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	Aspirin Cardio 100mg	Acetylsalicylic acid	Preganacy and Lactation	Addition of text to include "Narrowing of the ductus arteriosus has been reported after treatment in the second trimester, which resolved in most cases after treatment was discontinued." Under sub title Pregnancy Addition of text to include "Consider prenatal monitoring for stenosis of the ductus arteriosus after taking acetylsalicylic acid from 20 weeks of pregnancy. Discontinue acetylsalicylic acid treatment if stenosis of the ductus arteriosus occurs." Under sub title Pregnanacy for first and second trimeter	9/2/2024	Bayer
2	Benylin Daytime Flu	Pseudoephedrine hydrochloride 30mg Ibuprofen 200mg	Special warnings and precautions for use	Addition of text to read "NSAIDs, such as BENYLIN DAYTIME FLU TABLETS, is associated with an increased risk of renal tubular acidosis (RTA) and hypokalaemia."	31/01/2024	Johnson & Johnson (PTY) Ltd
			Fertility, pregnancy and lactation	Addition of text to read "This may occur shortly after treatment initiation and is usually reversible upon discontinuation." Under sub-section Pregnancy.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Benylin Daytime Flu	Pseudoephedrine hydrochloride 30mg Ibuprofen 200mg	Fertility, pregnancy and lactation	Addition of text to read "In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, BENYLIN DAYTIME FLU TABLETS should not be given unless clearly necessary. If BENYLIN DAYTIME FLU TABLETS is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to BENYLIN DAYTIME FLU TABLETS for several days from gestational week 20 onward. BENYLIN DAYTIME FLU TABLETS should be discontinued if oligohydramnios or ductus arteriosus constriction are found." Revision of text to read "Regular use of nonsteroidal anti-inflammatory medicines (NSAIDs) during the third trimester of pregnancy, may result in premature constriction/closure of the foetal ductus arteriosus in utero, renal dysfunction (see above), and possibly, in persistent pulmonary hypertension of the newborn, the onset of labour may be delayed, and its duration increased."	31/01/2024	Johnson & Johnson (PTY) Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
2	Benylin Daytime Flu	Pseudoephedrine hydrochloride 30mg Ibuprofen 200mg	Overdose	Addition of text to read “posterior, reversible encephalopathy syndrome, reversible cerebral vasoconstriction, syndrome.”	31/01/2024	Johnson & Johnson (PTY) Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Ca-C 1000 Effervescent	Calcium Lactate, Calcium Carbonate, Vitamin C And Gluconate	How to use Centrum Ca-C1000	Revision of text to read "Always use this medicine exactly as described in this leaflet or as your doctor or pharmacist has told you. Check with your doctor or pharmacist if you are not sure. Adults and children 7 years of age and older: the recommended dose is one effervescent tablet daily. Children from 3 to 7 years of age: the recommended dose is 1/2 effervescent tablet daily. Infants: as prescribed by your doctor. Dissolve the effervescent tablet in a glass of water (approx. 200 ml) and drink immediately. Centrum Ca-C 1000 effervescent tablet may be taken with or without food. This product is intended to complement your diet with calcium & vit C, and not for the treatment or prevention of bone conditions. Please talk to your healthcare professional to determine the appropriate requirement for calcium and Vit D for your bone conditions."	25/01/2024	Haleon

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Durogesic	Fentanyl	Side effects and DUROGESIC	Addition of text to read "This medicine contains fentanyl which is an opioid medicine. Repeated use of opioid painkillers can result in the drug being less effective (you become accustomed to it, known as drug tolerance). You may also become more sensitive to pain while using DUROGESIC. This is known as hyperalgesia. Increasing the dose of your patches may help to further reduce your pain for a while, but it may also be harmful. If you notice that your medicine becomes less effective, talk to your doctor. Your doctor will decide whether it is better for you to increase the dose or to gradually decrease your use of DUROGESIC." Under sub revised title Long-term use and tolerance Addition of text to read "Repeated use of DUROGESIC can also lead to dependence, abuse and addiction which may result in life threatening overdose. The risk of these side effects can increase with a higher dose and longer duration of use. Dependence or addiction can make you feel that you are no longer in control of how much medicine you need to use or how often you need to use it. You might feel that you need to carry on using your medicine, even when it doesn't help to relieve your pain." Under sub revised title Dependence and addiction.	26/01/2024	Janssen

