NOVARTIS

EXJADE® (deferasirox) film-coated tablets

90 mg, 180 mg, 360 mg film-coated tablets
(locally available strengths may differ)

Basic Succinct Statement (BSS)

Version 4.0

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This material is only meant for Healthcare Professionals

EXJADE® Film-coated Tablets

Important note: Before prescribing, consult full prescribing information.

Presentation:

Exjade® film-coated tablets

Film-coated tablets containing 90 mg, 180 mg or 360 mg of deferasirox.

Indications: ♦For adults and pediatric patients aged 2 years and over with chronic iron overload due to blood transfusions (transfusional hemosiderosis). ♦For adults and pediatric patients aged 10 years and over with non-transfusion-dependent thalassemia syndromes and iron overload.

Dosage: Transfusional iron overload

♦Starting daily dose:

For patients who are currently on chelation therapy with Exjade Film-coated Tablets and switching to Exjade dispersible tablets, the dose of Exjade dispersible tablets should be 40% higher than the dose of Exjade Film-coated Tablets, rounded to the nearest whole dispersible tablet.

Recommended initial daily dose is 14 mg/kg body weight; consider 21 mg/kg for patients receiving >14 mL/kg/month of packed red blood cells (>4 units/month), and for whom the objective is the reduction of iron overload; consider 7 mg/kg for patients receiving <7 mL/kg/month of packed red blood cells (<2 units/month), and for whom the objective is the maintenance of the body iron level**;** for patients already well-managed on treatment with deferoxamine, consider a starting dose of Exjade Film-coated Tablets that is numerically one third that of the deferoxamine dose. For patients who are currently on chelation therapy with Exjade dispersible tablet and switching to Exjade Film-coated Tablets, the dose of Exjade Film-coated Tablets should be 30% lower than the dose of Exjade dispersible tablets, rounded to the nearest whole tablet.

♦50% starting dose reduction in moderate hepatic impairment (Child-Pugh B). Should not be used in severe hepatic impairment (Child-Pugh C).

♦**Monthly monitoring of serum ferritin** for assessing patient's response to therapy and to minimize the risk of overchelation.

♦Dose adjustment:

If necessary every 3 to 6 months based on serum ferritin trends. Dose adjustments should be made in steps of 3.5 to 7 mg/kg. In patients not adequately controlled with doses of 21 mg/kg, doses of up to 28 mg/kg may be considered. In patients whose serum ferritin level has reached the target (usually between 500 and 1000 microgram/L), dose reductions in steps of 3.5 to 7 mg/kg should be considered to maintain serum ferritin levels within the target range. Exjade Film-coated Tablets should be interrupted if serum ferritin falls consistently below 500 micrograms/L.

♦Maximum daily dose:

The maximum daily dose of film-coated tablets is 28 mg/kg body weight.

Dosage: Non-transfusion-dependent thalassemia syndromes and iron overload

♦**Starting daily dose:**

For patients who are currently on chelation therapy with Exjade Film-coated Tablets and switching to Exjade dispersible tablets, the dose of Exjade dispersible tablets should be 40% higher than the dose of Exjade Film-coated Tablets, rounded to the nearest whole dispersible tablet.

Recommended initial daily dose is 7 mg/kg body weight. Therapy should only be initiated when there is evidence of iron overload: liver iron concentration (LIC) ≥5 mg Fe/g dry weight (dw) or serum ferritin consistently >800 microgram/L. In patients with no LIC assessment, caution should be taken during chelation therapy to minimize the risk of over-chelation. For patients who are currently on chelation therapy with Exjade dispersible tablet and switching to Exjade Film-coated Tablets, the dose of Exjade Film-coated Tablets should be 30% lower than the dose of Exjade dispersible tablets, rounded to the nearest whole tablet.

♦**Dose adjustment:**

Should be considered every 3 to 6 months in steps of 3.5 to 7 mg/kg if the patient's LIC is ≥7 mg Fe/g dw, or serum ferritin is consistently >2,000 microgram/L, and not showing a downward trend, and the patient is tolerating the drug well. Once a satisfactory body iron level has been achieved (LIC <3 mg Fe/g dw or serum ferritin <300 microgram/L), treatment should be interrupted.

♦50% starting dose reduction in moderate hepatic impairment (Child-Pugh B). Should not be used in severe hepatic impairment (Child-Pugh C).

♦**Maximum daily dose:**

The maximum daily dose of film-coated tablets is 14 mg/kg body weight.

Administration:

The film-coated tablets should be swallowed whole with some water. For patients who are unable to swallow whole tablets, Exjade Film-coated Tablets may be crushed and administered by sprinkling the full dose on soft food like yogurt or apple sauce (apple puree). The dose should be immediately and completely consumed, and not stored for future use. Exjade Film-coated Tablets should be taken once a day, preferably at the same time each day, and may be taken on an empty stomach or with a light meal.

Contraindications: ♦Hypersensitivity to deferasirox or to any of the excipients. ♦Creatinine clearance <40 mL/min or serum creatinine >2 times the age-appropriate upper limit of normal. ♦High risk MDS patients and patients with other hematological and non-hematological malignancies who are not expected to benefit from chelation therapy due to the rapid progression of their disease.

Warnings and precautions: ♦Caution in elderly patients due to a higher frequency of adverse reactions. ♦Caution in patients with creatinine clearance between 40 and less than 60 mL/min, particularly in cases where there are additional risk factors that may impair renal function. Monthly monitoring of creatinine clearance, serum creatinine and proteinuria: dose

reduction may be needed in some cases of non-progressive increase in serum creatinine; Exjade should be interrupted if serum creatinine shows a progressive rise beyond the age-appropriate upper limit of normal. More frequent creatinine monitoring recommended in patients with an increased risk of renal complications. Rare reports of acute renal failure, some of which required dialysis or with fatal outcome. Reports of renal tubulopathy mainly in children with beta-thalassemia and serum ferritin levels <1,500 microgram/L. Dose reduction or interruption may be considered if abnormalities occur in levels of markers of renal tubular function and/or as clinically indicated. ♦Not recommended in patients with severe hepatic impairment (Child-Pugh C). Monitoring of serum transaminases, bilirubin and alkaline phosphatase: before the initiation of treatment, every 2 weeks during the first month and monthly thereafter. Exjade should be interrupted if persistent and progressive unattributable increase in serum transaminases levels. Post-marketing cases of hepatic failure have been reported. ♦Gastrointestinal (GI) irritation may occur. Upper GI ulceration and hemorrhage have been reported in patients, including children and adolescents. Multiple ulcers have been observed in some patients. There have been reports of ulcers complicated with GI perforation (including fatal outcome). There have been rare reports of fatal GI hemorrhages, especially in elderly patients who had advanced hematologic malignancies and/or low platelet counts. Caution in patients with platelet counts $<50 \times 10^9$/L. ♦Severe cutaneous adverse reactions (SCARs) have been reported. Patients should be advised of the signs and symptoms of SCARs and be closely monitored. If any SCAR is suspected, Exjade should be discontinued immediately and should not be reintroduced. ♦Skin rashes: Exjade should be interrupted if severe rash develops. ♦Discontinue if severe hypersensitivity reaction occurs. Exjade should not be reintroduced in patients who have experienced previous hypersensitivity reactions on deferasirox due to the risk of anaphylactic shock. ♦Annual ophthalmological/audiological testing. ♦Monthly monitoring of serum ferritin recommended to assess patient's response and to avoid overchelation. Closer monitoring of serum ferritin levels, renal and hepatic function recommended when high doses of treatment and when serum ferritin levels decrease close to target range. Dose reduction may be considered. ♦ Deferasirox is not associated with growth retardation in children, however as a general precautionary measure body weight and longitudinal growth can be monitored (every 12 months). ♦ Cytopenia reported (relationship with Exjade/Jadenu uncertain), regular monitoring of blood counts recommended. ♦Caution when driving or operating machines if experiencing dizziness. ♦Should not be used during pregnancy unless clearly necessary. ♦Not recommended when breast-feeding.

Adverse drug reactions:

Very common: blood creatinine increased.

Common: nausea, vomiting, diarrhoea, abdominal pain, abdominal distension, constipation, dyspepsia, rash, pruritus, transaminases increased, proteinuria, headache.

Uncommon: anxiety, sleep disorder, dizziness, cataracts, maculopathy, deafness, laryngeal pain, gastrointestinal haemorrhage, gastric ulcer (including multiple ulcers), duodenal ulcer, gastritis, acute pancreatitis, hepatitis, cholelithiasis, pigmentation disorder, renal tubular disorder(Fanconi syndrome), pyrexia, oedema, fatigue.

Rare: optic neuritis, drug reaction with eosinophilia and systemic symptoms (DRESS), erythema multiforme, oesophagitis.

Adverse drug reactions from post-marketing (frequency unknown): renal tubular necrosis, gastrointestinal perforation, Stevens-Johnson syndrome, toxic epidermal necrolysis (TEN), acute renal failure, tubulointerstitial nephritis, hepatic failure, hypersensitivity vasculitis, urticaria, alopecia, hypersensitivity reaction (including anaphylactic reaction and angioedema), aggravated anaemia and cytopenia (relationship with Exjade uncertain).