of SmPC section 4.8 to include the new ADRs "somnolence", "throat irritation" and "infusion site pruritus" with the frequency 'not known', and SmPC section 4.7 to include "somnolence", and "tremor" and "hypotension" for consistency, based on the final report from non-interventional PASS Pompe Safety Sub-Registry - AGLU06909/LTS13930. This final study report is submitted to address the assessment report conclusion of the Pompe registry report 2020 (MEA024.15 and MEA025.15 Annual Pompe Registry Report 2020). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 06/10/2022 (II/0087 which also includes the II/0090 safety variation) which are available the Agency's website**

Name	EU number	Date of communication	Rationale
Mysildecard	All presentations	15/09/2022	To update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan, following assessment of the same change for Revatio (EMEA/H/C/PSUSA/00002700/202105). The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 01/07/2022 (IB/0012) which are available on the Agency's website**
Norvir	All presentations	15/10/2022	To update Sections 4.4 and 4.6 of the SmPC and Section 2 of the package leaflet to remove information related to sexual transmission and update the text regarding HIV transmission in breast-feeding women, following CHMP recommendation. The MAH took the opportunity: - to add information regarding sodium to Section 4.4 of the SmPC and Section 2 of the PL for the 100 mg film-coated tablets, to be in line with the current Annex to the European Commission guideline on 'Excipients in the labelling and package leaflet of medicinal products for human use' **Parallel distributors must use the annexes dated 24/08/2022 (IA/0164 which includes the IB/0162 safety scopes too) which are available on the Agency's website**
Nucala	All presentations	15/11/2022	Update of section 4.2 of the SmPC to add a clarification statement regarding administration of Nucala 100 mg in children aged 6 to 11 years. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/10/2022 (IB/0051) which are available on the Agency's website**
Nuwiq	All presentations	15/11/2022	Update of sections 4.8 and 5.1 of the SmPC in order to add safety and efficacy data based on the final CSR from the category 3 study GENA-21b; a prospective, open-label, multicentre phase 3b study to assess the efficacy and safety of personalized prophylaxis with Human-

Name	EU number	Date of communication	Rationale
			cl rhFVIII in previously treated adult patients with severe haemophilia A. Further, upon request by the CHMP following the assessment of Study GENA-05 (P46 013 and P46 014), the MAH is updating the numbers of evaluated subjects in SmPC section 4.8 and is removing of the sentence "A prospective open-label clinical study in PUPs with severe haemophilia A (<1% FVIII:C) is ongoing" in section 5.1 of the SmPC. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 13/10/2022 (WS2244) which are available on the Agency's website**
Oncaspar	All presentations	15/09/2022	Update of sections 4.2 and 4.4 of the SmPC to add advice on premedication to reduce the cases of hypersensitivity reactions based on literature review and guidelines. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 13/09/2022 (II/0048) which are available on the European Commission website**
Orladeyo	All presentations	15/11/2022	Update of sections 4.4 and 4.5 of the SmPC in order to remove the warning for women of childbearing potential and amend drug-drug interaction information with desogestrel based on final results from study BCX7353-111; this is a phase 1 drug interaction study to evaluate the effects of berotralstat on the pharmacokinetics of a combination oral contraceptive, desogestrel with ethinyl estradiol; the package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/09/2022 (II/0006) which are available on the Agency's website**
Pifeltro	All presentations	15/11/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual

Name	EU number	Date of communication	Rationale
			transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 10/10/2022 (IG1535) which are available on the Agency's website**
Piqray	All presentations	15/09/2022	Update of sections 4.2, 4.4 and 4.8 of the SmPC to add the adverse reactions colitis and angioedema with a frequency "not known". Update of section 5.1 of the SmPC based on final results from study CBYL719C2301 (SOLAR-1) listed as a PAES in the Annex II; this is a phase III, randomized, double-blind, placebo-controlled study of alpelisib in combination with fulvestrant for men and postmenopausal women with hormone receptor positive, HER2-negative advanced breast cancer which progressed on or after aromatase inhibitor treatment; the Annex II is updated accordingly. In addition, the MAH is updating the ATC code in the SmPC. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (II/0012; PSUSA/00010871/202111) which are available on both the European Commission and the Agency's website**
Plenadren	All presentations	15/09/2022	Update of section 4.4 of the SmPC in order to add a warning on pheochromocytoma crisis. The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 13/10/2022 (II/0038) which are available on the Agency's website**
Pregabalin Pfizer	All presentations	15/09/2022	Update SmPC sections 4.4 and 4.8 with a warning regarding severe cutaneous adverse reactions (SJS and TEN). The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 29/07/2022 (N/0049 which includes the WS/2261 safety scopes too) which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Pregabalin Mylan	All presentations	15/11/2022	Update sections 4.4 and 4.8 of SmPC to reflect new data on suicidal ideation following the review of the data provided in LEG 007 and 054 of the reference product, Lyrica (EMEA/H/C/WS2168, dated 22 April 2022). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 18/10/2022 (IB/0024) which are available on the Agency's website**
Pregabalin Sandoz	All presentations	15/09/2022	Update sections 4.4 of SmPC is updated to highlight that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential have to use effective contraception based on the new data on MCM and for section 4.6 of SmPC is being updated concerning the risks of pregabalin treatment during pregnancy, indicating that women of childbearing potential have to use effective contraception, pregabalin may cross the human placenta and the description of major congenital malformations (MCM). The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 30/06/2022 (IB/0026) which are available on the Agency's website**
Pregabalin Sandoz GmbH	All presentations	15/09/2022	To update sections 4.4 of SmPC is updated to highlight that pregabalin should not be used during pregnancy unless clearly necessary and women of childbearing potential have to use effective contraception based on the new data on MCM and for section 4.6 of SmPC is being updated concerning the risks of pregabalin treatment during pregnancy, indicating that women of childbearing potential have to use effective contraception, pregabalin may cross the human placenta and the description of major congenital malformations (MCM). The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 30/06/2022 (IB/0025) which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Prezista	All presentations	15/09/2022	Update of sections 4.3 and 4.5 of the SmPC to update the safety information based on final results from study to assess the effect of single and multiple doses of Darunavir in combination with Cobicistat or Ritonavir on the pharmacokinetics of single dose Dabigatran Etexilate in healthy participants. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/09/2022 (YU which includes the WS2250 safety scopes too) which are available on the European Commission's website**
Prialt	All presentations	15/09/2022	Update of section 4.2 of the SmPC to adjust the posology regimen. Update of sections 4.2, 4.3, 4.4 and 4.8 to add information regarding the increased risk of suicide. Update of section 5.1 to add a paragraph regarding responsive daily dose. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 02/08/2022 (II/0068) which are available on the European Commission's website**.
PritorPlus	All presentations	15/10/2022	To update sections 4.4 and 4.8 of the SmPC and sections 2 and 4 of the PL to implement the wording provided by PRAC assessment Report on the PSUR for hydrochlorothiazide/spironolactone regarding the adverse event Acute Respiratory Distress Syndrome (ARDS) affecting the medicinal products that contain hydrochlorothiazide (PSUSA/00001662/202101). **Parallel distributors must use the annexes dated 24/08/2022 (IG1549) which are available on the Agency's website**
Rapamune	All presentations	15/09/2022	To update Sections 4.4 and 4.5 of the SmPC to add the drug interaction with cannabidiol concerning the signal assessment leading to systematic calcineurin inhibitors and mTOR inhibitors serum levels increase and toxicity

Name	EU number	Date of communication	Rationale
			(EPITT no: 19614) The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 22/07/2022 (IB/0189) which are available on the Agency's website**
Remsima	All presentation	15/11/2022	Sections 4.4, 4.5 and 4.6 of the SmPC, Section 2 of the PL and the Patient Reminder Card have been updated with information regarding administration of live vaccines to infants exposed to infliximab during pregnancy. To include a note in the instructions for use that it is normal to see a drop at the end of the needle. **Parallel distributors must use the annexes dated 27/09/2022 (IB/0116) which are available on the Agency's website**
Retsevmo	All presentation	15/11/2022	Extension of indication to include first-line treatment of advanced RET-mutant medullary thyroid cancer (MTC) in adults and adolescents 12 years and older based on interim results from Study LIBRETTO-001 (LOXO-RET-17001) on the clinical safety and efficacy of selpercatinib in patients with RET-mutant MTC who are cabozantinib and vandetanib treatment-naïve (MTC:-Cab/-Van). LIBRETTO-001 is a global, multicohort, open-label, Phase 1/2 study in adult and adolescent patients with advanced RET-altered tumours. As a consequence, sections 4.1 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 02/09/2022 (II/0014/G) which are available on the Agency's website**
Revlimid	All presentation	15/11/2022	Update of section 4.2 of the SmPC to update the dosage for patients with impaired renal function (severe renal impairment and end stage renal disease) for the follicular lymphoma (FL) indication based on additional PK analysis. In addition, to update the existing warning in section 4.4 of the SmPC to highlight that male patients should not donate semen or sperm

