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	Co-diovan	Valsartan / hydrochlorothiazide	Pregnancy, lactation, females and males of reproductive potential	Revision of text to read "Valsartan: In embryofetal development studies in mice, rats and rabbits, fetotoxicity was observed in association with maternal toxicity in rats at valsartan doses of 600 mg/kg/day approximately 18 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient) and in rabbits at doses of 10 mg/kg/day approximately 0.6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). There was no evidence of maternal toxicity or fetotoxicity in mice up to a dose level of 600 mg/kg/day approximately 9 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Animal data-Pregnancy. Revision of text to read "Risk summary- It is not known whether valsartan is transferred into human milk. Valsartan was transferred into the milk of lactating rats. Hydrochlorothiazide crosses the placenta and is transferred into human milk. Thus, it is not advisable to use Co-Diovan in breast-feeding mothers." under Lactation.	5-Mar-21	Novartis International AG
2	Crestor	Rosuvastatin	Therapeutic Indications	Revision of text to read "Adults, adolescents and children aged 6 years or older with primary hypercholesterolaemia (type IIa including heterozygous familial hypercholesterolaemia) or mixed dyslipidaemia (type IIb) as an adjunct to diet when response to diet and other non-pharmacological treatments (e.g. exercise, weight reduction) is inadequate. Adults, adolescents and children aged 6 years or older with homozygous familial hypercholesterolaemia as an adjunct to diet and other lipid lowering treatments (e.g. LDL apheresis) or if such treatments are not appropriate." under the sub-heading Treatment of hypercholesterolaemia.	2-Mar-21	Sandoz dd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Posology and Method of Administration	Revision of text to read "Paediatric use should only be carried out by specialists. Children and adolescents 6 to 17 years of age (boys Tanner Stage <II-V Heterozygous familial hypercholesterolaemia In children and adolescents with heterozygous familial hypercholesterolaemia the usual start dose is 5 mg daily. • In children 6 to 9 years of age with heterozygous familial hypercholesterolaemia, the usual dose range is 5-10 mg orally once daily. Safety and efficacy of doses greater than 10 mg have not been studied in this population. • In children 10 to 17 years of age with heterozygous familial hypercholesterolaemia, Tthe usual dose range is 5-20 mg orally once daily. Titration should be conducted according to the individual response and tolerability in paediatric patients, as recommended by the paediatric treatment recommendations (see Special warnings and precautions for use). Children and adolescents should be placed on standard cholesterol-lowering diet before rosuvastatin treatment initiation; this diet should be continued during rosuvastatin treatment." under the sub-heading Paediatric Population.	2-Mar-21	Sandoz dd
				Revision of text of read "Homozygous familial hypercholesterolaemia In children 6 to 17 years of age with homozygous familial hypercholesterolaemia, the recommended maximum dose is 20 mg once daily. A starting dose of 5 to 10 mg once daily depending on age, weight and prior statin use is advised. Titration to the maximum dose of 20 mg once daily should be conducted according to the individual response and tolerability in paediatric patients, as recommended by the paediatric treatment recommendations (see Special warnings and precautions for use). Children and adolescents should be placed on standard cholesterol-lowering diet before rosuvastatin treatment initiation; this diet should be continued during rosuvastatin treatment. There is limited experience with doses other than 20 mg in this population. The 40 mg tablet is not suitable for use in paediatric patients. Children younger than 6 years The safety and efficacy of use in children younger than 6 years has not been studied. Therefore, Crestor is not recommended for use in children younger than 6 years. [….]." under the sub-heading Paediatric Population. Revision of text to read "Increased systemic exposure has been seen in Asian subjects (see Contraindications, Special warnings and precautions for use and Pharmacokinetic properties). The recommended start dose is 5 mg for patients of Asian ancestry. The 40mg dose is contraindicated in these patients." under the sub-heading Race.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Contraindications	Revision of text to read "Crestor is contraindicated: - in patients with hypersensitivity to rosuvastatin or to any of the excipients. - in patients with active liver disease including unexplained, persistent elevations of serum transaminases and any serum transaminase elevation exceeding 3 x the upper limit of normal (ULN). - in patients with severe renal impairment (creatinine clearance <30 ml/min). - in patients with myopathy. - in patients receiving concomitant combination of sofosbuvir/velpatasvir/voxilaprevir (see Interactions) - in patients receiving concomitant ciclosporin. - during pregnancy and lactation and in women of childbearing potential not using appropriate contraceptive measures."	2-Mar-21	Sandoz dd
			Special Warnings and Precautions for Use	Revision of text to read "Before treatment Crestor, as with other HMG-CoA reductase inhibitors, should be prescribed with caution in patients with predisposing factors for myopathy/rhabdomyolysis. Such factors include: • renal impairment • hypothyroidism • personal or family history of hereditary muscular disorders • previous history of muscular toxicity with another HMG-CoA reductase inhibitor or fibrate • alcohol abuse • age >70 years • situations where an increase in plasma levels may occur (see Posology and method of administration, Interactions and Pharmacokinetic properties) • concomitant use of fibrates In such patients the risk of treatment should be considered in relation to possible benefit and clinical monitoring is recommended. If CK levels are significantly elevated at baseline (>5xULN) treatment should not be started." under the sub-heading Skeletal muscle effects.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Special Warnings and Precautions for Use	Revision of text to read "Whilst on treatment In clinical trials there was no evidence of increased skeletal muscle effects in the small number of patients dosed with Crestor and concomitant therapy. However, an increase in the incidence of myositis and myopathy has been seen in patients receiving other HMG-CoA reductase inhibitors together with fibric acid derivatives including gemfibrozil, ciclosporin, nicotinic acid, azole antifungals, protease inhibitors and macrolide antibiotics. Gemfibrozil increases the risk of myopathy when given concomitantly with some HMG-CoA reductase inhibitors. Therefore, the combination of Crestor and gemfibrozil is not recommended. The benefit of further alterations in lipid levels by the combined use of Crestor with fibrates or niacin should be carefully weighed against the potential risks of such combinations. The 40 mg dose is contraindicated with concomitant use of a fibrate. (See Interactions and Undesirable effects.) Crestor must not be co-administered with systemic formulations of fusidic acid or within 7 days of stopping fusidic acid treatment. In patients where the use of systemic fusidic acid is considered essential, statin treatment should be discontinued throughout the duration of fusidic acid treatment. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving fusidic acid and statins in combination (see Interactions). Patients should be advised to seek medical advice immediately if they experience any symptoms of muscle weakness, pain or tenderness. Statin therapy may be re-introduced seven days after the last dose of fusidic acid. In exceptional circumstances, where prolonged systemic fusidic acid is needed, e.g. for the treatment of severe infections, the need for co-administration of Crestor and fusidic acid should only be considered on a case by case basis and under close medical supervision. Crestor should not be used in any patient with an acute, serious condition suggestive of myopathy or predisposing to the development of renal failure secondary to rhabdomyolysis (e.g. sepsis, hypotension, major surgery, trauma, severe metabolic, endocrine and electrolyte disorders; or uncontrolled seizures)." under the sub-heading Skeletal muscle effects.	2-Mar-21	Sandoz dd
				Revision of text to read "Pharmacokinetic studies show an increase in exposure in Asian subjects compared with Caucasians (see Posology and method of administration, Contraindications and Pharmacokinetic properties)." under Race.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Special Warnings and Precautions for Use	Revision of text to read "Some evidence suggests that statins as a class raise blood glucose and in some patients, at high risk of future diabetes, may produce a level of hyperglycaemia where formal diabetes care is appropriate. This risk, however, is outweighed by the reduction in vascular risk with statins and therefore should not be a reason for stopping statin treatment. Patients at risk (fasting glucose 5.6 to 6.9 mmol/l, BMI >30 kg/m2, raised triglycerides, hypertension) should be monitored both clinically and biochemically according to national guidelines. In the JUPITER study, the reported overall frequency of diabetes mellitus was 2.8% in rosuvastatin and 2.3% in placebo, mostly in patients with fasting glucose 5.6 to 6.9 mmol/l." under the sub-heading Diabetes Mellitus. Revision of text to read "The evaluation of linear growth (height), weight, BMI (body mass index), and secondary characteristics of sexual maturation by Tanner staging in paediatric patients 6 to 17 years of age taking rosuvastatin is limited to a two year period. After two years of study treatment, no effect on growth, weight, BMI or sexual maturation was detected (see Pharmacodynamic properties). In a clinical trial of children and adolescents receiving rosuvastatin for 52 weeks, CK elevations >10xULN and muscle symptoms following exercise or increased physical activity were observed more frequently compared to observations in clinical trials in adults (see Undesirable effects). under the sub-heading Paediatric Population.	