The underlisted safety variations have been submitted by Marketing Authorization Holders (MAHs) and approved by the Food and Drugs Authority in line with the Variation Guidelines for Allopathic Medicines.These safety variations are being shared with healthcare professionals and patients.

Safety Updates						
No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Aerius	Desloratadine	Special warnings and precautions for use	Addition of text to read "In the case of severe renal insufficiency, Aerius should be used with caution (see section 5.2)." under the heading Renal function Revision of text to read "Sorbitol is a source of fructose; patients with hereditary fructose intolerance (HFI) should not take this medicinal product." Revision of text to read "Aerius oral solution contains benzyl alcohol This medicinal product contains 0.75 mg benzyl alcohol in each ml of oral solution. Benzyl alcohol may cause anaphylactoid reactions. Increased risk due to accumulation in young children. It is not recommended to be used for more than a week in young children (less than 3 years old). High volumes should be used with caution and only if necessary, especially in subjects with liver or kidney impairment because of the risk of accumulation and toxicity (metabolic acidosis)." Deletion of text "In the case of severe renal insufficiency, Aerius should be used with caution (see section 5.2).] [This medicinal product contains sorbitol; thus, patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine." under the heading Paediatric population	20/04/2022	MSD

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Aerius	Desloratadine	Special warnings and precautions for use	Additon of text to read " A retrospective observational safety study indicated an increased incidence of new-onset seizure in patients 0 to 19 years of age when receiving desloratadine compared with periods not receiving desloratadine. Among children 0-4 years old, the adjusted absolute increase was 37.5 (95 % Confidence Interval (CI) 10.5-64.5) per 100,000 person years (PY) with a background rate of new onset seizure of 80.3 per 100,000 PY. Among patients 5-19 years of age, the adjusted absolute increase was 11.3 (95 % CI 2.3-20.2) per 100,000 PY with a background rate of 36.4 per 100,000 PY. (See section 4.4.)" under the heading Paediatric population.	20/04/2022	MSD
2	Anastrozole	Anastrozole	Possible side effects	Revision of text under subtitle" Very common side effects(may affect more than 1 in 10 people) " to read " •Headache. • Hot flushes. • Feeling sick (nausea). • Skin rash. • Pain or stiffness in your joints. • Inflammation of the joints (arthritis). • Feeling weak. • Bone loss (osteoporosis). • Depression"	13/04/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Anastrozole	Anastrozole	Contents of the pack and other information	Revision of text under subtitle"What Anastrozole 1 mg film-coated tablets contains" to read "•The active substance is anastrozole. Each film-coated tablet contains 1 mg of anastrozole. • The other ingredients are: Tablet core: lactose monohydrate, cellulose microcrystalline, sodium starch glycolate (Type A), magnesium stearate, silica colloidal anhydrous, hydroxypropylcellulose. Tablet coating: Opadry II white: lactose monohydrate, hypromellose, macrogol 4000, titanium dioxide (E 171)". Revision of text under subtitle "What Anastrozole 1 mg film-coated tablets looks like and contents of the pack" to read" White, round and biconvex film-coated tablets with embossment “A1” on one side. The film-coated tablets are packed in ALU/PVC blister and inserted in a carton. Pack sizes: 7, 10, 14, 20, 28, 30, 50, 56, 60, 84, 90, 98, 100 film-coated tablets. Not all pack sizes may be marketed."	13/04/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Contraindications	Inclusion of section "Contraindications" "• Hypersensitivity to the active substances or to any of the excipients listed in section 6.1 or to sulfonamide derived active substances. Hydrochlorothiazide is a sulfonamide derived active substance. • Second and third trimesters of pregnancy (see sections 4.4 and 4.6). • Severe renal impairment (creatinine clearance <30 ml/min/1.73 m2 BSA). • Severe hepatic impairment and/or cholestasis. • Refractory hypokalaemia and hypercalcaemia. • Gout. • The concomitant use of Candesan with aliskiren-containing products is contraindicated in patients with diabetes mellitus or renal impairment (GFR < 60 ml/min/1.73 m2) (see sections 4.5 and 5.1)".	