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	Aerinex	Erenumab	Dosage regimen and administration	Revision of text to read " Administration should be performed by an individual who has been trained to administer the product. To administer the 140 mg dose, give two consecutive subcutaneous injections of 70 mg each of Aerinex or one subcutaneous injection of 140 mg. " under the heading Method of administration.	04-Feb-21	Novartis
			Adverse drug reactions	Revision of text to read " Immune system disorders •Hypersensitivity reactions including rash, angioedema and anaphylactoid reactions [see section WARNINGS AND PRECAUTIONS]. Gastrointestinal disorders •Constipation with serious complications has been reported. In a majority of these cases, the onset was reported after the first dose of Aerinex; however patients have also experienced these events later on in the treatment. Many of the cases of constipation with serious complications were reported for patients who have a history of constipation or concurrently use medications associated with decreased gastrointestinal motility. In some severe cases hospitalization was required. •Oral sores (e.g., stomatitis, mouth ulceration, oral mucosal blistering) Skin and subcutaneous tissue disorders •Alopecia •Rash (e.g., rash papular, exfoliative rash, rash erythematous, urticaria, blister)" under the heading Post marketing experience.		
2	Daktarin cream	Miconazole nitrate	Driving and using machines	Addition of text under driving to read "Daktarin cream contains Benzoic Acid (E210) and Butylated hydroxyanisole (E320) This medicine contains 2 mg Benzoic acid per gram of cream, which is equivalent to 60 mg Benzoic acid in a 30 g tube of cream. Benzoic acid may increase jaundice (yellowing of the skin and eyes) in newborn babies (up to 4 weeks old) and may cause local irritation" under this section. Deletion of text under driving and using machines "Benzoic acid (E210). This can irritate your eyes, eyelids, mouth and nostrils if it comes into contact with them.	15-Feb-21	Janssen
			Possible side effects	Addition of text to read "By reporting side effects you can help provide more information on the safety of this medicine" under this section.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Gyno-Daktarin vaginal cream	Miconazole nitrate	What you need to know before you use Gyno-Daktarin cream	Revision of text to read "Gyno-Daktarin cream contains Benzoic Acid (E210) and Butylated hydroxyanisole (E320) This medicine contains 2 mg Benzoic acid (E210) and butylatedper gram of cream, which is equivalent to 30 mg Benzoic acid in a 15 g tube of cream 80 mg Benzoic acid in a 40 g tube of cream 156 mg Benzoic acid in a 78 g tube of cream Benzoic acid may cause local irritation. Butylated hydroxyanisole (E320). TheseThis can irritate yourcause local skin, eyes, eyelids, mouth and nostrils if they come into reactions (e.g. contact with them.dermatitis), or irritation to the eyes and mucous membranes" under this section.	15-Feb-21	Janssen
			How to use Gyno-Daktarin cream, For infections of the vagina	Revision of text to read "Your doctor may suggest treatment over 7 days: • Insert the cream into the vagina once daily before bedtime for 7 days " under this section.		
			Possible side effects	Addition of text to read "By reporting side effects you can help provide more information on the safety of this medicine" under this section.		
4	Jardiance	Empagliflozin	Therapeutic indications	Revision of texts to read "Jardiance is a member of a group of medicines called sodium glucose co-transporter-2 (SGLT2) inhibitors". Addition of texts to read "This medicine can also help prevent heart disease".	15-Feb-21	Boehringer Ingelheim
			Warnings and Precautions	Revision and addition of texts to read "if you have serious kidney or liver problems – your doctor may ask you to take a different medicine. Might be at risk of dehydration, for example:" Addition of texts to read "Talk to your doctor immediately if you develop a combination of symptoms of pain, tenderness, redness, or swelling of the genitals or the area between the genitals and the anus with fever or feeling generally unwell. These symptoms could be a sign of a rare but serious or even life-threatening infection, called necrotising fasciitis of the perineum or Fournier´s gangrene which destroys the tissue under the skin. Fournier's gangrene has to be treated immediately".		
