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	Amlodipine	Amlodpine	Undesirable effects	Addition of text "Myocardical infarction under adverse reaction with frequency very rare of system organ class vascular disorders" Addition of text "flushing under adverse reaction with frequency common of system organ class vascular disorders" Addition of text "Hypotension under adverse reaction with frequency uncommon if system organ class"	17/05/2023	Novartis
			Overdose	Inclusion of text to read "Non-cardiogenic pulmonary oedema has rarely been reported as a consequence of amlodipine overdose that may manifest with a delayed onset (24-48 hours post-ingestion) and require ventilatory support. Early resuscitative measures (including fluid overload) to maintain perfusion and cardiac output may be precipitating factors".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Dalacin C	Clindamycin Palmitate Hydrochloride	Warnings	Revision of text to read “Clindamycin is potentially nephrotoxic and cases with acute kidney injury have been reported. Consider monitoring of renal function particularly in patients with pre-existing renal dysfunction or those taking concomitant nephrotoxic drugs. In case of acute kidney injury, discontinue DALACIN C when no other etiology is identified.” Under the sub-heading Nephrotoxicity.	9/6/2023	Pfizer Specialties Limited
3	Deslatyne	Desloratadine	Possible side effects	Addition of text under sub section not known to read " depressed mood and dry eyes.”	30/05/2023	Novartis
4	Esmeron	Rocuronium bromide	Undersirable effects	Addition of text under subtitle tabulated list of adverse reactions "Mydriasis Fixed pupils" with MedDRA preferred term not known under MedDRA system organ clAass Eye disorder. Addition of text "In the context of a potential increase of permeability or compromise of the integrity of the Blood-Brain Barrier (BBB)"	3/5/2023	Worldwide Healthcare

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Hemlibra	Emicizumab	Special warnings and precautions for use	Revision of text under subtitle "Effects of emicizumab on coagulation tests" to read" Emicizumab restores the tenase cofactor activity of missing activated factor VIII (FVIIIa). Coagulation laboratory tests based on intrinsic clotting, including the activated clotting time (ACT), activated partial thromboplastin time (e.g. aPTT), measure the total clotting time including time needed for activation of FVIII to FVIIIa by thrombin. Such intrinsic pathway based tests will yield overly shortened clotting times with emicizumab, which does not require activation by thrombin. The overly shortened intrinsic clotting time will then disturb all single factor assays based on aPTT, such as the one stage FVIII activity assay (see section 4.4, Table 1). However, single factor assays utilising chromogenic or immuno-based methods are not affected by emicizumab and may be used to assess coagulation parameters during treatment, with specific considerations for FVIII chromogenic activity assays as described below. Chromogenic FVIII activity tests may be manufactured with either human or bovine coagulation proteins. Assays containing human coagulation factors are responsive to emicizumab but may overestimate the clinical haemostatic potential of emicizumab. In contrast, assays containing bovine coagulation factors are insensitive to emicizumab (no activity measured) and can be used to monitor endogenous or infused FVIII activity, or to measure anti FVIII inhibitors.	9/3/2023	Roche Product Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Hemlibra	Emicizumab	Special warnings and precautions for use	Emicizumab remains active in the presence of inhibitors against FVIII and so will produce a false negative result in clotting based Bethesda assays for functional inhibition of FVIII. Instead, a chromogenic Bethesda assay utilising a bovine based FVIII chromogenic test that is insensitive to emicizumab may be used. These two pharmacodynamic markers do not reflect the true haemostatic effect of emicizumab in vivo (aPTT is overly shortened and reported FVIII activity may be overestimated) but provide a relative indication of the pro-coagulant effect of emicizumab. In summary, intrinsic pathway clotting based laboratory test results in patients treated with Hemlibra should not be used to monitor its activity, determine dosing for factor replacement or anti coagulation, or measure FVIII inhibitors titers. Caution should be taken if intrinsic pathway clotting based laboratory tests are used, as misinterpretation of their results may lead to under-treatment of patients experiencing bleeding episodes, which can potentially result in severe or life-threatening bleeds. Laboratory tests affected and unaffected by emicizumab are shown in Table 1 below. Due to its long half-life, these effects on coagulation assays may persist for up to 6 months after the last dose (see section 5.2)."	9/3/2023	Roche Product Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Herceptin	Trastuzumab	Indications/Uses	Revision of text to read "Before the start of Herceptin therapy, overexpression of HER2 in the patient's tumour tissue must have been demonstrated either by immunohistochemistry at a 3+ level or by molecular biology (detection of HER2 gene amplification using fluorescence in situ hybridisation [FISH] or chromogenic in situ hybridisation [CISH])." under Breast cancer sub-section. Addition of text "Herceptin should only be used in patients with metastatic gastric cancer whose tumours overexpress HER2, as defined by IHC2+ and confirmed by a positive FISH+ or silver in situ hybridisation (SISH) result, or by IHC3+ determined in a validated test." under sub-section Metastatic gastric cancer or cancer of the gastro-oesophageal junction.	