22/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Special warnings and precautions for use	Inclusion of section "Special warnings and precautions for use" "Dual blockade of the renin-angiotensin-aldosterone system (RAAS)" "There is evidence that the concomitant use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren increases the risk of hypotension, hyperkalaemia and decreased renal function (including acute renal failure). Dual blockade of RAAS through the combined use of ACE-inhibitors, angiotensin II receptor blockers or aliskiren is therefore not recommended (see sections 4.5 and 5.1). If dual blockade therapy is considered absolutely necessary, this should only occur under specialist supervision and subject to frequent close monitoring of renal function, electrolytes and blood pressure. ACE-inhibitors and angiotensin II receptor blockers should not be used concomitantly in patients with diabetic nephropathy" Inclusion of section "Renal impairment": “As with other agents inhibiting the renin-angiotensin-aldosterone system, changes in renal function may be anticipated in susceptible patients treated with Candesan (see section 4.3)" Inclusion of section "Kidney transplantation": “There is limited clinical evidence regarding Candesan use in patients who have undergone renal transplant" Inclusion of section” Renal artery stenosis” “Medicinal products that affect the renin-angiotensin-aldosterone system, including angiotensin II receptor antagonists (AIIRAs), may increase blood urea and serum creatinine in patients with bilateral renal artery stenosis or stenosis of the	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Interaction with other medicinal products and other forms of interaction	Inclusion of section "Interaction with other medicinal products and other forms of interaction "Compounds which have been investigated in clinical pharmacokinetic studies include warfarin, digoxin, oral contraceptives (i.e. ethinylestradiol/levonorgestrel), glibenclamide and nifedipine. No pharmacokinetic interactions of clinical significance were identified in these studies. The potassium depleting effect of hydrochlorothiazide could be expected to be potentiated by other medicinal products associated with potassium loss and hypokalaemia (e.g. other kaliuretic diuretics, laxatives, amphotericin, carbenoxolone, penicillin G sodium, salicylic acid derivates, steroids, ACTH). Concomitant use of Candesan and potassium-sparing diuretics, potassium supplements or salt substitutes or other medicinal products that may increase serum potassium levels (e.g. heparin sodium, co-trimoxazole also known as trimethoprim/sulfamethoxazole) may lead to increases in serum potassium. Monitoring of potassium should be undertaken as appropriate (see section 4.4). Diuretic-induced hypokalaemia and hypomagnesaemia predisposes to the potential cardiotoxic effects of digitalis glycosides and antiarrhythmics. Periodic monitoring of serum potassium is recommended when Candesan is administered with such medicinal products, and with the following medicinal products that could induce torsades de pointes: • Class Ia antiarrhythmics (e.g. quinidine, hydroquinidine, disopyramide) • Class III antiarrhythmics (e.g. amiodarone, sotalol, dofetilide,	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Fertility, pregnancy and lactation	Inclusion of section "Fertility, pregnancy and lactation". "Angiotensin II Receptor Antagonists (AIIRAs)" under subsection “Pregnancy” "Epidemiological evidence regarding the risk ofteratogenicity following exposure to ACE-inhibitors during the first trimester of pregnancy has not been conclusive; however, a small increase in risk cannot be excluded. Whilst there is no controlled epidemiological data on the risk with AIIRAs, similar risks may exist for this class of medicinal products. Unless continued AIIRA therapy is considered essential, patients planning pregnancy should be changed to alternative antihypertensive treatments which have an established safety profile for use in pregnancy. When pregnancy is diagnosed, treatment with AIIRAs should be stopped immediately and, if appropriate, alternative therapy should be started. Exposure to AIIRA therapy during the second and third trimesters is known to induce human foetotoxicity (decreased renal function, oligohydramnios, skull ossification retardation) and neonatal toxicity (renal failure, hypotension, hyperkalaemia) (see section 5.3). Should exposure to AIIRAs have occurred from the second trimester of pregnancy, ultrasound check of renal function and skull is recommended. Infants whose mothers have taken AIIRAs should be closely observed for hypotension (see sections 4.3 and 4.4)" "Hydrochlorothiazide" under subsection “Pregnancy” "There is limited experience with hydrochlorothiazide during pregnancy, especially during the first trimester. Animal studies are insufficient.	