2-Mar-21	Sandoz dd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Interactions	Interactions requiring rosuvastatin dose adjustments Revision of text to read "When it is necessary to co-administer Crestor with other medicinal products known to increase exposure to rosuvastatin, doses of Crestor should be adjusted. Start with a 5 mg once daily dose of Crestor if the expected increase in exposure (AUC) is approximately 2-fold or higher. The maximum daily dose of Crestor should be adjusted so that the expected rosuvastatin exposure would not likely exceed that of a 40 mg daily dose of Crestor taken without interacting medicinal products, for example a 20 mg dose of Crestor with gemfibrozil (1.9-fold increase), and a 10 mg dose of Crestor with combination ritonavir/atazanavir (3.1fold increase). If medicinal product is observed to increase rosuvastatin AUC less than 2-fold, the starting dose need not be decreased but caution should be taken if increasing the Crestor dose above 20mg." under the sub-heading Interactions requiring rosuvastatin dose adjustments (see also Table 1) Revision of text in table concerning the effect of co-administered medicinal products on rosuvastatin exposure (AUC; in order of decreasing magnitude) from published clinical trials, Table 1 under the sub-heading Interactions requiring rosuvastatin dose adjustments (see also Table 1) Addition of text "The following medical product/combinations did not have a clinically significant effect on the AUC ratio of rosuvastatin at coadministration: Aleglitazar 0.3 mg 7 days dosing; Fenofibrate 67 mg 7 days TID dosing; Fluconazole 200mg 11 days OD dosing; Fosamprenavir 700 mg/ritonavir 100 mg 8 days BID dosing; Ketoconazole 200 mg 7 days BID dosing; Rifampin 450 mg 7 days OD dosing; Silymarin 140 mg 5 days TID dosing." under the sub-heading Interactions requiring rosuvastatin dose adjustments.	2-Mar-21	Sandoz dd
				Revision of text to read "Fusidic Acid: Interaction studies with rosuvastatin and fusidic acid have not been conducted. The risk of myopathy, including rhabdomyolysis may be increased by the concomitant administration of systemic fusidic acid with statins. The mechanism of this interaction (whether it is pharmacodynamic or pharmacokinetic, or both) is yet unknown. There have been reports of rhabdomyolysis (including some fatalities) in patients receiving this combination. If treatment with systemic fusidic acid is necessary, Crestor treatment should be discontinued throughout the duration of the fusidic acid treatment. Also see Special warnings and precautions for use. The frequencies of adverse reactions are ranked according to the following convention: Common (≥ 1/100 to <1/10); Uncommon (≥ 1/1,000 to <1/100); Rare (≥ 1/10,000 to <1/1000); Very rare (<1/10,000); Not known (cannot be estimated from the available data)." under the sub-heading Effect of rosuvastatin on co-administered medicinal products: Other medicinal products.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Undesirable Effects	Revision of text to read "The frequencies of adverse reactions are ranked according to the following convention: Common (≥ 1/100 to <1/10); Uncommon (≥ 1/1,000 to <1/100); Rare (≥ 1/10,000 to <1/1000); Very rare (<1/10,000); Not known (cannot be estimated from the available data)." under this section. Addition of "Lupus-like syndrome" and "Muscle rupture" with frequency Rare under the System Organ Class Musculoskeletal and connective tissue disorders under the heading Adverse reactions based on data from clinical studies and post-marketing experience.	2-Mar-21	Sandoz dd
			Pharmacological Properties	Revision of text to read "Clinical safety and Efficacy: In a force-titration, open label trial, 42 patients (including 8 paediatric patients) with homozygous familia hypercholesterolaemia were evaluated for their response to Crestor 20 - 40 mg. In the overall population, the mean LDL-C reduction was 22%. under the sub-heading Pharmacodynamic properties. Revision of text to read "Paediatric Population: After 52 weeks of study treatment, no effect on growth weight, BMI or sexual maturation was detected (see Specia warnings and precautions for use). This trial (n=176) was not suited for comparison of rare adverse drug events. Rosuvastatin was also studied in a 2-year open-label, titration-to-goal study in 198 children with heterozygous familial hypercholesterolaemia aged 6 to 17 years (88 male and 110 female, Tanner stage <II-V). The starting dose for all patients was 5 mg rosuvastatin once daily. Patients aged 6 to 9 years (n=64) could titrate to a maximum dose of 10 mg once daily and patients aged 10 to 17 years (n=134) to a maximum dose of 20 mg once daily. After 24 months of treatment with rosuvastatin, the LS mean percent reduction from the baseline value in LDL-C was 43% (Baseline: 236 mg/dL, Month 24: 133 mg/dL). For each age group, the LS mean percent reductions from baseline values in LDL-C were -43% (Baseline: 234 mg/dL, Month 24: 124 mg/dL), -45% (Baseline: 234 mg/dL, Month 24: 124 mg/dL) and -35% (Baseline: 241 mg/dL, Month 24: 153 mg/dL) in the 6 to <10, 10 to <14, and 14 to <18 age groups, respectively. Rosuvastatin 5 mg, 10 mg, and 20 mg also achieved statistically significant mean changes from baseline for the following secondary lipid and lipoprotein variables: HDL-C, TC, non-HDL-C, LDL-C/HDL-C, TC/HDL-C, TG/HDL-C, non-HDL C/HDL-C, ApoB, ApoB/ApoA-1. These changes were each in the direction of improved lipid responses and were sustained over 2 years. No effect on growth, weight, BMI or sexual maturation was detected after 24 months of treatment (see Special warnings and precautions for use)." under the sub-heading Pharmacodynamic propertes.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin	Pharmacological Properties	Revision of text to read " Paediatric population: Rosuvastatin was studied in a randomised, double-blind, placebo-controlled, multi-centre, cross-over study with 20 mg once daily versus placebo in 14 children and adolescents (aged from 6 to 17 years) with homozygous familial hypercholesterolaemia. The study included an active 4-week dietary lead-in phase during which patients were treated with rosuvastatin 10 mg, a cross-over phase that consisted of a 6-week treatment period with rosuvastatin 20 mg preceded or followed by a 6-week placebo treatment period, and a 12-week maintenance phase during which all patients were tre ated with rosuvastatin 20 mg. Patients who entered the study on ezetimibe or apheresis therapy continued the treatment throughout the entire study. A statistically significant (p=0.005) reduction in LDL-C (22.3%, 85.4 mg/dL or 2.2 mmol/L) was observed following 6 weeks of treatment with rosuvastatin 20 mg versus placebo. Statistically significant reductions in Total-C (20.1%, p=0.003), non-HDL-C (22.9%, p=0.003) and ApoB (17.1%, p=0.024) were observed. Reductions were also seen in TG, LDL-C/HDL-C, Total-C/HDL-C, non-HDLC/HDL-C and ApoB/ApoA-1 following 6 weeks of treatment with rosuvastatin 20 mg versus placebo. The reduction in LDL-C after 6 weeks of treatment with rosuvastatin 20 mg following 6 weeks of treatment with placebo was maintained over 12 weeks of continuous therapy. One patient had a further reduction in LDL-C (8.0%), Total-C (6.7%) and nonHDL-C (7.4%) following 6 weeks of treatment with 40 mg after up-titration. During an extended open-label treatment in 9 of these patients with 20 mg rosuvastatin for up to 90 weeks, the LDL-C reduction was maintained in the range of -12.1% to -21.3%. under the sub-heading Pharmacodynamic properties.	2-Mar-21	Sandoz dd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Crestor	Rosuvastatin		Revision of text to read "Paediatric population: In the 7 evaluable children and adolescent patients (aged from 8 to 17 years) from the force-titration open label study with homozygous familial hypercholesterolaemia (see above), the percent reduction in LDL-C (21.0%), Total-C (19.2%) and non-HDL-C (21.0%) from baseline following 6 weeks of treatment with rosuvastatin 20 mg was consistent with that observed in the aforementioned study in children and adolescents with homozygous familial hypercholesterolaemia." under the sub-heading Pharmacodynamic properties. Revision of text to read "Special precautions: Age and Sex: There was no clinically relevant effect of age or sex on the pharmacokinetics of rosuvastatin in adults. The exposure in children and adolescents with heterozygous familial hypercholesterolaemia appears to be similar to or lower than that in adult patients with dyslipidaemia (see “Paediatric population” below)." under te sub-heading Pharmacokinetic properties. Revision of text to read "Paediatric Population: Two pharmacokinetic studies with rosuvastatin given as tablets in paediatric patients with heterozygous familial hypercholesterolaemia 10 to 17 or 6 to 17 years of age (total of 214 patients) demonstrated that exposure in paediatric patients appears comparable to or lower than that in adult patients. Rosuvastatin exposure was predictable with respect to dose and time over a 2-year period." under the sub-heading Pharmacokinetic properties.	2-Mar-21	Sandoz dd
3	Diovan	Valsartan	Dosage regimen and administration	Revision of text to read "NOTE for all indications: No dosage adjustment is required for patients with renal impairment or for patients with hepatic impairment of non-biliary origin and without cholestasis." under Post-myocardial infarction.	5-Mar-21	Novartis International AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Diovan	Valsartan	Warnings and precautions	Revision of text to read " No dosage adjustment is required for patients with hepatic impairment. Valsartan is mostly eliminated unchanged in the bile, and patients with biliary obstructive disorders showed lower valsartan clearance (see section CLINICAL PHARMACOLOGY). Particular caution should be exercised when administering valsartan to patients with biliary obstructive disorders." under Patients with hepatic impairment. Revision of text to read "Valsartan: In embryofetal development studies in mice, rats and rabbits, fetotoxicity was observed in association with maternal toxicity in rats at valsartan doses of 600 mg/kg/day approximately 18 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient) and in rabbits at doses of 10 mg/kg/day approximately 0.6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). There was no evidence of maternal toxicity or fetotoxicity in mice up to a dose level of 600 mg/kg/day approximately 9 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Animal data-Pregnancy.	5-Mar-21	Novartis International AG
			Pregnancy, lactation, females and males of reproductive potential	Revision of text to read "Risk summary- It is not known whether valsartan is transferred into human milk. Since valsartan was transferred into the milk of lactating rats, it is not advisable to use Diovan in breast-feeding mothers." under Lactation.		
