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	Actemra	Tocilizumab	Composition	Revision of text to read "Tocilizumab (produced by recombinant DNA technology using CHO [Chinese hamster ovary] cells)." under Active substance. Revision of text to read "Concentrate for solution for infusion- Polysorbate 80, sucrose, disodium phosphate dodecahydrate, sodium dihydrogen phosphate dihydrate, water for injection q.s. 4 ml, 10 ml or 20 ml of solution corresponding, respectively, to 1.76 mg, 4.43 mg and 8.85 mg of sodium." under Excipients. Revision of text to read "Injection solution for subcutaneous use-Polysorbate 80, L arginine, L-arginine hydrochloride, L-methionine, L-histidine, L-histidine hydrochloride monohydrate, water for injection q.s. 0.9 ml of solution." under Excipients .	29-Sep-21	Roche Products Ghana Ltd
			Warnings and precautions	Addition of text to include "Additional remarks-Actemra concentrate for solution for infusion (i.v. formulation) contains less than 1 mmol of sodium (23 mg) per dose, i.e. it is virtually “sodium-free”."		
			Undesireable effects	Addition of text to include " Reporting of suspected adverse reactions after marketing authorisation is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected new or serious adverse reaction."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Actemra	Tocilizumab	Other information	Revision of text to read "Shelf life Do not use this medicine after the expiry date (“EXP”) stated on the container." Revision of text to read " Special precautions for storage Actemra, concentrate for solution for infusion Store concentrate in thea refrigerator (2–8°C). Do not freeze. Keep the container in the outer carton in order to protect the contents from light. Actemra, injection solution for subcutaneous use Store in the refrigerator at 2 8°C. Do not freeze. Keep in the outer carton in order to protect the contents from light. Instructions for handling Intravenous administration: Actemra is supplied in pyrogen-free single-use vials containing no preservatives. Sterile needles and syringes should be used for preparing Actemra. 1) Withdraw the required volume of Actemra from one or more unused vials under aseptic conditions using a sterile needle and syringe (a dose of 8 mg/kg BW corresponds to 0.4 ml/kg BW, 10 mg/kg corresponds to 0.5 ml/kg, 12 mg/kg corresponds to 0.6 ml/kg) . Discard any unused portion left in the vial. 2) Using another sterile needle and syringe, discard the same volume of isotonic sodium chloride solution (sterile, pyrogen-free 0.9% [w/v] sodium chloride solution) as the required volume of Actemra from a 100 ml infusion bag (for patients ≥ 30 kg) or from a 50 ml infusion bag (for PJIA or SJIA patients < 30 kg)."	29-Sep-21	Roche Products Ghana Ltd
2	Arthrotec	clofenac sodium/Misopros	Qualitative And Quantitative Composition	Revision of text to read “Diclofenac sodium 75 mg Misoprostol 200 mcg under the sub heading active ingredient ''75 mg''.	20-Oct-21	Pfizer
			Pharmaceutical Form	Addition of text to read '' White, round, biconvex tablets approximately 10 mm to11 mm in diameter. Each tablet consists of an enteric-coated core containing 75 mg of diclofenac sodium surrounded by an outer mantle containing 200 mcg misoprostol''.		
			Posology and method of administration	Deletion of text '' 50 mg/200 mcg—1 tablet two or three times daily'' under the sub heading Osteoarthritis, Rheumatoid arthritis. Deletion of text '' 50 mg/200 mcg—1 tablet two, three, or four times daily'' under the sub heading ankylosing spondylitis. Deletion of text '' 50 mg/200 mcg—1 tablet two or three times daily'' under the sub heading Musculoskeletal disorders.		
			Interaction with other medicinal products and other forms of interaction	Deletion of text ''Voriconazole: Voriconazole increased Cmax and AUC of diclofenac (50 mg single dose) by 114% and 78%, respectively.''		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Avastin	Bevacizumab	Dosage and Administration	Revision of text under Dosage and administration to read "Do not administer as an intravenous bolus injection." Revision of text under Children and adolescents to read " Avastin is not approved for children and adolescents under 18 years of age. The safety and efficacy of Avastin in this population have not been established (see end of “Properties/Effects” and “Pharmacokinetics” sections). "	29-Sep-21	Roche Products Ghana Ltd
			Interactions	Revision of text under Radiotherapy to read " There is evidence that infection rates are increased when Avastin is used in conjunction with radiotherapy (not approved for any disease; see « Undesirable effects »)."		