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Effects on ability to drive and use machines	Inclusion of section "Effects on ability to drive and use machines" "No studies on the effects on the ability to drive and use machines have been performed. When driving vehicles or operating machines, it should be taken into account that occasionally dizziness or weariness may occur during treatment with Candesan"	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Undesirable effects	Inclusion of section "Undesirable effects" "In controlled clinical studies with candesartan cilexetil/hydrochlorothiazide adverse reactions were mild and transient. Withdrawals from treatment due to adverse events were similar with candesartan cilexetil/hydrochlorothiazide (2.3-3.3%) and placebo (2.7-4.3%). In clinical trials with candesartan cilexetil/hydrochlorothiazide, adverse reactions were limited to those that were reported previously with candesartan cilexetil and/or hydrochlorothiazide. The table below presents adverse reactions with candesartan cilexetil from clinical trials and post marketing experience. In a pooled analysis of clinical trial data of hypertensive patients, adverse reactions with candesartan cilexetil were defined based on an incidence of adverse events with candesartan cilexetil at least 1% higher than the incidence seen with placebo. The frequencies used in the tables throughout section 4.8 are: very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data).Inclusion of two tables that show the frequency of undesirable effect on system organ class for candesartan as well as frequency of undesirable effect on system organ class for hydrochlorothiazide of dose 25mg or higher" "Reporting of suspected adverse reactions:" "Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan Cilexetil/Hydrochlorothiazide	Overdose	Inclusion of section "Overdose" "Symptoms ”Based on pharmacological considerations, the main manifestation of an overdose of candesartan cilexetil is likely to be symptomatic hypotension and dizziness. In individual case reports of overdose (of up to 672 mg candesartan cilexetil) patient recovery was uneventful. The main manifestation of an overdose of hydrochlorothiazide is acute loss of fluid and electrolytes. Symptoms such as dizziness, hypotension, thirst, tachycardia, ventricular arrhythmias, sedation/impairment of consciousness and muscle cramps can also be observed" "Management" "No specific information is available on the treatment of overdose with Candesan. The following measures are, however, suggested in case of overdose.When indicated, induction of vomiting or gastric lavage should be considered. If symptomatic hypotension should occur, symptomatic treatment should be instituted and vital signs monitored. The patient should be placed supine with the legs elevated. If this is not sufficient, plasma volume should be increased by infusion of isotonic sodium chloride solution. Serum electrolyte and acid balance should be checked and corrected, if needed. Sympathomimetic medicinal products may be administered if the above-mentioned measures are not sufficient. Candesartan cannot be removed by haemodialysis. It is not known to what extent hydrochlorothiazide is removed by haemodialysis”	21/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Enbrel	Etanercept	Pediatric population with juvenile idiopathic arthritis	Addition of text to read under "Of the 127 patients in the parent study, 109 participated in the open-label extension study and were followed for a total of 10 years. At the end of the extension study, 84/109 (77%) patients had completed the study; 27 (25%) while actively taking Enbrel, 7 (6%) had withdrawn from treatment due to low/inactive disease; 5 (5%) had re-started Enbrel following an earlier withdrawal from treatment; and 45 (41%) had stopped Enbrel (but remained under observation); 25/109 (23%) patients permanently discontinued from the study. Improvements in clinical status achieved in the parent study were generally maintained for all efficacy endpoints during the entire follow-up period. Patients actively taking Enbrel could enter an optional withdrawal re-treatment period once during the extension study based on investigator's judgement of clinical response. 30 patients entered the withdrawal period. 17 patients were reported to have a flare (defined as ≥30% worsening in at least 3 of the 6 ACR Pedi components with ≥30% improvement in not more than 1 of the remaining 6 components and a minimum of 2 active joints); median time to flare after Enbrel withdrawal was 190 days. 13 patients were re-treated and the median time to re-treatment from withdrawal was estimated as 274 days. Due to the small number of data points, these results should be interpreted with caution.One malignancy, Hodgkin's disease was reported in the first year of the extension study in an 18 year old EO JIA patient. The number (exposure-adjusted rate per 100 patient years) of serious adverse events, malignancies, and serious infections was 40 (5.85 EP100PY), 1 (0.15 EP100PY), and	20/04/2022	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Enbrel	Etanercept	Adult patients with non-radiographic axial spondyloarrrthritis	Addition of text to read under " This multi-center, open-label, phase 4, 3-period study evaluated the withdrawal and re-treatmentof Enbrel in patients with active nr-AxSpa who achieved an adequate response (inactive disease defined as Ankylosing Spondylitis Disease Activity Score (ASDAS) C-reactive protein (CRP) less than 1.3) following 24 weeks of treatment. 209 adult patients with active nr-AxSpa (18 to 49 years of age), defined as those patients meeting the Assessment of SpondyloArthritis International Society (ASAS) classification criteria of axial spondyloarthritis (but not meeting the modified New York criteria for AS), having positive MRI findings (active inflammation on MRI highly suggestive of sacroiliitis associated with SpA) and/or positive hsCRP (defined as high sensitivity C-reactive protein [hsCRP] > 3 mg/l), and active symptoms defined by an ASDAS CRP greater than or equal to 2.1 at the screening visit received open-label Enbrel 50 mg weekly plus stable background NSAID at the optimal tolerated anti-inflammatory dosage for 24 weeks in Period 1. Patients were also required to have an inadequate response or intolerance to two or more NSAIDs. At week 24, 119 (57%) patients achieved inactive disease and entered into the Period 2 40-week withdrawal phase where subjects discontinued etanercept, yet maintained the background NSAID. The primary measure of efficacy was the occurrence of flare (defined as an ASDAS erythrocyte sedimentation rate (ESR) greater than or equal to 2.1) within 40 weeks following withdrawal of Enbrel. Patients who flared were	20/04/2022	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Enbrel	Etanercept	Pharmacitual Form/ Nature and contents of container	Revision of text to read "Cartons contain single-use pre-filled syringes of Enbrel (50 mg) and alcohol swabs."	20/04/2022	Pfizer
5	Fentanyl Sandoz	Fentanyl	Warning and Precautions	Revision of text to read under the sub heading Take special care with Fentanyl Sandoz " • You have ever abused or been dependent on alcohol, prescription medicines or illegal drugs. If any of the above apply to you (or you are not sure), talk to your doctor or pharmacist before using Fentanyl Sandoz. • All patients on opioids including Fentanyl Sandoz may develop reduced pain relief, increased sensitivity to pain, physical and psychological dependence to the medication with repeated use; it is important not to discontinue the medication suddenly. Talk to your doctor before stopping the medicine if you ever feel there is a reason to stop."	28/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Fentanyl Sandoz	Fentanyl	Side Effects and Fentanyl Sandoz	Revision of text to read " • Fentanyl Sandoz may make you unusually drowsy, and make your breathing more slow or shallow. • Repeated, long term use of the patches may make the medicine less effective (you become 'tolerant' to it) or you may become dependent on it. See section 4 for a full list of possible side effects. • . Fentanyl Sandoz can cause an increased sensitivity to feeling pain and an extreme response to pain. If this is suspected, talk to	28/03/2022	Novartis
5	Fentanyl Sandoz	Fentanyl	Other medicines and Fentanyl Sandoz	Revision of text to read " • Some medicines used to treat cancer of the blood (such as idelalisib). • Some medicines used to treat pain and sometimes seizures called gabapentinoids (gabapentin and pregabalin)."	28/03/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Feldene	Piroxicam	Special warnings and precautions for use	Revision of text under the heading Skin reactions to read as "Serious skin reactions, some of which have fatal outcomes, including drug reaction with eosinophilia and systemic symptoms (DRESS syndrome), exfoliative dermatitis, Stevens-Johnson syndrome and toxic section 4.8). Cases of fixed drug eruption (FDE) have been reported with piroxicam. Piroxicam should not be reintroduced in patients with history of piroxicam-related FDE. Potential cross reactivity might occur with other oxicams. Studies have suggested that piroxicam may be associated with a higher risk of serious skin reactions compared with other non-oxicam NSAIDs. The incidence of these adverse effects appears to be more significant at the start of treatment with the latency period in most cases during the first month of treatment. Treatment with piroxicam should be stopped at the first appearance of a skin rash, mucosal lesions or any other sign of hypersensitivity " Revision of text under the heading Elderly subjects to read as " When prescribing, the physician must take into account the fact that cases of secondary anovulatory infertility by non-rupture of Graffian follicles, reversible upon discontinuation of treatment have been reported in patients treated chronically by some inhibitors synthesis of prostaglandins."	16/02/2022	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Feldene	Piroxicam	Interaction with other medicinal products and other forms of interactions	Revision of text under the subheading Oral anticoagulants to read as "NSAIDs, including piroxicam, are likely to enhance the effects of anticoagulants, such as coumarin-typederivatives (warfarin) and direct oral anticoagulants (for example, apixaban, dabigatran, rivaroxaban). Increase in the risk of haemorrhage from oral anticoagulant (aggression of the gastroduodenal mucosa by non-steroidal anti-inflammatories). Consequently, the concomitant use of piroxicam and anticoagulants should be avoided. If the association cannot be avoided, carry out close clinical, or even biological, monitoring (see section 4.4)."	16/02/2022	Pfizer
6	Feldene	Piroxicam	Undesirable effects	Revision of text under the heading Cutaneo-mucous reactions to read as " • Stomatitis, • Eruptions, pruritus, rare cases of photosensitisation, • Rare cases of bullous skin reactions, such as erythema multiforme, erosive pluriorificialis or epidermal necrolysis (Stevens-Johnson, Lyell syndrome), angio-oedema, exfoliative dermatitis, multiforme erythema, onycholysis, DRESS Syndrome, fixed drug eruption have been reported- frequency unknown (see section 4.4)." Revision of text under the heading Renal and urinary effects to read as " •Functional acute renal failure (ARF) in patients presenting with risk factors (see section 4.4). • Organic renal involvement that could translate into ARF: isolated cases of interstitial nephritis, acute tubular necrosis, nephrotic syndrome, glomerulonephritis and papillary necrosis have been reported	16/02/2022	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Feldene	Piroxicam	Pharmacokinetic properties	Addition of text to read "The global bioavailability and significance of the absorption are not modified baby food, with the latter slightly slowing the absorption rate." under the	16/02/2022	Pfizer
7	Pregabalin Sandoz	Pregabalin	What you need to know before you take Pregabalin Sandoz	Revision of text under subtitle "Before taking this medicine you should tell your doctor if you have a history of heart disease" to read "There have been reports of kidney failure in some patients when taking Pregabalin Sandoz. If while taking Pregabalin Sandoz you notice decreased urination, you should tell your doctor as stopping the medicine may improve this. · A small number of people being treated with anti-epileptics such as Pregabalin Sandoz have had thoughts of harming or killing themselves. If at any time you have these thoughts, immediately contact your doctor. · When Pregabalin Sandoz is taken with other medicines that may cause constipation (such as some types of pain medicines) it is possible that gastrointestinal problems may occur (e.g., constipation, blocked or paralysed bowel). Tell your doctor if you experience constipation, especially if you are prone to this problem. · Before taking this medicine you should tell your doctor if you have a history of alcoholism or drug dependence. Let your doctor know if you think you need more medicine than prescribed. · There have been reports of convulsions when taking Pregabalin Sandoz or shortly after stopping Pregabalin Sandoz. If you experience a convulsion, contact your doctor immediately. · There have been reports of reduction in brain function (encephalopathy) in some patients