15 April 2024
EMA/169204/2024
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
Abecma	All presentations	15/04/2024	Extension of indication to include treatment of adult patients with relapsed and refractory multiple myeloma (RRMM) who have received at least two prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD-38 antibody and have demonstrated disease progression on the last therapy for Abecma (idecabtagene vicleucel, ide-cel), based on results from study BB2121-MM-003 (MM-003, KarMMa-3). Consequently, sections 2.1, 2.2, 4.1, 4.2, 4.4, 4.5, 4.8, 5.1, 5.2, 6.1, 6.3, 6.4 and 6.6 of the SmPC are updated. The package leaflet and labelling are updated in accordance. **Parallel distributors must use the annexes dated 19/03/2024 (II/0031), which are available on both the European Commission website and the Agency's website.**
Adrovance	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-marketing case reports and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (WS2467), which are available on the Agency's website**
Aldurazyme	All presentations	15/03/2024	To update section 4.2 of the SmPC in order to modify the administration instructions following the assessment of procedure PSUSA/00001830/202104 based on literature review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0085), which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Alkindi	All presentations	15/02/2024	Update of section 4.2 of the SmPC in order to update posology recommendations in case of incomplete dosing. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0019), which are available on both the European Commission website and the Agency's website.**
Ameluz	All presentations	15/03/2024	Update of section sections 4.2, 4.4, 4.5, 4.8, 5.1 and 6.6 of the SmPC in order to include artificial daylight lamps as an additional light source for photodynamic therapy in combination with Ameluz for the treatment of actinic keratoses based on final results from non-clinical study PT-0042-A and literature (investigator-initiator trials). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/12/2023 (II/0055), which are available on the Agency's website**
Azacitidine Accord	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 04/01/2024 (IAIN/0018), which are available on the Agency's website.**
Azacitidine betapharm	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IAIN/0017), which are available on the Agency's website.**

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Azacitidine Mylan	All presentations	15/02/2024	To update section 4.8 of the SmPC to implement the signal recommendations on 'Azacitidine (injectable formulations) - leading to Cutaneous vasculitis (EPITT no 19929)' adopted at the 25-28 September 2023 PRAC meeting (EMA/PRAC/416575/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IAIN/0017), which are available on the Agency's website.**
Benlysta	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to change the frequency of urticaria and rash from uncommon to common and to change the frequency of diarrhoea and nausea from very common to common and to update the Summary of the safety profile based on a cumulative review of clinical trials. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0117 which includes the II/0118 safety updates too), which are available on the Agency's website**
BESPONSA	All presentations	15/03/2024	Update of sections 4.2, 4.6, 4.8, 5.1 and 5.2 of the SmPC in order to update paediatric information based on final results from studies ITCC-059 (WI203581) and INO-Ped-ALL-1 (WI235086). Study WI203581 is a Phase 1/2, multicenter, European, multi-cohort, open-label study in pediatric patients (≥1 and <18 years of age) with R/R CD22-positive Acute Lymphoblastic Leukemia (ALL); and study WI235086 is an open-label, multi-center Phase 1 study to assess safety and tolerability of InO in Japanese pediatric patients with R/R CD22-positive ALL. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 14/12/2023 (II/0026), which are available on the Agency's website.**
Blincyto	All presentations	15/04/2024	Update of sections 6.6 of the SmPC in order to add a statement that the administration of

Name	EU number	Date of communication	Rationale
			Blincyto for BSA of less than 0.4 m2 has not been established. In addition, the MAH took the opportunity to update the name of ATC pharmacological subgroup according to WHO ATC Index and to delete "intravenous catheter" from the important note statement regarding flushing and to introduce minor editorial changes to the PI. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2024 (II/0053/G), which are available on the Agency's website.**
Bonviva	All presentations	15/04/2024	Update of section 4.4 of the SmPC to add information regarding the risk of "Atypical fractures of other long bones", and section 4.8 of the SmPC to add "Atypical fractures of long bones other than the femur" as a new ADR with frequency 'not known', based on literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (WS2451), which are available on the Agency's website.**
Brilique	All presentations	15/04/2024	Update of sections 4.2 and 4.4 of the SmPC in order to include a warning related to Single Antiplatelet Therapy (SAPT) in patients with Acute Coronary Syndrome (ACS) who have undergone a Percutaneous Coronary Intervention (PCI) procedure and who have an increased risk of bleeding based on literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/03/2024 (II/0061), which are available on the European Commission website.**
Cibinqo	All presentations	15/04/2024	Extension of indication to include treatment of adolescents 12 to < 18 years of age with moderate to severe atopic dermatitis for CIBINQO based on final results from non-clinical study 00655292 [21GR211] and interim results from clinical study B7451015. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of