			Clinical pharmacology	Revision of text to read "About 70% of the absorbed dose is excreted in the bile mainly as unchanged compound. Valsartan does not undergo extensive biotransformation, and, as expected, systemic exposure to valsartan is not correlated with the degree of liver dysfunction. No dose adjustment for valsartan is therefore necessary in patients with hepatic impairment of non-biliary origin and without cholestasis. The AUC with valsartan has been observed to approximately double in patients with biliary cirrhosis or biliary obstruction (see section WARNINGS AND PRECAUTIONS)." under Hepatic impaiment- Pharmacokinetics (PK).		
			Non-clinical safety data	Revision of text to read " Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day, approximately 18 6 times the maximum recommended human dose on a mg/m² basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). " under Reproductive toxicity		
4	Daktacort	Miconazole nitrate and hydrocortisone	What you need to know before you use daktacort cream	Addition of text to include "• 60 mg benzoic acid in each tube of 30 g cream which is equivalent to 2 mg/g cream. • Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old)." under the subheading Daktacort cream contains	21-Jan-21	Janssen Pharmaceuticals

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Exforge	Amlodipine besylate/valsartan	Pregnancy, lactation, females and males of reproductive potential	Revision of text " Valsartan-In embryofetal development studies in mice, rats and rabbits, fetotoxicity was observed in association with maternal toxicity in rats at valsartan doses of 600 mg/kg/day approximately 18 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient) and in rabbits at doses of 10 mg/kg/day approximately 0.6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). There was no evidence of maternal toxicity or fetotoxicity in mice up to a dose level of 600 mg/kg/day approximately 9 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Animal data- Pregnancy. Revision of text to read " It is not known whether valsartan is transferred into human milk. It is reported that amlodipine is transferred into human milk. The proportion of the maternal dose received by the infant has been estimated with an interquartile range of 3 – 7%, with a maximum of 15%. The effect of amlodipine on infants is unknown. Valsartan was transferred into the milk of lactating rats. It is therefore not advisable for women who are breast-feeding to use Exforge."	5-Mar-21	Novartis International AG
			Overdosage	Deletion of text to read "Overdosage with amlodipine may result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and potentially prolonged systemic hypotension up to and including shock with fatal outcome have been reported." under Overdosage.		
			Non-clinical safety data	Revision of text to read " Reproductive toxicity: In a rat fertility study, valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day, approximately 6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Valsartan.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Exforge HCT	Amlodipine besylate / valsartan / hydrochlorothiazide	Pregnancy, lactation, females and males of reproductive potential	Revision of text to read "In embryofetal development studies in mice, rats and rabbits, fetotoxicity was observed in association with maternal toxicity in rats at valsartan doses of 600 mg/kg/day approximately 18 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient) and in rabbits at doses of 10 mg/kg/day approximately 0.6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). There was no evidence of maternal toxicity or fetotoxicity in mice up to a dose level of 600 mg/kg/day approximately 9 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). " under Valsartan-Animal data. Revision of text to read "It is not known whether valsartan is transferred into human milk. It is reported that amlodipine is transferred into human milk. The proportion of the maternal dose received by the infant has been estimated with an interquartile range of 3 – 7%, with a maximum of 15%. The effect of amlodipine on infants is unknown. Valsartan was transferred into the milk of lactating rats. Hydrochlorothiazide is transferred into human milk. It is therefore not advisable for women who are breast-feeding to use Exforge HCT." under Lactation.	5-Mar-21	Novartis International AG
			Overdosage	Deletion of text "Overdosage with amlodipine may result in excessive peripheral vasodilatation and possibly reflex tachycardia. Marked and potentially prolonged systemic hypotension up to and including shock with fatal outcome have been reported. " under Overdosage.		
			Non-clinical safety data	Revision of text to read " In a rat fertility study, valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day, approximately 6 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Reproductive toxicity-Valsartan.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Hexaxim	Diphtheria, tetanus, pertussis (acellular, component), hepatitis B (rDNA), poliomyelitis (inactivated) and Haemophilus influenzae type b conjugate vaccine (adsorbed).	Qualitative and Quantitative Composition	Addition of text "Excipient with known effect Phenylamine…….. 85 micrograms (See section 4.4)" under this section.	11-Feb-21	Sanofi-Aventis
			Posology and method of administration	Revision of text to read "Where a dose of hepatitis B vaccine is given at birth; - Hexacima can be used for supplementary doses of hepatitis B vaccine from the age of 6 weeks. If a second dose of hepatitis B vaccine is required before this age, monovalent hepatitis B vaccine should be used. - Hexacima can be used for a mixed hexavalent/pentavalent/hexavalent combined vaccine immunisation schedule in accordance with official recommendations." under the sub-heading Posology. Deletion of text "After a 3-dose WHO EPI schedule with Hexacima (6, 10, 14 weeks) and in the absence of hepatitis B vaccination at birth, a hepatitis B vaccine booster must be given. At the very least, a booster dose of polio vaccine should be given. Hexacima can be considered for the booster." under the sub-heading Posology. Revision of text to read "WHO-EPI schedule (6, 10, 14 weeks): After a WHO-EPI schedule, a booster dose should be given - As a minimum, a booster dose of polio vaccine should be given - In absence of hepatitis B vaccine at birth, a hepatitis B vaccine booster must be given Hexacima can be considered for the booster" under the sub-heading Posology.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Lamisil	Terbinafine hydrochloride	Interactions	Addition of texts to include "Pregnancy: Risk summary There are no adequate or well-controlled clinical trials using terbinafine in pregnant women. In an observational, registry-based cohort study, there was no increase in the risk of major malformations or spontaneous abortion in pregnancies exposed to oral terbinafine in comparison to those not exposed to oral terbinafine (see Human Data). In animal reproduction studies, terbinafine did not cause reproductive toxicity in rats and rabbits at oral doses up to 12 and 23 times the maximum recommended human dose (MRHD) based on body surface (BSA), respectively (see Animal Data). The use of terbinafine may be considered during pregnancy, if necessary." under Pregnancy, lactation, females males of reproductive potential Addition of text to include "Data: Human data A nationwide, observational, registry-based cohort study was conducted in Denmark from January 1, 1997 to December 31, 2016 in a cohort of 1,650,649 pregnancies. Pregnancies were matched on propensity scores comparing pregnancies exposed to oral terbinafine versus those not exposed to oral terbinafine in a 1:10 ratio to evaluate the risk of major malformations (522 versus 5220) and spontaneous abortions (891 versus 8910). The prevalence odds ratio for the risk of major malformations was 1.01 (95% CI, 0.63-1.62) for pregnancies exposed versus not exposed to oral terbinafine. The hazard ratio for the risk of spontaneous abortion was 1.06 (95% CI, 0.86-1.32) for the same comparison. No increased risk of major malformations or spontaneous abortion was identified among pregnancies exposed to oral terbinafine. Animal data: In embryo-fetal development studies in rats and rabbits, terbinafine was administered orally (30, 100, or 300 mg/kg/day) during the period of organogenesis. There were no embryotoxic or teratogenic effects up to the maximum tested dose of 300 mg/kg/day in rats and rabbits (corresponding to 12 and 23 times the MRHD based on BSA, respectively). Subcutaneous administration of terbinafine (10, 30 or 100 mg/kg/day) to rats during the period of organogenesis showed no teratogenic or embryotoxic effect up at doses up to 100 mg/kg/day (corresponding to 4 times the MRHD based on BSA). In a rat peri-and postnatal development study, oral administration of terbinafine (30, 100 or 300 mg/kg/day) had no adverse effects on pregnancy and lactation at doses up to 300 mg/kg/day (corresponding to 12 times the MRHD based on BSA). No treatment related effects in F1 and F2 generations were noted."	12-Feb-21	Novartis International AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Lamisil	Terbinafine hydrochloride	Interactions	Addition of text to include "Lactation: Risk summary Terbinafine is transferred into human breast milk. There are no data on the effects of terbinafine on the breastfed child or on milk production. The maximum ratio of terbinafine in milk to plasma is 7:1, and the maximum amount of terbinafine ingested by the infant is expected to be 16% of the dose administered to the nursing mother. The highest concentration of terbinafine in breast milk was observed within 6 hours after administration, and thereafter the concentration of terbinafine decreased by approximately 70% in the 6-12 hour time window after administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for Lamisil and any potential adverse effects on the breast-fed child from Lamisil." Revision of text that reads "There are no data to support special recommendations for women of child-bearing potential." under the subheading Women of child-bearing potential Deletion of text that reads "Pregnancy: Foetal toxicity studies with terbinafine in animals suggest no adverse effects. Since documented clinical experience in pregnant women is very limited, Lamisil tablets should not be used during pregnancy unless the potential benefits outweigh any potential risks. Breast-feeding: Terbinafine is excreted in breast milk; mothers receiving oral treatment with Lamisil should therefore not breast-feed." under the subheading Females and males of reproductive potential	12-Feb-21	Novartis International AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Lamisil	Terbinafine hydrochloride	Non-clinical safety data	Addition of texts that includes "Repeat dose toxicity, Mutagenicity and carcinogenicity ". Revision of texts to read "In a 32-week repeated dose study in monkeys, refractile irregularities were observed in the retina at the higher doses (non-toxic effect level 50 mg/kg/day). These irregularities were associated with the presence of a terbinafine metabolite in ocular tissue and disappeared after drug discontinuation. They were not associated with histological changes. In 4-week studies, intravenous administration of terbinafine resulted in central nervous system disturbances including hypoactivity, ataxia and convulsions in rats (> 30 mg/kg/day) and monkeys (75 mg/kg/day)" Addition of texts that includes "Reproductive toxicity: No adverse effects on fertility or other reproduction parameters were observed in studies in rats or rabbits. In a fertility and reproductive study, rats were treated orally with terbinafine (10, 50, or 250 mg/kg/day) starting 9 weeks (males) or 2 weeks (females) prior to mating and continued through pregnancy and lactation. There were no effects on fertility or general reproductive performance. However at 250 mg/kg/day (corresponding to 10 times the MRHD based on BSA), there was evidence of parental toxicity (reduced body weight gain, lower pregnancy rate and litter size), increased pre- and perinatal offspring mortality, and retarded postnatal offspring development. For information on embryofetal and pre- and postnatal toxicity, (see section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL). Juvenile animal studies"	12-Feb-21	Novartis International AG
			Information for Patients	Addition of text that includes "Pediatrics: The scored tablets are divisible for dosing in children according to body weight (see section 4 Dosage regimen and administration)."		
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Composition	Revision of text to read "Sodium dihydrogen phosphate monohydrate, anhydrous sodium sulphate, mannitol, L	9-Jul-21	F. Hoffmann-La Roche AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Pharmaceutical form and active substance quantity per unit	Deletion of text that reads "Excipients sufficient for 0.3 ml of solution." under Mircera 30 to 250µg/0.3 ml solution for injection in prefilled syringe" Deletion of text that reads "MIRCERA 360 µg/0.6 ml solution for injection in a prefilled syringe Each prefilled syringe with ready-to-use solution for injection contains 360 µg methoxy polyethylene glycol-epoetin beta. Excipients sufficient for 0.6 ml of solution." Revision of text to read "The quoted dosage strength in µg relates to the protein moiety of the methoxy polyethylene glycol-epoetin beta molecule without consideration of glycosylation." Adittion of text that reads "Initiation of treatment" under dosage/administration Revision of text to read "The recommended starting dose of 0.6 µg/kg body weight may be administered once every two weeks as a single i.v. or s.c. injection." under subheading patients on dialysis Adittion of text that reads "Dose adjustment" under dosage/administration Revision of text to reads "The MIRCERA dose may be increased by approximately 25% of the previous dose if the rise in hemoglobin is less than 1.0 g/dl (0.621 mmol/l) over a month. Further dose increases of approximately 25% may be made every 4 weeks until the individual target hemoglobin level is achieved. If the rise in hemoglobin exceeds 2 g/dl (1.24 mmol/l) in one month or if the hemoglobin level exceeds 12 g/dl, the dose should be reduced by approximately 25%. If the hemoglobin level continues to increase, therapy should be interrupted until the hemoglobin level begins to decrease, at which point therapy should be restarted at a dose approximately half the previously administered dose. After dose interruption a hemoglobin decrease of approximately 0.35 g/dl (0.22 mmol/l) per week is expected. Dose adjustments should not be made more frecuently than once a month."	9-Jul-21	F. Hoffmann-La Roche AG
				Revision of text to read "In patients treated once every two weeks whose hemoglobin concentration is above the target range, may receive MIRCERA once monthly at twice the dose previously administered once every two weeks. Switching from erythropoiesis stimulating agent (ESA) treatment to Mircera Patients currently treated with an ESA, can be switched to MIRCERA administered once a month as a single intravenous or subcutaneous injection. The starting dose of MIRCERA is calculated from the previous weekly ESA dose at the time of the treatment switch, as described in Table 1. The first MIRCERA injection should be given at the time of the next scheduled dose of the previously administered darbepoetin alfa or epoetin."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Pharmaceutical form and active substance quantity per unit	Revision of text to read "After dose interruption a haemoglobin decrease of approximately 0.35 g/dl (0.22 mmol/l) per week is expected. Dose adjustments should not be made more frequently than once a month." Addition of text to include "To ensure the traceability of biological medicinal products, it is recommended that the trade name and batch number be documented with every treatment." Addition of text to include "Special dosage instructions Patients with hepatic impairment-No adjustments of the starting dose or dose modification rules are required in patients with any degree of hepatic impairment (see “Kinetics in specific patient groups”). Deletion of text that reads "If a dose of MIRCERA is missed, the missed dose should be administered as soon as possible and treatment with MIRCERA continued at the prescribed dosing frequency. Use in children- Due to limited safety and efficacy data, no dosage recommendations can be given for use in patients under 18 years of age. Use in the elderly-Use in patients with hepatic impairment No adjustment of the starting dose and no dosage adjustment rule are necessary in patients with hepatic impairment, regardless of its severity (see Pharmacokinetics in special patient populations)."	9-Jul-21	F. Hoffmann-La Roche AG
				Addition of text to include "Children and adolescents Due to limited safety and efficacy data, no dosage recommendations can be given for use in patients under 18 years of age. Delayed administration If a dose of Mircera is missed, the missed dose should be administered as soon as possible and treatment with Mircera continued at the prescribed dosing frequency. Mode of administration Intravenous and subcutaneous administration."		
