The underlisted safety variations have been submitted by Marketing Authorization Holders 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 to help make the best therapeutic decision regarding benefit-risk profile of these medicines to ensure patient safety.

No.	Name of Drug	Active ingredient(s)	Section(s) updated	Updates	Marketing Authorization Holder
1	Artesunate/Amodiaquine - Winthrop 25mg/67.5mg, 50mg/135mg, 100mg/270mg (bisters of 3 and 6)	Artesunate/ Amodiaquine	Safety and efficacy following repeated administration.	Removal of "It is not known, whether the toxicity of amodiaquine, observed with prophylactic use (i.e. agranulocytosis, hepatotoxicity) may also develop after repeated cycles of curative treatment "	Sanofi-Aventis
2	Avastin	Bevacizumab	Dosage and Administration	To ensure the traceability of biological medicinal products, it is recommended that the trade name and batch number be documented with every treatment.	Roche
			Undesirable Effects	The number of patients with various malignancies treated in clinical studies with Avastin (mostly in combination with chemotherapy) changed from over 5,400 to 5,700. Hypomagnesemia, hyponatremia were added to metabolism and nutritional disorders. Cough was added to respiratory organ disorders. The phrase "receiving frontline therapy" was excluded from gastrointestinal perforation and fistula, under Investigations	
			Warnings and precautions	In order to improve the traceability of biological medicinal Products, the trade name Avastin should be clearly recorded on the patient card. Substitution of another biological medicinal product requires the consent of the prescribing physician. The particulars in this prescribing information apply to Avastin only, has been removed.	
3	Kivexa	Abacavir sulfate /Lamivudine	Interactions	Coadministration of sorbitol solution (3.2 g, 10.2 g, 13.4 g) with a single 300 mg dose of lamivudine oral solution resulted in dose-dependent decreases of 14%, 32%, and 36% in lamivudine exposure (AUC) and 28%, 52%, and 55% in the Cmax of lamivudine in adults. When possible, avoid chronic coadministration of sorbitol-containing medicines with lamivudine. Consider more frequent monitoring of HIV-1 viral load when chronic coadministration cannot be avoided.	GlaxoSmithkline
				Zalcitabine was removed from the interactions section	
			Warnings and Precautions	Several observational, epidemiological studies have reported an association with abacavir use and the risk of myocardial infarction. Meta-analyses of randomised controlled trials have observed no excess risk of myocardial infarction with abacavir use. To date, there is no established biological mechanism to explain a potential increase in risk. In totality the available data from observational studies and from controlled clinical trials show inconsistency and therefore the evidence for a causal relationship between abacavir treatment and the risk of myocardial infarction is inconclusive.	
				Pneumocystis jiroveci pneumonia (often referred to as PJP)	

No.	Name of Drug	Active ingredient(s)	Section(s) updated	Updates	Marketing Authorization Holder
4	NovoRapid	Insulin aspart	Therapeutic Indication	Reviewed to include the use of the product for the treatment of diabetes mellitus in children aged 1 year and above.	Novo Nordisk
			Avoidance of Medication Errors	Patient information leaflet/ Product pack insert updated to provide instructions to patients on how to avoid mix up of the medication with other Novo Nordisk insulin aspart products as "Avoidance of accident mix-ups/medication error"	
5	Tritazide	Ramipril/ Hydrochlorothiazide	Interactions with mechanistic target of rapamycin (mTOR) or dipeptidyl peptidase 4 (DPP-IV) inhibitors	There is a possible increased risk of angioedema in patients treated with ACE inhibitors including ramipril, who are taking concomitant medications such as mTOR inhibitors (e.g. temsirolimus, everolimus, sirolimus) or vildagliptin. Caution should be used when starting therapy.	Sanofi-Aventis
6	Victoza	Liraglutide	Pharmacokinetic properties	Hepatic impairment: The pharmacokinetics of liraglutide was evaluated in subjects with varying degree of hepatic impairment in a single-dose trial. Liraglutide exposure was decreased by 13–23% in subjects with mild to moderate hepatic impairment compared to healthy subjects. Exposure was significantly lower (44%) in subjects with severe hepatic impairment (Child Pugh score >9).	Novo Nordisk
			Overdose	From clinical trials and marketed use, overdoses have been reported up to 40 times (72 mg) the recommended maintenance dose. Generally, the patients reported severe nausea, vomiting and diarrhoea. None of the patients reported severe hypoglycaemia. All patients recovered without complications. In the event of overdose, appropriate supportive treatment should be initiated according to the patient's clinical signs and symptoms.	