Name	EU number	Date of communication	Rationale
			the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 21/03/2024 (II/0010), which are available on both the European Commission website and the Agency's website.**
Clopidogrel ratiopharm	All presentations	15/04/2024	To update sections 4.1, 4.2, 4.4 and 5.1 of the SmPC to include the extension of indication "clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI)", following the assessment and approval of the same changes in the reference product. To update sections 4.4 and 4.8 of the SmPC in order to update an existing warning on`Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention, following the assessment and approval of the same changes in the reference product. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (IB/0024/G), which are available on both the European Commission website and the Agency's website.**
Clopidogrel Teva	All presentations	15/03/2024	To update the below listed sections of the SmPC following assessment of the same for the reference product, Plavix: Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence, section 4.1, 4.2 and 5.1 of the SmPC is updated. To update the below listed sections of the SmPC and PL following assessment of the same for the reference product, Plavix: - Update of section 4.4 of the SmPC in order to update an existing warning on 'Bleeding and haematological

Name	EU number	Date of communication	Rationale
			disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (IB/0059/G), which are available on both the European Commission website and the Agency's website.**
Cotellic	All presentations	15/04/2024	To update the section 4.8 of the SmPC and section 4 of the PL to implement the signal recommendation on "Cobimetinib; vemurafenib – Aphthous ulcer, mouth ulceration, stomatitis" (EPITT no 19961), adopted at the 8-11 January 2024 PRAC meeting. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/03/2024 (IG1730), which are available on the Agency's website.**
Dynastat	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to update skin reactions information based on literature and post-marketing data. pdate of section 4.6 of the SmPC to amend the available data on use during pregnancy, based on the PRAC advice for non-steroidal anti-inflammatory drugs (NSAID)-containing medicinal products (EMA/CMDh/642745/2022). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0088 which includes the PSUSA/00002314/202303 too), which are available on the Agency website.**
Effentora	All presentations	15/04/2024	Update of sections 4.2, 4.4, and 4.8 of the SmPC to inform prescribers about Opioid Use Disorder (OUD). The package leaflet is updated accordingly. Update of section 4.4 of the SmPC to add requirement regarding safe storage space. The package leaflet is updated accordingly. Update of SmPC section 4.9 to add toxic leukoencephalopathy as possible

Name	EU number	Date of communication	Rationale
			symptom of fentanyl overdose. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/03/2024 (PSUSA/ 00001369/202304), which are available on both the European Commission website and the Agency's website.**
Erelzi	All presentations	15/02/2024	Update of section 4.8 of the SmPC to add Glomerulonephritis with frequency "not known". The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/12/2023 (PSUSA/10795/202302), which are available on both the European Commission website and the Agency's website.**
Esbriet	All presentations	15/04/2024	To update section 4.4 and 4.8 to implement the signal recommendations on "Pirfenidone – Drug reaction with eosinophilia and systemic symptoms (DRESS)" (EPITT 19920) adopted at 27-30 November 2023 PRAC meeting (EMA/PRAC/539397/2023). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 19/03/2024 (IAIN/0081), which are available on the Agency's website.**
Fosavance	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-marketing case reports and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (WS2467), which are available on the Agency's website.**