Name	EU number	Date of communication	Rationale
			during treatment and for at least seven days after the end of treatment in order to align with the Revlimid Annex IID requirements for the patient educational brochures and to align with similar wording in the Imnovid (pomaldiomide) and Thalidomide BMS (thalidomide) SmPCs. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/10/2022 (II/0122) which are available on the European Commission website**
Reyataz	All presentation	15/11/2022	Update SmPC (sections 4.4 and 4.6) and PIL (section 2) in line with CHMP recommendation for all approved HIV products with respect to the removal of the disease information relating to sexual transmission of HIV and amending sections relating to breast-feeding. Furthermore, the MAH has taken the opportunity to update the section 6.1 of REYATAZ SmPC to support the implementation of the identification of medicinal products (IDMP) and the harmonization of the REYATAZ PI with the information currently in the REYATAZ Module 3 and revise "Gelatine" by "Gelatin" (in Ph. Eur.). **Parallel distributors must use the annexes dated 17/10/2022 (IB/0136) which are available on the Agency's website**
Rezolsta	All presentation	15/09/2022	Update of sections 4.3 and 4.5 of the SmPC to update the safety information based on final results from study to assess the effect of single and multiple doses of Darunavir in combination with Cobicistat or Ritonavir on the pharmacokinetics of single dose Dabigatran Etexilate in healthy participants. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/05/2022 (WS2250) which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Rilutek	All presentation	15/11/2022	Update of section 4.8 of the SmPC to add the adverse reaction rash with a frequency 'not known'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2022 (PSUSA/00002645/202112) which are available on the European Commission website**
Rinvoq	All presentation	15/09/2022	Update of section 4.5 of the SmPC to add information about drug interaction with grapefruit as a CYP3A4 inhibitor based on literature references; the package leaflet is updated accordingly. Extension of indication to include the treatment of active non-radiographic axial spondyloarthritis in adult patients with objective signs of inflammation as indicated by elevated C-reactive protein (CRP) and/or magnetic resonance imaging (MRI), who have responded inadequately to nonsteroidal anti-inflammatory drugs (NSAIDs) As a consequence, SmPC sections 4.1, 4.2, 4.8, 5.1 and 5.2 have been updated and the package leaflet has been updated in accordance. **Parallel distributors must use the annexes dated 27/07/2022 (II/0016 which includes the II/0019 safety scopes too) which are available the Agency's website**
Rixathon	All presentation	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 31/08/2022 (PSUSA/00002652/202111) which are available on both the European Commission and the Agency's website**
Riximyo	All presentation	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral

Name	EU number	Date of communication	Rationale
			infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (PSUSA/00002652/202111) which are available on both the European Commission and the Agency's website**
Ruxience	All presentation	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/08/2022 (PSUSA/00002652/202111) which are available on both the European Commission and the Agency's website**
Rybelsus	All presentation	15/09/2022	Update of section 4.8 of the SmPC to add 'Hypersensitivity' to the list of adverse drug reactions (ADRs) with frequency "uncommon". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 23/06/2022 (II/0025), which are available on the Agency's website**
Sildenafil Actavis	All presentation	15/09/2022	To update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan, following assessment of the same change for Revatio. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/06/2022 (IB/0023), which are available on the Agency's website.**
Sildenafil ratiopharm	All presentation	15/09/2022	To update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan, following assessment of the same change for Revatio. The package leaflet is updated accordingly.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 21/06/2022 (IB/0052), which are available on the Agency's website.
Sildenafil Teva	All presentation	15/09/2022	To update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan, following assessment of the same change for Revatio. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/07/2022 (IB/0041), which are available on the Agency's website.**
SomaKit TOC	All presentation	15/11/2022	Update of section 4.4 of the SmPC to amend a warning on errors of interpretation of gallium (68Ga) edotreotide images. Update of section 4.8 of the SmPC to add a description of cases in which physiological uptake of gallium (68Ga) edotreotide by splenic tissue has been misdiagnosed as neuroendocrine tumour, leading to unnecessary intervention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 19/09/2022 (PSUSA/00010552/202112), which are available on both the European Commission and the Agency's website**
Stelara	All presentation	15/11/2022	Update of sections 4.4 and 4.8 of the SmPC to add a warning regarding lupus-related conditions and to add the adverse reactions cutaneous lupus and lupus-like syndrome with a frequency "very rare". Update of section 4.4 of the SmPC to amend a warning regarding opportunistic infections. Update of section 2 of the package leaflet to amend a warning regarding breast-feeding. Additionally, minor editorial changes have been included throughout the PI. Update of the SmPC section 4.4, 4.5 and 4.6 with recommendation not to administer live vaccines to infants for six months following birth unless ustekinumab infant serum levels are undetectable or there is clear clinical benefit for the individual infant.

