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	Coversyl	Perindopril	Undesirable effects	Addition of texts under vascular disorders to include "Raynaud's phenomenon-frequency not known"	05-Jul-20	Les Laboratoires Servier
2	Inegy	Ezetimibe/ simvastatin	Undesirable effects	Addition of texts to read "Eye disorders: vision blurred (rare); visual impairment (rare) ". Addition of texts under Skin and subcutaneous tissue disorders to include "lichenoid drug eruptions (very rare) . Addition of texts under Musculoskeletal and connective tissue disorders to include "muscle rupture (very rare)". Addition of texts under Reproductive system and breast disorders to include "gynecomastia (very rare)".	18-Jun-20	MSD
3	Janumet	(Sitagliptin + Metformin)	Special warnings and precautions for use	Addition of texts to read "Sodium: This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free''	20-Jul-20	MSD
4	Januvia	Sitagliptin	Special warnings and precautions for use	Addition of texts to read "Sodium; This medicinal product contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free''	20-Jul-20	MSD
5	Singulair	Montelukast	Fertility, pregnancy and lactation	Revision of texts to read "Available data from published prospective and retrospective cohort studies with montelukast use in pregnant women evaluating major birth defects have not established a drug-associated risk. Available studies have methodologic limitations, including small sample size, in some cases retrospective data collection, and inconsistent comparator groups".	18-Jun-20	MSD
6	Triplixam	Perindopril arginine/indapamide /amlodipine	Undesirable effects	Addition of texts under vascular disorders to include "Raynaud's phenomenon-frequency not known"	05-Jul-20	Les Laboratoires Servier
7	Vastarel MR	Trimetazidine dihydrochloride	Posology and method of administration	Revision of texts to read "Oral route: The dose is one tablet of 35 mg of trimetazidine twice daily, i.e. once in the morning and once in the evening, during meals"	12-Aug-20	Les Laboratoires Servier

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Vastarel MR	Trimetazidine dihydrochloride	Interaction with other medicinal products and other forms of interaction	Revision of texts to read "No drug interactions have been identified".	12-Aug-20	Les Laboratoires Servier
			Fertility, pregnancy and lactation	Revision of texts to read "Pregnancy: There is no data from the use of trimetazidine in pregnant women. Animal studies do not indicate direct or indirect harmful effects with respect to reproductive toxicity (see section 5.3). As a precautionary measure, it is preferable to avoid the use of VASTAREL during pregnancy".		
				Revision of texts to read "Breastfeeding: It is unknown whether trimetazidine/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded. VASTAREL should not be used during breastfeeding"		
				Addition of texts to read "Fertility: Reproductive toxicity studies have shown no effect on fertility in female and male rats (see section 5.3).		
			Undesirable effects	Addition of texts to read "Ear and labyrinth-vertigo (frequency not known).		
				Addition of texts to include "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. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system.		
			Pharmacological properties	Addition of texts to include "Trimetazidine exposure may be increased in elderly patients due to an age-related decrease in renal function. A pharmacokinetics study performed specifically in elderly (75-84 years) and very elderly (≥ 85 years) participants showed that in the event of moderate renal impairment (creatinine clearance between 30 and 60 mL/min) trimetazidine exposure was increased by a factor of 1.0 and 1.3 respectively in comparison with younger participants (30-65 years) with moderate renal impairment.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Vastarel MR	Trimetazidine dihydrochloride	Pharmacological properties	Addition of texts to include "Renal impairment: On average, trimetazidine exposure is multiplied by 1.7 in patients with moderate renal impairment (creatinine clearance between 30 and 60 mL/min) and by 3.1 in patients with severe renal impairment (creatinine clearance below 30 mL/min) compared with healthy young volunteers with normal renal function. No safety concerns were observed in this population as compared with the general population.	12-Aug-20	Les Laboratoires Servier
				Addition of texts to include "Paediatric population The pharmacokinetics of trimetazidine have not been studied in the paediatric population (< 18 years)"		
			Preclinical safety data	Revision of texts to read "Chronic oral toxicity studies in dogs and rats showed a good safety profile".		
8	Xeloda	Capecitabine	Composition	Revision of texts to read "Excipients-Tablet core: Xeloda 150 mg: anhydrous lactose 15.6 mg, sodium 1.12 mg Xeloda 500 mg: anhydrous lactose 52 mg, sodium 3.75 mg Croscarmellose sodium (produced from genetically modified cotton), hypromellose, microcrystalline cellulose, magnesium stearate. Film coating:Hypromellose, talc, titanium dioxide, yellow iron oxide, red iron oxide"	06-Aug-20	Roche
			Indication/uses	Revision of heading from "Indications and potential uses" to "Indications/uses"		
			Dosage and Administration	Revision of texts to read "usual dosage"		
			Warnings and Precautions	Addition of texts to read "This medicinal product contains less than 1 mmol of sodium (23 mg) per film-coated tablet, i.e. it is virtually “sodium-free”"		
			Interactions	Addition and revision of texts to read "Enzyme inducers-Phenytoin: Increased plasma concentrations of phenytoin (a CYP2C9 substrate) have been observed during concomitant use of Xeloda with phenytoin. Patients taking phenytoin concomitantly with Xeloda should be regularly monitored for increased plasma phenytoin concentrations and associated clinical symptoms."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Xeloda	Capecitabine	Interactions	Addition of heading to include "Enzyme inhibitors"	06-Aug-20	Roche
				Revision of texts to include " other interactions:Allopurinol-Interactions between allopurinol and 5-FU have been reported. Concomitant use of allopurinol and capecitabine should be avoided. Oxaliplatin-No clinically significant differences in exposure to capecitabine or its metabolites, free platinum or total platinum occurred when capecitabine was administered in combination with oxaliplatin with or without bevacizumab."		
				Addition of heading and revision of texts to read ''Effect of Xeloda on other medicinal products: Docetaxel/paclitaxel-Studies evaluating the effects of Xeloda on the pharmacokinetics of docetaxel and paclitaxel and vice versa showed no effect by Xeloda on the pharmacokinetics of docetaxel or paclitaxel (Cmax and AUC) nor any effect by docetaxel or paclitaxel on the pharmacokinetics of 5'-DFUR, a major metabolite of capecitabine''.		
				Addition of heading to read "Effect of other medicinal products on Xeloda"		
			Undesirable effects	Addition of texts under cardiac disorders to read "uncommon:angina unstable, angina pectoris"		
				Addition of texts 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".		
			Overdose	Revision of heading from overdosage to overdose		
				Addition of subheading to read "Signs and symptoms" and "Treatment".		
			Properties and effects	Revision of texts that read "mechanism of action/pharmacodynamics" to read "mechanism of action"		
				Addition of texts to read "Pharmacodynamics-Not applicable".		
			Preclinical data	Revision of subheading to read "Long-term or repeated dose toxicity".		
			Special precautions for storage	Addition of texts to read "Keep out of the reach of children".		