			Pregnancy,lactation	Revision of text under Fertility to read "A substudy in the ongoing clinical development programme with 295 premenopausal women has shown a higher incidence of new cases of ovarian failure in the bevacizumab group compared to the control group. After discontinuation of bevacizumab treatment, ovarian function recovered in the majority of patients. The long-term effects of treatment with bevacizumab on fertility are unknown (see “Warnings and precautions” and “Undesirable effects”). Repeated-dose safety studies in animals have shown that bevacizumab may have an adverse effect on female fertility (see “Properties/Effects” and “Preclinical data”)."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Avastin	Bevacizumab	Undesirable effects	Revision of text under Gastrointestinal disorders to read "Common: intestinal perforation, ileus, intestinal obstruction, rectovaginal fistula (occurring most commonly classified asin the enterovaginal fistula category), gastrointestinal disorder, stomatitis, proctalgia" Revision of text under Gastrointestinal perforation and fistula (see “Warnings and precautions”) to read "Gastrointestinal perforation has been reported in clinical trials with an incidence of less than 1% in patients with non-squamous non-small cell lung cancer, up to 1.3% in patients with metastatic breast cancer, up to 2% in patients with metastatic renal cell cancer or ovarian cancer and up to 2.7% (including gastrointestinal fistula and abscess) in patients with metastatic colorectal cancer. Cases of gastrointestinal perforation have also been observed in patients with relapsed glioblastoma. In a clinical trial in patients with persistent, recurrent or metastatic cervical cancer (study GOG-0240), gastrointestinal perforations (all grades) occurred in 3.2% of patients, all of whom had a history of prior pelvic radiation. Fatal outcome was reported in approximately a third of serious cases of gastrointestinal perforation, which represents 0.2%–1% of all Avastin treated patients. In Avastin clinical trials, gastrointestinal fistulae (all grades) have been reported with an incidence of up to 2% in patients with metastatic colorectal cancer and ovarian cancer, and less commonly also in patients with other types of cancer." Revision of text under Haemorrhage to read "In clinical trials across all indications, the overall incidence of NCI-CTC Grade 3–5 bleeding events ranged from 0.4% to 6.9% in Avastin treated patients, compared with 0% to 4.5% of patients in the chemotherapy control group.Tumour-associated haemorrhage (see below) and mild mucocutaneous bleeding (e.g. epistaxis) accounted for the majority of bleeding events observed." Revision of text under Tumour-associated haemorrhage to read "Across all Avastin clinical trials, mucocutaneous bleeding was observed in up to 50% of patients treated with Avastin. In most cases, it consisted of Grade 1 epistaxis lasting under 5 minutes, resolving without medical intervention and necessitating no change in the Avastin treatment regimen, and less frequently of low-grade bleeding from the oral mucosa or vagina. Occurrence appears to be dose dependent." Addition of text under Changes in laboratory values to read "Reporting of suspected adverse reactions after marketing authorisation is very important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected new or serious adverse reaction."	29-Sep-21	Roche Products Ghana Ltd
			Properties/Effects	Revision of text under Pharmacodynamics to read "Avastin (bevacizumab) is a recombinant humanised monoclonal antibody (IgG1 kappa) which binds selectively to human vascular endothelial growth factor (VEGF) and inhibits its biological activity. Bevacizumab contains human sequences with antigen-binding regions of a humanised murine antibody that binds to VEGF. Bevacizumab is produced by recombinant DNA technology in a Chinese hamster ovarian cell expression system. The subsequent purification process comprises specific virus inactivation and impurity removal steps. Bevacizumab consists of 214 amino acids and has a molecular weight of approximately 149,000 daltons.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Campto	Irinotecan Hydrochloride Trihydrate	Special warnings and precautions for use	Revision of text under Patients with reduced UGT1A1 activity to read "Another specific polymorphism of UGT1A1 gene (that reduces the activity of this enzyme) is a missense mutation known as UGT1A1*6 variant. Patients with UGT1A1*28 or *6 variants (especially if homozygous) are at increased risk of experiencing adverse events such as neutropenia and diarrhea. A reduced irinotecan starting dose should be considered for homozygous patients (see Section 4.2 Posology and method of administration). In addition, *28 and *6 homozygous and heterozygous patients should be closely monitored for neutropenia and diarrhea. The exact reduction in starting dose in this patient population has not been established and any subsequent dose modifications should be based on individual patient tolerance to treatment. In order to identify patients at increased risk of experiencing neutropenia and diarrhea, UGT1A1 genotyping can be useful. More in detail, UGT1A1*28 genotying can be useful in Caucasians, Africans and Latinos, UGT1A1*6 in East-Asians and combined UGT1A1*28 and *6 in Chinese and Japanese, since these are the populations in which these variants are more prevalent."	30-Sep-21	Pfizer
5	Concor	Bisoprolol fumarate	Possible side effects	Addition of text "You should see your doctor straight away if you experience more severe allergic reactions which may involve face, neck, tongue, mouth or throat swelling or difficulty breathing" under the subheading " Skin and subcutaneous tissue disorders" Addition of text "and angioedema " as part of the rare undesirable effects under the subheading "skin and subcutaneous tissue disorders".	7-Sep-21	Merck

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Diclofenac	Diclofenac Potassium	Fertility, Pregnancy and lactation	Revision of text to read “There are insufficient data on the use of diclofenac in pregnant women. Some epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy, however the overall data are inconclusive. Diclofenac should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus (see sections 4.3 and 5.3).” under Pregnancy.	20-Oct-21	Sandoz Pharmaceuticals d.d.