Name	EU number	Date of communication	Rationale
			The update follows assessment of the final safety registry report of CNTO1275PSO4007 "Pregnancy Research Initiative: Exposure to ustekinumab during pregnancy: A review and analysis of birth outcomes from the Swedish, Danish, and Finnish medical birth registers." The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2021 (PSUSA/00003085/202112), which are available on European Commission and the Agency's website**.
Stocrin	All presentation	15/11/2022	Update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors can use the annexes dated 09/11/2021 (YU which includes the IAIN/0129 safety scopes) which are available on European Commission website**.
Suliqua	All presentation	15/09/2022	Update of section 4.8 of the SmPC to add the adverse reaction delayed gastric emptying with a frequency "rare". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/08/2022 (PSUSA/00010577/202111), which are available on both the European Commission and the Agency's website.**
Sustiva	All presentation	15/11/2022	Update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 13/10/2022 (IAIN/0158), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Tagrisso	All presentations	15/10/2022	Update of sections 4.2, 4.4 and 4.8 of the SmPC to amend the table regarding dose modifications to recommend permanently discontinuation in case of adverse reactions Stevens-Johnson Syndrome and Aplastic anaemia, to add a warning on Aplastic anaemia, to add the adverse reaction Aplastic Anaemia with frequency "rare" and amend the description for haematologic events, to add the adverse reaction left ventricular ejection fraction decreased with frequency "common" and cardiac failure with frequency "uncommon". The package leaflet is updated accordingly **Parallel distributors must use the annexes dated 19/09/2022 (PSUSA/00010472/202111), which are available on both the European Commission and the Agency's website**
Tarceva	All presentations	15/10/2022	Update of section 4.8 of the SmPC to add the adverse reactions hepatitis and acute hepatitis and update of section 4.4 of the SmPC to amend a warning/precaution regarding hepatotoxicity. The package leaflet is updated accordingly. Update of section 4.8 to add the adverse reaction pneumatosis with a frequency rare. **Parallel distributors must use the annexes dated 19/09/2022 (PSUSA/00001255/202111), which are available on the European Commission website**
Telzir	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 19/08/2022 (IG1531), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Tivicay	All presentations	15/10/2022	Update Sections 4.4 and 4.6 of the SmPC and Section 2 of the package leaflet to remove information related to sexual transmission and update the text regarding HIV transmission in breast-feeding women, following CHMP recommendation. The MAH took the opportunity: - to reintroduce the statement regarding the recommendation for HIV positive women not to breastfeed in section 4.6 of the SmPC in Croatian, Swedish, Czech, Rumanian and Greek language; - to correct the statements regarding excretion of Tivicay in milk for the PIs in Bulgarian, Romanian, Latvian, Maltese and Slovak language. To update section 4.8 of the SmPC and section 4 of the PL to include the ADR "weight increased" with a frequency "common". **Parallel distributors must use the annexes dated 01/09/2022 (WS2323/0081 which includes the WS/2268 and IB/0083 safety scopes too) which are available on the Agency's website**
Torisel	All presentations	15/09/2022	Update sections 4.4 and 4.5 of the SmPC and section 2 of the PL, to implement the signal recommendation on drug interaction with cannabidiol leading to systemic calcineurin inhibitors and mTOR inhibitors serum levels increased and toxicity (EPITT 19614) **Parallel distributors must use the annexes dated 20/06/2022 (IB/0087), which are available on the Agency's website**
Trelegy Ellipta	All presentations	15/09/2022	Update of section 4.8 of the SmPC to add the ADR ('dysgeusia') and change frequencies for already reported ADRs ('nasopharyngitis', 'viral respiratory tract infection', and 'dysphonia') based on an updated safety analysis. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/07/2022 (R/0023, this includes WS2130/0020/G safety scopes), which**