			Qualitative and quantitative composition	Addition of texts to read "Jardiance contains sodium: This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium free'.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
4	Jardiance	Empagliflozin	Possible side effects	Addition of texts to read "Severe allergic reaction, seen with unknown frequency (frequency cannot be estimated from the available data) Possible signs of severe allergic reaction may include: □ swelling of the face, lips, mouth, tongue, or throat that may lead to difficulty breathing or swallowing)". Deletion of texts that read "severe allergic reaction (may include swelling of the face, lips, mouth, tongue, or throat that may lead to difficulty breathing or swallowing)". Addition of texts under side effects not known to include "necrotising fasciitis of the perineum or Fournier´s gangrene, a serious soft tissue infection of the genitals or the area between the genitals and the anus Addition of texts in paragraph 3 to include " or in combination with other medicinal products for the treatment of diabetes,"	15-Feb-21	Boehringer Ingelheim

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Mircera	Methoxy polyethylene glycol-epoetin beta	Dosage and administration	Addition of text to read "As recommended in current guidelines, the rate of increase in Hb and the target Hb should be determined for each patient individually. In CKD patients, the aim of treatment is to reach a target Hb level of 10-12 g/dl. Patients should be monitored closely to ensure that the lowest effective dose of Mircera is used to provide adequate control of the symptoms of anaemia." under the sub-heading Treatment of symptomatic anemia in CKD patients. Revision of text to read "Patients not on dialysis – The recommended starting dose is 1.2 µg/kg body weight administered once monthly as a single subcutaneous injection. Alternatively a starting dose of 0.6 µg/kg body weight can be administered once every two weeks as a single i.v. or s.c. injection. Patients on dialysis –The starting dose of 0.6 µg/kg body weight can be administered once every two weeks as a single i.v. or s.c. injection. The 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 at monthly intervals until the 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 is increasing and approaching 12 g/dl (7.45 mmol/l), 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. A hemoglobin decrease of approximately 0.35 g/dl (0.22 mmol/l) per week is expected after treatment interruption. Dose adjustments should not be made more than once a month. In patients treated once every two weeks whose hemoglobin concentration exceeds the target range, MIRCERA can be administered once monthly at double the dose previously administered once every two weeks." under the sub-heading Patients not currently treated with an erythropoiesis-stimulating agent (ESA).	15-Jan-21	Roche

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Mircera	Methoxy polyethylene glycol-epoetin beta	Dosage and administration	Revision of text to read " In patients currently treated with an ESA, MIRCERA can be administered once a month as a single intravenous or subcutaneous injection. The starting dose of MIRCERA is calculated on the basis of the weekly ESA dose previously administered at the time of the treatment switch, as described in Table 1. The first injection should start on the date scheduled in the previous administration regime comprising darbepoetin alfa or epoetin. If a dose adjustment is required to maintain the target hemoglobin concentration above 10 g/dl (6.21 mmol/l), the monthly dose may be increased by approximately 25%. If the rise in hemoglobin levels exceeds 2 g/dl (1.24 mmol/l) in one month or if the hemoglobin level exceeds 12 g/dl (7.45 mmol/l), 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. A hemoglobin decrease of approximately 0.35 g/dl (0.22 mmol/l) per week is expected after treatment interruption. Dose adjustments should not be made more than once a month." under the sub-heading Patients currently treated with an erythropoiesis-stimulating agent (ESA). Revision of text to read " Due to limited In the absence of safety and efficacy data, no dosage recommendations can be givenMIRCERA is not recommended for use in children and adolescentspatients under 18 years of age." under the sub-heading Use in children.	15-Jan-21	Roche