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Gavreto	All presentations	15/04/2024	Update of sections 4.2, 4.4 and 4.5 of the SmPC in order to amend posology recommendations, warnings and drug-drug interaction information regarding the co-administration with CYP3A4 inhibitors, P-gp inhibitors and CYP3A4 inducers based on final results from the DDI study GP43162, listed as a category 3 study in the RMP, as well as results from the physiologically based pharmacokinetic (PBPK) analyses summarised in the PBPK Report 1120689. The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 25/03/2024 (II/0012), which are available on both the European Commission and the Agency's website.**
Grepid	All presentations	15/02/2024	To update sections 4.1, 4.2, 4.4 and 5.1 of the SmPC to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI). To update sections 4.4 and 4.8 of the SmPC in order to update an existing warning on`Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (IB/0057/G), which are available on both the European Commission and the Agency's website.**
HyQvia	All presentations	15/02/2024	Extension of indication to include treatment of Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) as maintenance therapy after stabilization with IVIg in adults, children and adolescents for HyQvia. As a consequence, sections 4.1, 4.2, 4.4, 4.7, 4.8, 5.1, 5.2 and 6.6 of the SmPC are updated. The package leaflet and labelling are updated in accordance.

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			Parallel distributors must use the annexes dated 25/01/2024 (II/0087), which are available on the European Commission website.
Imfinzi	All presentations	15/03/2024	Update of sections 4.2, 4.4 and 4.8 of the SmPC to add the adverse reactions of 'uveitis' and 'arthritis', a warning/precaution regarding these adverse reactions, and recommendations for treatment modifications when these adverse reactions occur. The package leaflet is updated accordingly. Update of section 4.4. of the SmPC to add a warning regarding patients with pre-existing autoimmune disease **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00010723/202304), which are available on the European Commission website.**
Instanyl	All presentations	15/04/2024	Update of sections 4.2, 4.4, and 4.8 of the SmPC to inform prescribers about Opioid Use Disorder (OUD). The package leaflet is updated accordingly. Update of section 4.4 of the SmPC to add requirement regarding safe storage space. The package leaflet is updated accordingly. Update of SmPC section 4.9 to add toxic leukoencephalopathy as possible symptom of fentanyl overdose. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/03/2024 (PSUSA/ 00001369/202304), which are available on both the European Commission website and the Agency's website.**
Imraldi	All presentations	15/02/2024	To update section 3 of the SmPC to add "opalescent" and "pale brown" to the pharmaceutical form description. The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 23/01/2024 (IB/0070), which are available on the Agency's website.**

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Increlex	All presentations	15/02/2024	Update of sections 4.2, 4.6, and 4.8 of the SmPC in order to modify administration instructions recommendation regarding the monitoring of pre-prandial blood glucose in pre-prandial condition and in case of symptoms and to prevent the risk of lipohypertrophy, delete wording in the pregnancy section and update on number of patients with severe primary IGFD based on the cumulative review of safety database, scientific literature and clinical trials data. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/10/2023 (II/0080), which are available on the Agency's website.**
Incruse Ellipta	All presentations	15/02/2024	Update of sections 4.2, 4.6 and 4.8 of the SmPC to add 'Dysphonia' and 'Oropharyngeal pain' to the list of adverse drug reactions (ADRs) with frequency rare, and to update the wording regarding the administration instructions and for pregnancy and breast-feeding. ***Both the package leaflet and the labelling are updated accordingly.*** **Parallel distributors must use the annexes dated 14/12/2023 (WS2485), which are available on the Agency's website.**
Jakavi	All presentations	15/04/2024	Update of section 4.4 of the SmPC in order to add new warnings on 'Major adverse cardiac events (MACE)', 'Thrombosis', and 'Second primary malignancies', following an Art. 20 Class Referral involving JAK inhibitors approved to treat rheumatoid arthritis. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (II/0068), which are available on the Agency's website.**
Kaftrio	All presentations	15/03/2024	To update Sections 4.2, 4.4, and 4.8 of the SmPC to emphasise the warning about the risk of drug induced elevated transaminases as requested in Article 46 WS procedures EMEA/H/C/005269/P46/013 and EMEA/H/C/005269/P46/014. Update of section