15/03/2023	Roche Product Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Herceptin	Trastuzumab	Dosage / Administration	Revision of text to read "The following initial and subsequent doses are recommended both for monotherapy and for combination with chemotherapy:" under sub-section Metastatic breast cancer – weekly schedule Revision of text to read "The recommended initial dose is Herceptin 4 mg/kg body weight administered as a 90- minute intravenous infusion. " under sub-section Monotherapy, Initial dose Revision of text to read "The recommended weekly maintenance dose is Herceptin 2 mg/kg body weight which can be administered as a 30-minute infusion if the initial dose was well tolerated. " under sub-section Montherapy, subsequent doses	15/03/2023	Roche Product Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Herceptin	Trastuzumab	Dosage / Administration	Deletion of sub-section "Missed doses" Revision of sub-section title to read "Children and adolescents" under sub-section Special dosage instructions Addition of sub-section "Delayed administration" Addition of text "If the patient has missed a dose of Herceptin by one week or less, then the usual maintenance dose (weekly regimen: 2 mg/kg body weight; 3-weekly regimen: 6 mg/kg body weight) should be given as soon as possible (do not wait until the next planned cycle). Subsequent Herceptin maintenance doses should be given 7 or 21 days later according to the weekly or 3-weekly schedule, respectively." under sub-section Delayed administration. Revision of text to read "Herceptin and anthracyclineanthracyclines should not be given concurrently in the metastatic breast cancer or adjuvant treatment setting. In the neoadjuvant treatment setting, concurrent administration of Herceptin and anthracyclines should be used with caution and only in chemotherapy-naïve patients.Herceptin is contraindicated in patients suffering dyspnoea at rest due to advanced malignancy or comorbidities." under sub-section Contraindications	15/06/2023	Roche Product Ghana Ltd
			Interactions	Deletion of sub-section "Pharmacokinetic/pharmacodynamic interactions"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Herceptin	Trastuzumab	Pregnancy and Lactation	Revision of sub-section to read "Pregancy" Revision of text to read "A study in which cynomolgus monkeys received doses 25 times the weekly human maintenance dose of 2 mg/kg Herceptin i.v. from day 120 to 150 of gestation demonstrated that trastuzumab is secreted in the milk post partum. Trastuzumab exposure in utero and the presence of trastuzumab in the serum of infant monkeys were not associated with adverse effects on their growth or development from birth to 1 month of age. It is not known whether trastuzumab is secreted in human milk. Nevertheless, as human IgG passes from serum into breast milk and the potential for harm to the infant is unknown, women should not breastfeed during Herceptin therapy." under sub-section Lactation	15/06/2023	Roche Product Ghana Ltd
			Effects on ability to drive and use machines	Revision of text to read "Herceptin has a minor influence on the ability to drive and use machines. Dizziness and somnolence may occur during treatment with Herceptin (see “Undesirable effects”). Patients experiencing infusion-related symptoms (see “Warnings and precautions”) should be advised not to drive or use machines until their symptoms have fully resolved."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Kadcyla	Trastuzumab emtansine	Kadcyla dose adjustment guidelines	Revision of text to read "Do not administer Kadcyla until the platelet count has recovered to ≤ Grade 1 (≥75,000/mm3). Then continue treatment at the same dose level. If a patient requires 2 treatment breaks due to thrombocytopenia, dose reduction by one level should be considered." under sub-section "Grade 2-3 on day of scheduled treatment (25,000 to <75,000/mm3)" of Thrombocytopenia	21/06/2023	Roche Product Ghana Ltd
			Warnings and precautions	Revision of text to read "It is recommended that treatment with Kadcyla be permanently discontinued in patients diagnosed with ILD or pneumonitis, except for radiotherapy pneumonitis as part of adjuvant treatment. In this case, Kadcyla should be permanently discontinued if radiotherapy pneumonitis is ≥Grade 3 or 2 and does not respond to standard treatment (see "Dosage/Administration, Dose adjustment")." under sub-section Pulmonary Toxicity Addition of text "Rare cases of severe and persistent thrombocytopenia (thrombocytopenia ≥ Grade 3 lasting over 90 days) have been reported with Kadcyla. In most of these cases, patients have received concomitant recombinant human thrombopoietin (rhTPO)." to sub-section Thrombocytopenia		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Kadcyla	Trastuzumab emtansine	Pregnancy and Lactation	Revision of text to read "Trastuzumab, a component of Kadcyla, may cause fetal harm or death when administered to a pregnant woman. In the post-marketing setting, cases of oligohydramnios, of which some have been associated with fatal pulmonary hypoplasia of the foetus, have been reported in pregnant women who have received trastuzumab. Animal studies have also shown reproductive toxicity (see “Preclinical data”). Kadcyla must not be administered in pregnancy unless clearly necessary. If Kadcyla is administered during pregnancy or if a patient becomes pregnant during treatment, inform the patient of the potential hazard to the fetus." under sub-section Pregnancy Revision of text to read "It is not known whether Kadcyla passes into human milk. Since many medicinal products pass into human milk and Kadcyla may cause serious adverse reactions in breast-feeding infants, women should discontinue breast-feeding before starting treatment with Kadcyla and not breast-feed during treatment. Breast-feeding may not be initiated until seven months after completing treatment. " under sub-section Lactation	21/06/2023	Roche Product Ghana Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Kadcyla	Trastuzumab emtansine	Preclinical data	Revision of text to read "No fertility studies in animals have been performed to evaluate the effect of Kadcyla. In addition, the developmental toxicity of maytansine has been identified in non-clinical studies, which suggests that DM1, the microtubule-inhibiting cytotoxic maytansinoid component of trastuzumab emtansine, has similar teratogenic and potentially embryotoxic activity." under sub-section Reproductive Toxicity	21/06/2023	Roche Product Ghana Ltd
			This is a medicament	Addition of text "A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you. Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold the medicament. The doctor and the pharmacist are experts in medicine, its benefits and risks. Do not by yourself interrupt the period of treatment prescribed for you. Do not repeat the same prescription without consulting your doctor"		