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Durogesic	Fentanyl	Side effects and DUROGESIC	Addition of text to read " The risk of becoming dependent or addicted varies from person to person. You may have a greater risk of becoming dependent or addicted on DUROGESIC if: • You or anyone in your family have ever abused or been dependent on alcohol, prescription medicines or illegal drugs (“addiction”). • You are a smoker. • You have ever had problems with your mood (depression, anxiety or a personality disorder) or have been treated by a psychiatrist for other mental illness. □ If you notice any of the following signs whilst using DUROGESIC, it could be a sign that you have become dependent or addicted. • You need to use the medicine for longer than advised by your doctor. • You need to use more than the recommended dose. • You are using the medicine for reasons other than prescribed, for instance, ‘to stay calm’ or ‘help you sleep’. • You have made repeated, unsuccessful attempts to quit or control the use of the medicine.	26/01/2024	Janssen

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Durogesic	Fentanyl	Side effects and DUROGESIC	• When you stop taking the medicine you feel unwell, and you feel better once using the medicine again (‘withdrawal effects’). If you notice any of these signs, speak to your doctor to discuss the best treatment pathway for you, including when it is appropriate to stop and how to stop safely.	26/01/2024	Janssen
			How to use DUROGESIC	Addition of text to read "Before starting treatment and regularly during treatment, your doctor will also discuss with you what you may expect from using DUROGESIC, when and how long you need to take it, when to contact your doctor, and when you need to stop it (see also section 2 ‘Withdrawal symptoms when stopping DUROGESIC’).		
			More about using DUROGESIC	Addition of text to read " An overdose may also result in a brain disorder known as toxic leukoencephalopathy." Under subtitle If you use too many patches or the wrong strength patch.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Jardiance	Empagliflozin	What Jardiance is and what it is used for	Revision of text to read "Jardiance is used to treat heart failure in adult patients with symptoms due to impaired heart function" Under sub-section heart failure. Revision of text to read "Heart failure occurs when the heart is too weak or stiff and cannot work properly. This can lead to serious medical problems and need for hospital care. The most common symptoms of heart failure are feeling breathless, feeling tired or very tired all the time, and ankle swelling. Jardiance helps protect your heart from getting weaker and improves your symptoms" Under sub-section what is heart failure.	16/01/2024	Boehringer Ingelheim International
			Therapeutic indications	Addition of sub-section "Chronic kidney disease." Addition of text "Jardiance is indicated in adults for the treatment of chronic kidney disease." Under sub-section chronic kidney disease.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Jardiance	Empagliflozin	Special warnings and precautions for use	Addition of text to read "Although ketoacidosis is less likely to occur in patients without diabetes mellitus, cases have also been reported in these patients." Under sub-section Ketoacidosis. Deletion of text "For the indication of type 2 diabetes mellitus, in patients with an eGFR below 60 ml/min/1.73 m2 or CrCl <60 ml/min the daily dose of empagliflozin is limited to 10 mg (see section 4.2). Empagliflozin is not recommended when eGFR is below 30 ml/min/1.73 m2 or CrCl below 30 ml/min. For the indication of heart failure, Jardiance is not recommended in patients with eGFR<20 ml/min/1.73 m2. Empagliflozin should not be used in patients with ESRD or in patients on dialysis. There are insufficient data to support use in these patients" Under sub-section Renal impairment. Deletion of text "There is experience with empagliflozin for the treatment of diabetes in patients with chronic kidney disease (eGFR ≥30 mL/min/1.73 m2) both with and without albuminuria." Under sub-section chronic kidney disease.	16/01/2024	Boehringer Ingelheim International

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Jardiance	Empagliflozin	Undesirable effects	Addition of sub-section "chronic kidney disease" Addition of text "The EMPA-KIDNEY study included patients with chronic kidney disease (N= 6 609) treated with 10 mg empagliflozin or placebo. About 44% of the patients had type 2 diabetes mellitus. The most frequent adverse events in the EMPA-KIDNEY study were gout (empagliflozin 7.0% vs placebo 8.0%), and acute kidney injury (empagliflozin 2.8% vs placebo 3.5%) which were more frequently reported in patients on placebo." Under sub-section chronic kidney disease.	16/01/2024	Boehringer Ingelheim International
6	Keytruda	Pembrolizumab	What KEYTRUDA is and what it is used for	Addition of text to include "a kind of cancer called cervical cancer." Deletion of text "a kind of cancer called colon or rectal cancer that is determined to be microsatellite instability high (MSI-H) or mismatch repair deficient (dMMR)." Revision of text to include "KEYTRUDA is used in children and adolescents: • aged 3 years and older to treat a kind of cancer called classical Hodgkin lymphoma. • aged 12 years and older to treat a kind of cancer called melanoma	16/02/2024	MSD