Name	EU number	Date of communication	Rationale
			4.6 of the SmPC to amend the wording regarding breast-feeding. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00010868/202304 which also includes the IB/0045 scopes), on both the European Commission and the Agency's website**
Kesimpta	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to amend an existing warning on injection-related reactions and to add 'Hypersensitivity reactions' to the list of adverse drug reactions (ADRs) with frequency not known. The package leaflet is updated accordingly. Addition of a statement in the pre-filled syringes (PFS) instructions for use when PFS has been dropped on a hard surface. The instructions for use have been updated accordingly. **Parallel distributors must use the annexes dated 09/02/2024 (II/0006) which are available on the Agency's website.**
Keytruda	All presentations	15/04/2024	Extension of indication to include in combination with platinum-containing chemotherapy as neoadjuvant treatment, and then continued as monotherapy as adjuvant, for the treatment of resectable non small cell lung carcinoma at high risk of recurrence in adults for Keytruda based on study KEYNOTE-671. Consequently, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 25/03/2024 (II/0134), which are available on the European Commission website.**
Kineret	All presentations	15/04/2024	Update of section 4.8 of the SmPC in order to add 'Injection site amyloid deposits' to the list of adverse drug reactions (ADRs) with frequency not known, based on a review of the clinical study and post-marketing data to

Name	EU number	Date of communication	Rationale
			evaluate a possible causal association between anakinra (Kineret) and amyloidosis. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (II/0092) which are available on the Agency's website.**
Kinzalcomb	All presentations	15/04/2024	Update of sections 4.2, 4.3, 4.4, 4.5, and 5.2 of the SmPC in order to align with reference labels for both active substances. The package leaflet is updated accordingly. Update section 4.7 of the SmPC to replace the term "drowsiness" by "syncope or vertigo" to align it with adverse reactions table in section 4.8 of SmPC. The package leaflet is updated accordingly. Update section 5.3 of the SmPC based on the EMA request dated 31 Jan 2023 for the HCTZ containing medicinal products to remove the sentence '…the extensive human experience with hydrochlorothiazide has failed to show an association between its use and an increase in neoplasms' in order to address an inconsistency in the PI. **Parallel distributors must use the annexes dated 25/01/2024 (WS2573/G) which are available on the Agency's website.**
Komboglyze	All presentations	15/04/2024	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on 'Vitamin B12 decrease/deficiency' and to change the frequency of 'Vitamin B12 decrease/deficiency' in the list of adverse drug reactions (ADRs) from frequency 'very rare' to 'common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (WS2544) which are available on the Agency's website.**
Lopinavir/Ritonavir Mylan	All presentations	15/02/2024	To update section 4.5 of the SmPC to reflect an additional drug-drug interaction with dabigatran etexilate and edoxaban. The package leaflet has been updated accordingly.

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			Parallel distributors must use the annexes dated 16/01/2024 (IB/0027) which are available on the Agency's website
Lunsumio	All presentations	15/04/2024	Update of sections 4.4 and 4.8 of the SmPC to add the adverse reaction haemophagocytic lymphohistiocytosis with a frequency 'uncommon' (both for all cases, and grade 3-4, based on review of available cases) and a warning/precaution regarding haemophagocytic lymphohistiocytosis. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (PSUSA/ 00010999/202306), which are available on both the European Commission website and the Agency's website.**
Mavenclad	All presentations	15/02/2024	Update of sections 4.5 and 4.6 of the SmPC to add information regarding the use of mavenclad with oral contraceptives based on the final study results from the drug-drug interaction study (MS 700568-0031). Annex II and the package leaflet are updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (II/0027), which are available on the Agency's website.**
Mayzent	All presentations	15/02/2024	Update of section 4.8 of the SmPC to amend the PML frequency from "unknown" to "rare". The package leaflet is updated accordingly. Update of section 4.4 of the SmPC to amend a warning regarding reduction in heart rate and atrioventricular conduction. **Parallel distributors must use the annexes dated 05/01/2024 (PSUSA/00010818/202303) which are available on the European Commission website.**
Mekinist	All presentations	15/04/2024	Update of section 4.8 of the SmPC to add the adverse reaction AV block with a frequency "not known" for mono therapy and "uncommon" for combination therapy with