7	Glivec	Imatinib mesilate	Description and Composition	Deletion of text "50mg capsules, White to yellow powder in a light yellow to orange opaque capsule, marked "NVRSH" under Pharmaceutical forms-Hard capsules. Repositioning of text “Certain dosage strengths and dosage forms may not be available in all countries.” from heading Active substance to Pharmaceutical forms. Deletion of text "50mg capsules- Capsule content: Cellulose microcrystalline; Crospovidone; Magnesium stearte; Silica colloidal, anhydrous. Capsule shell: Gelatin; Iron oxide, yellow (E172); Titanium dioxide (E171). Printing ink: Iron oxide, red (E172).” From sub-heading Excipients.	13-Oct-21	Novartis International AG
			Adverse Drug Reaction	Addition of text "Rare: pemphigus "under the System Organ Class Skin and subcutaneous tissue disorders in Table 3 Addition of text "Uncommon: Osteonecrosis" under the System Organ Class Musculoskeletal and connective tissue disorders in Table 3. Deletion of text “Rare: Avascular necrosis/hip osteonecrosis” under the System Organ Class Musculoskeletal and connective tissue disorders in Table 3.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Herceptin	Trastuzumab	Posology and method of administration	Revision of text to read" In order to prevent medication errors, it is important to check the vial labels to ensure that the drug being prepared and administered is Herceptin (trastuzumab) and not another trastuzumab-containing product (e.g. trastuzumab emtansine or trastuzumab deruxtecan)." Revision of text to read" The 600 mg dose should be administered as a subcutaneous injection only over 2 5 minutes every three weeks. The injection site should be alternated between the left and right thigh. New injections should be given at least 2.5 cm from the old site and never into areas where the skin is red, bruised, tender, or hard. During the treatment course with Herceptin subcutaneous formulation other medicinal products for subcutaneous administration should preferably be injected at different sites. Patients should be observed for 30 minutes after the first injection and for 15 minutes after subsequent injections for signs or symptoms of administration-related reactions (see sections 4.4 and 4.8). For instructions on use and handling of Herceptin subcutaneous formulation refer to section 6.6." under Method of administration.	18-Oct-21	Roche Products Ghana Ltd
			Special warnings and precautions for use	Revision of text to read" Administration related reactions (ARRs) are known to occur with Herceptin subcutaneous formulation. Pre-medication may be used to reduce risk of occurrence of ARRs. Although serious ARRs, including dyspnea, hypotension, wheezing, bronchospasm, tachycardia, reduced oxygen saturation and respiratory distress, were not reported in the clinical trial with the Herceptin subcutaneous formulation, caution should be exercised as these have been associated with the intravenous formulation. Patients should be observed for ARRs for 30 minutes after the first injection and for 15 minutes after subsequent injections. ARRs considered mild in severity can be treated with an analgesic/antipyretic such as meperidine or paracetamol, or an antihistamine such as diphenhydramine. Serious reactions to intravenous Herceptin have been treated successfully with supportive therapy such as oxygen, beta-agonists, and corticosteroids. In rare cases, these reactions were associated with a clinical course culminating in a fatal outcome. Patients experiencing dyspnea at rest due to complications of advanced malignancy and comorbidities may be at increased risk of a fatal ARR. Therefore, these patients should not be treated with Herceptin (see section 4.3)." under Administration related reactions. Addition of text to read "Herceptin contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially sodium free." under Sodium.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Lyrica	Pregabalin	Special warnings and precautions	Addition of text "precautionary warning for women of childbearing potential to use contraception while taking pregabalin".	3-Nov-21	Pfizer
			Fertility, pregnancy, and lactation	Deletion of text "potential risk to humans is unknown".		
