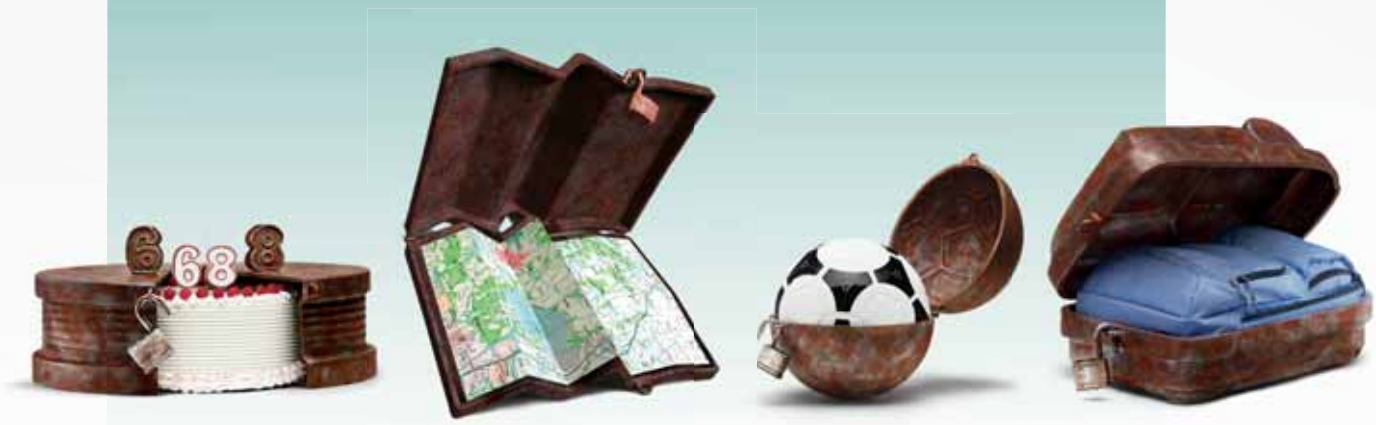
EXJADE® IMPORTANT RENAL AND HEPATIC INFORMATION

This information will help when prescribing EXJADE, with particular reference to patient monitoring, contraindications, and warnings and precautions related to the renal and hepatic profile of EXJADE.



EXJADE® deferasirox

Indications[1]

EXJADE® is indicated for the treatment of chronic iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) in patients with beta thalassemia major aged 6 years and older.

EXJADE is also indicated for the treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups:

- In patients with beta thalassemia major with iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) aged 2 to 5 years
- In patients with beta thalassemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells) aged 2 years and older
- In patients with other anaemias aged 2 years and older

EXJADE is also indicated for the treatment of chronic iron overload requiring chelation therapy when deferoxamine therapy is contraindicated or inadequate in patients with non-transfusion-dependent thalassemia syndromes aged 10 years and older.

Dosage for patients with chronic transfusional iron overload[1]

It is recommended that treatment be started after the transfusion of approximately 20 units (about 100 ml/kg) of packed red blood cells or when there is evidence from clinical monitoring that chronic iron overload is present (e.g. serum ferritin >1,000 µg/l). Doses (in mg/kg) must be calculated and rounded to the nearest whole tablet size.

Dosage for patients with non-transfusion-dependent thalassemia syndromes[1]

Chelation 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 µg/l). LIC is the preferred method of iron overload determination and should be used wherever available. Caution should be taken during chelation therapy to minimize the risk of over-chelation in all patients.

Contraindications[1]

- Hypersensitivity to the active substance or to any of the excipients
- Combination with other iron chelator therapies as the safety of such combinations has not been established
- Patients with estimated creatinine clearance <60 ml/min

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RENAL SAFETY PROFILE

Findings from clinical trials

Parameters measured in clinical trials[1]

In EXJADE® clinical trials, only patients with a serum creatinine within the normal range for their age and gender were enrolled. The individual baseline value of serum creatinine was calculated as the average of two (and for some patients three) pre-treatment values of serum creatinine. The mean intra-patient coefficient of variation of these two or three pre-treatment measurements was approximately 10%.[2] This is why duplicate serum creatinine values are recommended before initiating treatment with EXJADE. During treatment, serum creatinine was monitored monthly, and when indicated, dose adjustments were made for increases of serum creatinine as described below.