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			dabrafenib, and include a footnote with the information; xx Including atrioventricular block complete. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 18/03/2024 (PSUSA/ 00010262/202305), which are available on both the European Commission website and the Agency's website.**
Mektovi	All presentations	15/04/2024	Update of sections 4.4 and 4.8 of the SmPC to add the adverse reaction Tumour lysis syndrome with a frequency not known and a warning/precaution regarding Tumour lysis syndrome. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (PSUSA/ 00010717/202306), which are available on both the European Commission website and the Agency's website.**
Mirapexin	All presentations	15/02/2024	Update of section(s) 4.2, 4.4 and 4.8 of the SmPC to highlight that the lowest effective dose should be used, amend the warning/precaution regarding restless legs augmentation syndrome and to add the adverse reaction restless legs augmentation syndrome with a frequency 'very common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/01/2024 (PSUSA/00002491/202304) which are available on the European Commission website.**
Myozyme	All presentations	15/03/2024	Update of section 4.2 of the SmPC in order to add home infusion upon request by PRAC following the assessment of PSUSA/00000086/202109 I based on a cumulative search of the MAH Global Pharmacovigilance database and literature. The Package Leaflet and Annex II are updated accordingly.

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			Parallel distributors must use the annexes dated 25/01/2024 (II/0094), which are available on the Agency's website.
Nevanac	All presentations	15/03/2024	To remove from SmPC section 4.8 (undesirable effect) "Uncommon: hypertension" as blood pressure increase is listed in the annexes as well.To replace the statement "Rinse your eye out with warm water" with "Contact your doctor for detailed instruction" in the package leaflet section 3. In addition the MAH has updated the translations with minor linguistic correction and to comply with QRD. **Parallel distributors must use the annexes dated 28/02/2024 (IAIN/0055 which includes the IB/0054/G safety scopes), which are available on the Agency's website**
Ninlaro	All presentations	15/04/2024	Update of sections 4.4 and 4.8 of the SmPC to add the adverse reactions TEN, anaphylactic reaction and angioedema (frequency Rare) and a warning/precaution regarding TEN. The package leaflet is updated accordingly, in addition to include previously missing symptoms for SJS/TEN. **Parallel distributors must use the annexes dated 19/03/2024 (PSUSA/ 00010535/202305), which are available on both the European Commission website and the Agency's website.**
Ontozry	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC to amend /add information relating to suicidality following the use of cenobamate. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 12/01/2024 (PSUSA/00010921/202303), which are available on both the European Commission website and the Agency's website.**
Ozempic	All presentations	15/04/2024	Update of sections 4.5 and 4.8 of the SmPC to add the adverse reaction intestinal obstruction

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			with a frequency not known and an interaction regarding other coumarin derivatives. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (PSUSA/ 00010671/202305), which are available on both the European Commission website and the Agency's website.**
PecFent	All presentations	15/04/2024	Update of sections 4.2, 4.4, and 4.8 of the SmPC to inform prescribers about Opioid Use Disorder (OUD). The package leaflet is updated accordingly. Update of section 4.4 of the SmPC to add requirement regarding safe storage space. The package leaflet is updated accordingly. Update of SmPC section 4.9 to add toxic leukoencephalopathy as possible symptom of fentanyl overdose. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/03/2024 (PSUSA/ 00001369/202304), which are available on both the European Commission website and the Agency's website.**
Pregabalin Zentiva	All presentations	15/04/2024	To update sections 4.4, 4.8 of the SmPC to include suicidal ideation as part of the observed withdrawal symptoms following the same changes adopted for the parent product Lyrica. Section 3 of the PL is updated accordingly. **Parallel distributors must use the annexes dated 15/03/2024 (IB/0050) which is available on the Agency's website.**
Prevenar 20	All presentations	15/04/2024	Extension of indication to include infants, children and adolescents from 6 weeks to less than 18 years of age for the prevention of invasive disease, pneumonia and acute otitis media caused by Streptococcus pneumoniae, based on final results from studies B7471003, B7471011, B7471012, B7471013 and B7471014. As a consequence, sections 4.1, 4.2, 4.4, 4.5, 4.8 and 5.1 of the SmPC are