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Keytruda	Pembrolizumab	What you need to know before you are given KEYTRUDA	Revision of text to include "type 1 diabetes, including diabetic ketoacidosis (acid in the blood produced from diabetes), symptoms may include feeling more hungry or thirsty than usual, need to urinate more often or weight loss, feeling tired or feeling sick, stomach pain, fast and deep breathing, confusion, unusual sleepiness, a sweet smell to your breath, a sweet or metallic taste in your mouth, or a different odour to your urine or sweat." Addition of text to include " inflammation and scarring of the bile ducts, which may include pain in the upper right part of the stomach, swelling of the liver or spleen, fatigue, itching, or yellowing of the skin or the whites of eyes (cholangitis sclerosing).” Addition of text include " inflammation of the stomach (gastritis)." Addition of text include" decreased function of the parathyroid gland, which may include muscle cramps or spasms, fatigue and weakness (hypoparathyroidism)." Addition of text to include under subtitle children and adolescent “Do not give KEYTRUDA to children under 18 years of age, except for children: • with classical Hodgkin lymphoma aged 3 years and older and • with melanoma aged 12 years and older.”	16/02/2024	MSD

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Keytruda	Pembrolizumab	Possible side effects	Addition of text to include “ • (Guillain-Barré syndrome); inflammation of the brain, which may present as confusion, fever, memory problems or seizures (encephalitis). • swelling of the optic nerve that may result in vision loss in one or both eyes, pain with eye movement, and/or loss of colour vision (optic neuritis).” Under subtitle Rare (may affect up to 1 in 1,000 people). Addition of text to include “ abnormal kidney function test; increased blood level of the liver enzyme alkaline phosphatase; increased calcium in the blood; increased bilirubin in the blood.” Under subtitle common (may affect up to 1 in 10 people).”	16/02/2024	MSD
7	Mirena 20 mcg IUS	52 mg of Levonrgestrel	Posology and method of administration	Revision of text to read Under sub section Insertion "Before insertion, the patient should be carefully examined to detect any contraindication to IUS insertion. Exclude pregnancy before insertion. Consider the possibility of ovulation and conception before using this product. Mirena is not suitable for use as a postcoital contraceptive (see sections 4.3 and 4.4 under “Medical examination and precautions”).	15/01/2024	Bayer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Mirena 20 mcg IUS	52 mg of Levonrgestrel	Posology and method of administration	Revision of text to read in table 1 "Starting Mirena with • Mirena should be inserted into the uterine cavity within 7 days of the onset of menstruation. In this case, Mirena provides contraceptive protection upon insertion and no back-up contraception is needed. • If insertion within 7 days of the onset of menstruation is not possible or the woman experiences irregular menses, Mirena may be inserted at any time during the menstrual cycle provided that the healthcare professional can reliably exclude the possibility of prior conception. However, in this case immediate contraceptive protection upon insertion is not ensured. Therefore, a barrier method of contraception should be used, or the patient should abstain from vaginal intercourse for the next 7 days to prevent pregnancy. Revision of text to read in table 1"Postpartum insertion with In addition to the instructions above (Starting Mirena): Postpartum insertions should be postponed until the uterus is fully involuted, and insertion should not be performed earlier than 6 weeks after delivery. If involution is substantially delayed, consider waiting until 12 weeks postpartum."	15/01/2024	Bayer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Mirena 20 mcg IUS	52 mg of Levonrgestrel	Posology and method of administration	Revision of text to read in table 1 "Insertion after first-trimester abortion with Mirena can be inserted immediately after first-trimester abortion. In this case, no back-up contraception is needed." Revision of text to read in table 1 "Replacing Mirena with Mirena can be replaced by a new system at any time in the menstrual cycle. In this case, no back-up contraception is needed." Revision of text to read in table 1 "Changing from another contraceptive method (e.g., combined hormonal contraceptives, implant) with • Mirena can be inserted immediately if it is reasonably certain that the woman is not pregnant. • Need for back-up contraception: If it has been more than 7 days since menstrual bleeding began, the woman should abstain from vaginal intercourse or use additional contraceptive protection for the next 7 days. Revision of text to read "After insertion, women should be re-examined after 4 to 12 weeks to check the threads and ensure that the IUS is in the correct position"	15/01/2024	Bayer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Mirena 20 mcg IUS	52 mg of Levonrgestrel	Special warnings and precautions for use	Addition of text to read under sub section precautions at time of removal "The use of excessive force or sharp instruments during removal may cause breakage of the device (see section 4.2). After removal of Mirena, the system should therefore be examined to ensure that it has been removed entirely.	15/01/2024	Bayer
			Undesirable effects	Addition of text to read " A separate study with 362 women who have used Mirena for more than 5 years showed a consistent adverse reaction profile in years 6 through 8.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
9	Pentasa 500mg, 1g Enema and 1000mg Suppositories	Mesalazine	What you need to know before you take pentasa	Revision of text to read "Mesalazine may produce red-brown urine discoloration after contact with sodium hypochlorite bleach in the toilet water. It concerns a chemical reaction between mesalazine and bleach and is harmless." Under sub section warnings and precautions. Addition of text to include "Serious skin reactions including Drug reaction with eosinophilia and systemic symptoms (DRESS syndrome),Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) have been reported in association with mesalazine treatment." Under sub section warnings and precautions, take special care with this medicine.	11/1/2024	Ferring pharmaceuticals
			Possible Side effects	Revision of text to read "reddish non-elevated, target-like or circular patches on the trunk, often with central blisters, skin peeling, ulcers of mouth, throat, nose, genitals and eyes, widespread rash, fever and enlarged lymph nodes. These serious skin rashes can be preceded by fever and flu-like symptoms."		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Tazocin	Piperacillin /Tazobactam	Special warnings and precautions for use	Addition of text to include "Rhabdomyolysis has been reported with the use of piperacillin/tazobactam. If signs or symptoms of rhabdomyolysis are observed, piperacillin/tazobactam should be discontinued and appropriate therapy initiated	25/01/2024	Pfizer
			Undesirable effects	Addition of text in Table 1 under adverse drug reaction to include "rhabdomyolysis" in system organ class		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
11	Talzenna	Talazoparib tosylate	Dose modifications and reductions	Revision of text under sub title to include ”Complete blood count should be obtained prior to starting TALZENNA therapy and monitored monthly and as clinically indicated.” Revision of text in table 1 dose adjustment for adverse reactions Haemoglobin <8 g/dL under section ≥9 g/dL with Resume TALZENNA at a reduced dose.” ” Platelet count <50,000/µL ≥50,000/µL Resume TALZENNA at a reduced dose.” ” Neutrophil count <1,000/µL ≥1,500/µL Resume TALZENNA at a reduced dose.”Non-haematologic adverse reaction Grade 3 or Grade 4 ≤Grade 1 Consider resuming TALZENNA at a reduced dose or discontinue.” gBRCAm HER2-negative locally advanced or metastatic breast cancer. Revision of text in table 2 dose reduction levels for talazoparib monotherapy (breast cancer) Talazoparib dose level (breast cancer) Recommended starting dose 1mg once daily. First dose reduction 0.75 mg once daily Revision of text in Concomitant treatment with inhibitors of P-glycoprotein (P-gp) gBRCAm HER2-negative locally advanced or metastatic breast cancer	18/01/2024	Pfizer