Name	EU number	Date of communication	Rationale
			are available on both the European Commission and the Agency's website
Triumeq	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. To update section 4.8 of the SmPC and section 4 of the PL to include the ADR "weight increased" with a frequency "common" **Parallel distributors must use the annexes dated 01/09/2022 (WS2323/0106 which includes the WS/2268 and IG/1532 safety scopes too) which are available on the Agency's website**
Trizivir	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. **Parallel distributors must use the annexes dated 11/08/2022 (IG1532) which are available on the Agency's website**
Truxima	All presentations	15/09/2022	Update of section 4.6 of the SmPC to amend a warning on breastfeeding and of section 4.8 of the SmPC to add the risk of serious viral infections with a frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (PSUSA/00002652/202111), which are available on both the European Commission and the Agency's website**

Name	EU number	Date of communication	Rationale
Veklury	All presentations	15/11/2022	Grouped variations to update sections 4.5 and 5.2 of the SmPC to update prescribing information related to interactions with other medicinal products, effect of intrinsic factors and COVID-19 disease on the pharmacokinetics (PK) of Veklury® and its metabolites in the adult population. This variation covers the Recommendations 9,11 ,12 and 13 listed at the time of the conditional marketing authorization (EMEA/H/C/005622/0000) for Veklury®. The package leaflet is updated accordingly. In addition, the marketing authorisation holder (MAH) took the opportunity to introduce some linguistic amendments. Furthermore two extensions of indication to include: - treatment of paediatric patients (at least 4 weeks of age and weighing at least 3 kg) with pneumonia requiring supplemental oxygen (low- or high-flow oxygen) or other non-invasive ventilation at start of treatment, based on interim results from Study GS-US-540-5823; a phase 2/3 single-arm, open-label study to evaluate the safety, tolerability, pharmacokinetics, and efficacy of Remdesivir in participants from birth to <18 years of age with COVID-19; - treatment of paediatric patients (weighing at least 40 kg) who do not require supplemental oxygen and who are at increased risk of progressing to severe COVID 19, based on data from 8 adolescent patients who were included in Study GS-US-540-9012, which was initially assessed by the CHMP as part of procedure II/16 (Extension of Indication to include treatment of adults). As a consequence, sections 4.1, 4.2, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet as well as the instructions for healthcare professionals have been updated accordingly **Parallel distributors must use the annexes dated 20/10/2022 (II/0037/G which includes II/0035/G variations too), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Veltassa	All presentations	15/11/2022	Update of sections 4.2 and 4.5 of the SmPC in order to introduce new drug-drug interaction information based on results from four in vitro studies: RLY-TR-0174, titled "In Vitro Evaluation of Potential RLY5016S and Immunosuppressant Drug-Drug Interactions"; RLY-TR-018, titled "In Vitro Evaluation of Potential Drug-Drug Interactions Between Patiromer and Sevelamer Hydrochloride"; "In Vitro Evaluation of Drug-Drug Interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS" and "Drug-drug interactions of commonly prescribed renal and cardiovascular Drugs with Patiromer DS in a simulated GI tract passage study". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 06/10/2022 (II/0029), which are available on the Agency's website**
Vemlidy	All presentations	15/09/2022	Update of section 4.4 to amend the existing warning on nephrotoxicity. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 17/08/2022 (PSUSA/00010575/202111), which are available on both the European Commission and the Agency's website**
Viagra	All presentations	15/10/2022	Update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 29/08/2022 (IB/0114), which are available on the Agency's website**

Name	EU number	Date of communication	Rationale
Viramune	All presentations	15/10/2022	Update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/08/2022 (IAIN/0155), which are available on the Agency's website.**
Vizarsin	All presentations	15/09/2022	Update section 4.5 of the SmPC to add a warning about the increase in hypotension observed with concomitant use of sildenafil and sacubitril/valsartan, following assessment of the same change for Revatio. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 01/07/2022 (IB/0035), which are available on the Agency's website**
Vocabria	All presentations	15/11/2022	Update of sections 4.2 and 5.1 of the SmPC in order to describe data regarding oral bridging using other suppressive regimens than oral bridging with cabotegravir and rilpivirine based on studies 201584 (FLAIR), 207966 (ATLAS-2M), 200056 (LATTE 2) and 201585 (ATLAS). To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/09/2022 (II/0012), which are available on the Agency's website**
Votubia	All presentations	15/09/2022	Update sections 4.4 and 4.5 of the SmPC, and sections 2 of the PL to implement the signal recommendations on 'interaction with cannabidiol leading to systemic calcineurin inhibitors and mTOR inhibitors serum levels increased and toxicity (EPITT no 19614)'