10	Nimenrix	polysaccharide groups A,	Posology and method of administration	Revision of text to read "Long-term antibody persistence data following vaccination with Nimenrix are available up to 10 years after vaccination (see sections 4.4 and 5.1).'' under the sub heading posology.	29-Oct-21	Pfizer
			Pharmacodynamic properties	Addition of text to read ''The Netherlands introduced Nimenrix into the national immunization program in 2018 as a single dose at 14 months of age. A catch-up campaign for individuals 14-18 years of age initiated in 2018 and in 2020 a single dose of Nimenrix at 14 years of age became routine, resulting in a toddler and adolescent national immunization program. Within two years, the incidence of meningococcal disease caused by groups C, W, and Y was significantly reduced by 100% (95% CI: 14, 100) in individuals 14-18 years of age, 85% (95% CI: 32, 97) in all vaccine eligible ages (direct effect), and 50% (95% CI: 28, 65) in non-vaccine eligible ages (indirect effect)'' under the sub-heading Impact of a single dose of Nimenrix.		
11	Prazolin	Pantoprazole	Warnings and Precautions	Addition of text "This usually resolves with replacement of the magnessium and stopping the medication".	31-Jul-21	Sandoz Pharmaceuticals d.d.
			Possible side effects	Addition of text " skin rash, fever, lymph node enlargement and internal organ involvement (Drug rash with Eosinophila and systemic symptoms DRESS)" under the subheading "serious skin conditions".		
12	Tacrolimus	Tacrolimus	Warnings and Precautions	Revision of text to read "Please avoid taking any herbal remedies e.g. St. John's wort (Hypericum perforatum) , Chinese herbal remedies containing Schisandra sphenanthera or any other herbal products as this may affect the effectiveness and the dose of Tacrolimus Sandoz that you need to receive".	30-Jul-21	Sandoz Pharmaceuticals d.d.
			Possible side effects	Addition of text "(May affect up to every 1 in 10000 people). Torsades de pointes" and deletion of text "echocardiogram abnormal" under the sub heading "very rare side effects".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
13	Tamoxifen	Tamoxifen citrate	Special warnings and precautions for use	Addition of text to include " Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported with the use of Tamoxifen tablet. At the time of prescription, patients should be advised of the signs and symptoms and closely monitored for skin reactions. If signs and symptoms suggestive of these side effects occur, Tamoxifen tablet should be discontinued immediately and, if necessary, alternative therapy should be considered. If the patient has developed a serious side effect such as SJS or TEN while using Tamoxifen tablet, treatment with Tamoxifen tablet must not be re-initiated in this patient at any time. Tamoxifen may induce or worsen symptoms of angioedema in patients with hereditary angioedema."	28-Sep-21	Sandoz Pharmaceuticals d.d.
			Fertility, pregnancy and lactation	Addition of text under Lactation to include " Limited data indicate that Tamoxifen tablet and its active metabolites are excreted in breast milk and accumulate over the time. Therefore, the use of the drug is not recommended during breastfeeding. When deciding whether to wean or discontinue using Tamoxifen tablet, the importance of the drug for the mother should be taken into consideration."		
			Side effects	Revision of text under Skin and subcutaneous tissue disorders to read "Rare: cutaneous vasculitis, toxic epidermal necrolysis" Addition of text under Skin and subcutaneous tissue disorders to include "Not known: exacerbation of hereditary angioedema"		
14	Voltfast	Diclofenac potassium	Women Of Child-Bearing Potential Pregnancy Breast-Feeding And Fertility	Revision of text under Pregnancy to read "There are insufficient data on the use of diclofenac in pregnant women. Some epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy, however the overall data are inconclusive. Voltfast should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the foetus. Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus (see sections CONTRAINDICATIONS and NON-CLINICAL SAFETY DATA)."	13-Sep-21	Novartis International AG
Label Updates						

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Amoksiclav	Amoxicillin/Clavulanic acid	What you need to know before you take Amoksiclav dispersible	Addition of text "Amoksiklav dispersible can make some existing conditions worse, or cause serious side effects. These include: allergic reactions, convulsions (fits) and inflammation of the large intestine. You must look out for certain symptoms while you are taking Amoksiklav dispersible, to reduce the risk of any problems. See 'Conditions you need to look out for' in Section 4" under the subheading "conditions you need to look out for". Addition of text "If you are having blood tests (such as red blood cell status tests or liver function tests) or urine tests (for glucose), let the doctor or nurse know that you are taking Amoksiklav dispersible. This is because Amoksiklav dispersible can affect the results of these types of tests" under the subheading "blood and urine tests".	6-Sep-21	Sandoz Pharmaceuticals d.d.