Name	EU number	Date of communication	Rationale
			updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 11/03/2024 (II/0012) which are available on both the European Commission website and the Agency's website.**
Protopic	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend the warning/precaution recommending against use in patients with a skin barrier defect. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/02/2024 (PSUSA/00002840/202303) which are available on both the European Commission website and the Agency's website.**
Puregon	All presentations	15/04/2024	Update of section 4.8 of the SmPC to add the adverse reaction "anaphylactic reaction" with a frequency not known. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/03/2024 (PSUSA/00001465/ 202305) which are available on the European Commission website.**
Reblozyl	All presentations	15/03/2024	Submission of the final report from study ACE-536-MDS-005 listed as a category 3 study in the RMP. This is a non-interventional post-authorisation safety study (PASS) to evaluate the effectiveness of the additional risk minimisation measure (aRMM) for Reblozyl among Healthcare Providers (HCPs) in the EU/EEA. Update of section 4.6 of the PI and Annex II.D. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 11/01/2024 (II/0023) which is available on the Agency's website.**
Reblozyl	All presentations	15/04/2024	Extension of indication to include treatment of adult patients with anaemia due to very low, low and intermediate-risk myelodysplastic

Name	EU number	Date of communication	Rationale
			syndromes (MDS), who may require RBC transfusions for Reblozyl, based on results from study ACE-536-MDS-002 (COMMANDS), and studies ACE-536-MDS-001(MEDALIST), ACE-536-MDS-004 , A536-03, A536-05 and ACE-536-LTFU-001. Consequently, sections 4.1, 4.2, 4.4, 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 27/03/2024 (II/0021) which are available on the European Commission website.**
Retsevmo	All presentations	15/03/2024	Extension of indication to include the treatment of adults and adolescents 12 years and older with advanced RET fusion-positive thyroid cancer in the first-line setting for RETSEVMO based on interim data from studies LIBRETTO-001 (LOXO-RET-17001) and LIBRETTO-121; LIBRETTO-001 is an open-label, multicentre, global Phase 1/2 study of selpercatinib in patients with RET-altered advanced solid tumors. LIBRETTO-121 is a Phase 1/2 study of selpercatinib in paediatric patients with advanced RET-altered solid or primary central nervous system tumours. As a consequence, sections 4.1, 4.2, 4.8 and 5.1 of the SmPC are updated. The package leaflet is updated in accordance. **Parallel distributors must use the annexes dated 29/02/2024 (II/0021) which are available on both the European Commission website and the Agency's website.**
Ritonavir Mylan	All presentations	15/02/2024	To update section 4.5 in order to reflect additional Drug-Drug Interaction with dabigatran etexilate and edoxaban. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/01/2024 (IB/0020/G) which is available on the Agency's website.**
Rivastigmine Actavis	All presentations	15/03/2024	To update sections 4.4 and 4.5 of the SmPC to strengthen the existing warning on QT

Name	EU number	Date of communication	Rationale
			prolongation based on post-marketing data and literature, following assessment of the same change for the reference product, Exelon. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/02/2024 (IB/0032) which is available on the Agency's website**
Rybelsus	All presentations	15/04/2024	Update of sections 4.5 and 4.8 of the SmPC to add the adverse reaction intestinal obstruction with a frequency not known and an interaction regarding other coumarin derivatives. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 27/03/2024 (PSUSA/ 00010671/202305), which are available on both the European Commission website and the Agency's website.**
Sarclisa	All presentations	15/04/2024	Update of sections 4.2, 4.4 and 5.2 of the SmPC based on final results from study TED16414, listed as a category 3 study in the RMP. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2022 (II/0026) which are available on the Agency's website.**
Sifrol	All presentations	15/02/2024	Update of section(s) 4.2, 4.4 and 4.8 of the SmPC to highlight that the lowest effective dose should be used, amend the warning/precaution regarding restless legs augmentation syndrome and to add the adverse reaction restless legs augmentation syndrome with a frequency 'very common'. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 05/01/2024 (EMEA/H/C/PSUSA/00002491/202304) which are available on both the European Commission website and the Agency's website.**