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Mircera	Methoxy polyethylene glycol-epoetin beta	Warnings and precautions	Revision of text to read "To ensure effective erythropoiesis, iron status should be determined in all patients before and during treatment. As a rule, supplemental iron therapy should be given in accordance with current treatment guidelines. Failure to respond to MIRCERA therapy should prompt an immediate search for causative factors. Deficiencies of iron, folic acid or vitamin B12 reduce the efficacy of ESAs and should therefore be corrected. Intercurrent infections, inflammatory or traumatic episodes, occult blood loss, hemolysis, severe aluminum toxicity, underlying hematological disease or myelofibrosis may also compromise the erythropoietic response. A reticulocyte count should be considered part of the bone marrow work-up. If all the conditions mentioned have been excluded and the patient has a sudden drop of hemoglobin associated with reticulocytopenia and antierythropoietin antibodies, bone marrow examination for erythroblastopenia (pure red cell aplasia [PRCA]) should be considered. If PRCA is diagnosed, it is mandatory to discontinue MIRCERA administration and withhold all other ESAs." under the sub-heading Iron supplementation. Addition of text to read " SCAR Severe cutaneous adverse reactions (SCARs) including Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), which can be life-threatening or fatal, have been reported in association with epoetin treatments. More severe cases have been observed with long-acting epoetins. At the time of prescription, patients should be advised of the signs and symptoms and monitored closely for skin reactions. Typical signs include fever, a spreading painful rash that is often preceded by fever and flu-like symptoms, blistering, and inflammation of the eyes and mucous membranes. If signs and symptoms suggestive of such hypersensitivity reactions appear, Mircera should be discontinued immediately. If a patient has developed a severe skin reaction such as SJS or TEN due to the use of Mircera, treatment with Mircera must not be restarted in this patient at any time." under this section. Revision of text to read "Misuse by non-anaemic persons (e.g. for doping) may lead to an excessive increase in hemoglobin levels. This carries a risk of life-threatening cardiovascular complications (risk of thrombosis due to hemoconcentration in erythrocytosis). Hemoglobin concentration: in CKD patients the maintenance hemoglobin concentration should not persistently exceed the upper limit of the target hemoglobin concentration recommended under Dosage and administration. In clinical trials an increased risk of death and serious cardiovascular events was observed when ESAs were used to achieve a target hemoglobin level exceeding 12 g/dl (7.5 mmol/l). Controlled clinical trials have not shown significant benefits attributable to the administration of epoetins when the hemoglobin concentration is increased beyond the level necessary to control symptoms of anemia and avoid blood transfusion." under the sub-heading Misuse.	15-Jan-21	Roche

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
5	Mircera	Methoxy polyethylene glycol-epoetin beta	Undesireable effects	Addition 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." under this section. Addition of "skin exfoliation, erythema multiforme, Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) as adverse reactions with frequency rRare under the System Organ Class Skin and subcutaneous disorders under the sub-sub-heading Clinical-trial experience. Revision of text to read "Platelet counts below 100 × 109/l were observed in 7.5% of patients treated with MIRCERA and in 4.4% of those receiving another ESA. The safety profile in the paediatric population was consistent with that in adults." under the sub-heading Clinical-trial experience.	15-Jan-21	Roche
			Properties and effects	Addition of text to read "Paediatric patients A phase II, dose-finding, open-label, repeated-dose, multicentre study was conducted in 64 paediatric haemodialysis patients (5 to 17 years old) with CKD to determine the effective starting dose of Mircera i.v. when switching from maintenance treatment with another ESA (epoetin alfa/beta or darbepoetin alfa). The primary efficacy endpoint in this study (change in Hb concentration [g/dl] between the baseline and evaluation periods) has been met." under the heading Mechanism of action and pharmacodynamics.		
