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	Aldactone	Spironolactone	Preclinical safety data	Revision of texts to read "Orally administered spironolactone has been shown to be a tumorigen in dietary administration studies performed in rats, with its proliferative effects manifested on endocrine organs and the liver. In an 18-month study using doses of about 50, 150 and 500 mg/kg/day, there were statistically significant increases in benign adenomas of the thyroid and testes and, in male rats, a dose-related increase in proliferative changes in the liver (including hepatocytomegaly and hyperplastic nodules). In a 24-month study in which the same strain of rat was administered doses of about 10, 30 and 100 mg/kg/day of spironolactone, the range of proliferative effects included significant increases in hepatocellular adenomas and testicular interstitial cell tumors in males, and significant increases in thyroid follicular cell adenomas and carcinomas in both sexes. There was also a statistically significant, but not dose-related, increase in benign uterine endometrial stromal polyps in females." under section Carcinogenesis, Mutagenesis, Impairment of Fertility Revision of texts to read "A dose-related (above 30 mg/kg/day) incidence of myelocytic leukemia was observed in rats fed daily doses of potassium canrenoate (a compound chemically similar to spironolactone and whose primary metabolite, canrenone, is also a major product of spironolactone in man) for a period of 1 year. In 2-year studies in the rats, oral administration of potassium canrenoate was associated with myelocytic leukemia and hepatic, thyroid, testicular and mammary tumors."under section Carcinogenesis, Mutagenesis, Impairment of Fertility.	14-Apr-21	Pfizer
2	Betoptic	Betaxolol	Posology and Method of Administration	Addition of text: "If more than one topical ophthalmic product is being used, the products must be administered at least 5 minutes apart. Eye ointments should be administered last" under Method of Administration.	7-May-21	Novartis International AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Betoptic	Betaxolol	Special warnings and precautions for use	Addition of text: "BETOPTIC ophthalmic solution, a cardioselective beta-blocker, has produced only minimal effects in patients with reactive airway disease. Caution should be exercised in the treatment of glaucoma patients with excessive restriction of pulmonary function". Addition of heading "Chroidal detachment". Addition of text: "Choroidal detachment has been reported with administration of aqueous suppressant therapy (e.g. timolol, acetazolamide) after filtration procedures" under Choroidal detachment. Addition of text: "Consideration should be given to the gradual withdrawal of beta-blockers prior to general anaesthesia because of the reduced ability of the heart to respond to beta-adrenergically mediated sympathetic reflex stimuli. Addition of heading "Ocular". Addition of text: "When BETOPTIC ophthalmic solution is used to reduce elevated intraocular pressure in angle-closure glaucoma, it should be used with a miotic and not alone. In patients with angle-closure glaucoma, the immediate treatment objective is to reopen the angle by constriction of the pupil with a miotic agent. Betaxolol has little or no effect on the pupil. • As with the use of other anti-glaucoma drugs, diminished responsiveness to BETOPTIC ophthalmic solution after prolonged therapy has been reported in some patients. However, in one long-term study in which 250 patients have been followed for up to three years, no significant difference in mean-intraocular pressure has been observed after initial stabilization." under the heading Ocular.	7-May-21	Novartis International AG
			Interaction with other Medicinal Products and Other Forms of Interaction	Addition of text: "There is a potential additive effect on the intraocular pressure when BETOPTIC ophthalmic solution is administered concomitantly with oral beta-blockers". Addition of text: Addition of text: "• Although BETOPTIC ophthalmic solution used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with BETOPTIC ophthalmic solution and adrenaline has been reported occasionally".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Betoptic	Betaxolol	Undesirable Effects	Addition of "dysthymic disorder" with frequency rare under the System Organ Class Immune System Disorders. Addition of hypoaesthesia eye, corneal staining, pupils unequal with frequency rare under the System Organ Class Eye Disorders. Addition of heading "Paediatric population". Addition o f text: "The safety and IOP-lowering effect of betaxolol 2.5 mg/ml eye drops, suspension has been demonstrated in paediatric patients in a 3-month, multi-centre, double-masked, active-controlled trial. The adverse drug reaction profile of betaxolol 2.5 mg/ml eye drops, suspension was comparable to that seen in adult patients". under Paediatric population.	7-May-21	Novartis International AG
			Overdose	Addition of text "An ocular overdose of BETOPTIC ophthalmic solution may be flushed from the eye(s) with lukewarm tap water".		