			Other medicines and Amoksiklav dispersible	Addition of text "Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This includes medicines that can be bought without a prescription and herbal medicines. If you are taking allopurinol (used for gout) with Amoksiklav dispersible, it may be more likely that you'll have an allergic skin reaction. If you are taking probenecid (used for gout), your doctor may decide to adjust your dose of Amoksiklav dispersible. If medicines to help stop blood clots (such as warfarin) are taken with Amoksiklav dispersible then extra blood tests may be needed. Amoksiklav dispersible can affect how methotrexate (a medicine used to treat cancer or rheumatic diseases) works. Amoksiklav dispersible may affect how mycophenolate mofetil (a medicine used to prevent the rejection of transplanted organs) works".		
			Driving and using machines	Addition of text " Amoksiklav dispersible can have side effects and the symptoms may make you unfit to drive. Don't drive or operate machinery unless you are feeling well. Amoksiklav dispersible contains aspartame (E951), which is a source of phenylalanine. This may be harmful for people with phenylketonuria. Amoksiklav dispersible contains castor oil, which may cause stomach upset and diarrhea".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Amoksiclav	Amoxicillin/Clavulanic acid	How to take Amoksiclav dispersible	Addition of text "The usual dose is: 1 tablet three times a day". Addition of text "If you have kidney problems the dose might be changed. A different strength or a different medicine may be chosen by your doctor. • If you have liver problems you may have more frequent blood tests to check how your liver is working" under the subheading "patients with kidney and liver problems". Addition of text "If you forget to take a dose, take it as soon as you remember. You should not take the next dose too soon, but wait about 4 hours before taking the next dose" under the subheading "if you forget to take Amoksiclav dispersible".	6-Sep-21	Sandoz Pharmaceuticals d.d.
			Possible side effects	Addition of text " Inflammation of the liver (hepatitis) • Jaundice, caused by increases in the blood of bilirubin (a substance produced in the liver) which may make your skin and whites of the eyes appear yellow • Inflammation of tubes in the kidney • Blood takes longer to clot • Hyperactivity • Convulsions (in people taking high doses of Amoksiklav dispersible or who have kidney problems) • Black tongue which looks hairy • Stained teeth (in children), usually removed by brushing Side effects that may show up in your blood or urine tests: • Severe reduction in the number of white blood cells • Low number of red blood cells (haemolytic anaemia) • Crystals in urine. Reporting of side effects If you get any side effects, talk to your doctor or pharmacist. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via drug.safetyssa@novartis.com. By reporting side effects you can help provide more information on the safety of this medicine" under the subheading "contact a doctor immediately if you see any of these symptoms".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
1	Amoksiclav	Amoxicillin/Clavulanic acid	Contents of the pack and other information	Addition of text "Antibiotics are used to treat infections caused by bacteria. They have no effect against infections caused by viruses. Sometimes an infection caused by bacteria does not respond to a course of an antibiotic. One of the commonest reasons for this to occur is because the bacteria causing the infection are resistant to the antibiotic that is being taken. This means that they can survive and even multiply despite the antibiotic. Bacteria can become resistant to antibiotics for many reasons. Using antibiotics carefully can help to reduce the chance of bacteria becoming resistant to them. When your doctor prescribes a course of an antibiotic it is intended to treat only your current illness. Paying attention to the following advice will help prevent the emergence of resistant bacteria that could stop the antibiotic working. 1. It is very important that you take the antibiotic at the right dose, at the right times and for the right number of days. Read the instructions on the label and if you do not understand anything ask your doctor or pharmacist to explain. 2. You should not take an antibiotic unless it has been prescribed specifically for you and you should use it only to treat the infection for which it was prescribed. 3. You should not take antibiotics that have been prescribed for other people even if they had an infection that was similar to yours. 4. You should not give antibiotics that were prescribed for you to other people. 5. If you have any antibiotic left over when you have taken the course as directed by your doctor you should take the remainder to a pharmacy for appropriate disposal" under the subheading : "Advice/medical education"	6-Sep-21	Sandoz Pharmaceuticals d.d.