			Pharmacokinetics	Addition of text to read "Paediatric patients The pharmacokinetics of Mircera were studied in 64 paediatric CKD patients (5 to 17 years old) receiving haemodialysis. At steady state (after the third dose of Mircera), a Cmax of 66.1 ng/ml and AUC0 tau of 7170 ng.hr/ml (both geometric means) were measured as the maximum observed exposure. Subsequently, Mircera serum concentrations declined with an apparent mean half-life of approximately 121 to 147 hours (geometric mean) in a manner similar to that in adults." under this section.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
6	Nizoral cream	Ketoconazole	Posology and method of administration	Revision of text to read "Cutaneous candidosis, tinea corporis, tinea cruris, tinea manus, tinea pedis and tinea (pityriasis) versicolor: It is recommended that Nizoral 2% cream be applied once or twice daily to cover the affected and immediate surrounding area" under this section. Addition of text to read "The usual duration of treatment is: tinea versicolor 2–3 weeks, yeast infections 2-3 weeks, tinea cruris 2-4 weeks, tinea corporis 3–4 weeks, tinea pedis 4-6 weeks" under this section Revision of text to read "Seborrheic dermatitis: Nizoral 2% cream should be applied to the affected areas once or twice daily. Nizoral 2% cream should be applied to the affected areas once or twice daily., depending on the severity of the infection. The usual initial duration of treatment in seborrheic dermatitis is 2 to 4 weeks. Maintenance therapy can be applied intermittently (once weekly) in seborrheic dermatitis. Treatment should be continued until a few days after the disappearance of all symptoms" under sub-heading Seborrheic dermatitis. Revision of sub -heading to read paediatric patients. Addition of text to read "The safety and efficacy of Nizoral 2% cream in children (17 years of age and younger) has not been established." under sub heading paediatric patients.	15-Feb-21	Janssen
			How to store Nizoral cream	Revision text to read "Store the cream in its original packaging. Store below 30 ºC under this section.		
			Contents of the pack and other information	Addition of text to read "Nizoral cream comes in a tube containing 15 g or 30 g of white cream. Not all pack sizes may be marketed" under this section.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
7	Trajenta	Linagliptin	Possible side effects	Addition of texts in paragraph 3 to include " or in combination with other medicinal products for the treatment of diabetes," Revision of texts to read " Some patients have experienced inflammation of the pancreas (pancreatitis; frequency rare, may affect up to 1 in 1000 people) while taking Trajenta alone or in combination with other medicinal products for the treatment of diabetes. Revision of texts to read "Some patients have had the following side effects while taking Trajenta alone or in combination with other medicinal products for the treatment of diabetes: □ Common: level of lipase in the blood increased. □ Uncommon: inflamed nose or throat (nasopharyngitis), cough, constipation (in combination with insulin), level of amylase in the blood increased. Deletion of texts that read "Some patients have had the following side effects while taking Trajenta and metformin: Common: level of lipase in the blood increased. Uncommon: inflamed nose or throat (nasopharyngitis), allergic reactions, (hypersensitivity), cough, level of amylase in the blood increased. Deletion of texts that read "Some patients have had the following side effects while taking Trajenta and insulin: Common: level of lipase in the blood increased. Uncommon: inflamed nose or throat (nasopharyngitis), allergic reactions (hypersensitivity), cough, pancreatitis, constipation. Not known: level of amylase in the blood increase". Deletion of texts that read "Some patients have had the following side effects while taking Trajenta, metformin and a sulphonylurea: □ Common: level of lipase in the blood increased. □ Uncommon: allergic reactions (hypersensitivity), level of amylase in the blood increased. □ Not known: inflamed nose or throat (nasopharyngitis), cough. Deletion of texts that read "Some patients have had the following side effects while taking Trajenta, metformin and empagliflozin: □ Common: level of lipase in the blood increased. □ Uncommon: level of amylase in the blood increased. □ Not known: inflamed nose or throat (nasopharyngitis), allergic reactions (hypersensitivity), cough.	12-Nov-21	Boehringer Ingelheim

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
8	Twynsta	Telmisartan/Amlodipine	Warnings and precautions for use	Addition of texts under do not take Twynsta to read "if you have narrowing of the aortic heart valve (aortic stenosis) or cardiogenic shock (a condition where your heart is unable to supply enough blood to the body). • if you suffer from heart failure after a heart attack. Addition of texts to include "if you are elderly and your dose needs to be increased" under Talk to your doctor before taking Twynsta.	10-Feb-21	Boehringer Ingelheim
			Interactions	Addition of texts to include "St. John's wort, Dantrolene (infusion for severe body temperature abnormalities), Medicines used to alter the way your immune system works (e.g. sirolimus, temsirolimus and everolimus)".		