taking Pregabalin Sandoz when they have other conditions. Tell your doctor if you have a	11/04/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Pregabalin Sandoz	Pregabalin	Pregnancy and breast-feeding	Revision of text to read" Pregabalin Sandoz should not be taken during pregnancy, unless you are told otherwise by your doctor. There is a risk of congenital malformations especially in the first trimester. Effective contraception must be used by women of child-bearing potential. If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine. It is not recommended to breast-feed your baby while using Pregabalin Sandoz as it is not known if Pregabalin Sandoz may be found in breast milk. Ask your doctor or pharmacist for advice before taking any medicine while breast-feeding."	11/04/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Pregabalin Sandoz	Pregabalin	Possible side effects	Revision of text under subtitle" Rare side-effects which may affect less than 1 person in 1000 are listed below:" to read "- Abnormal sense of smell -swinging vision -altered perception of depth -visual brightness, -vision loss · Dilated pupils, cross eyes. · Cold sweat, tightness of the throat, swollen tongue. · Inflammation of the pancreas. · Difficulty in swallowing. · Slow or reduced movement of the body. · Difficulty with writing properly. · Increased fluid in the abdomen. · Fluid in the lungs · Convulsions · Changes in the recording of electrical changes (ECG) in the heart which correspond to heart rhythm disturbances · Muscle damage. · Breast discharge, abnormal breast growth, breast growth in males. · Interrupted menstrual periods. · Kidney failure, reduced urine volume, urinary retention. · Decrease in white blood cell count. · Inappropriate behaviour. · Allergic reactions (which may include difficulty breathing, inflammation of the eyes (keratitis) and a serious skin reaction	11/04/2022	Novartis
8	Robester	Rosuvastatin	Other medicines and Robester	Addition of text to read " • ticagrelor (used for the prevention of stroke, heart attack and other similar conditions)"	14/04/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Sandoz	Piperacillin /Tazobactam	Warnings and precautions	Revision of text to read " • Haemophagocytic lymphohistiocytosis (HLH) - it is a rare life-threatening disorder in which histiocytes and lymphocytes (types of white blood cells) build up in organs including the skin, spleen, and liver, and destroy other blood cells. clinical signs and symptoms of an excessive systemic inflammation (e.g. fever, hepatosplenomegaly, hypertriglyceridaemia, hypofibrinogenaemia, high serum ferritin, cytopenias and haemophagocytosis). • Patients should be evaluated immediately if they develop pathologic immue activation. If diagnosis of HLH is established, piperacillin/tazobactam treatment should be discontinued • Beta-lactam Antibiotic Class Effect • Beta-lactam antibiotics, including piperacillin tazobactam, may led to manifestations of damage or disease that affects the brain	24/02/2022	Novartis
			Possible Side Effects	Revision of text to read under the sub heading uncommon side effects"- joint and muscle pain - chills - Convulsion (seizure)"		
10	Vizimpro	Dacomitinib monohydrate	Pharmaceutical form	Revision of text to read " VIZIMPRO 15 mg film-coated tablets. Blue film-coated, round biconvex tablet, debossed with “Pfizer” on one side and “DCB15” on the other. VIZIMPRO 30 mg film-coated tablets. Blue film-coated, round biconvex tablet, debossed with “Pfizer” on one side and “DCB30” on the other. VIZIMPRO 45 mg film-coated tablets. Blue film-coated, round biconvex tablet, debossed with “Pfizer” on one side and “DCB45”	14/04/2022	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Vizimpro	Dacomitinib monohydrate	Special Warnings and Precautions for use	Revision of text to read under the subheading drug metabolized by CYP2D6 " Lactose VIZIMPRO contains lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption should not take this medicine. Sodium VIZIMPRO contains < 1 mmol sodium (23 mg) per tablet, that is to say essentially “sodium-free ”.	14/04/2022	Pfizer
			Shelf Life	Revision of text to read " 60 months "		
11	Voltaren emulgel 1%	Diclofenac	Warnings and Precautions	Addition of text: "Be cautious when smoking or near naked flames due to risk of severe burns. Voltaren emulgel 1 % contains paraffin which is potentially flammable when it builds up on fabric (clothing, bedding, dressings, etc.) and may not be totally removed by laundering)" under the heading "warnings and precautions".	06/04/2022	GSK