			Pregnancy and Lactation	Addition of text: "A decision must be made whether to discontinue breast-feeding or to discontinue or abstain from BETOPTIC ophthalmic solution therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman." under the heading Breast-feeding.		
			Effects on ability to drive and use machines	Addition of text: "BETOPTIC ophthalmic solution has no or negligible influence on the ability to drive and use machines".		
			Pharmacological Properties	Addition of text: "Elevated intraocular pressure (IOP) is a major risk factor in glaucomatous field loss. The higher the level of IOP, the greater the likelihood of optic nerve damage and visual field loss". Under Mechanism of Action.		
			Pharmacokinetic Properties	Revision of text to read "Following oral or i.v. administration, betaxolol plasma concentrations decline with a terminal half-life of 15 to 16 hours. Oral bioavailability is about 80%. Following a 20 mg oral dose, a mean maximum plasma concentration of about 46 ng/ml was achieved at 4 hours. Plasma drug levels increase in a dose-proportional manner with increasing dose. Plasma exposure to betaxolol is low following topical ocular administration. Following topical ocular administration of 0.5% betaxolol solution to normal volunteers for 1 week, maximum steady-state plasma drug concentrations were about 1 ng/ml or less". under the heading Absorption.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Betoptic	Betaxolol	Clinical Studies	Revision of text read "In controlled, double-masked studies, the magnitude and duration of the ocular hypotensive effect of betaxolol 0.25% eye drops, suspension and betaxolol 0.5% eye drops, solution were clinically equivalent". Clinical studies show that topical betaxolol reduces mean intraocular pressure 25% from baseline. In trials using 22 mmHg as a generally accepted index of intraocular pressure control, betaxolol was effective in more than 94% of the population studies, of which 73% were treated with the beta-blocker alone. Data obtained during controlled clinical trials in patients with chronic open-angle glaucoma and ocular hypertension indicates that treatment with betaxolol has a superior long-term benefit on the visual field as compared to treatment with timolol, a non-selective beta-blocker. In three-way masked crossover studies comparing ophthalmic betaxolol to timolol and placebo, betaxolol was found to have minimal effect on pulmonary and cardiovascular parameters. In contrast, timolol significantly decreased pulmonary function and produced a lowering of the mean heart rate. Ophthalmic betaxolol solution at 1% (one drop in each eye) was compared to placebo in a cross-over study challenging nine patients with reactive airway disease. Betaxolol had no significant effect on pulmonary function as measured by the Forced Expiratory Volume per Second (FEV1), the Forced Vital Capacity (FVC) and the relation between them (FEV1/FVC) and was not significantly different from placebo. The action of isoproterenol, a beta-stimulant, administered at the end of the study was not inhibited by ophthalmic betaxolol. Ophthalmic betaxolol has minimal effect on pulmonary and cardiovascular parameters. Additionally, during therapy with betaxolol, no negative effect on the blood supply to the optic nerve has been observed. Rather, betaxolol maintained or improved ocular blood flow/perfusion. Clinical observation of glaucoma patients treated with betaxolol for up to 3 years shows that the intraocular pressure lowering effect is well maintained".	7-May-21	Novartis International AG
			Special precautions for storage	Revision of text to read "Store at room temperature (8°C – 30°C). Keep the bottle in the outer carton. Do not use this medicine after the expiry date which is stated on the packaging. Discard 4 weeks after first opening. Keep this medicine out of the sight and reach of children".		