			Contraindication	Revision of text to read "Hypersensitivity to the active substance or to any of the constituent excipients listed under “Composition”. MIRCERA must not be used in patients with untreated or poorly controllable controlled hypertension."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Warnings and precautions	Revision of text to read "Hemoglobin target levels exceeding above 12 g/dl may be assosiated with an increased the risk of cardiovascular events, including death. Controlled clinical studies have shown no significant benefit of ESAattributable to epoetin use when the hemoglobin level is higher than that necessary to control symptoms of anemia and avoid blood transfusion. Deficiencies of iron, folic acid or vitamin B12 reduce the effectiveness of ESAs and should therefore be corrected. Intercurrent infections, inflammatory or traumatic episodes, occult blood loss, hemolysis, severe aluminium toxicity, underlying hematological disease or bone marrow fibrosis may also compromise the erythropoietic response. A reticulocyte count should be considered as part of the evaluation. If all the conditions mentioned are excluded and the patient has a sudden drop of hemoglobin associated with reticulocytopenia and antierythropoietin antibodies, examination of the bone marrow for (the diagnosis of pure red cell aplasia [PRCA]) should be considered. If PRCA is diagnosed, therapy with Mircera must be discontinued and patients must not be switched to another ESA. Pure red cell aplasia (PRCA) Pure red cell aplasia due to antierythropoietin antibodies has been reported during treatment with ESAs, including MIRCERA. These antibodies cross-react with all ESAs, and patients suspected or confirmed to have antibodies to erythropoietin must not be switched to Mircera."	9-Jul-21	F. Hoffmann-La Roche AG
				Revision of text to read "Blood pressure should be adequately monitored in all patients before, at initiation of and during treatment with MIRCERA. If high blood pressure is difficult to control by medication or diet, MIRCERA must be reduced in dose or withheld (see Contraindications)." under blood pressure monitoring Revision of text to read "The safety and efficacy of MIRCERA therapy have not been established investigated in patients with hemoglobinopathies, seizure disorders, bleeding or a recent history of bleeding requiring transfusions or with platelet counts exceeding above 500 × 109/l. Caution is therefore required in such these patients." under other Revision of text to read "In clinical trials an increased risk of death and serious cardiovascular events was observed when erythropoiesis stimulating agents (ESAs) were administered to achieve a target hemoglobin of greater than 12 g/dl (7.5 mmol/l)." Addition of text to include "This medicinal product contains less than 1 mmol of sodium (23 mg) per prefilled syringe, i.e. it is virtually “sodium-free”."		
			Interactions	Revision of text to read "No interaction studies have been performed. Clinical studies have produced no evidence that MIRCERA interacts with other medicinal products. The effects of other drugs on the MIRCERA pharmacokinetics and pharmacodynamics was investigated in a population analysis. No evidence was found of an effect on MIRCERA pharmacokinetics pharmacodynamics of MIRCERA"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Pregnancy, lactation	Revision of text to read "There are insufficient data on use in pregnant women. Animal studies have shown no direct or indirect toxicity affecting pregnancy, embryonic development, or delivery fetal development, parturition (see Preclinical data) and/or postnatal development. Caution is required if used during pregnancy." Revision of text to read "It is unknown whether methoxy polyethylene glycol-epoetin beta is excreted in human breast milk. One animal study has shown excretion of methoxy polyethylene glycol-epoetin beta in maternal milk. In deciding whether to continue or discontinue breastfeeding during treatment with MIRCERA or to discontinue therapy, the benefit of breastfeeding to the child should be weighed against the benefit of MIRCERA therapy to the woman." under lactation	9-Jul-21	F. Hoffmann-La Roche AG
			Undesirable effects	Deletion of text that reads "Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), skin exfoliation and erythema multiforme, have been reported with Mircera in the post-marketing setting (see Warnings and precautions). Frequencies are not known. Clinical-trial experience" Revision of text to read "The MIRCERA safety data from clinical trials are based on 3042 CKD patients, including 1939 patients treated with MIRCERA and 1103 with another ESA. Undesirable effects must be expected in some 6% of patients treated with MIRCERA. The most frequent reported undesirable effect was hypertension (common)." Revision of text to read "Vascular disorders, General disorders and administration site conditions, Nervous system disorders, Skin and subcutaneous tissue disorders, Immune system disorders" under organ class Revision of text to read "All other reactions attributed to MIRCERA were rare and in most cases mild to moderate in severity. Thesereactions could be explained by comorbidities known in the population. inIn clinical studies, the platelet count decreased slightly during treatment with MIRCERA, but remained within the normal range. Platelet counts below 100 × 109/l were observed in 7.5% of patients treated with MIRCERA and 4.4% of patients treated with ESA. The safety profile in the paediatric population was consistent with that in adults."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Undesirable effects	Revision of text to read "Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), skin exfoliation and erythema multiforme, have been reported with Mircera in the post-marketing setting (see “Warnings and precautions”). Frequencies are not known.The occurrence of neutralizing antierythropoietin antibody-mediated pure red cell aplasia (AEAB-PRCA) has been reported in association with MIRCERA therapy during post-marketing experience (see Warnings and precautions)." under Undesirable effects after market launch. Addition of text that 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." under Description of selected adverse reactions	9-Jul-21	F. Hoffmann-La Roche AG
			Overdose	Revision of text to read "MIRCERA has a wide therapeutic range. Individual response must be considered when initiating treatment with MIRCERA."		
			Treatment	Addition of text to include "In case of excessive haemoglobin levels, Mircera should be temporarily withheld (see “Dosage/Administration”). If clinically indicated, phlebotomy may be performed."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Mircera	Methoxy polyethylene glycol-epoetin beta	Properties/Effects	Addition of text to read "Mircera stimulates erythropoiesis by interaction with the erythropoietin receptor on progenitor cells in the bone marrow. As primary growth factor for erythroid development, the natural hormone erythropoietin is produced by the kidney and released into the bloodstream according to the level of tissue oxygen saturation. In response to hypoxia, the natural hormone erythropoietin interacts with erythroid progenitor cells, increasing their production." Revision of text to read "Methoxy polyethylene glycol-epoetin beta, the active substance of MIRCERA, is a continuous erythropoietin receptor activator that differs from erythropoietin in its activity at the receptor level, which is characterized by slower association with and faster dissociation from the receptor, reduced specific activity in vitro with increased activity in vivo, and an increased half-life. Its average molecular weight is about 60 kDa, of which the protein portion plus the carbohydrate portion accounts for approximately 30 kDa." under Pharmacodynamics Revision of text to read "MIRCERA pharmacokinetics in patients with severe liver failure are similar to those in healthy subjects (see Special dosage instructions)." under Hepatic impairment Revision of text to read "Population analysesfound no evidence that age, gender or ethnicity have a relevant pharmacokinetic effect. A population-based pharmacokinetic analysis likewise showed no relevant difference in pharmacokinetics between dialyzed and nondialyzed patients." under Other special populations	9-Jul-21	F. Hoffmann-La Roche AG
			Preclinical data	Deletion of text that reads "In addition, in a panel of human tissues, in vitro binding of MIRCERA was only observed in target cells (bone marrow progenitor cells)." under Carcinogenicity Addition of text to include "In a panel of human tissues, in vitro binding of MIRCERA was only observed in target cells (bone marrow progenitor cells)." under Additional data		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Paclitaxel	Paclitaxel	Undesirable side effects	Revision of text to read "Adverse reactions associated with the administration of single agent paclitaxel administered as a three hour infusion in the metastatic setting (812 patients treated in clinical studies) and as reported in the post-marketing surveillance* of paclitaxel are listed below. The latter ones may be attributed to paclitaxel regardless of the treatment regimen.". Addition of footnote "Can persist beyond 6 months of paclitaxel discontinuation" under the System Organ Class Nervous System Disorders. Addition of "Palmar-plantar erythrodysesthesia syndrome * with frequency Not known under System Organ Class Skin and subcutaneous tissue disorders.	10-Dec-19	Sandoz dd
			Pharmacological Properties	Revision of text "Pharmacotherapeutic group: Antineoplastic agents (taxanes) ATC code: L01CD01" under the sub heading Pharmacodynamic Properties.		
11	Polygynax	Polymyxin, Neomycin, Nystatin	Therapeutic indication	Revision of text to read "Local treatment of vaginitis due to sensitive germs (bacterial vaginitis, vulvovaginitis due to Candida albicans and Candida non-albicans, mixed vaginitis) and bacterial vaginosis"	24-Sep-19	Innotech
			Undesirable side effects	Revison of text to read " Undesirable effects are classified by system organ class. For undesirable effects reported from spontaneous notifications, the frequency is not known (cannot be estimated from available data)" Addition of table for sytem organ class, frequency and undesirable effects under this section.		
