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	Bisoprolol	Bisoprolol fumarate	Possible side effects	Revision to read under the text "You should see a doctor straight away if you experience more severe allergic reactions, which may involve face, neck, tongue, mouth or throat swelling, or difficulty breathing."	5/10/2022	Novartis
			How to store Bisoprolol	Revision of text to read "Do not use the medicine packed in bottles after 6 months after first opening the bottle"		
2	Cataflam 50mg	Diclofenac potassium 50mg tablet	Dosage regimen and administration	Insertion of subtitle " Renal impairment" under title Special populations	5/10/2022	Novartis
				Insertion of text under subtitle Renal impairment to read" Cataflam is contraindicated in patients with renal failure (GFR <15 mL/min/1.73m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Cataflam to patients with renal impairment(see section WARNINGS AND PRECAUTIONS)."		
				Insertion of subtile "Hepatic impairment" under title Special populations		
				Insertion of text under subtitle Hepatic impairment to read "Cataflam is contraindicated in patients with hepatic failure(see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Cataflam to patients with mild to moderate hepatic impairment(see section WARNINGS AND PRECAUTIONS)."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Cataflam 50mg	Diclofenac potassium 50mg tablet	Contraindications	Revsion of text to read"•Known hypersensitivity to the active substance or any of the other excipients. •Active gastric or intestinal ulcer, bleeding or perforation (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS). •Last trimester of pregnancy (see section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL). •Hepatic failure. •Renal failure (GFR <15 mL/min/1.73 m2). •Severe cardiac failure (see section WARNINGS AND PRECAUTIONS). •Like other non-steroidal anti-inflammatory drugs (NSAIDs), Cataflam is also contraindicated in patients in whom the use of acetylsalicylic acid or other NSAIDs can precipitate asthma, angioedema, urticaria, or acute rhinitis (i.e., NSAID-induced cross-reactivity reactions) (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS)."	5/10/2022	Novartis
			Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of title to read" Pregnancy,Lactation, Females and Males of Reproductive Potential"		
				Revision of text under Pregnancy with subtitle Risk Summary to read"There are insufficient data on the use of diclofenac in pregnant women. Some epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy, however the overall data are inconclusive. Diclofenac has been shown to cross the placental barrier in humans. Use of NSAIDs, including diclofenac, can cause uterine inertia, premature closure of the fetal ductus arteriosus and fetal renal impairment leading to oligohydramnios. Because of these risks, Cataflam should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. In addition, Cataflam should not be used during the third trimester of pregnancy (see section CONTRAINDICATIONS). In animal reproduction studies, no evidence of teratogenicity was observed in mice, rats, or rabbits given diclofenac daily during the period of organogenesis at doses up to approximately 0.41, 0.41, and 0.81 times, respectively, the maximum recommended human dose (MRHD) of Cataflam, despite the presence of maternal and fetal toxicity (see Animal data)."		
				Insertion of subtitle "Clinical Considerations"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Cataflam 50mg	Diclofenac potassium 50mg tablet	Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of text under Fetal Adverse Drug Reactions with subtitle Premature Closure of Fetal Ductus Arteriosus to read"As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of premature closure of the fetal ductus arteriosus (see section CONTRAINDICATIONS)."	5/10/2022	Novartis
				Revision of text under Fetal Adverse Drug Reactions with subtitle Oligohydramnios/Fetal Renal Impairment to read"Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. If an NSAID is necessary from the 20th week gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible (see section DOSAGE REGIMEN AND ADMINISTRATION). If Cataflam treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Cataflam and follow up according to clinical practice."		
				Revision of text under Fetal Adverse Drug Reactions with subtitle Labor or Delivery to read"There are no studies on the effects of Cataflam during labor or delivery. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia (see section CONTRAINDICATIONS). In animal studies, NSAIDS, including diclofenac, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth."		
				Insertion of subtitle" Data"		
				Revision of text under Human Data with subtitle Premature Closure of Fetal Ductus Arteriosus to read"Published literature reports that the use of NSAIDs during the third trimester of pregnancy may cause premature closure of the fetal ductus arteriosus."		
				Revision of text under Human data with subtitle Oligohydramnios/Fetal Renal Impairment to read"Published studies and post-marketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal impairment leading to oligohydramnios. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Cataflam 50mg	Diclofenac potassium 50mg tablet	Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of subtitle Breastfeeding to read"Lactation" Revision of text under Females amd males of reproductive potential with subtitle Male Fertility to read"There is no human data on the effect of Cataflam on male fertility. Diclofenac administered to male and female rats at 4 mg/kg/day (approximately 0.16 times the MRHD based on BSA comparison) did not affect fertility."	5/10/2022	Novartis
3	Diclofenac Sandoz	Diclofenac sodium	Pregnancy and breast-feeding	Revision of text to read "If pregnancy is diagnosed during use of Diclofenac Sandoz , the doctor should be informed. You may use Diclofenac Sandoz in the first and second 'thirds' of pregnancy only after consulting your doctor. If use of Diclofenac Sandoz is necessary between the 20th week and end of the second 'third' of pregnancy, it is advisable to use the lowest dose possible and for as short a time as possible. Using it beyond 48 hours may require your doctor monitoring your pregnancy for reduced amniotic fluid. In the last 'third' of pregnancy, Diclofenac Sandoz must not be used without your doctor's go ahead and possible fetal monitoring by ultrasound due to an increased risk of complications for mother and child."under sub heading pregnancy	19/10/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Flotac	Diclofenac Resinate	Dosage Regimen and Administration	Insertion of subheading "Renal impairment" Insertion of text "Flotac is contraindicated in patients with renal failure (GFR <15 mL/min/1.73m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Flotac to patients with renal impairment (see section WARNINGS AND PRECAUTIONS)" under the subheading "renal impairment". Insertion of subheading "Hepatic impairment" Insertion of text "Flotac is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren Resinate to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)" under the subheading "hepatic impairment". Deletion of subheading "Renal impairment" under the subtitle "Established cardiovascular disease or significant cardiovascular risk factors". Deletion of text "Flotac is contraindicated in patients with renal failure (GFR <15 mL/min/1.73m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Flotac to patients with renal impairment (see section WARNINGS AND PRECAUTIONS)" under the subheading "Renal impairment". Deletion of subheading "Hepatic impairment" under the subtitle "Established cardiovascular disease or significant cardiovascular risk factors". Deletion of text "Flotac is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren Resinate to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)" under the subheading "hepatic impairment".	22/09/2022	Novartis
			Contraindications	Revision of text to read "Last trimester of pregnancy (see sections PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL)		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Flotac	Diclofenac Resinate	Interactions	Revision of subheading to read "PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL" Deletion of subheading "Women of childbearing potential" Deletion of text "There are no data to suggest any recommendations for women of childbearing potential".	22/09/2022	Novartis
6	Pasurta	Erenumabum (genetically engineered using ovarian cells of Chinese hamsters).	Warnings and precautions	Addition of text to read under the heading Constipation with serious complications "Aimovig can lead to constipation with severe complications (see «Undesirable effects»). Patients taking Aimovig should therefore be monitored for signs of severe constipation and treated clinically appropriately. Concomitant use of drugs associated with decreased gastrointestinal motility may increase the risk of severe constipation and potential complications."	13/10/2022	Novartis
			Undesirable effects	Revision of text to read "The overall population for assessing safety, including patients in the unblinded extension phase with Aimovig, consisted of 2537 patients (3040.2 patient years) who received at least one dose of Aimovig 2280 patients were treated for at least 6 months, 1320 patients received at least 12 months and 217 patients were treated for over 5 years. The overall safety profile of Aimovig remained consistent over the 5 years of unblinded treatment."		
			Immunogenicity	Revision of text to read "In the four clinical studies on migraine prophylaxis (20120178, 20120295, 20120296 and 20120297), the incidence of the development of antibodies to erenumab during the double-blind treatment phase was 6.3 % (56/884) in patients treated with 70 mg Aimovig (3 of them showed -neutralizing activity in vitro) and 2.6% (13/504) in patients treated with 140 mg (Aimovig (none of them showed neutralising activity in vitro). Taking into account the overall data from the 4 studies up to the unblinded extension phase, the incidence of the development of antibodies to erenumab was 8.0% (185/2303) in patients receiving only 70 mg or 140 mg of Aimovig throughout the study (8 of them had neutralizing activity in vitro). In an open-label study with a treatment duration of up to 256 weeks, patients who received only 70 mg or 140 mg of Aimovig throughout the study had an incidence of anti-erenumab antibody development of 11.0% (25/225) (2 of them showed neutralizing activity in vitro). The development of antibodies to erenumab did not affect the efficacy or safety of Aimovig."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Ultane	sevoflurance	Warnings and special precautions	Inclusion of new text to read under Bradycardia in Down Syndrome "Episodes of severe bradycardia and cardiac arrest, not related to underlying congenital heart disease, have been reported during anaesthesia induction with sevoflurane in paediatric patients with Down syndrome. In most cases, bradycardia improved with decreasing the concentration of sevoflurane, manipulating the airway, or administering an anticholinergic or epinephrine. During induction, closely monitor heart rate, and consider incrementally increasing the inspired sevoflurane concentration until a suitable level of anaesthesia is achieved. Consider having an anticholinergic and epinephrine available when administering sevoflurane for induction in this patient population."	25/10/2022	AbbVie (Pty) Ltd
8	Voltaren 75mg&100mg modified release tablets	Diclofenac sodium 75mg&100mg prolonged-release tablets	Dosage Regimen and Administration	Insertion of subtitle " Renal impairment" under title Special populations	5/10/2022	Novartis
				Revision of text under Renal Impairment to read"Voltaren is contraindicated in patients with renal failure (GFR <15 mL/min/1.73 m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren to patients with renal impairment (see section WARNINGS AND PRECAUTIONS). "		
				Insertion of subtitle " Hepatic impairment" under title Special populations		
				Revision of text under Hepatic Impairment to read"Voltaren is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Voltaren 75mg&100mg modified release tablets	Diclofenac sodium 75mg&100mg prolonged-release tablets	Contraindications	Revision of text to read"•Known hypersensitivity to the active substance or to any of the other excipients. •Active gastric or intestinal ulcer, bleeding or perforation (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS). •Last trimester of pregnancy (see section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL). •Hepatic failure. •Renal failure (GFR <15 mL/min/1.73 m2). •Severe cardiac failure (see section WARNINGS AND PRECAUTIONS). •Like other non-steroidal anti-inflammatory drugs (NSAIDs), Voltaren is also contraindicated in patients in whom the use of acetylsalicylic acid or other NSAIDs can precipitate asthma, angioedema, urticaria, or acute rhinitis (i.e., NSAID-induced cross-reactivity reactions) (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS).	5/10/2022	Novartis
			Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of title to read" Pregnancy,Lactation, Females and Males of Reproductive Potential"		
				Revision of text under Pregnancy with subtitle Risk Summary to read" There are insufficient data on the use of diclofenac in pregnant women. Some epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy, however the overall data are inconclusive. Diclofenac has been shown to cross the placental barrier in humans. Use of NSAIDs, including diclofenac, can cause uterine inertia, premature closure of the fetal ductus arteriosus and fetal renal impairment leading to oligohydramnios. Because of these risks, Voltaren should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. In addition, Voltaren should not be used during the third trimester of pregnancy (see section CONTRAINDICATIONS). In animal reproduction studies, no evidence of teratogenicity was observed in mice, rats, or rabbits given diclofenac daily during the period of organogenesis at doses up to approximately 0.41, 0.41, and 0.81 times, respectively, the maximum recommended human dose (MRHD) of Voltaren, despite the presence of maternal and fetal toxicity (see Animal data)."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Voltaren 75mg&100mg modified release tablets	Diclofenac sodium 75mg&100mg prolonged-release tablets	Pregnancy,Lactation, Females and Males of Reproductive Potential	Insertion of subtitle "Clinical Considerations"	5/10/2022	Novartis
				Revision of text under Fetal Adverse Drug Reactions with subtitle Premature Closure of Fetal Ductus Arteriosus to read"As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of premature closure of the fetal ductus arteriosus (see section CONTRAINDICATIONS)."		
				Revision of text under Fetal Adverse Drug Reactions with subtitle Oligohydramnios/Fetal Renal Impairment to read"Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. If an NSAID is necessary from the 20th week gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible (see section DOSAGE REGIMEN AND ADMINISTRATION). If Voltaren treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Voltaren and follow up according to clinical practice."		
				Revision of text under Fetal Adverse Drug Reactions with subtitle Labor or Delivery to read"There are no studies on the effects of Voltaren during labor or delivery. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia (see section CONTRAINDICATIONS). In animal studies, NSAIDS, including diclofenac, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth."		
				Insertion of subtitle" Data"		
				Revision of text under Human Data with subtitle Premature Closure of Fetal Ductus Arteriosus to read"Published literature reports that the use of NSAIDs during the third trimester of pregnancy may cause premature closure of the fetal ductus arteriosus."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Voltaren 75mg&100mg modified release tablets	Diclofenac sodium 75mg&100mg prolonged-release tablets	Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of text under Human data with subtitle Oligohydramnios/Fetal Renal Impairment to read"Published studies and post-marketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal impairment leading to oligohydramnios. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug." Revision of subtitle Breastfeeding to read"Lactation" Revision of text under Females amd males of reproductive potential with subtitle Male Fertility to read"There is no human data on the effect of Voltaren on male fertility. Diclofenac administered to male and female rats at 4 mg/kg/day (approximately 0.16 times the MRHD based on BSA comparison) did not affect fertility."	5/10/2022	Novartis
9	Voltaren Suppository.	Diclofenac sodium	Dosage regimen and administration	Revision of text to read under special population "Voltaren is contraindicated in patients with renal failure (GFR <15 mL/min/1.73 m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren to patients with renal impairment (see section WARNINGS AND PRECAUTIONS)" subheading renal impairment. Revision of read under special population "Voltaren is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltaren to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)."subheading hepatic impairment.	5/10/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Voltaren Suppository.	Diclofenac sodium	Pregnancy. Lactation, Females and Males of Reproductive potential	Revision of text to read under heading Pregnancy " Diclofenac has been shown to cross the placental barrier in humans. Use of NSAIDs, including diclofenac, can cause uterine inertia, premature closure of the fetal ductus arteriosus and fetal renal impairment leading to oligohydramnios. Because of these risks, Voltaren should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. In addition, Voltaren should not be used during the third trimester of pregnancy (see section CONTRAINDICATIONS)." Deletion of text to read under heading Pregnancy " Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia and/or premature closure of the ductus arteriosus (see sections CONTRAINDICATIONS and NON-CLINICAL SAFETY DATA	5/10/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Voltaren Suppository.	Diclofenac sodium	Clinical consideration	Revision of text to read under fetal adverse drug reactions "As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of premature closure of the fetal ductus arteriosus (see section CONTRAINDICATIONS). "sub heading premature closure of fetal ductus arteriosus. Revision of text to read under subheading oligohydramnios/fetal renal impairment "Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. If an NSAID is necessary from the 20th week gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible (see section DOSAGE REGIMEN AND ADMINISTRATION). If Voltaren treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Voltaren and follow up according to clinical practice." Revision of text to read under subheading labor or delivery "There are no studies on the effects of Voltaren during labor or delivery. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia (see section CONTRAINDICATIONS). In animal studies, NSAIDS, including diclofenac, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth." Revision of text to read under subheading human data "Diclofenac was detected in a low concentration (100 ng/mL) in breast milk in one nursing mother treated orally with a diclofenac salt of 150 mg/day. The estimated dose ingested by an infant consuming breast milk is equivalent to 0.03 mg/kg/day."	5/10/2022	Novartis
10	Voltfast 50mg	Diclofenac potassium 50mg powder	Dosage regimen and administration	Insertion of subtitle " Renal impairment" under title Special populations Revision of text under Renal Impairment to read"Voltfast is contraindicated in patients with renal failure (GFR <15 mL/min/1.73m2) (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with renal impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltfast to patients with renal impairment (see section WARNINGS AND PRECAUTIONS)." Insertion of subtitle " Hepatic impairment" under title Special populations	6/10/2022	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Volfast 50mg	Diclofenac potassium 50mg powder	Contraindications	Revision of text under Hepatic Impairment to read"Voltfast is contraindicated in patients with hepatic failure (see section CONTRAINDICATIONS). No specific studies have been carried out in patients with hepatic impairment, therefore, no specific dose adjustment recommendations can be made. Caution is advised when administering Voltfast to patients with mild to moderate hepatic impairment (see section WARNINGS AND PRECAUTIONS)."	6/10/2022	Novartis
				Revision of text to read"•Known hypersensitivity to the active substance or to any of the other excipients. •Active gastric or intestinal ulcer, bleeding or perforation (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS). •Last trimester of pregnancy (see section PREGNANCY, LACTATION, FEMALES AND MALES OF REPRODUCTIVE POTENTIAL). •Hepatic failure. •Renal failure (GFR <15 mL/min/1.73 m2). •Severe cardiac failure (see section WARNINGS AND PRECAUTIONS). •Like other non-steroidal anti-inflammatory drugs (NSAIDs), Voltfast is also contraindicated in patients in whom the use of acetylsalicylic acid or other NSAIDs can precipitate asthma, angioedema, urticaria, or acute rhinitis (i.e., NSAID-induced cross-reactivity reactions) (see sections WARNINGS AND PRECAUTIONS and ADVERSE DRUG REACTIONS).		
			Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of title to read" Pregnancy,Lactation, Females and Males of Reproductive Potential"		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Volfast 50mg	Diclofenac potassium 50mg powder	Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of text under Pregnancy with subtitle Risk Summary to read" There are insufficient data on the use of diclofenac in pregnant women. Some epidemiological studies suggest an increased risk of miscarriage after use of a prostaglandin synthesis inhibitor (such as NSAIDs) in early pregnancy, however the overall data are inconclusive. Diclofenac has been shown to cross the placental barrier in humans. Use of NSAIDs, including diclofenac, can cause uterine inertia, premature closure of the fetal ductus arteriosus and fetal renal impairment leading to oligohydramnios. Because of these risks, Voltfast should not be used during the first two trimesters of pregnancy unless the expected benefits to the mother outweigh the risks to the fetus. In addition, Voltfast should not be used during the third trimester of pregnancy (see section CONTRAINDICATIONS). In animal reproduction studies, no evidence of teratogenicity was observed in mice, rats, or rabbits given diclofenac daily during the period of organogenesis at doses up to approximately 0.41, 0.41, and 0.81 times, respectively, the maximum recommended human dose (MRHD) of Voltfast, despite the presence of maternal and fetal toxicity (see Animal data)."	6/10/2022	Novartis
				Insertion of subtitle "Clinical Considerations"		
				Revision of text under Fetal Adverse Drug Reactions with subtitle Premature Closure of Fetal Ductus Arteriosus to read"As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of premature closure of the fetal ductus arteriosus (see section CONTRAINDICATIONS)."		
				Revision of text under Fetal Adverse Drug Reactions with subtitle Oligohydramnios/Fetal Renal Impairment to read"Risk of fetal renal impairment with subsequent oligohydramnios has been observed when NSAIDs (including diclofenac) were used from the 20th week of pregnancy onwards. If an NSAID is necessary from the 20th week gestation to the end of the 2nd trimester, limit the use to the lowest effective dose and shortest duration possible (see section DOSAGE REGIMEN AND ADMINISTRATION). If Voltfast treatment extends beyond 48 hours, consider monitoring with ultrasound for oligohydramnios. If oligohydramnios occurs, discontinue Voltfast and follow up according to clinical practice."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Volfast 50mg	Diclofenac potassium 50mg powder	Pregnancy,Lactation, Females and Males of Reproductive Potential	Revision of text under Fetal Adverse Drug Reactions with subtitle Labor or Delivery to read"There are no studies on the effects of Voltaren during labor or delivery. As with other NSAIDs, use of diclofenac during the third trimester of pregnancy is contraindicated owing to the possibility of uterine inertia (see section CONTRAINDICATIONS). In animal studies, NSAIDS, including diclofenac, inhibit prostaglandin synthesis, cause delayed parturition, and increase the incidence of stillbirth."	6/10/2022	Novartis
				Insertion of subtitle" Data"		
				Revision of text under Human Data with subtitle Premature Closure of Fetal Ductus Arteriosus to read"Published literature reports that the use of NSAIDs during the third trimester of pregnancy may cause premature closure of the fetal ductus arteriosus."		
				Revision of text under Human data with subtitle Oligohydramnios/Fetal Renal Impairment to read"Published studies and post-marketing reports describe maternal NSAID use at about 20 weeks gestation or later in pregnancy associated with fetal renal impairment leading to oligohydramnios. These adverse outcomes are seen, on average, after days to weeks of treatment, although oligohydramnios has been infrequently reported as soon as 48 hours after NSAID initiation. In many cases, but not all, the decrease in amniotic fluid was transient and reversible with cessation of the drug."		
				Revision of subtitle Breastfeeding to read"Lactation"		
				Revision of text under Females amd males of reproductive potential with subtitle Male Fertility to read"There is no human data on the effect of Voltfast on male fertility. Diclofenac administered to male and female rats at 4 mg/kg/day (approximately 0.16 times the MRHD based on BSA comparison) did not affect fertility."		