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
12	Sinutab 3 way Tablets	Psedoephedrine hydrochloride 30mg ibuprofen 200mg	Special warnings and precautions for use	Addition of text to read SINUTAB® 3-WAY might increase the likelihood of developing renal tual acidosis (RTA) (a kidney disease where your kidneys do not remove acids from your blood into the urine as they should) and hypokalaemia (low potassium levels in your blood causing weakness, confusion, tiredness, muscle cramps or changes in the way your heart beats).	31/01/2024	Johnson & Johnson (PTY) Ltd

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
12	Sinutab 3 way Tablets	Psedoephedrine hydrochloride 30mg ibuprofen 200mg	Fertility, pregnancy and lactation	Addition of text to read "You should not take SINUTAB® 3-WAY during the first 6months of pregnancy unless absolutely necessary and advised by your doctor. If you need treatment during this period or while you are trying to get pregnant, the lowest dose for the shortest time possible should be used. It may affect your and your baby's tendency to bleed and cause labour to be later or longe than expected." Addition of text to read "If SINUTAB® 3-WAY is taken for more than a few days from 20 weeks of pregnancy onward, SINUTAB®3-WAY can cause kidney problems in your unborn baby that may lead to low levels of amniotic fluid that surrounds the baby (oligohydramnios) or narrowing of a blood vessel (ductus than a few days, your doctor may recommend additional monitoring.	31/01/2024	Johnson & Johnson (PTY) Ltd
			Undesirable effects	Adition of tex to read • Sudden onset of severe headache, nausea, vomiting, confusion, fits, visual disturbances."		