12	Remicade	Infliximab	Possible side effects	Addition of text to include "Kaposi's sarcoma, a rare cancer related to infection with human herpes virus 8. Kaposi's sarcoma most commonly appears as purple lesions on the skin." under the subheading Not known: frequency cannot be estimated from the available data.	21-Jan-21	Janssen Pharmaceuticals
13	Rhinathiol	Carbocisteine	Posology	Revision of text to read "This medicinal product is indicated in adults (over 15years of age) in the event of a recent respiratory disease with expectoration difficulties (difficulty in clearing brochial secretions via sputum)." Addition of text "FOR ADULTS ONLY"	2-Mar-21	Sanofi-Aventis-Aventis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
13	Rhinathiol	Carbocisteine	Special warnings and precautions for use	Revision of text to read "Hyperactivity to the active substance or to any of the excipients (particularly methyl parahydroxybenzoate) listed in section 6.1. In case of active gastroduodenal ulcer" under subheading contraindication Addition of text to read "This medicine contains sucrose. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take this medicine." Addition of text to read "Caution is recommended in the elderly, in those with history of gastroduodenal ulcers, or those taking concomitant medications known to cause gastrointestinal bleeding. If gastrointestinal bleeding occurs, patients should discontinue medication" Addition of text to include "Animal studies do not indicate any teratogenic effects. There is no available data on carbocisteine use in pregnant women. The use of carbocisteine in pregnant women is therefore not recommended." Addition of text to include "There are no available data on the presence of carbocisteine in milk. The use of carbocisteine in breast feeding women is therefore not recommended" Revision of text to read "Possibility of cases of digestive intolerance (gastric pain, nausea, vomiting, and diarrhoea). If these occur, the dose should be reduced" Addition of text to include "Gastrointestinal bleeding. Treatment should be discontinued. Allergic skin erruption and anaphylatic reactions such as urticaria, angioedema, pruritis and erythematous rash. under undesirable effects	2-Mar-21	Sanofi-Aventis-Aventis
14	Rocephin	Ceftriaxone	Indications/Uses	Revision of text to read "Infections caused by pathogens sensitive to ceftriaxone, e.g.: - respiratory tract infections, particularly pneumonia, and ear, nose and throat infections; - abdominal infections (peritonitis, infections of the biliary and gastrointestinal tracts); - renal and urinary tract infections; - genital infections, including gonorrhea; - sepsis; - infections of the bones, joints, soft tissue, skin and of wounds; - infections in patients with impaired immunity; - meningitis; - disseminated Lyme borreliosis (stages II and III). Perioperative prophylaxis of infections associated with gastrointestinal, biliary , urogenital, gynaecological surgery, but only in cases of potential or definite contamination. Official recommendations on the appropriate use of antibiotics should be followed, especially usage recommendations to prevent the increase in antibiotic resistance." .	20-May-21	F. Hoffmann-La Roche AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
14	Rocephin	Ceftriaxone	Dosage/Administration	Revision of text to read "The usual dosage is 1–2 g of Rocephin once daily (every 24 hours). In severe infections or those caused by moderately sensitive organisms, the once daily dose may be raised to 4 g." under Adults and children over twelve years. Revision of text to read "A daily dose of 20–50 mg per kg body weight; it must not exceed 50 mg per kg. Rocephin is contraindicated in premature neonates up to a postmenstrual age of 41 weeks (gestational age + postnatal age) (see Contraindications). Rocephin is contraindicated in neonates (≤28 days) if they require (or are expected to require) treatment with calcium-containing intravenous solutions, including continuous calcium-containing infusions such as in parenteral nutrition, because of the risk of calcium ceftriaxone precipitation (see Contraindications)." under Neonates (up to 14 days old). Revision of text to read "A daily dose of 20–80 mg per kg. For children with body weights of 50 kg or more, the usual adult dosage must be used. Intravenous doses of 50 mg or more per kg body weight in infants and children up to 12 years of age should be given by slow infusion over at least 30 minutes. In neonates, intravenous doses should be given over 60 minutes to reduce the potential risk of bilirubin encephalopathy." under Infants and children (15 days to twelve years).	20-May-21	F. Hoffmann-La Roche AG
			Warnings and Precautions	Revision of text to read "As with all beta-lactam antibiotics, there have been reports of serious and occasionally fatal hypersensitivity reactions (see Undesirable effects – After market launch). In case of severe hypersensitivity reactions, treatment with ceftriaxone must be discontinued immediately and adequate emergency measures must be initiated. Before starting treatment, it should be established whether the patient has ever had hypersensitivity reactions to ceftriaxone, to other cephalosporins or to any other beta-lactam agent. Caution is required when administering ceftriaxone to patients with a history of hypersensitivity to other beta-lactam agents. Hypersensitivity reactions (including anaphylactic shock) may be caused by lidocaine (contained in the solvent for i.m. injection). Severe cutaneous adverse reactions (SCARs) such as Stevens-Johnson syndrome, toxic epidermal necrolysis, drug rash with eosinophilia and systemic symptoms (DRESS), erythema multiforme and acute generalised exanthematous pustulosis (AGEP) have been reported in patients receiving treatment with beta-lactam antibiotics including Rocephin or ceftriaxone (see “Undesirable effects”). In the event of such reactions, Rocephin should be immediately discontinued and alternative therapy considered." under Hypersensitivity.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
14	Rocephin	Ceftriaxone	Warnings and Precautions	Revision of text to read "On long-term use of Rocephin, non-susceptible microorganisms may become difficult to control. Close patient supervision is therefore essential. If superinfection occurs during treatment, appropriate measures should be taken." Under Superinfections. Revision of text to read "Rare cases of pancreatitis possibly due to cholestasis have been reported in patients treated with Rocephin. Most patients presented with risk factors for cholestasis and biliary sludge, e.g. extensive prior therapy, severe illness and total parenteral nutrition. The possibility cannot be excluded that Rocephin-induced precipitation in the gallbladder acts as a trigger or cofactor. Ceftriaxone can displace bilirubin from its binding to serum albumin. Treatment of hyperbilirubinemic neonates is therefore contraindicated (see Contraindications)." under Pancreatitis.	20-May-21	F. Hoffmann-La Roche AG
			Interactions	Revision of text to read "No impairment of renal function has been observed after concurrent admini¬stration of large doses of Rocephin and potent diuretics such as furosemide. There are conflicting data regarding a potential increase in renal toxicity of aminoglycosides when used with cephalosporins. The recommendations on monitoring of aminoglycoside levels and renal function in clinical practice should be closely adhered to in such cases. Nevertheless, the two products must be administered separately (see Incompatibilities). No disulfiram-like effect has been demonstrated after Rocephin administration alcohol ingestion. Ceftriaxone does not contain the N-methyl¬thio¬tetra¬zole moiety that could lead to ethanol intolerance and bleeding problems as is the casewith other cephalosporins. Probenecid has no effect on the elimination of ceftriaxone. Bacteriostatics may adversely interfere with the bactericidal effect of cephalosporins. Antagonistic effects were observed in an in vitro study of ceftriaxone in combi¬nation with chloramphenicol.".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
14	Rocephin	Ceftriaxone	Undesirable effects	Revision of text to read "Edema, chills, anaphylactic or anaphylactoid reactions. Vein wall inflammatory reactions after i.v. administration. These may be minimised by slow injection (over two to four minutes)." with frequency rare under the System Organ Class General Disorders and Administration Site Conditions. Addition of sub-heading "Undesirable effects after market launch" under this section. Revision of text "Not known: Severe cutaneous adverse reactions (SCARs) (see “Warnings and precautions”)." under Undesirable effects after market launch. Lidocaine (contained in the solvent for i.m. injection) Revision of text to read "Common: Oedema, sensation of cold or heat. 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." under General Disorders and Administration Site Conditions	20-May-21	F. Hoffmann-La Roche AG
			Properties and Effects	Addition of sub-heading " Clinical Efficacy" . Addition of text "Not applicable" under Clinical Efficacy"		
			Pharmacokinetics	Revision of text to read "Ceftriaxone is not metabolized systemically but is converted to inactive metabolites by gut flora after biliary excretion into the intestinal lumen." under the sub-heading Metabolism.		
			Other Information	Addition of sub-heading "Shelf life after opening" .		
15	Sandimmun Neoral	Ciclosporin	Instructions for use and handling	Revision of text to read "Remove the grey stopper and throw it away." under Instructions for use and handling of Sandimmun Neoral solution: Initial use of Sandimmun Neoral oral solution	19-Feb-21	Novartis International AG
16	Simponi	Golimumab	Possible side effects	Addition of text to include "• Kaposi’s sarcoma, a rare cancer related to infection with human herpes virus 8. Kaposi’s sarcoma most commonly appears as purple lesions on the skin." under the subheading Side effects of which the frequency is not known	21-Jan-21	Janssen Pharmaceuticals

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
17	Tavanic	Levofloxacin	Special warnings and precautions for use	Revision of texts to read "Severe cutaneous adverse reactions: Severe cutaneous adverse reactions (SCARs) including toxic epidermal necrolysis (TEN: also known as Lyell's syndrome), Stevens Johnson syndrome (SJS) and drug reaction with eosinophilia and systemic symptoms (DRESS), which could be life-threatening or fatal, have been reported with levofloxacin (see section 4.8). At the time of prescription, patients should be advised of the signs and symptoms of severe skin reactions, and be closely monitored. If signs and symptoms suggestive of these reactions appear, levofloxacin should be discontinued immediately and an alternative treatment should be considered. If the patient has developed a serious reaction such as SJS, TEN, or DRESS with the use of levofloxacin, treatment with levofloxacin must not be restarted in this patient at any time." Revision of texts to read "As with all quinolones, disturbances in blood glucose, including both hypoglycaemia and hyperglycaemia have been reported, occurring more frequently in the elderly, usually in diabetic patients receiving concomitant treatment with an oral hypoglycaemic agent (e.g. glibenclamide) or with insulin. Cases of hypoglycaemic coma have been reported. In diabetic patients, careful monitoring of blood glucose is recommended (see section 4.8). Tavanic treatment should be stopped immediately if a patient reports blood glucose disturbance and alternative nonfluoroquinolone antibacterial therapy should be considered." under the sub heading dysglycaemia Revision of texts to read "Psychotic reactions have been reported in patients receiving quinolones, including levofloxacin. In very rare cases these have progressed to suicidal thoughts and self-endangering behaviour-sometimes after only a single dose of levofloxacin (see section 4.8). In the event that the patient develops these reactions, levofloxacin should be discontinued immediately at the first signs or symptoms of these reactions and patients should be advised to contact their prescriber for advice. Alternative nonfluoroquinolone antibacterial therapy should be considered, and appropriate measures instituted. Caution is recommended if levofloxacin is to be used in psychotic patients or in patients with history of psychiatric disease." Under subheading Psychotic reactions	2-Jul-21	Sanofi-Aventis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
17	Tavanic	Levofloxacin	Undesirable effects	Addition of texts that read "Endocrine disorders (Rare) Syndrome of inappropriate secretion of antidiuretic hormone (SIADH)" Addition of texts that read "Hypoglycaemic coma" under the subheading Metabolism and nutrition disorder(Rare) Deletion of texts that read "Hypoglycaemic coma" under the subheading Metabolism and nutrition disorder [Not known (cannot be estimated from available data)] Addition of texts that read "Delirium, Memory impairment" under the subheading Psychiatric disorders (Rare) Addition of texts that read "Drug Reaction with Eosinophilia and Systemic Symptoms (DRESS) (see section 4.4), Fixed drug eruption" under the subheading Skin and subcutaneous tissue disorders(Rare)	2-Jul-21	Sanofi-Aventis
			What you need to know before you take [Tradename]	Addition of texts that read "You have ever developed a severe skin rash or skin peeling, blistering and/or mouth sores after taking levofloxacin. Serious skin reactions Serious skin reactions including Stevens-Johnson syndrome, toxic epidermal necrolysis, and drug reaction with eosinophilia and systemic symptoms (DRESS) have been reported with the use of levofloxacin. SJS/TEN can appear initially as reddish target-like spots or circular patches often with central blisters on the trunk. Also, ulcers of mouth, throat, nose, genitals and eyes (red and swollen eyes) can occur. These serious skin rashes are often preceded by fever and/or flu-like symptoms. The rashes may progress to widespread peeling of the skin and life-threatening complications or be fatal. DRESS appears initially as flu-like symptoms and a rash on the face then an extended rash with a high body temperature, increased levels of liver enzymes seen in blood tests and an increase in a type of white blood cell (eosinophilia) and enlarged lymph nodes. If you develop a serious rash or another of these skin symptoms, stop taking levofloxacin and contact your doctor or seek medical attention immediately." under warnings and precautions (Talk to your doctor or pharmacist before taking your medicine if)		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
17	Tavanic	Levofloxacin	Possible side effects	Addition of texts to include "Widespread rash, high body temperature, liver enzyme elevations, blood abnormalities (eosinophilia), enlarged lymph nodes and other body organs involvement (Drug Reaction with Eosinophilia and Systemic Symptoms which is also known as DRESS or drug hypersensitivity syndrome) (see section 2) Syndrome associated with impaired water excretion and low levels of sodium (SIADH) Lowering of your blood sugar levels (hypoglycaemia) or lowering of your blood sugar levels leading to coma (hypoglycaemic coma). This important for people that have diabetes." under Stop Taking Tavanic and see a doctor straight away if you notice any of the following serious side effects – you may need urgent medical treatment Revision of texts to read "Severe skin rashes including Stevens-Johnson syndrome and toxic epidermal necrolysis. These 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 can be preceded by fever and flu-like symptoms (see section 2) Loss of appetite, skin and eyes becoming yellow in colour, dark-coloured urine, itching, or tender stomach (abdomen). These may be signs of liver problems which may include a fatal failure of the liver." under not known Addition of texts to include "Sharply demarcated, erythematous patches with/without blistering that develop within hours of administration of levofloxacin and heals with postinflammatory residual hyperpigmentation; it usually recurs at the same site of the skin or mucous membrane upon subsequent exposure to levofloxacin Memory impairment" under Tell you doctor if any of the following side effects gets serious or lasts longer than a few days	2-Jul-21	Sanofi-Aventis
18	Taxotere	Docetaxel	Special warnings and precautions for use	Addition of text to read "Tumour lysis syndrome has been reported with docetaxel after the first or the second cycle (see section 4.8). Patients at risk of tumour lysis syndrome (e.g. with renal impairment, hyperuricemia, bulky tumour, rapid progression) should be closely monitored. Correction of dehydration and treatment of high uric acid levels are recommended prior to initiation of treatment" under subheading "tumour lysis syndrome"	10-Feb-21	Sanofi-Aventis
			Undesirable effects	Addition of text to read " Tumour lysis syndrome, potentially fatal, has been reported (frequency not known)" under subheading "Metabolism and nutrition disorders" Addition of text to read "Myositis has been reported with docetaxel (frequency not known)." under subheading "musculoskeletal disorder"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
19	Tienam	Imipenem/ Cilastatin	Qualitative and quantitative composition	Revision of text to read " Each vial contains 37.6 mg (1.6 mmol) of sodium (as bicarbonate)" under subheading Excipient with known effect.	19-Nov-20	MSD Idea Pharmaceuticals
			Special warnings and precautions for use	Revision of text to read "This medicinal product contains 37.6 mg sodium (1.6 mmol) per vial, equivalent to 1.9% of the WHO recommended maximum daily intake of 2 g sodium for an adult. This should be taken into consideration by patients on a controlled sodium diet" .		
			Pharmacological properties	Revision of table under subheading "Pharmacodynamic properties". Revision of texts to read " The intrinsically low activity of imipenem against Morganella morganii, Proteus spp. and Providencia spp. requires the high exposure of imipenem. 4 Non-susceptible isolates are rare or not yet reported. The identification and antimicrobial susceptibility test result on any such isolate must be confirmed and the isolate sent to a reference laboratory" unnder subheading pharmacodynamic properties of this section.		
20	Triveram	Atorvastatin / Perindopril arginine / Amlodipine	Warnings and precautions	Addition of text to read " Make sure to tell your doctor if you are taking any of the following medicines: letermovir, a medicine that helps stop you from getting ill from cytomegalovirus" under subheading "Other medicines and Triveram"	10-Feb-21	Servier Laboratories
			Possible side effects	Revision of text to read "Stop taking the medicinal product and see a doctor immediately, if you experience any of the following side effects or symptoms that can be serious: Aggravated dizziness or fainting due to low blood pressure" .		
			Posology and method of administration	Addition of text to read "Use of TRIVERAM is not recommended in patients taking letermovir co-administered with ciclosporin" .		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
21	Valsartan	Valsartan	Description and composition	Deletion of text " Oral Solution: Clear, colorless to pale yellow solution" under Pharmaceutical forms. Deletion of text " Each mL oral solution contains 3 mg of valsartan." under Active substance. Deletion of text "Oral Solution: sucrose, methyl parahydroxybenzoate (E218), potassium sorbate, poloxamer (188), citric acid, anhydrous, sodium citrate, artificial blueberry flavour (538926 C), propylene glycol (E1520), sodium hydroxide, hydrochloric acid, purified water" under Excipients.	5-Mar-21	Novartis International AG
			Indication	Revision of text to read " Treatment of hypertension in children, adolescents and adults (see section 4 Dosage regimen and administration)".		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
21	Valsartan	Valsartan	Dosage regimen and administration	Revision of text to read ' NOTE for all indications: No dosage adjustment is required for patients with renal impairment or for patients with hepatic impairment of non-biliary origin and without cholestasis." under Hypertensive adult patients with Impaired Glucose Tolerance at cardiovascular risk. Deletion of text "Oral Solution For children and adolescents who are unable to swallow tablets, the use of the Valsartan oral solution is recommended. The systemic exposure and peak plasma concentration of valsartan is about 1.7-fold and 2.2-fold higher with the oral solution compared to the tablets. The initial dose for the Valsartan oral solution is 20 mg (corresponding to approx.7 mL of the solution) once daily for children and adolescents below 35 kg of weight and 40 mg (corresponding to approx.13 mL of the solution) once daily for those weighing 35 kg or more. The dose should be adjusted based on blood pressure response up to a maximum dose of 40 mg valsartan once daily (corresponding to approx. 13 mL of the solution) for children and adolescents with body weight below 35 kg and 80 mg valsartan (corresponding to 27 mL of the solution) for children and adolescents with body weight of 35 kg or more. Switching between Valsartan tablets and Valsartan oral solution. It is not recommended to switch between Valsartan tablets and Valsartan oral solution unless clinically required. •If switching from Valsartan tablets to Valsartan oral solution is considered essential on clinical grounds, the Valsartan dose should be adjusted as described in the table below and blood pressure should be carefully monitored. The dose should be titrated based on blood pressure response and tolerability. •If switching from Valsartan oral solution to Valsartan tablets is considered clinically essential, initially the same dose in milligrams should be given. Subsequently, frequent blood pressure monitoring should be performed taking into account potential under-dosing and the dose should be titrated further based on blood pressure response and tolerability." and deletion of dosing table for oral solution under Children and adolescents 6-18 years of age. Revision of text to read "The safety and efficacy of Valsartan in children less than 1 year of age have not been established. Children less than 1 year of age must not receive Diovan." under Children less than 1 year of age. Deletion of text " Oral solution: Valsartan may be taken independently of a meal." under Method of administration.	5-Mar-21	Novartis International AG

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
21	Valsartan	Valsartan	Warnings and precautions	Revision of text to read "No dosage adjustment is required for patients with hepatic impairmentinsufficiency. Valsartan is mostly eliminated unchanged in the bile, and patients with biliary obstructive disorders showed lower valsartan clearance (see section CLINICAL PHARMACOLOGY). Particular caution should be exercised when administering valsartan to patients with biliary obstructive disorders." under Patients with hepatic impairment. Deletion of text "Valsartan oral solution contains 0.3 g sucrose per milliliter. This should be taken into account in patients with diabetes mellitus. Patients with rare hereditary problems of fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not take Valsartan oral solution as it contains sucrose. Valsartan oral solution contains methyl parahydroxybenzoate which may cause allergic reactions (possibly delayed). Valsartan oral solution contains poloxamer (188) which may cause softened stools" under Special excipients (Valsartan oral solution). Deletion of text "Valsartan oral solution is not bioequivalent to the tablet formulation and patients should not be switched unless clinically essential. For dosing recommendations in this case, see section DOSAGE AND ADMINISTRATION." under Change of pharmaceutical form.	5-Mar-21	Novartis International AG
			Adverse drug reactions	Revision of text to read "In a double-blind randomized study in 90 children aged 1 to less than 6 years, which was followed by a one-year open-label extension, two deaths and isolated cases of marked liver transaminases elevations were observed. In a second study in which 75 children aged 1 to less than 6 years were randomized, no deaths and one case of marked liver transaminase elevations occurred during a one year open-label extension. These cases occurred in a population who had significant comorbidities. A causal relationship to Valsartan has not been established. Hyperkalaemia has been observed in children and adolescents aged 6 to less than 18 years with underlying chronic kidney disease." under Pediatric population (Hypertension).		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
21	Valsartan	Valsartan	Pregnancy lactation, females and fertility males of reproductive potential	Revision of text to read "In embryofetal development studies in mice, rats and rabbits, fetotoxicity was observed in association with maternal toxicity in rats at valsartan doses of 600 mg/kg/day approximately 18 times the maximum recommended human dose on a mg/m2 basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient) and in rabbits at doses of 10 mg/kg/day approximately 0.6 times the maximum recommended human dose on a mg/m² basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). There was no evidence of maternal toxicity or fetotoxicity in mice up to a dose level of 600 mg/kg/day approximately 9 times the maximum recommended human dose on a mg/m² basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient)." under Animal data. Revision of text to read "Risk summary-It is not known whether valsartan is transferred excreted into human milk. Since valsartan was transferred excreted into the milk of lactating rats, it is not advisable to use Valsartan in breast-feeding mothers." under Lactation.	5-Mar-21	Novartis International AG
			Clinical pharmacology	Revision of text to read "Pediatric population-In a study of 26 pediatric hypertensive patients (aged 1 to 16 years) given a single dose of a suspension of valsartan (mean: 0.9 to 2 mg/kg, with a maximum dose of 80 mg), the clearance (liters/h/kg) of valsartan was comparable across the age range of 1 to 16 years and similar to that of adults receiving the same formulation (see section WARNINGS AND PRECAUTIONS in pediatric patients). Valsartan pharmacokinetics have not been investigated in pediatric patients less than 1 year of age "under Special populations-Pharmacodynamics (PD)		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
21	Valsartan	Valsartan	Clinical studies	Revision of text to read "The antihypertensive effect of valsartan have been evaluated in four randomized, double-blind clinical studies in 561 pediatric patients from 6 to less than 18 years of age and 291 pediatric patients 1 to less than 6 years of age. Renal and urinary disorders, and obesity were the most common underlying medical conditions potentially contributing to hypertension in the children and adolescents enrolled in these studies." under Pediatric population (Hypertension) Revision of text "Three clinical studies were conducted in 291 patients aged 1 to less than 6 years. No children below the age of 1 year were enrolled in these studies. In the first study (CVAL489A2307) of 90 patients, the efficacy of valsartan was confirmed compared to placebo but a dose-response could not be demonstrated. In the second study (CVAL489K2303) of 75 patients, higher doses of valsartan were associated with greater BP reductions, but the dose response trend did not achieve statistical significance and the treatment difference compared to placebo was not significant. The third study (CVAL489K2306) was a 6 week, randomized double-blind study to evaluate the dose response of valsartan in 126 children 1 to less than 6 years of age with hypertension, with or without chronic kidney disease (CKD) randomized to either 0.25 mg/kg or 4 mg/kg body weight. At endpoint, the reduction in Mean systolic blood pressure (MSBP)/ Mean diastolic blood pressure (MDBP) with valsartan 4.0 mg/kg compared to valsartan 0.25 mg/kg was 8.5/6.8 mmHg vs. 4.1/0.3 mmHg, respectively; (p=0.0157/p<0.0001). Similarly the CKD subgroup also showed reductions in MSBP/MDBP with valsartan 4.0 mg/kg compared to 0.25 mg/kg (9.2/6.5 mmHg vs 1.2/ +1.3 mmHg)." under Clinical experience in children 1 to less than 6 years of age.	5-Mar-21	Novartis International AG
			Non-clinical safety data	Revision of text to read "Valsartan had no adverse effects on the reproductive performance of male or female rats at oral doses up to 200 mg/kg/day, approximately 6 times the maximum recommended human dose on a mg/m² basis (calculations assume an oral dose of 320 mg/day and a 60-kg patient). " under Reproductive toxicity. Revision of text to read "Consequently, a clinical relevance in children < less than 1 year of age cannot be excluded, while preclinical data do not indicate a safety concern for children older than 1 year." under Pediatric population.		
			Storage	Deletion of text "Oral solution: Once opened, the bottle can be stored for up to 3 months at temperatures below 30°C." under Storage.		
			Information for patients	Deletion of text and graphics related to oral solution under this entire section.		
22	Vermox	Mebendazole	Before you use Vermox suspension	Addition of text to include "• Convulsions (seizures) have been reported, including in infants. Vermox should only be given to children under 2 year of age if your doctor has specifically prescribed it." under the subheading Warnings and precautions	14-May-21	Janssen Pharmaceuticals

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
22	Vermox	Mebendazole	How to use Vermox suspension	Addition of text to include "• Consider using Vermox oral suspension for patients such as young children who are unable to swallow the tablet. • Vermox should only be given to children under 2 year of age if your doctor has specifically prescribed it." under the subheading Using this medicine	14-May-21	Janssen Pharmaceuticals