Name	EU number	Date of communication	Rationale
Sutent	All presentations	15/04/2024	Update of sections 4.4 and 4.8 of the SmPC to add the adverse reaction Hyperammonaemic encephalopathy with a frequency unknown and add a warning regarding Hyperammonaemic encephalopathy. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 24/03/2024 (PSUSA/00002833/ 202304) which are available on both the European Commission website and the Agency's website.**
Tafinlar	All presentations	15/04/2024	To update the section 4.8 of the SmPC to include the signal "peripheral neuropathy" following the PRAC's recommendation adopted on 30 November 2023 (EMA/PRAC/539397/2023; EPITT No. 19947). The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 07/03/2024 (IG1710) which are available on the Agency's website.**
Tagrisso	All presentations	15/04/2024	Update of section 4.8 of the SmPC to add 'Skin Hyperpigmentation' to the list of adverse drug reactions (ADRs) with frequency 'uncommon' based on literature. The package leaflet has been updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (II/0054) which are available on the Agency's website.**
Tecentriq	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding the risk of immune-related adverse reactions in patients with pre-existing autoimmune disease. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2024 (PSUSA/00010644/202305) which are available on both the European Commission and the Agency's website**

Name	EU number	Date of communication	Rationale
Tegsedi	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to modify the warning on liver monitoring and drug-induced liver injury and to add 'drug-induced liver injury' to the list of adverse drug reactions (ADRs) with frequency not known. Annex II and the package leaflet are updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (II/0038) which are available on the Agency's website.**
Teysuno	All presentations	15/02/2024	To update section 4.6 of the SmPC according to WP/NcWP recommendation on the 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 15/01/2024 (IB/0055) which are available on the Agency's website.**
Truvada	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding Bone effects. Update of section 4.8 of the SmPC to add the adverse reaction bone mineral density decreased with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/1210/202304) which are available on both the European Commission and the Agency's website.**
Tysabri	All presentations	15/03/2024	Update of sections 4.2 and 4.4 of the SmPC to modify administration instructions and update educational guidance to enable the subcutaneous formulation to be administered outside a clinical setting by healthcare professionals based on the cumulative review of post marketing and clinical study data. The package leaflet and Annex IID are updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0136) which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Vabysmo	All presentations	15/04/2024	Update of section 4.8 of the SmPC in order to add 'Retinal Vasculitis' and 'Retinal Occlusive Vasculitis' to the list of adverse drug reactions (ADRs) with frequency not known, based on a drug safety report and post-marketing data; the Package Leaflet is updated accordingly. **Parallel distributors must use the annexes dated 08/02/2024 (II/0009) which are available on the Agency's website.**
Vantavo	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to include information on the risk of 'atypical fractures of other bones' (than the femur), and update of section 4.8 to add 'atypical fractures of other bones' as a new ADR with frequency 'not known' and to include further information about the risk of 'atypical subtrochanteric and diaphyseal femoral fractures', based on post-marketing case reports and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 30/11/2023 (WS2467) which are available on the Agency's website.**
Verzenios	All presentations	15/03/2024	Update of section 4.4 of the SmPC in order to add a new warning on "arterial thromboembolic events", based on a safety review. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 09/11/2023 (II/0028) which are available on the Agency's website**
Viread	All presentations	15/03/2024	Update of section 4.4 of the SmPC to amend a warning/precaution regarding Bone effects. Update of section 4.8 of the SmPC to add the adverse reaction bone mineral density decreased with a frequency common. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 16/02/2024 (PSUSA/00002892/202303) which are available on both the European Commission and the Agency's website**