			Qualitative and quantitative composition	Addition of texts to read "Twynsta contains sodium • This medicine contains less than 1 mmol sodium (23 mg) per tablet, that is to say essentially 'sodium-free".		
9	Voltaren	Diclofenac sodium	Exciepients	Deletion of text "Printing ink:Iron oxide black, Shellac" from text under the heading "Tablet coating for 100 mg"	02-Feb-21	Novartis

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Xeloda	Capecitabine	Dosage and Administration	Movement of texts " Combination therapy; Treatment of advanced or metastatic gastric cancer, oesophageal cancer or cancer of the gastro-oesophageal junction: In combination with oxaliplatin and epirubicin- The recommended dose of Xeloda is 625 mg/m2 twice daily with no treatment break for 24 weeks in combination with oxaliplatin 130 mg/m2 (every 3 weeks) and epirubicin 50 mg/m2 (every 3 weeks). For detailed information on premedication to maintain adequate hydration and antiemesis before oxaliplatin administration, see the prescribing information on oxaliplatin. Treatment of HER2-positive metastatic adenocarcinoma of the stomach or gastro-oesophageal junction: In combination with Herceptin and cisplatin- Following Herceptin and cisplatin (80 mg/m2) given as a 2-hour intravenous infusion, treatment is started on the same day with Xeloda 1000 mg/m2 twice daily for two weeks, followed by a 7-day rest period, continued for 6 cycles. Detailed information on the use of Herceptin and cisplatin and on administration of a premedication can be found in the relevant prescribing information." from the heading "Dose adjustment following undesirable effects/interactions" to "Treatment of locally advanced or metastatic breast cancer" under this section.	08-Jan-21	Roche

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Xeloda	Capecitabine	Warnings and Precautions	Addition of text to read "Dihydropyrimidine dehydrogenase (DPD) deficiency: DPD activity is rate-limiting in the catabolism of 5-fluorouracil (see “Pharmacokinetics”). Patients with DPD deficiency are therefore at increased risk of fluoropyrimidine-related toxicity, including for example stomatitis, diarrhoea, mucosal inflammation, neutropenia and neurotoxicity. DPD deficiency-related toxicity usually occurs during the first cycle of treatment or after a dose increase. Complete DPD deficiency: Complete DPD deficiency is rare (0.01-0.5% of Caucasians). Patients with complete DPD deficiency are at high risk of life-threatening or fatal toxicity and must not be treated with Xeloda (see “Contraindications”). Partial DPD deficiency: Partial DPD deficiency is estimated to affect 3-9% of the Caucasian population. Patients with partial DPD deficiency are at increased risk of serious and potentially life-threatening toxicity. A reduced starting dose should be considered to limit this toxicity. DPD deficiency should be regarded as a parameter to be taken into account in conjunction with other routine measures for dose reduction. Initial dose reduction may impact the efficacy of treatment. In the absence of serious toxicity, subsequent doses may be increased with careful monitoring. Testing for DPD deficiency: Phenotype and/or genotype testing prior to the initiation of treatment with Xeloda is recommended despite uncertainties regarding optimal pre-treatment testing methods. Consideration should be given to applicable clinical guidelines. Genotypic characterisation of DPD deficiency: Pre-treatment testing for rare mutations of the DPYD gene can identify patients with DPD deficiency. The four DPYD variants c.1905+1G>A [also known as DPYD*2A], c.1679T>G [DPYD*13], c.2846A>T and c.1236G>A/HapB3 can cause complete absence or reduction of DPD enzymatic activity. Other rare variants may also be associated with an increased risk of severe or life-threatening toxicity. Certain homozygous and compound heterozygous mutations in the DPYD gene locus (e.g. combinations of the four variants with at least one allele of c.1905+1G>A or c.1679T>G) are known to cause complete or near-complete absence of DPD enzymatic activity. Patients with certain heterozygous DPYD variants (including c.1905+1G>A, c.1679T>G, c.2846A>T and c.1236G>A/HapB3 variants) have increased risk of serious toxicity when treated with fluoropyrimidines.	08-Jan-21	Roche