3	Candesan Plus	Candesartan cilexetil/ hydrochlorothiazide	Clinical particulars	Addition of texts to include sections on "Contraindications; Special warnings and precautions for use; Interaction with other medicinal products and other forms of interaction; Fertility, pregnancy and lactation; Effects on ability to drive and use machines; Undesirable effects; Overdose"	26-Mar-21	Sandoz Pharmaceticals d.d
			Pregnancy and breast-feeding	Revision of texts to read "Candesan Plus is not recommended in pregnancy, and must not be taken when more than 3 months pregnant, as it may cause serious harm to your baby if used after the third month of pregnancy." Revision of texts to read "Do NOT take Candesan Plus, if: you are pregnant (it is also better to avoid Candesan Plus in pregnancy – see pregnancy section)"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Candesan Plus	Candesartan cilexetil/ hydrochlorothiazide	Warnings and precautions	Addition of texts to include "Talk to your doctor or pharmacist before taking Candesan Plus, if: you are taking any of the following medicines used to treat high blood pressure: - an ACE-inhibitor (for example enalapril, lisinopril, ramipril), in particular if you have diabetes related kidney problems. - aliskiren" Addition of texts to include "Do NOT take Candesan Plus, if: you have diabetes or impaired kidney function and you are treated with a blood pressure lowering medicine containing aliskiren."	26-Mar-21	Sandoz Pharmaceticals d.d
4	Esmeron	Rocuronium Bromide	Clinical Particulars	Revision of texts to read as "Posology- As with other neuromuscular blocking agents, the dosage of Esmeron should be individualized for each patient. The method of anesthesia and the expected duration of surgery, the method of sedation and the expected duration of mechanical ventilation, possible interaction with other drugs that are administered concomitantly, and the condition of the patient should be taken into account when determining the dose." under sub heading Posology and method of administration Revision of texts to read as "Method of administration- Esmeron is administered intravenously either as a bolus injection or as a continuous infusion (see section 6.6)" under sub heading Posology and method of administration Addition of texts to include "Sodium- This medicine contains less than 1 mmol sodium (23 mg) per vial, that is to say essentially 'sodium-free'." under sub heading Special warnings and precautions for use.	17-Mar-21	MSD (Pty) Limited
5	Herceptin	Trastuzumab	Effects on ability to drive and use machines	Revision of texts to read "Herceptin has a minor influence on the ability to drive or use machines (see section 4.8). Dizziness and somnolence may occur during treatment with Herceptin (see section 4.8). Patients experiencing administration-related symptoms (see section 4.4) should be advised not to drive and use machines until symptoms abate."	17-Mar-21	Roche Products Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Herceptin	Trastuzumab	Undesirable effects	Deletion of texts that read; “Herpes zoster, common; Erysipelas,common; cellulitis,common; sepsis,uncommon” under Infections and infestations Revision of texts to read; +Anaphylactic reaction,Rare, +Anaphylactic shock, Rare” under Immune system disorders Deletion of texts that read; “Thinking abnormal, common” under Psychiatric disorders Deletion of texts that read; “Ataxia, common; Paresis,Rare; Brain oedema, Not known” under Nervous system disorders Deletion of texts that read; “Palpitation,very common; Pericarditis, Not known; Bradycardia, Not known” under Cardiac disorders Addition of texts to include; “Wheezing,uncommon” under Respiratory, thoracic and mediastinal disorders Revision of texts to include; “Pneumonitis,uncommon” under Respiratory, thoracic and mediastinal disorders Deletion of texts to include, “Hepatic Failure, Not known” under Hepatobiliary disorders	17-Mar-21	Roche Products Ghana Ltd
6	Invanz	Ertapenem	Special warnings and precautions for use	Addition of texts to read " This medicinal product contains approximately 137 mg sodium per 1.0 g dose, equivalent to 6.85 % of the WHO recommended maximum daily intake of 2 g sodium for an adult." Addition of text to read "hypersensitivity vasculitis" under "Skin and subcutaneous tissue disorders"	15-Feb-21	MSD Idea Pharmaceuticals
7	Mezolyn	Meropenem	Warnings and precautions	Addition of texts to read "Severe skin related adverse reactions have been reported in patients receiving Meropenem. If signs and symptoms suggestive of these reactions appear, Meropenem should be withdrawn immediately and an alternative treatment should be considered"	12-Jul-21	Sandoz
			Possible side effects	Revison of texts to read Addition of texts to read "Rare; Delirium (altered consciousness), Frequency not known (cannot be estimated from available data); Reddish skin rash/pustules (AGEP rash)" under subheading "other possible side effects"		