Name	EU number	Date of communication	Rationale
Vipdomet	All presentations	15/02/2024	Update of sections 4.4 and 4.8 of the SmPC in order to add a new warning on Vitamin B12 decrease or deficiency and to update the list of adverse drug reactions (ADRs) in accordance with the recent update of the PI for Glucophage, which is the reference label for the compound metformin, and following the request by MHRA on 20 June 2022 for all products containing metformin. **Parallel distributors must use the annexes dated 26/10/2023 (II/0044) which are available on the Agency's website.**
Wegovy	All presentations	15/04/2024	Update of sections 4.5 and 4.8 of the SmPC to add the adverse reaction intestinal obstruction with a frequency not known and an interaction regarding other coumarin derivatives. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 21/03/2024 (PSUSA/ 00010671/202305), which are available on both the European Commission website and the Agency's website.**
Xultophy	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to add Dizziness and Delayed gastric emptying to the list of adverse drug reactions (ADRs) with frequency common and unknown, respectively, based on the cumulative review of clinical studies data, post marketing data, class labels and biological plausibility. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 07/12/2023 (II/0050), which are available on the Agency's website**
Yervoy	All presentations	15/04/2024	Update of section 4.4 and 4.8 of the SmPC in order to add 'myelitis' as a warning under the subsection "Other immune-mediated adverse reactions" and to the list of adverse drug reactions (ADRs) with their calculated frequencies for monotherapy (not known) and in combination (rare), based on post marketing

Name	EU number	Date of communication	Rationale
			data and literature. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/02/2024 (WS2597), which are available on the Agency's website**
Yescarta	All presentations	15/03/2024	To update section 4.4 of the SmPC and section 2 of the PL to implement the signal recommendation on 'Axicabtagene ciloleucel - Progressive multifocal leukoencephalopathy (PML)' (EPITT no 19940), adopted at the 27-30 November 2023 PRAC meeting. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 22/02/2024 (IAIN/0071), which are available on the Agency's website.**
Zavicefta	All presentations	15/03/2024	Update of section 4.4 of the SmPC with information regarding the fact that cases of Crohn's disease have been reported post-marketing. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0033), which are available on the Agency's website.**
Zaltrap	All presentations	15/02/2024	Update of section 4.6 of the SmPC in order to update information regarding the duration of contraceptive use after cessation of treatment. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (Yearly update which includes II/0070), which are available on the European Commission website.**
Zeffix	All presentations	15/04/2024	Update of section 4.4 of the SmPC in order to amend an existing warning on HIV co-infection. The Package Leaflet is updated accordingly. **Parallel distributors must use the annexes dated 15/02/2024 (II/0087), which are available on the Agency's website.**

Name	EU number	Date of communication	Rationale
Zelboraf	All presentations	15/04/2024	To update the section 4.8 of the SmPC and section 4 of the PL to implement the signal recommendation on "Cobimetinib; vemurafenib – Aphthous ulcer, mouth ulceration, stomatitis" (EPITT no 19961), adopted at the 8-11 January 2024 PRAC meeting. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 26/03/2024 (IG1730), which are available on the Agency's website.**
Zinforo	All presentations	15/03/2024	Update of section 4.8 of the SmPC in order to add 'Kounis Syndrome' to the list of adverse drug reactions (ADRs). The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (II/0063) which are available on both the European Commission and the Agency's website**
Zinplava	All presentations	15/02/2024	Extension of indication to include treatment of the paediatric population (1 to 18 years of age) for ZINPLAVA, based on final results from study MK-6072-001 (MODIFY III) listed as a category 3 study in the RMP. 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 accordingly. **Parallel distributors must use the annexes dated 26/01/2024 (II/0037), which are available on the European Commission website.**
Zyllt	All presentations	15/03/2024	To update the below listed sections of the SmPC and PL following assessment of the same for the reference product Plavix: - Extension of indication to include clopidogrel in combination with acetylsalicylic acid in ST segment elevation acute myocardial infarction (STEMI) patients undergoing percutaneous coronary intervention (PCI); as a consequence section 4.1, 4.2 and 5.1 of the SmPC is updated. C.I.2.a - To update the below listed sections of the SmPC and the package leaflet following assessment of the same for the reference product Plavix: - Update

Name	EU number	Date of communication	Rationale
			of section 4.4 of the SmPC in order to update an existing warning on 'Bleeding and haematological disorders' by adding a statement on triple antiplatelet therapy (clopidogrel + aspirin + dipyridamole) for stroke secondary prevention. The package leaflet is updated accordingly. **Parallel distributors must use the annexes dated 25/01/2024 (IB/0045/G) which are available on both the European Commission and the Agency's website**

Index: