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Deferasirox Tablets 180 mg & 360 mg

Ferasiro

फेरासीरो

To be sold on the prescription of medical specialist

MSN

PRESCRIBING INFORMATION

WARNING: RENAL FAILURE, HEPATIC FAILURE, and GASTROINTESTINAL HEMORRHAGE

Renal Failure
- **Deferasirox can cause acute renal failure and death, particularly in patients with comorbidities and those who are in the advanced stages of their hematologic disorders.**
- **Evaluate baseline renal function prior to starting or increasing Deferasirox dosing in all patients. Deferasirox is contraindicated in adult and pediatric patients with eGFR less than 40 mL/min/1.73 m². Measure serum creatinine in duplicate prior to initiation of therapy. Monitor renal function at least monthly. For patients with baseline renal impairment or increased risk of acute renal failure, monitor renal function weekly for the first month, then at least monthly. Reduce the starting dose in patients with preexisting renal disease. During therapy, increase the frequency of monitoring and modify the dose for patients with an increased risk of renal impairment, including use of concomitant nephrotoxic drugs, and pediatric patients with volume depletion or overchelation.**

Hepatic Failure
- **Deferasirox can cause hepatic injury including hepatic failure and death.**
- **Measure serum transaminases and bilirubin in all patients prior to initiating treatment, every 2 weeks during the first month, and at least monthly thereafter.**
- **Avoid use of Deferasirox in patients with severe (Child-Pugh C) hepatic impairment and reduce the dose in patients with moderate (Child-Pugh B) hepatic impairment.**

Gastrointestinal Hemorrhage
- **Deferasirox can cause gastrointestinal (GI) hemorrhages, which may be fatal, especially in elderly patients who have advanced hematologic malignancies and/or low platelet counts.**
- **Monitor patients and discontinue Deferasirox for suspected GI ulceration or hemorrhage.**

1. GENERIC NAME
Deferasirox film coated tablets 180 mg and 360 mg

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Deferasirox film coated tablets 180 mg:
Each tablet contains
Deferasirox………180 mg

Deferasirox film coated tablets 360 mg:
Each tablet contains
Deferasirox………360 mg

3. DOSAGE FORM AND STRENGTH
Deferasirox film coated tablets 180 mg and 360 mg

4. CLINICAL PARTICULARS

4.1 Therapeutic Indications
- Indicated for the treatment of chronic iron overload due to blood transfusions (Transfusional haemosiderosis) in adult and paediatric patients (aged 2 years and above)
- For the treatment of chronic iron overload in patients with non-transfusion dependent thalassemia (NTDT) syndromes aged 10 years and older.

4.2 Posology and Method of Administration
Transfusional Iron Overload
Deferasirox therapy should only be considered when a patient has evidence of chronic transfusional iron overload. The evidence should include the transfusion of at least 100 mL/kg of packed red blood cells (e.g., at least 20 units of packed red blood cells for a 40 kg person or more in individuals weighing more than 40 kg), and a serum ferritin consistently greater than 1,000 mcg/L.
Prior to starting therapy, or increasing dose, evaluate:
- Serum ferritin level
- Baseline renal function:
  – Obtain serum creatinine in duplicate (due to variations in measurements).
  – Calculate the estimated glomerular filtration rate (eGFR). Use a prediction equation appropriate for adult patients (e.g., CKD-EPI, MDRD method) and in pediatric patients (e.g., Schwartz equations).
  – Obtain urinalyses and serum electrolytes to evaluate renal tubular function.
- Serum transaminases and bilirubin
- Baseline auditory and ophthalmic examinations

Initiating Therapy:
The recommended initial dose of Deferasirox for patients 2 years of age and older with eGFR greater than 60 mL/min/1.73 m is 14 mg per kg body weight orally, once daily. Calculate doses (mg per kg per day) to the nearest whole tablet or nearest whole sachet content for granules. Changes in weight of pediatric patients over time must be taken into account when calculating the dose.

During Therapy:
- Monitor serum ferritin monthly and adjust the dose of Deferasirox, if necessary, every 3 to 6 months based on serum ferritin trends.
- Use the minimum effective dose to achieve a trend of decreasing ferritin.
- Make dose adjustments in steps of 3.5 or 7 mg per kg and tailor adjustments to the individual patient's response and therapeutic goals.
- In patients not adequately controlled with doses of 21 mg per kg (e.g., serum ferritin levels persistently above 2,500 mcg/L and not showing a decreasing trend over time), doses of up to 28 mg per kg may be considered. Doses above 28 mg per kg are not recommended.
- Adjust dose based on serum ferritin levels:
  – If the serum ferritin falls below1,000 mcg/L at 2 consecutive visits, consider dose reduction especially if the Deferasirox dose is greater than 17.5 mg/kg/day.
  – If the serum ferritin falls below500 mcg/L, interrupt Deferasirox therapy to minimize the risk of overchelation, and continue monthly monitoring.
  – Evaluate the need for ongoing chelation therapy for patients whose conditions no longer require regular blood transfusions.
  – Use the minimum effective dose to maintain iron burden in the target range.
- Monitor blood counts, liver function, renal function and ferritin monthly.
- Interrupt Deferasirox for pediatric patients who have acute illnesses, which can cause volume depletion, such as vomiting, diarrhea, or prolonged decreased oral intake, and monitor more frequently. Resume therapy as appropriate, based on assessments of renal function, when oral intake and volume status are normal.

Iron Overload in Non-Transfusion-Dependent Thalassemia Syndromes
Deferasirox therapy should only be considered when a patient with NTDT syndrome has an LIC of at least 5 mg Fe/g dw and a serum ferritin greater than 300 mcg/L.
Prior to starting therapy, obtain:
- LIC by liver biopsy or by an FDA-cleared or approved method for identifying patients for treatment with deferasirox therapy
- Serum ferritin level on at least 2 measurements 1-month apart [see Clinical Studies (14)]
- Baseline renal function:
  – Obtain serum creatinine in duplicate (due to variations in measurements).
  – Calculate the estimated glomerular filtration rate (eGFR). Use a prediction equation appropriate for adult patients (e.g., CKD-EPI, MDRD method) and in pediatric patients (e.g., Schwartz equations).
  – Obtain urinalyses and serum electrolytes to evaluate renal tubular function.
- Serum transaminases and bilirubin.
- Baseline auditory and ophthalmic examinations

Initiating Therapy:
- The recommended initial dose of Deferasirox for patients with eGFR greater than 60 mL/min/1.73 m² is 7 mg per kg body weight orally once daily. Calculate doses (mg per kg per day) to the nearest whole tablet or nearest whole sachet content for granules.
- If the baseline LIC is greater than 15 mg Fe/g dw, consider increasing the dose to 14 mg/kg/day after 4 weeks.

During Therapy:
- Monitor serum ferritin monthly to assess the patient's response to therapy and to minimize the risk of overchelation. Interrupt treatment when serum ferritin is less than 300 mcg/L and obtain an LIC to determine whether the LIC has fallen to less than 3 mg Fe/g dw.
- Use the minimum effective dose to achieve a trend of decreasing ferritin.
- Monitor LIC every 6 months.
- After 6 months of therapy, if the LIC remains greater than 7 mg Fe/g dw, increase the dose of
- Deferasirox to a maximum of 14 mg/kg/day. Do not exceed a maximum of 14 mg/kg/day.
- If after 6 months of therapy, the LIC is 3 to 7 mg Fe/g dw, continue treatment with deferasirox at no more than 7 mg/kg/day.
- When the LIC is less than 3 mg Fe/g dw, interrupt treatment with deferasirox and continue to monitor the LIC.
- Monitor blood counts, liver function, renal function and ferritin monthly.
- Increase monitoring frequency for pediatric patients who have acute illness, which can cause volume depletion, such as vomiting, diarrhea, or prolonged decreased oral intake. Consider dose interruption until oral intake and volume status are normal.

Restart treatment when the LIC rises again to more than 5 mg Fe/g dw.

Administration
Swallow Deferasirox tablets once daily with water or other liquids, preferably at the same time each day. Take Deferasirox tablets on an empty stomach or with a light meal (contains less than 7% fat content and approximately 250 calories). Examples of light meals include 1 whole wheat English muffin, 1 packet jelly (0.5 ounces), and skim milk (8 fluid ounces) or a turkey sandwich (2 oz. turkey on whole wheat 2bread w/ lettuce, tomato, and 1 packet mustard). Do not take Deferasirox tablets with aluminium-containing antacid products. For patients who have difficulty swallowing whole tablets, Deferasirox tablets may be crushed and mixed with soft foods (e.g., yogurt or applesauce) immediately prior to use and administered orally. Commercial crushers with serrated surfaces should be avoided for crushing a single 90 mg tablet. The dose should be immediately and completely consumed and not stored for future use.

Take Deferasirox Sprinkle granules on an empty stomach or with a light meal. Administer Deferasirox Sprinkle granules by sprinkling the full dose on soft food (e.g., yogurt or applesauce) immediately prior to use and administered orally. Deferasirox Sprinkle granules should be taken once a day, preferably at the same time each day. Do not take Deferasirox Sprinkle granules with aluminium-containing antacid products.

For patients who are currently on chelation therapy with Deferasirox tablets for oral suspension and converting to Deferasirox, the dose should be about 30% lower, rounded to the nearest whole tablet or nearest whole sachet content for granules. The table below provides additional information on dosing conversion to Deferasirox.

	Deferasirox Tablets for oral suspension	Deferasirox film coated Tablets
Transfusion-Dependent Iron Overload		
Starting Dose	20 mg/kg/day	14 mg/kg/day
Titration Increments	5–10 mg/kg	3.5–7 mg/kg
Maximum Dose	40 mg/kg/day	28 mg/kg/day
Non-Transfusion-Dependent Thalassemia Syndromes		
Starting Dose	10 mg/kg/day	7 mg/kg/day
Titration Increments	5–10 mg/kg	3.5–7 mg/kg
Maximum Dose	20 mg/kg/day	14 mg/kg/day

Use in Patients with Baseline Hepatic or Renal Impairment
Patients with Baseline Hepatic Impairment
Mild (Child-Pugh A) Hepatic Impairment: No dose adjustment is necessary.
Moderate (Child-Pugh B) Hepatic Impairment: Reduce the starting dose by 50%.
Severe (Child-Pugh C) Hepatic Impairment: Avoid Deferasirox tablets.
Patients with Baseline Renal Impairment
Do not use Deferasirox in adult or pediatric patients with eGFR less than 40 mL/min/1.73 m².
For patients with renal impairment (eGFR 40-60 mL/min/1.73 m), reduce the starting dose by 50%.
Exercise caution in pediatric patients with eGFR between 40 and 60 mL/minute/1.73 m². If treatment is needed, use the minimum effective dose and monitor renal function frequently. Individualize dose titration based on improvement in renal injury.

Dose Modifications for Decreases in Renal Function While on Deferasirox
Deferasirox is contraindicated in patients with eGFR less than 40 mL/min/1.73 m².
For decreases in renal function while receiving Deferasirox, modify the dose as follows:
Transfusional Iron Overload
Adults:
If the serum creatinine increases by 33% or more above the average baseline measurement, repeat the serum creatinine within 1 week, and if still elevated by 33% or more, reduce the dose by 7 mg per kg.
Pediatric Patients (ages 2 years–17 years):
- Reduce the dose by 7 mg per kg if eGFR decreases by greater than 33% below the average baseline measurement and repeat eGFR within 1 week.
- Interrupt Deferasirox for acute illnesses, which can cause volume depletion, such as vomiting,
- Diarrhea, or prolonged decreased oral intake, and monitor more frequently. Resume therapy as appropriate, based on assessments of renal function, when oral intake and volume status are normal. Avoid use of other nephrotoxic drugs.
- In the setting of decreased renal function, evaluate the risk benefit profile of continued Deferasirox use. Use the minimum effective Deferasirox dose and monitor renal function more frequently, by evaluating tubular and glomerular function. Titrate dosing based on renal injury. Consider dose reduction or interruption and less nephrotoxic therapies until improvement of renal function. If signs of renal tubular or glomerular injury occur in the presence of other risk factors such as volume depletion, reduce or interrupt Deferasirox to prevent severe and irreversible renal injury.

All Patients (regardless of age):
Discontinue therapy for eGFR less than 40 mL/min/1.73 m².

Non-Transfusion-Dependent Thalassemia Syndromes
Adults:
- If the serum creatinine increases by 33% or more above the average baseline measurement, repeat the serum creatinine within 1 week, and if still elevated by 33% or more, interrupt therapy if the dose is 3.5 mg per kg, or reduce by 50% if the dose is 7 or 14 mg per kg.

Pediatric Patients (ages 10 years–17 years):
- Reduce the dose by 3.5 mg per kg if eGFR decreases by greater than 33% below the average baseline measurement and repeat the eGFR within 1 week.
- Increase monitoring frequency for pediatric patients who have acute illnesses, which can cause volume depletion, such as vomiting, diarrhea, or prolonged decreased oral intake. Consider dose interruption until oral intake and volume status are normal. Avoid use of other nephrotoxic drugs.
- In the setting of decreased renal function, evaluate the risk benefit profile of continued Deferasirox use. Use the minimum effective Deferasirox dose and monitor renal function more frequently, by evaluating tubular and glomerular function. Titrate dosing based on renal injury. Consider dose reduction or interruption and less nephrotoxic therapies until improvement of renal function. If signs of renal tubular or glomerular injury occur in the presence of other risk factors such as volume depletion, reduce or interrupt Deferasirox to prevent severe and irreversible renal.

All Patients (regardless of age):
- Discontinue therapy for eGFR less than 40 mL/min/1.73 m².

Dose Modifications Based on Concomitant Medications
UDP-glucuronosyltransferases (UGT) Inducers
Concomitant use of UGT inducers decreases systemic exposure. Avoid the concomitant use of strong UGT inducers (e.g., rifampicin, phenytoin, phenobarbital, ritonavir). If you must administer Deferasirox tablets or Deferasirox Sprinkle granules with a strong UGT inducer, consider increasing the initial dose by 50%, and monitor serum ferritin levels and clinical responses for further dose modification.
Bile Acid Sequestrants
Concomitant use of bile acid sequestrants decreases systemic exposure. Avoid the concomitant use of bile acid sequestrants (e.g., cholestyramine, colesevelam, colestipol). If you must administer Deferasirox tablets or Deferasirox Sprinkle granules with a bile acid sequestrant, consider increasing the initial dose by 50%, and monitor serum ferritin levels and clinical responses for further dose modification.

4.3 Contraindications
- Deferasirox is contraindicated in patients with:
- Estimated GFR less than 40 mL/min/1.73 m²
- Poor performance status
- High-risk myelodysplastic syndromes (this patient population was not studied and is not expected to benefit from chelation therapy)
- Advanced malignancies
- Platelet counts less than 50 x 10 /L
- Known hypersensitivity to deferasirox or any component of Deferasirox.

4.4 Special Warnings and Precautions for Use
Acute Kidney Injury, Including Acute Renal Failure Requiring Dialysis and Renal Tubular Toxicity Including Fanconi Syndrome
Deferasirox is contraindicated in patients with eGFR less than 40 mL/min/1.73 m². Exercise caution in pediatric patients with eGFR between 40 and 60 mL/min/1.73 m². If treatment is needed, use the minimum effective dose and monitor renal function frequently. Individualize dose titration based on improvement in renal injury. For patients with renal impairment (eGFR 40-60 mL/min/1.73 m²) reduce the starting dose by 50%.

Deferasirox can cause acute kidney injury including renal failure requiring dialysis that has resulted in fatal outcomes. Based on postmarketing experience, most fatalities have occurred in patients with multiple comorbidities and who were in advanced stages of their hematological disorders. In the clinical trials, adults and pediatric deferasirox-treated patients with no preexisting renal disease experienced dose-dependent mild, non-progressive increases in serum creatinine and proteinuria. Preexisting renal disease and concomitant use of other nephrotoxic drugs may increase the risk of acute kidney injury in adult and pediatric patients. Acute illnesses associated with volume depletion and overchelation may increase the risk of acute kidney injury in pediatric patients. In pediatric patients, small decreases in eGFR can result in increases in deferasirox exposure, particularly in younger patients with body surface area typical of patients less than age 7 years. This can lead to a cycle of worsening renal function and further increases in Deferasirox tablets for oral suspension exposure, unless the dose is reduced or interrupted. Renal tubular toxicity, including acquired Fanconi syndrome, has been reported in patients treated with deferasirox, most commonly in pediatric patients with beta-thalassemia and serum ferritin levels less than 1,500 mcg/L.

Evaluate renal glomerular and tubular function before initiating therapy or increasing the dose. Use prediction equations validated for use in adult and pediatric patients to estimate GFR. Obtain serum electrolytes and urinalysis in all patients to evaluate renal tubular function.

Monitor all patients for changes in eGFR and for renal tubular toxicity weekly during the first month after initiation or modification of therapy and at least monthly thereafter. Dose reduction or interruption may be considered if abnormalities occur in levels of markers of renal tubular function and/or as clinically indicated. Monitor serum ferritin monthly to evaluate for overchelation. Use the minimum dose to establish and maintain a low iron burden. Monitor renal function more frequently in patients with pre-existing renal disease or decreased renal function. In pediatric patients, interrupt Deferasirox during acute illnesses, which can cause volume depletion such as vomiting, diarrhea, or prolonged decreased oral intake, and monitor renal function more frequently. Promptly correct fluid deficits to prevent renal injury. Resume therapy as appropriate, based on assessments of renal function, when oral intake and volume status are normal.

Hepatic Toxicity and Failure
Deferasirox can cause hepatic injury, fatal in some patients. In Study 1, 4 patients (1.3%) discontinued deferasirox because of hepatic toxicity (drug-induced hepatitis in 2 patients and increased serum transaminases in 2 additional patients). Hepatic toxicity appears to be more common in patients greater than 55 years of age. Hepatic failure was more common in patients with significant comorbidities, including liver cirrhosis and multiorgan failure.

Acute liver injury and failure, including fatal outcomes, have occurred in pediatric deferasirox-treated patients. Liver failure occurred in association with acute kidney injury in pediatric patients at risk for overchelation during a volume-depleting event. Interrupt Deferasirox therapy when acute liver injury or acute kidney injury is suspected and during volume depletion. Monitor liver and renal function more frequently in pediatric patients who are receiving Deferasirox in the 14-28 mg/kg/day range and when iron burden is approaching normal. Use the minimum effective dose to achieve and maintain a low iron burden.

Measure transaminases [aspartate transaminase (AST) and alanine transaminase (ALT)] and bilirubin in all patients before the initiation of treatment and every 2 weeks during the first month and at least monthly thereafter. Consider dose modifications or interruption of treatment for severe or persistent elevations.

Avoid the use of Deferasirox in patients with severe (Child-Pugh C) hepatic impairment. Reduce the starting dose in patients with moderate (Child-Pugh B) hepatic impairment [see Dosage and Administration (2.4), Use in Specific Populations (8.7)]. Patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment may be at higher risk for hepatic toxicity.

Gastrointestinal (GI) Ulceration, Hemorrhage, and Perforation
GI hemorrhage, including deaths, has been reported, especially in elderly patients who had advanced hematologic malignancies and/or low platelet counts. Nonfatal upper GI irritation, ulceration and hemorrhage have been reported in patients, including children and adolescents, receiving deferasirox. Monitor for signs and symptoms of GI ulceration and hemorrhage during Deferasirox therapy, and promptly initiate additional evaluation and treatment if a serious GI adverse reaction is suspected. The risk of GI hemorrhage may be increased when administering Deferasirox in combination with drugs that have ulcerogenic or hemorrhagic potential, such as nonsteroidal anti-inflammatory drugs (NSAIDs), corticosteroids, oral bisphosphonates, or anticoagulants. There have been reports of ulcers complicated with GI perforation (including fatal outcome).

Bone Marrow Suppression
Neutropenia, agranulocytosis, worsening anemia, and thrombocytopenia, including fatal events, have been reported in patients treated with deferasirox. Pre-existing hematologic disorders may increase this risk. Monitor blood counts in all patients. Interrupt treatment with Deferasirox in patients who develop cytopenias until the cause of the cytopenia has been determined. Deferasirox is contraindicated in patients with platelet counts below 50 x 10^9/L.

Age-Related Risk of Toxicity
Elderly Patients
Deferasirox has been associated with serious and fatal adverse reactions in the postmarketing setting among adults, predominantly in elderly patients. Monitor elderly patients treated with Deferasirox more frequently for toxicity.

Pediatric Patients
Deferasirox has been associated with serious and fatal adverse reactions in pediatric patients in the postmarketing setting. These events were frequently associated with volume depletion or with continued Deferasirox tablets for oral suspension doses in the 20-40 mg/kg/day range equivalent to 14-28 mg/kg/day Deferasirox when body iron burden was approaching or in the normal range. Interrupt Deferasirox in patients with volume depletion, and resume Deferasirox when renal function and fluid volume have normalized. Monitor liver and renal function more frequently during volume depletion and in patients receiving Deferasirox in the 14-28 mg/kg/day range when iron burden is approaching the normal range. Use the minimum effective dose to achieve and maintain a low iron burden.

Overchelation
For patients with transfusional iron overload, measure serum ferritin monthly to assess the patient's response to therapy and minimize the risk of overchelation. An analysis of pediatric patients treated with Deferasirox tablets for oral suspension in pooled clinical trials (n = 158), found a higher rate of renal adverse reactions among patients receiving doses greater than 25 mg/kg/day equivalent to 17.5 mg/kg/day Deferasirox while their serum ferritin values were less than 1,000 mcg/L. Consider dose reduction or closer monitoring of renal and hepatic function, and serum ferritin levels during these periods. Use the minimum effective dose to maintain a low-iron burden.

If the serum ferritin falls below 1,000 mcg/L at 2 consecutive visits, consider dose reduction, especially if the Deferasirox dose is greater than 17.5 mg/kg/day [see Adverse Reactions (6.1)]. If the serum ferritin falls below 500 mcg/L, interrupt therapy with Deferasirox and continue monthly monitoring. Evaluate the need for ongoing chelation for patients whose conditions do not require regular blood transfusions. Use the minimum effective dose to maintain iron burden in the target range. Continued administration of Deferasirox in the 14 to 28 mg/kg/day range, when the body iron burden is approaching or within the normal range can result in life-threatening adverse reactions.

For patients with NTDT, measure LIC by liver biopsy or by using an FDA-cleared or approved method for monitoring patients receiving deferasirox therapy every 6 months on treatment. Interrupt Deferasirox administration when the LIC is less than 3 mg Fe/g dw. Measure serum ferritin monthly, and if the serum ferritin falls below 300 mcg/L, interrupt Deferasirox and obtain a confirmatory LIC.

Hypersensitivity
Deferasirox may cause serious hypersensitivity reactions (such as anaphylaxis and angioedema), with the onset of the reaction usually occurring within the first month of treatment. If reactions are severe, discontinue Deferasirox and institute appropriate medical intervention. Deferasirox is contraindicated in patients with known hypersensitivity to deferasirox products and should not be reintroduced in patients who have experienced previous hypersensitivity reactions on deferasirox products due to the risk of anaphylactic shock.

Severe Skin Reactions
Severe cutaneous adverse reactions (SCARs), including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN) and drug reaction with eosinophilia and systemic symptoms (DRESS) which could be life-threatening or fatal have been reported during deferasirox therapy. Cases of erythema multiforme have been observed. Advise patients of the signs and symptoms of severe skin reactions, and closely monitor. If any severe skin reactions are suspected, discontinue Deferasirox immediately and do not reintroduce Deferasirox therapy.

Skin Rash
Rashes may occur during Deferasirox treatment. For rashes of mild to moderate severity, Deferasirox may be continued without dose adjustment, since the rash often resolves spontaneously. In severe cases, interrupt treatment with Deferasirox. Reintroduction at a lower dose with escalation may be considered after resolution of the rash.

Auditory and Ocular Abnormalities
Auditory disturbances (high frequency hearing loss, decreased hearing), and ocular disturbances (lens opacities, cataracts, elevations in intraocular pressure, and retinal disorders) were reported at a frequency of less than 1% with deferasirox therapy in the clinical studies. The frequency of auditory adverse reactions was increased among pediatric patients, who received Deferasirox tablets for oral suspension doses greater than 25 mg/kg/day equivalent to 17.5 mg/kg/day Deferasirox when serum ferritin was less than 1,000 mcg/L.
Perform auditory and ophthalmic testing (including slit lamp examinations and dilated fundoscopy) before starting Deferasirox treatment and thereafter at regular intervals (every 12 months). If disturbances are noted, monitor more frequently. Consider dose reduction or interruption.

4.5 Drug Interactions
Aluminium-Containing Antacid Preparations
The concomitant administration of Deferasirox and Aluminium-containing antacid preparations has not been formally studied. Although deferasirox has a lower affinity for Aluminium than for iron, do not take Deferasirox with Aluminium-containing antacid preparations.

Agents Metabolized by CYP3A4
Deferasirox may induce CYP3A4 resulting in a decrease in CYP3A4 substrate concentration when these drugs are coadministered. Closely monitor patients for signs of reduced effectiveness when deferasirox is administered with drugs metabolized by CYP3A4 (e.g., alfentanil, aprepitant, budesonide, buspirone, conivaptan, cyclosporine, darifenacin, darunavir, dasatinib, dihydroergotamine, dronedarone, eletriptan, eplerenone, ergotamine, everolimus, felodipine, fentanyl, hormonal contraceptive agents, indinavir, fluticasone, lopinavir, lovastatin, lurasidone, maraviroc, midazolam, nisoldipine, pimozide, quetiapine, quinidine, saquinavir, sildenafil, simvastatin, sirolimus, tacrolimus, tolvaptan, tipranavir, triazolam, ticagrelor, and vardenafil).

Agents Metabolized by CYP2C8
Deferasirox inhibits CYP2C8 resulting in an increase in CYP2C8 substrate (e.g., repaglinide and paclitaxel) concentration when these drugs are coadministered. If Deferasirox and repaglinide are used concomitantly, consider decreasing the dose of repaglinide and perform careful monitoring of blood glucose levels. Closely monitor patients for signs of exposure related toxicity when Deferasirox is coadministered with other CYP2C8 substrates.

Agents Metabolized by CYP1A2
Deferasirox inhibits CYP1A2 resulting in an increase in CYP1A2 substrate (e.g., alosetron, caffeine, duloxetine, melatonin, ramelteon, tacrine, theophylline, tizanidine) concentration when these drugs are coadministered. An increase in theophylline plasma concentrations could lead to clinically significant theophylline induced CNS or other adverse reactions. Avoid the concomitant use of theophylline or other CYP1A2 substrates with a narrow therapeutic index (e.g., tizanidine) with Deferasirox. Monitor theophylline concentrations and consider theophylline dose modification if you must coadminister theophylline with Deferasirox. Closely monitor patients for signs of exposure related toxicity when Deferasirox is coadministered with other drugs metabolized by CYP1A2.

Agents Inducing UDP-glucuronosyltransferase (UGT) Metabolism
Deferasirox is a substrate of UGT1A1 and to a lesser extent UGT1A3. The concomitant use of Deferasirox with strong UGT inducers (e.g., rifampicin, phenytoin, phenobarbital, ritonavir) may result in a decrease in Deferasirox efficacy due to a possible decrease in deferasirox concentration. Avoid the concomitant use of strong UGT inducers with Deferasirox. Consider increasing the initial dose of Deferasirox if you must coadminister these agents together.

Bile Acid Sequestrants
Avoid the concomitant use of bile acid sequestrants (e.g., cholestyramine, colesevelam, colestipol) with Deferasirox due to a possible decrease in deferasirox concentration. If you must coadminister these agents together, consider increasing the initial dose of Deferasirox.

Busulfan
Increased exposure of busulfan was observed with concomitant use with deferasirox. Monitor plasma concentrations of busulfan when coadministered with deferasirox to allow dose adjustment of Busulfan as needed.

4.6 Use in Special Populations Use in Special Populations (such as pregnant women, lactating women, paediatric patients, geriatric patients etc.)
Pregnancy
There are no studies with the use of Deferasirox in pregnant women to inform drug-associated risks. Administration of deferasirox to rats during pregnancy resulted in decreased offspring viability and an increase in renal anomalies in male offspring at doses that were about or less than the recommended human dose on a mg/m basis. No fetal effects were noted in pregnant rabbits at doses equivalent to the human recommended dose on an mg/m basis. Deferasirox should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

The background risk of major birth defects and miscarriage for the indicated population is unknown. All pregnancies had a background risk of birth defect, loss, or other adverse outcomes.

Lactation
No data are available regarding the presence of Deferasirox or its metabolites in human milk, the effects of the drug on the breastfed child, or the effects of the drug on milk production. Deferasirox and its metabolites were excreted in rat milk. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in a breastfeeding child from deferasirox and its metabolites, a decision should be made whether to discontinue breastfeeding or to discontinue the drug, taking into account the importance of the drug to the mother.

Females and Males of Reproductive Potential
Counsel patients to use non-hormonal method(s) of contraception since Deferasirox can render hormonal contraceptives ineffective.

Paediatric Use
Transfusional Iron Overload
The safety and effectiveness of Deferasirox have been established in pediatric patients 2 years of age and older for the treatment of transfusional iron overload.
Safety and effectiveness have not been established in pediatric patients less than 2 years of age for the treatment of transfusional iron overload.
Iron Overload in Non-Transfusion-Dependent Thalassemia Syndromes
The safety and effectiveness of Deferasirox have been established in patients 10 years of age and older for the treatment of chronic iron overload with non-transfusion-dependent thalassemia (NTDT) syndromes.

Safety and effectiveness have not been established in patients less than 10 years of age with chronic iron overload in NTDT syndromes.

Pediatric approval for treatment of NTDT syndromes with liver iron (Fe) concentration (LIC) of at least 5 mg Fe per gram of dry weight and a serum ferritin greater than 300 mcg/L was based on 16 pediatric patients treated with deferasirox therapy (10 years to less than 16 years of age) with chronic iron overload and NTDT. Use of Deferasirox in these age groups is supported by evidence from adequate and well-controlled studies of deferasirox in adult and pediatric patients.

In general, risk factors for deferasirox-associated kidney injury include pre-existing renal disease, volume depletion, overchelation, and concomitant use of other nephrotoxic drugs. Acute kidney injury, and acute liver injury and failure has occurred in pediatric patients. In a pooled safety analysis, pediatric patients with higher deferasirox exposures had a greater probability of renal toxicity and decreased renal function, resulting in increased deferasirox exposure and progressive renal toxicity/kidney injury. Higher rates of renal AEs have been identified among pediatric patients receiving Deferasirox tablets for oral suspension doses greater than 25 mg/kg/day equivalent to 17.5 mg/kg/day Deferasirox when their serum ferritin values were less than 1,000 mcg/L.

Monitoring recommendations for all pediatric patients with Transfusional Iron Overload and NTDT It is recommended that serum ferritin be monitored every month to assess the patient's response to therapy and to minimize the risk of overchelation.

Monitor renal function by estimating GFR using an eGFR prediction equation appropriate for pediatric patients and evaluate renal tubular function. Monitor renal function more frequently in pediatric patients in the presence of renal toxicity risk factors, including episodes of dehydration, fever and acute illness that may result in volume depletion or decreased renal perfusion. Use the minimum effective dose.

Interrupt Deferasirox in pediatric patients with transfusional iron overload, and consider dose interruption in pediatric patients with non-transfusion-dependent iron overload, for acute illnesses, which can cause volume depletion, such as vomiting, diarrhea, or prolonged decreased oral intake, and monitor more frequently. Resume therapy as appropriate, based on assessments of renal function, when oral intake and volume status are normal. Evaluate the risk benefit profile of continued Deferasirox use in the setting of decreased renal function. Avoid use of other nephrotoxic drugs.

Geriatric Use
In elderly patients, including those with MDS, individualize the decision to remove accumulated iron based on clinical circumstances and the anticipated clinical benefit and risks of deferasirox tablets for oral suspension therapy.

Renal Impairment
Deferasirox is contraindicated in patients with eGFR less than 40 mL/min/1.73 m². For patients with renal impairment (eGFR 40 to 60 mL/min/1.73 m), reduce the starting dose by 50%. Exercise caution in pediatric patients with an eGFR between 40 and 60 mL/min/1.73 m². If treatment is needed, use the minimum effective dose with enhanced monitoring of glomerular and renal tubular function. Individualize dose titration based on improvement in renal injury.

Deferasirox can cause glomerular dysfunction, renal tubular toxicity, or both, and can result in acute renal failure. Monitor all patients closely for changes in eGFR and renal tubular dysfunction during Deferasirox treatment. If either develops, consider dose reduction, interruption or discontinuation of Deferasirox until glomerular or renal tubular function returns to baseline.

Hepatic Impairment
Avoid use in patients with severe (Child-Pugh C) hepatic impairment. For patients with moderate (ChildPugh B) hepatic impairment, reduce the starting dose by 50%. Closely monitor patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment for efficacy and adverse reactions that may require dose titration.

4.7 Effects on Ability to Drive and Use Machines
Deferasirox has minor influence on the ability to drive and use machines. Patients experiencing the uncommon adverse reaction of dizziness should exercise caution when driving or operating machines.

4.8 Undesirable Effects
Adverse reactions reported with bempedoic acid are displayed by system organ class and frequency in table 1. Frequencies are defined as: very common (≥ 1/10); common (≥ 1/100 to < 1/10); uncommon (≥ 1/1,000 to < 1/100); rare (≥ 1/10,000 to < 1/1,000); very rare (< 1/10,000); and not known (cannot be estimated from the available data)

Table 1: Adverse reactions

Blood and lymphatic system disorders	
Not known:	Pancytopenia, thrombocytopenia, anaemia aggravated, neutropenia
Immune system disorders	
Not known:	Hypersensitivity reactions (including anaphylactic reactions and angioedema)
Metabolism and nutrition disorders	
Not known:	Metabolic acidosis
Psychiatric disorders	
Uncommon:	Anxiety, sleep disorder
Nervous system disorders	
Common:	Headache
Uncommon:	Dizziness
Eye disorders	
Uncommon:	Cataract, maculopathy
Rare:	Optic neuritis
Ear and labyrinth disorders	
Uncommon:	Deafness
Respiratory, thoracic and mediastinal disorders	
Uncommon:	Laryngeal pain
Gastrointestinal disorders	
Common:	Diarrhoea, constipation, vomiting, nausea, abdominal pain, abdominal distension, dyspepsia
Uncommon:	Gastrointestinal haemorrhage, gastric ulcer (including multiple ulcers), duodenal ulcer, gastritis
Rare:	Oesophagitis
Not known:	Gastrointestinal perforation[1], acute pancreatitis[1]
Hepatobiliary disorders	
Common:	Transaminases increased
Uncommon:	Hepatitis, cholelithiasis
Not known:	Hepatic failure
Skin and subcutaneous tissue disorders	
Common:	Rash, pruritus
Uncommon:	Pigmentation disorder
Rare:	Drug reaction with eosinophilia and systemic symptoms (DRESS)
Not known:	Stevens-Johnson syndrome, hypersensitivity vasculitis, urticaria, erythema multiforme[1], alopecia[1], toxic epidermal necrolysis (TEN)
Renal and urinary disorders	
Very common:	Blood creatinine increased
Common:	Proteinuria
Uncommon:	Renal tubular disorder (acquired Fanconi syndrome), glycosuria
Not known:	Acute renal failure, tubulointerstitial nephritis, nephrolithiasis, renal tubular necrosis
General disorders and administration site conditions	
Uncommon:	Pyrexia, oedema, fatigue

Description of selected adverse reactions

Gallstones and related biliary disorders were reported in about 2% of patients. Elevations of liver transaminases were reported as an adverse reaction in 2% of patients. Elevations of transaminases greater than 10 times the upper limit of the normal range, suggestive of hepatitis, were uncommon (0.3%). During post-marketing experience, hepatic failure, sometimes fatal, has been reported with deferasirox. There have been post-marketing reports of metabolic acidosis. The majority of these patients had renal impairment, renal tubulopathy (Fanconi syndrome) or diarrhoea, or conditions where acid-base imbalance is a known complication. Cases of serious acute pancreatitis were observed without documented underlying biliary conditions. As with other iron chelator treatment, high-frequency hearing loss and lenticular opacities (early cataracts) have been uncommonly observed in patients treated with deferasirox.

Creatinine clearance in transfusional iron overload
In a retrospective meta-analysis of 2,102 adult and paediatric beta-thalassaemia patients with transfusional iron overload treated with deferasirox dispersible tablets in two randomised and four open label studies of up to five years' duration, a mean creatinine clearance decrease of 13.2% in adult patients (95% CI: -14.4% to -12.1%; n=935) and 9.9% (95% CI: -11.1% to -8.6%; n=1,142) in paediatric patients was observed during the first year of treatment. In 250 patients who were followed for up to five years, no further decrease in mean creatinine clearance levels was observed.

Clinical study in patients with non-transfusion-dependent thalassaemia syndromes
In a 1-year study in patients with non-transfusion-dependent thalassaemia syndromes and iron overload (dispersible tablets at a dose of 10 mg/kg/day), diarrhoea (9.1%), rash (9.1%), and nausea (7.3%) were the most frequent study drug-related adverse events. Abnormal serum creatinine and creatinine clearance values were reported in 5.5% and 1.8% of patients, respectively. Elevations of liver transaminases greater than 2 times the baseline and 5 times the upper limit of normal were reported in 1.8% of patients.

Paediatric population
In two clinical studies, growth and sexual development of paediatric patients treated with deferasirox for up to 5 years were not affected.
Diarrhoea is reported more commonly in paediatric patients aged 2 to 5 years than in older patients.
Renal tubulopathy has been mainly reported in children and adolescents with beta-thalassaemia treated with deferasirox. In post-marketing reports, a high proportion of cases of metabolic acidosis occurred in children in the context of Fanconi syndrome.
Acute pancreatitis has been reported, particularly in children and adolescents.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. To report Suspected Adverse Reactions, contact MSN Laboratories Private Limited at pharmacovigilance@msnlabs.com or through company website www.msnlabs.com->Contact us->Medical Enquiry/ to report a side effect. You can also report side effects directly via the National Pharmacovigilance Programme of India by calling on **1800 180 3024** or you can report to MSN Labs on +91- 40 38265227. By reporting side effects, you can help provide more information on the safety of this product.

4.9 Overdose
Early signs of acute overdose are digestive effects such as abdominal pain, diarrhea, nausea, and vomiting. Hepatic and renal disorders have been reported, including cases of liver enzyme and creatinine increased with recovery after treatment discontinuation. An erroneously administered single dose of 90 mg/kg led to Fanconi syndrome which resolved after treatment.
There is no specific antidote for Deferasirox. In case of overdose, it may be treated with induction of vomiting or gastric lavage, and by symptomatic treatment.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic Properties
Mechanism of Action
Deferasirox is an orally active chelator that is selective for iron (as Fe^{3+}). It is a tridentate ligand that binds iron with high affinity in a 2:1 ratio. Although deferasirox has very low affinity for zinc and copper, there are variable decreases in the serum concentration of these trace metals after the administration of deferasirox. The clinical significance of these decreases is uncertain.

Pharmacodynamic Properties
Pharmacodynamic effects tested in an iron balance metabolic study with the tablet for oral suspension formulation showed that deferasirox (10, 20, and 40 mg per kg per day) was able to induce a mean net iron excretion (0.119, 0.329, and 0.445 mg Fe/kg body weight per day, respectively) within the clinically relevant range (0.1 to 0.5 mg per kg per day). Iron excretion was predominantly faecal. An analysis of pooled pediatric clinical trial data found a statistically significant relationship between exposure and the probability of renal toxicity (increase in serum creatinine and urinary protein), resulting in a decrease in renal function. Decreases in renal function resulted in an increase in deferasirox exposure which may increase the probability of renal toxicity.

Cardiac Electrophysiology
At the maximum approved recommended dose, deferasirox does not prolong the QT interval to any clinically relevant extent..

5.2 Pharmacokinetic Properties
Absorption
Based on studies in patients with the tablet for oral suspension, deferasirox is absorbed following oral administration with median times to maximum plasma concentration (T_{max}) of about 1.5 to 4 hours. In healthy subjects, Deferasirox showed comparable T_{max}. The maximal concentrations (C_{max}) and area under the curve (AUC_{0-24h}, AUC_t) of deferasirox increase approximately linearly with dose after both single administration and under steady-state conditions. Exposure to deferasirox increased by an accumulation factor of 1.3 to 2.3 after multiple doses with the tablet for oral suspension formulation.
The absolute bioavailability [as measured by area under the curve over time to infinity (AUC_{inf})] of deferasirox tablets for oral suspension is 70% compared to an intravenous dose. The bioavailability (as measured by AUC_{inf}) of Deferasirox tablets was 36% greater than with deferasirox tablets for oral suspension. After strength-adjustment, the mean AUC_{inf} of Deferasirox tablets (i.e., 360 mg strength) was similar to that of deferasirox tablets for oral suspension (i.e., 500 mg strength) under fasting conditions; however the mean C_{max} was increased by 30%. The 30% increase in C_{max} observed with Deferasirox tablets is not clinically meaningful.

The administration of Deferasirox tablets with a light meal (approximately 250 calories with fat content less than 7% of total calories) indicated that the AUC_{inf} and C_{max} were similar to that under fasting conditions. The administration of Deferasirox tablets with a high-fat meal (approximately 1,000 calories with fat content greater than 50% of total calories), increased AUC_{inf} by 18% and C_{max} by 29% compared to that under fasting conditions

Distribution
Deferasirox is highly (99%) protein bound to plasma proteins, almost exclusively serum albumin, and has a small volume of distribution of approximately 14 litres in adults.

Metabolism
Glucuronidation is the main metabolic pathway for deferasirox, with subsequent biliary excretion. Deconjugation of glucuronidates in the intestine and subsequent reabsorption (enterohepatic recycling) is likely to occur: in a healthy volunteer study, the administration of cholestyramine after a single dose of deferasirox resulted in a 45% decrease in deferasirox exposure (AUC).

Deferasirox is mainly glucuronidated by UGT1A1 and to a lesser extent UGT1A3. CYP450-catalysed (oxidative) metabolism of deferasirox appears to be minor in humans (about 8%). No inhibition of deferasirox metabolism by hydroxyurea was observed *in vitro*.

Excretion
Deferasirox and its metabolites are primarily excreted in the faeces (84% of the dose). Renal excretion of deferasirox and its metabolites is minimal (8% of the dose). The mean elimination half-life (t1/2) ranged from 8 to 16 hours. The transporters MRP2 and MXR (BCRP) are involved in the biliary excretion of deferasirox.

Linearity / non-linearity
The C_{max} and AUC_{0-24h} of deferasirox increase approximately linearly with dose under steady-state conditions. Upon multiple dosing exposure increased by an accumulation factor of 1.3 to 2.3.

Specific Populations
Pediatric: Following oral administration of single or multiple doses, systemic exposure of adolescents and children to deferasirox was less than in adult patients. In children less than 6 years of age, systemic exposure was about 50% lower than in adults.
Sex: The apparent clearance is 17.5% lower in females compared to males.

Renal Impairment: Compared to patients with MDS and eGFR greater than 60 mL/min/1.73 m², patients with MDS and eGFR 40 to 60 mL/min/1.73 m (n = 34) had approximately 50% higher mean deferasirox trough plasma concentrations.

Hepatic Impairment: In a single dose (20 mg/kg) study in patients with varying degrees of hepatic impairment, deferasirox exposure was increased compared to patients with normal hepatic function. The average total (free and bound) AUC of deferasirox increased 16% in 6 patients with mild (Child-Pugh A) hepatic impairment, and 76% in 6 patients with moderate (Child-Pugh B) hepatic impairment compared to 6 patients with normal hepatic function. The impact of severe (Child-Pugh C) hepatic impairment was assessed in only 1 patient.

Drug Interactions
Midazolam: The concomitant administration of deferasirox tablets for oral suspension and CYP3A4 probe substrate midazolam resulted in a decrease of midazolam C by 23% and AUC by 17%. In the clinical setting, this effect may be more pronounced, as the study was not adequately designed to conclusively assess the potential induction of CYP3A4 by deferasirox.

Repaglinide: The concomitant administration of deferasirox tablets for oral suspension (30 mg per kg/day for 4 days) and the CYP2C8 probe substrate repaglinide (single dose of 0.5 mg) increased repaglinide AUC to 2.3-fold and C of 1.6-fold.

Theophylline: The concomitant administration of deferasirox tablets for oral suspension (repeated dose of 30 mg per kg/day) and the CYP1A2 substrate theophylline (single dose of 120 mg) resulted in an approximate doubling of the theophylline AUC and elimination half-life. The single dose C was not affected, but an increase in theophylline C is expected to occur with chronic dosing.

Rifampicin: The concomitant administration of deferasirox tablets for oral suspension (single dose of 30 mg per kg) and the strong uridine diphosphate glucuronosyltransferase (UGT) inducer rifampicin (600 mg per day for 9 days) decreased deferasirox AUC by 44%.

Cholestyramine: The concomitant administration of cholestyramine after a single dose of deferasirox tablets for oral suspension decreased deferasirox AUC by 45%.

Busulfan: Concomitant administration of deferasirox and busulfan resulted in an increase of Busulfan exposure (AUC).

In vitro Studies:
Deferasirox inhibited human CYP2A6, CYP2D6, and CYP2C19 *in vitro*.
Deferasirox is not a substrate of P-glycoprotein, MRP1 or MRP

6. NONCLINICAL PROPERTIES
Nonclinical Toxicology
Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity or carcinogenic potential. The main findings were kidney toxicity and lens opacity (cataracts). Similar findings were observed in neonatal and juvenile animals. The kidney toxicity is considered mainly due to iron deprivation in animals that were not previously overloaded with iron.

Tests of genotoxicity in vitro were negative (Ames test, chromosomal aberration test) while deferasirox caused formation of micronuclei *in vivo* in the bone marrow, but not liver, of non-iron-loaded rats at lethal doses. No such effects were observed in iron-preloaded rats. Deferasirox was not carcinogenic when administered to rats in a 2-year study and transgenic p53+/- heterozygous mice in a 6-month study.

The potential for toxicity to reproduction was assessed in rats and rabbits. Deferasirox was not teratogenic, but caused increased frequency of skeletal variations and stillborn pups in rats at high doses that were severely toxic to the non-iron-overloaded mother. Deferasirox did not cause other effects on fertility or reproduction.

7. PHARMACEUTICAL PARTICULARS
8.1 Incompatibilities
None

8.2 Packing Information
10's Blister pack

8.3 Storage and Handling Instructions
Do not store above 30°C.

8. PATIENT COUNSELLING INFORMATION
Dosing Instructions
Advise patients to take Deferasirox tablets with water or other liquids. Advise patients to swallow Deferasirox tablets once daily with water or other liquids, preferably at the same time each day. Advise patients to take Deferasirox tablets on an empty stomach or with a light meal (contains less than 7% fat content and approximately 250 calories). Examples of light meals include 1 whole wheat English muffin, 1 packet jelly (0.5 ounces), and skim milk (8 fluid ounces) or a turkey sandwich (2 oz. turkey on whole wheat bread w/lettuce, tomato, and 1 packet mustard). For patients who have difficulty swallowing whole tablets, Deferasirox tablets may be crushed and mixed with soft foods (e.g., yogurt or applesauce) immediately prior to use and administered orally. Advise against the use of commercial crushers with serrated surfaces for crushing a single 90 mg tablet. Advise patients to immediately and completely consume the dose and not store it for future use.

Advise patients to take Deferasirox Sprinkle granules by sprinkling the full dose on soft food (e.g., yogurt or applesauce) immediately prior to use and administered orally. Advise patients to take Deferasirox Sprinkle granules once a day, preferably at the same time each day. Deferasirox Sprinkle granules may be taken on an empty stomach or with a light meal.

Blood Testing
Advise patients that blood tests will be performed frequently to check for damage to kidneys, liver, or blood cells.

Acute Kidney Injury, Including Acute Renal Failure
Caution patients about the potential for kidney toxicity when taking Deferasirox tablets or Deferasirox Sprinkle granules. Inform patients of the signs and symptoms of kidney injury. Advise patients to contact their healthcare provider immediately if they experience any of these symptoms.

Hepatic Toxicity and Failure
Caution patients about the potential for hepatic toxicity when taking Deferasirox tablets or Deferasirox Sprinkle granules. Inform patients of the signs and symptoms of hepatic toxicity. Advise patients to contact their healthcare provider immediately if they experience any of these symptoms.

GI Ulceration and Hemorrhage
Caution patients about the potential for the development of GI ulcers or bleeding when taking Deferasirox in combination with drugs that have ulcerogenic or hemorrhagic potential, such as NSAIDs, corticosteroids, oral bisphosphonates, or anticoagulants. Inform patients of the signs and symptoms of GI ulcers or bleeding. Advise patients to contact their healthcare provider for symptoms of heartburn but to seek immediate medical attention for symptoms of GI hemorrhage.

Allergic Reactions
Serious allergic reactions (which include swelling of the throat) have been reported in patients taking Deferasirox, usually within the first month of treatment. If reactions are severe, advise patients to stop taking Deferasirox immediately and seek immediate medical attention.

Severe Skin Reactions
Severe skin reactions have been reported in patients taking Deferasirox tablets or Deferasirox Sprinkle granules. Inform patients of the signs and symptoms of severe skin reactions. If reactions are severe, advise patients to stop taking Deferasirox tablets or Deferasirox Sprinkle granules immediately and seek immediate medical attention.

Skin Rash
Skin rashes may occur during Deferasirox treatment. If the skin rash is severe, advise patients to stop taking Deferasirox and seek medical attention.

Pediatric Patients with Acute Illness
Instruct pediatric patients and their caregivers to contact their healthcare provider during episodes of acute illness, especially if the patient has not been drinking fluids or the patient has volume depletion due to fever, vomiting, or diarrhea.

Auditory and Ocular Testing
Because auditory and ocular disturbances have been reported with deferasirox, conduct auditory testing and ophthalmic testing before starting Deferasirox treatment and thereafter at regular intervals. Advise patients to contact their healthcare provider if they develop visual or auditory changes during treatment.

Drug Interactions
Caution patients not to take Aluminium containing antacids and Deferasirox tablets or granules simultaneously.
Caution patients about potential loss of effectiveness of drugs metabolized by CYP3A4 (e.g., cyclosporine, simvastatin, hormonal contraceptive agents) when Deferasirox is administered with these drugs.

Caution patients about potential loss of effectiveness of Deferasirox when administered with drugs that are potent UGT inducers (e.g., rifampicin, phenytoin, phenobarbital, ritonavir). Based on serum ferritin levels and clinical response, consider increases in the dose of Deferasirox when concomitantly used with potent UGT inducers.

Caution patients about potential loss of effectiveness of Deferasirox when administered with drugs that are bile acid sequestrants (e.g., cholestyramine, colesevelam, colestipol). Based on serum ferritin levels and clinical response, consider increases in the dose of Deferasirox when concomitantly used with bile acid sequestrants.

Caution patients with diabetes to monitor their glucose levels more frequently when repaglinide is used concomitantly with Deferasirox.

Handling Instructions
Advise patients to store Deferasirox in a dry, room-temperature environment.

Driving and Using Machines
Caution patients experiencing dizziness to avoid driving or operating machinery

9. DETAILS OF MANUFACTURER
MSN Laboratories Private Limited,
Formulation Division, Unit II,
Sy.no.1277, 1319 to 1324,
Nandigama (Village & Mandal),
Ranga Reddy District,
Telangana-509228,
India

10. DETAILS OF PERMISSION OR LICENCE NUMBER WITH DATE
5/MN/TS/2014/F/G, 26/08/2019

11. DATE OF REVISION
July-2021

D030203-00