10	Xeloda	Capecitabine	Warnings and Precautions	Addition of text to read"The frequency of the heterozygous c.1905+1G>A genotype in the DPYD gene in Caucasian patients is around 1%, 1.1% for c.2846A>T, 2.6-6.3% for c.1236G>A/HapB3 variants and 0.07-0.1% for c.1679T>G. Data on the frequency of these four DPYD variants in other populations than Caucasian is limited. At present the four DPYD variants (c.1905+1G>A, c.1679T>G, c.2846A>T and c.1236G>A/HapB3) are assumed to be virtually absent in populations of African (-American) or Asian origin. "under this section.	08-Jan-21	Roche

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
10	Xeloda	Capecitabine	Warnings and Precautions	Deletion of text "Rare cases of unexpected severe toxicity associated with 5-FU (e.g. stomatitis, diarrhea, mucosal inflammation, neutropenia and neurotoxicity) have been attributed to a deficiency of DPD activity. Patients with low or absent DPD activity, an enzyme involved in fluorouracil degradation, are at increased risk of severe, life-threatening or fatal adverse reactions caused by fluorouracil, and are contraindicated from using Xeloda (see Contraindications). Such patients with certain homozygous or certain compound heterozygous mutations in the DPYD gene locus that cause complete or near-complete absence of DPD activity have the highest risk of life-threatening or fatal toxicity and should not be treated with Xeloda. No dose has been proven safe for patients with complete absence of DPD activity. Patients with certain heterozygous DPYD variants (e.g. DPYD*2A variant) that may cause partial DPD deficiency have been shown to be at increased risk of severe toxicity when treated with capecitabine. Patients with partial DPD deficiency in whom the benefits of Xeloda are considered to outweigh the risks (taking into account the possible suitability of an alternative non-fluoropyrimidine chemotherapeutic regimen) must be treated with extreme caution, initially with a substantial dose reduction and frequent subsequent monitoring and dose adjustment according to toxicity. Testing for DPD deficiency should be considered, based on local availability and current guidelines. In patients with unrecognized DPD deficiency treated with capecitabine, as well as in patients who test negative for specific DPYD variants, life-threatening toxicities manifesting as overdose may occur. In the event of grade 2–4 acute toxicity, treatment must be discontinued immediately. Permanent discontinuation should be considered based on clinical assessment of the onset, duration and severity of the observed toxicities (see Overdose)." from this section.	08-Jan-21	Roche
11	Zytiga 250mg	Abiraterone acetate	Undesirable effects	Addition of text to read "anaphylactic reactions under the System Organ class Immune system disorders as an adverse reaction with frequency - not known" in Table 1 under this section.	15-Feb-21	Janssen
			Interaction with other medicinal products and other forms of interaction	Revision of text to read "In a CYP2C8 drug-drug interaction trial in healthy subjects, the AUC of pioglitazone was increased by 46% and the AUCs for M-III and M-IV, the active metabolites of pioglitazone, each decreased by 10% when pioglitazone was given together with a single dose of 1,000 mg abiraterone acetate. Patients should be monitored for signs of toxicity related to a CYP2C8 substrate with a narrow therapeutic index if used concomitantly. Examples of medicinal products metabolised by CYP2C8 include pioglitazone and repaglinide (see section 4.4)." under this section.		