8	Ocrevus	Ocrelizumab	Dosage/Administration	Addition of texts to include "If patients have not had an infusion-related reaction (IRR) during previous OCREVUS infusions, the duration of the infusion can be shortened (to 2 hours) for subsequent doses (see Table 1, Option 2)."	17-Mar-21	Roche Products Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Ocrevus	Ocrelizumab	Infections	Revision of texts under Progressive multifocal leukoencephalopathy (PML) to read as "Infections with the John Cunningham (JC) virus which led to PML have been observed in patients who were treated with anti-CD20 antibodies and other MS therapies and exposed to risk factors (e.g. patient population, polytherapy with immuno¬suppressants). The risk of PML with Ocrevus cannot be ruled out. Postmarketing cases of progressive multifocal leukoencephalopathy (PML) have been reported during the use of Ocrevus. The cases of PML in ocrelizumab-treated patients reported to date involved additional possible risk factors such as other previous drug-modifying treatments (DMTs) known to increase the risk of PML or low lymphocyte counts."	17-Mar-21	Roche Products Ghana Ltd
			Description of selected undesirable effects from clinical trials	Addition of texts with subheading Alternative shorter infusion for maintenance therapy; to include "In a study (MA30143 substudy on shortening the infusion duration) to characterize the safety profile of shorter (2-hour) OCREVUS infusions in patients with the relapsing remitting form of multiple sclerosis , the incidence, intensity and nature of IRR symptoms were comparable to those occurring with infusions over approximately 3.5 hours (see “Clinical efficacy”). In both infusion groups, the total number of necessary interventions was low but in the group with the shorter (2-hour) infusions, more interventions (reduction in the rate or temporary interruptions of the infusion) were needed to manage IRR symptoms than in the group with infusions given over 3.5 hours (8.7% vs. 4.8%)."		
			Substudy on shortening the infusion duration	Addition of texts to include "The safety of the shorter (2-hour) OCREVUS infusion was evaluated in a prospective, multicentre, randomized, double-blind, controlled, parallel-arm substudy of MA30143 (ENSEMBLE study) in patients with relapsing remitting multiple sclerosis who had not previously had disease-modifying treatment. The first dose of OCREVUS was given as two 300 mg infusions (600 mg in total), with an interval of 14 days between each. From the second dose onwards (dose 2 to 6), patients were randomized in a 1:1 ratio either to the group with a conventional OCREVUS infusion (over approximately 3.5 hours every 24 weeks) or to the group with a shorter OCREVUS infusion (over approximately 2 hours every 24 weeks). Randomization was stratified according to the region and dose at which the patients had first been randomized. The primary endpoint was the proportion of patients with IRRs during or within 24 hours of the first randomized infusion of OCREVUS. The primary analysis was conducted when 580 patients had been randomized. The proportion of patients with IRRs during or within 24 hours after the first randomized infusion was 24.6% in the group with the shorter infusion, compared with 23.1% in the group with the conventional infusion. The group difference was similar after stratification. Overall, the IRRs at all randomized doses were for the most part mild or moderate and there were only two severe IRRs (one IRR per group). No life-threatening, fatal or serious IRRs occurred"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Simvastatin	Simvastatin	Special warnings and precautions for use	Addition of texts to include "Daptomycin- Cases of myopathy and/or rhabdomyolysis have been reported with HMG-CoA reductase inhibitors (e.g. simvastatin) co-administered with daptomycin. Caution should be used when prescribing HMG-CoA reductase inhibitors with daptomycin, as either agent can cause myopathy and/or rhabdomyolysis when given alone. Consideration should be given to temporarily suspend simvastatin in patients taking daptomycin unless the benefits of concomitant administration outweigh the risk. Consult the prescribing information of daptomycin to obtain further information about this potential interaction with HMG-CoA reductase inhibitors (e.g. simvastatin) and for further guidance related to monitoring. (See section 4.5.)"	7-Dec-20	Sandoz Pharmaceticals d.d
			Drug-drug Interactions	Addition of texts to include "Daptomycin- It should be considered to temporarily suspend simvastatin in patients taking daptomycin unless the benefits of concomitant administration outweigh the risk (see section 4.4)" in the table under section Pharmacokinetic interactions Addition of texts to include "Ticagrelor-Co-administration of ticagrelor with simvastatin increased simvastatin Cmax by 81% and AUC by 56% and increased simvastatin acid Cmax by 64% and AUC by 52% with some individual increases equal to 2- to 3-fold. Co-administration of ticagrelor with doses of simvastatin exceeding 40 mg daily could cause adverse reactions of simvastatin and should be weighed against potential benefits. There was no effect of simvastatin on ticagrelor plasma levels. The concomitant use of ticagrelor with doses of simvastatin greater than 40 mg is not recommended." Addition of texts to include "Daptomycin-The risk of myopathy and/or rhabdomyolysis may be increased by concomitant administration of HMG-CoA reductase inhibitors (e.g. simvastatin) and daptomycin (see section 4.4)."		
			Undesirable effects	Addition of texts to include "Eye disorders- Rare: vision blurred, visual impairment" in the table Addition of texts to include “Skin and subcutaneous tissue disorders- Very rare: lichenoid drug eruptions” in the table Addition of texts to include “Musculoskeletal and connective tissue disorders Very rare: muscle rupture” in the table Addition of texts to include “Reproductive system and breast disorders- Very rare: gynecomastia” in the table Addition of texts to include “Post-marketing Experience The additional adverse reactions have been reported in post- marketing use with ezetimibe/simvastatin or during clinical studies or post-marketing use with one of the individual components.”		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Tagrisso	Osimertinib	Undesirable effects	Addition of texts to include " Erythema multiforme (EM)" as an adverse drug reaction.	3-Mar-21	Astrazeneca AB
			Possible side effects	Addition of texts to include "Stevens-Johnson syndrome, which can appear as reddish target-like macules or circular patches often with central blisters on the trunk, skin peeling, ulcers of mouth, throat, nose, genitals and eyes and be preceded by fever and flu-like symptoms. This side effect is rare: it may affect up to 1 in 1000 people. See also section 2" under subsection Serious side effects Addition of texts to include "Target lesions, which are skin reactions that look like rings (suggestive of Erythema multiforme). This side effect is uncommon: it may affect up to 1 in 100 people" Revision of texts to read "Skin and nail problems- signs may include pain, itching, dry skin, rash, redness around the fingernails. This is more likely in areas exposed to the sun using moisturisers regularly on your skin and nails can help with this. Tell your doctor if your skin or nail problems get worse" under subsection Other side effects; Very common.		
11	Tecentriq	Atezolizumab	Posology and method of administration	Addition of texts to read "Patients with first-line (1L) UC should be selected for treatment based on the tumour expression of PD-L1 confirmed by a validated test (see section 5.1)" under subheading "Tecentriq monotherapy" Revision of text to read "Severe cutaneous adverse reactions; Grade 3; Withhold Tecentriq; or suspected Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN); Treatment may be resumed when the symptoms improve to Grade 0 or Grade 1 within 12 weeks rash is resolved and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day. Grade 4 or confirmed Stevens-Johnson syndrome (SJS) or toxic epidermal necrolysis (TEN); Permanently discontinue Tecentriq" under "Table 1: Dose modification advice for Tecentriq"	1-Apr-21	Roche Products Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
11	Tecentriq	Atezolizumab	Special warnings and precautions for use	Addition of texts to read "Immune-related severe cutaneous adverse reactions (SCARs), including cases of Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), have been reported in patients receiving atezolizumab. Patients should be monitored for suspected severe skin reactions and other causes should be excluded. For suspected SCARs, patients should be referred to a specialist for further diagnosis and management. Based on the severity of the adverse reaction, atezolizumab should be withheld for Grade 3 skin reactions and treatment with systemic corticosteroids at a dose of 1-2 mg/kg/day of prednisone or equivalent should be started. Treatment with atezolizumab may be resumed if the event improves to ≤ Grade 1 within 12 weeks, and corticosteroids have been reduced to ≤ 10 mg prednisone or equivalent per day. Treatment with atezolizumab should be permanently discontinued for Grade 4 skin reactions, and corticosteroids should be administered. Atezolizumab should be withheld for patients with suspected SJS or TEN. For confirmed SJS or TEN, atezolizumab should be permanently discontinued. Caution should be used when considering the use of atezolizumab in a patient who has previously experienced a severe or life-threatening skin adverse reaction on prior treatment with other immune-stimulatory anticancer agents." under subheading "Immune-related severe cutaneous adverse reactions"	1-Apr-21	Roche Products Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
11	Tecentriq	Atezolizumab	Undesirable effects	Addition of texts to read "Endocrine disorders; hypothyroidism, hyperthyroidism; common, Skin and subsutaneous tissue disorders; pemphigoid; rare, Renal and urinary disorders; nephritis; Uncommon" under "Table 2: Summary of adverse reactions occurring in patients treated with atezolizumab" Revision of texts to read "Myocarditis occurred in < 0.1% (1/3,854) of patients who received atezolizumab monotherapy 4.9 months. The duration was 14 days. Myocarditis led to the discontinuation of atezolizumab in 1 (<0.1%) patient." under subheading "Description of selected adverse reactions; Immune-related myocarditis " Addition of texts to read "Severe cutaneous adverse reactions (SCARs) occurred in 0.7% (26/3,854) of patients who received atezolizumab monotherapy. Of the 26 patients, one experienced a fatal event. The median time to onset was 5.9 months (range: 4 days to 15.5 months). The median duration was 2.3 months (range: 1 day to 22.1+ months; + denotes a censored value). SCARs led to discontinuation of atezolizumab in 3 (<0.1%) patients. SCARs requiring the use of systemic corticosteroids occurred in 0.2% (8/3,854) of patients receiving atezolizumab monotherapy." under subheading "Description of selected adverse reactions; Immune-related severe cutaneous adverse reactions" Revison of texts to read "Across multiple phase II and III studies, 13.1% to 54.1% of patients developed treatment-emergent anti-drug antibodies (ADAs). Patients who developed treatment-emergent ADAs tended to have overall poorer health and disease characteristics at baseline. Those imbalances in health and disease characteristics at baseline can confound the interpretation of pharmacokinetic (PK), efficacy and safety analyses. Exploratory analyses adjusting for imbalances in baseline health and disease characteristics were conducted to assess the effect of ADA on efficacy. These analyses did not exclude possible attenuation of efficacy benefit in patients who developed ADA compared to patients who did not develop ADA. The median time to ADA onset ranged from 3 weeks to 5 weeks." under subheading "Description of selected adverse reactions; Immunogenicity"	1-Apr-21	Roche Products Ghana Ltd
12	Topamax	Topiramate	Warnings and precautions	Revision of texts to read "If you have an intolerance to some sugars, contact your doctor before taking this medicinal product" under subheading Topamax contains lactose Addition of texts to include "Topamax can cause serious skin reactions, tell your doctor immediately if you develop a skin rash and/or blisters (see also section 4 'Possible side effects')." Addition of texts to include "You are responsible for judging whether you are fit to drive motorized vehicles or carry out work that needs focused attention. One of the factors that can affect your abilities in these respects is the use of medicines due to their effects and/or side effects. Therefore read all the information in this package leaflet for guidance. Discuss the matter with your doctor or pharmacist if you are unsure." under subheading Driving and using machines.	15-Apr-21	Janssen Pharmaceuticals

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
12	Topamax	Topiramate	Possible side effects	Addition of texts to include "Serious skin reactions, such as Stevens-Johnson syndrome and toxic epidermal necrolysis - these may appear as rashes with or without blisters. Skin irritation, sores or swelling in the mouth, throat, nose, eyes and around the genitals. The skin rashes may develop into serious widespread skin damage (peeling of the epidermis and superficial mucous membranes) with life-threatening consequences." under subheading Rare. Deletion of texts that read "Stevens Johnson syndrome, a potentially life-threatening condition that may present with sores in multiple mucosal sites (such as the mouth, nose, and eyes), a skin rash, and blistering" under subheading Common. Deletion of texts that read "Toxic epidermal necrosis, a life-threatening condition related to, yet more severe than, Stevens-Johnson syndrome, characterized by widespread blistering and sloughing of the outer layers of the skin (see rare side effects)" under subheading Not known (frequency cannot be estimated from the available data).	15-Apr-21	Janssen Pharmaceuticals