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 24/06/2022 (IG/1518), which are available on the Agency's website
Xalkori	All presentations	15/11/2022	Extension of indication to include treatment of paediatric patients (age ≥ 6 to < 18 years) with relapsed or refractory systemic anaplastic lymphoma kinase (ALK)-positive anaplastic large cell lymphoma (ALCL) and with unresectable, recurrent, or refractory ALK-positive inflammatory myofibroblastic tumour (IMT) for XALKORI based on the results from Studies ADVL0912 and A8081013; as a consequence, sections 4.1, 4.2, 4.4, 4.8, 5.1 and 5.2 of the SmPC are updated. Information regarding the educational pack in annex II has also been added. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 28/10/2022 (II/0072), which are available on the European Commission website**
Xeljanz	All presentations	15/09/2022	Update of section 4.4 of the SmPC to add a warning/precaution regarding hypoglycaemia. Update of section 4.4 of the SmPC to add a warning/precaution regarding retinal venous thrombosis and update of footnote under the ADR table in section 4.8 to indicate that venous thromboembolism also includes retinal venous thrombosis. Update of section 4.4, 4.8 and 5.1 to add warnings and safety data on serious infections, viral reactivation, non-melanoma skin cancer and fractures. In addition to update the **Outer carton** (section 4 **for oral solution**) to include a total volume of 240 mL The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 13/09/2022 (PSUSA/00010588/202111) which are available on the European Commission website**

Name	EU number	Date of communication	Rationale
Xiliarx	All presentations	15/11/2022	Update of section 4.8 of the SmPC in order to add the new ADRs 'cutaneous vasculitis' with the frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/07/2022 (WS2253), which are available on the Agency's website**
Xyrem	All presentations	15/11/2022	Update the Product Information, Annex IIIB (Package Leaflet), in order to include additional instructions for the use of the dosing cup cap closure in the child-resistant manner, following PRAC Rapporteur's Final Assessment Report dated on 05th May 2022 for the PSUR single assessment procedure number EMEA/H/C/PSUSA/00010612/202110. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/10/2022 (IB/0099), which are available on the Agency's website**
Yescarta	All presentations	15/11/2022	Update of section 4.8 of the SmPC to add the adverse reaction status epilepticus with a frequency of "common". Extension of indication to include treatment of adult patients with relapsed or refractory (r/r) diffuse large B-cell lymphoma (DLBCL) and high-grade B-cell lymphoma (HGBL) for Yescarta; as a consequence, sections 4.1, 4.2, 4.8, 5.1 and 5.2 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 14/10/2022 (II/0046) which are available on the European Commission website**
Ziagen	All presentations	15/10/2022	To update sections 4.4 and 4.6 of the SmPC and section 2 of the PL to implement the recommendation of the CHMP to remove the disease information relating to sexual transmission of HIV and to amend the sections related to breast-feeding.

Name	EU number	Date of communication	Rationale
			Parallel distributors must use the annexes dated 11/08/2022 (IG1532), which are available on the Agency's website
Zirabev	All presentations	15/09/2022	Update of section 4.2 and 6.6 of the SmPC and section 3 of the package leaflet by adding "Do not shake the vial". **Parallel distributors must use the annexes dated 26/07/2022 (IB/0028), which are available on the Agency's website**
Zomarist	All presentations	15/11/2022	Update of section 4.8 of the SmPC in order to add the new ADRs 'cutaneous vasculitis' with the frequency "not known". Update of section 4.8 of the SmPC in order to update the list of ADRs and update the ADR table in line with the EC SmPC guideline (2009). The package leaflet has is accordingly. **Parallel distributors must use the annexes dated 14/10/2022 (YU which includes the WS2224 and WS2253 safety scopes) which are available on the European Commission website**
Zyllt	All presentations	15/09/2022	Update section 4.5 of the SmPC to add the drug-drug interaction between clopidogrel and rosuvastatin to align the PI with its parent product Plavix. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/06/2022 (IB/0043), which are available on the Agency's website.**

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