			Special warnings and precautions for use	Addition of text to read "Hypoglycaemia- Cases of hypoglycaemia have been reported when ZYTIGA plus prednisone/prednisolone was administered to patients with pre-existing diabetes receiving pioglitazone or repaglinide (see section 4.5); therefore, blood sugar should be monitored in patients with diabetes."under this section.		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
Label Updates						
1	Daktarin Oral Gel	Miconazole	Before you use Daktarin oral gel	Revision of text to read "Daktarin oral gel contains 0.00773 g of alcohol (ethanol) in each 1 g which is equivalent to 0.00773 mg/mg (0.773 % w/w). The amount in 1 g is equivalent to less than 1 mL beer or 1 mL wine. The small amount of alcohol in this medicine will not have any noticeable effects. •Daktarin oral gel contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium-free'." under the heading Important information about some of the ingredients of Daktarin oral gel.	05-Jan-21	Janssen
2	Motilium	Domperidone	Warnings and Precautions	Revision of text to read "•Each orodispersible tablet contains 0,75 mg aspartame, which is a source of phenylalanine. It may be harmful if you have phenylketonuria. (PKU), a rare genetic disorder in which phenylalanine builds up because the body cannot remove it properly" •The film-coated tablets contain lactose (a type of sugar). If you have been told by your doctor that you have an intolerance to some sugars, contact your doctor before using this medicinal product. •Each film coated tablet of domperidone contains less than 1 mmol sodium (23 mg) per dose, that is to say essentially 'sodium free'" under the heading What MOTILIUM contains.	03-Feb-21	Janssen
			Possible side effects	Revision of text to read " If you experience side effects, contact your doctor or pharmacist. This also applies to possible side effects not listed in this leaflet. By reporting side effects, you can help us to obtain more information on the safety of a medicine." under the heading Reporting of side effects		
			How to store this Medicine	Revision of text to read " •Keep this medicine out of the sight and reach of children. •Do not use this medicine after the expiry date which is stated on the pack. The expiry date "exp" refers to the last day of the month shown where the first two figures indicate the month, the next, the year. •Store between 15and 30 ºC , protect from light . •Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. These measures will help to protect the environment." under this section		

No.	Name of Drug	Active Ingredient(s)	Updated Section	Update	Date of Update	MAH
3	Vermox	Mebendazole	Before you use Vermox suspension	Revision of text to read "Do not use Vermox suspension if: •You are allergic to anything in Vermox suspension (listed in section 6 below) •You are pregnant Do not use this medicine if any of the above applies to you. If you are not sure, talk to your doctor or pharmacist before using Vermox suspension." under this section. Revision of text to read "Warnings and precautions •Vermox suspension should not be given to children under 2 years of age. Vermox should only be given to younger children if your doctor has specifically prescribed it. Your doctor will decide whether Vermox is suitable for your child. You must follow the doctor's instructions carefully." under this section. Deletion of text "Ask your doctor or pharmacist for advice before taking any medicine if you are pregnant or breast-feeding." under the heading Pregnancy and breast-feeding.	03-Feb-21	Janssen
			Possible side effects	Addition of text "Feeling sick (nausea) or being sick (vomiting)" with frequency Uncommon under the heading "Tell your doctor or pharmacist if you notice any of the following side effects:" Addition of text "Inflammation of the kidneys" with frequency Rare under the heading "Tell your doctor or pharmacist if you notice any of the following side effects:" Revision of text to read "If you get any side effects, talk to your doctor, pharmacist or nurse. This includes any possible side effects not listed in this leaflet. By reporting side effects you can help provide more information on the safety of this medicine." under the heading Reporting of side effects.		
4	Zytiga	Abiraterone acetate	What you need to know before you take ZYTIGA	Revision of text to read "Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines. This is important because ZYTIGA may increase the effects of a number of medicines including heart medicines, tranquilisers, some medicines for diabetes, herbal medicines (e.g., St John's wort) and others. Your doctor may want to change the dose of these medicines. Also, some medicines may increase or decrease the effects of ZYTIGA. This may lead to side effects or to ZYTIGA not working as well as it should." under the sub-heading Other medicines and ZYTIGA.	11-Feb-21	Janssen