Results from the one-year core studies[1]

During clinical trials, increases in serum creatinine of >33% on ≥2 consecutive occasions, sometimes above the upper limit of the normal range, occurred in about 36% of patients. These were dose-dependent. About two-thirds of the patients showing serum creatinine increase returned below the 33% level without dose adjustment. In the remaining third the serum creatinine increase did not always respond to a dose reduction or a dose interruption. Indeed, in some cases, only a stabilization of the serum creatinine values has been observed after dose reduction.

Long-term renal safety data[2]

Additional long-term follow-up data of 5 years is available for a total of 185 patients enrolled in the core clinical trial. The 5-year follow-up study included pediatric and adult sickle cell disease patients with transfusional hemosiderosis. The evidence of changes in median serum creatinine and calculated creatinine clearance indicates a comparable renal safety profile to other patient populations, and no progression of renal abnormalities with prolonged exposure to EXJADE.

Monitoring serum creatinine and creatinine clearance[1]

It is recommended that serum creatinine be assessed in duplicate before initiating therapy. **Serum creatinine, creatinine clearance** (estimated with the Cockcroft-Gault or MDRD formula in adults and with the Schwartz formula in children) and/or plasma cystatin C levels **should be monitored weekly in the first month after initiation or modification of therapy with EXJADE, and monthly thereafter.** Patients with pre-existing renal conditions and patients who are receiving medicinal products that depress renal function may be more at risk of complications. Care should be taken to maintain adequate hydration in patients who develop diarrhea or vomiting.

This booklet is intended to describe how to manage these effects on renal and hepatic function.

Methods for estimating creatinine clearance[1]

For your reference, here is a brief overview of methods to estimate creatinine clearance in adults and children when prescribing EXJADE.

Adult

Once a method has been selected you should not interchange between formulas.

Cockcroft–Gault formula[3]
The Cockcroft–Gault formula employs creatinine measurements and the patient's weight to predict creatinine clearance.

The formula states creatinine clearance in ml/min.

$$\text{Creatinine clearance}^{a} = \frac{(140 - \text{age}) \times \text{weight (kg)}}{72^{b} \times \text{serum creatinine (mg/100 ml)}}$$

Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[4,5]
A general practice and public health perspective favors adoption of the CKD-EPI equation in North America, Europe, and Australia and using it as a comparator for new equations in all locations.

Glomerular filtration rate (GFR) = $141 \times \min(\text{Scr}/\kappa, 1)^{\alpha} \times \max(\text{Scr}/\kappa, 1)^{-1.209} \times 0.993^{\text{Age}} \times 1.018$ [if female] × 1.159 [if black], where Scr is serum creatinine, κ is 0.7 for females and 0.9 for males, α is −0.329 for females and −0.411 for males, min indicates the minimum of Scr/κ or 1, and max indicates the maximum of Scr/κ or 1.

Pediatric

Schwartz formula[6]

$$\text{Creatinine clearance (ml/min)} = \frac{\text{constant}^{c} \times \text{height (cm)}}{\text{serum creatinine (mg/dl)}}$$

[a]In female patients creatinine clearance is multiplied by 0.85.
[b]If serum creatinine is provided in mmol/l instead of mg/dl the constant should be 815 instead of 72.
[c]The constant is 0.55 in children and adolescent girls, or 0.70 in adolescent boys.

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Dose adjustment according to serum creatinine level[1]

Dose adjustment for adults

For adult patients, the daily dose may be reduced by 10 mg/kg if a rise in serum creatinine by >33% above the average of the pre-treatment measurements **and** estimated creatinine clearance decreases below the lower limit of the normal range (<90 ml/min) are seen at two consecutive visits, and cannot be attributed to other causes.

Dose adjustment for pediatric patients

For pediatric patients, the dose may be reduced by 10 mg/kg if estimated creatinine clearance decreases below the lower limit of the normal range (<90 ml/min) **and/or** serum creatinine levels rise above the age-appropriate upper limit of normal at two consecutive visits.

After a dose reduction, for adult and pediatric patients, treatment should be interrupted if a rise in serum creatinine >33% above the average of the pre-treatment measurements is observed and/or the calculated creatinine clearance falls below the lower limit of the normal range. Treatment may be reinitiated depending on the individual clinical circumstances.

Particular attention should therefore be paid to monitoring of serum creatinine in patients who are concomitantly receiving medicinal products that depress renal function.

Tests for proteinuria should be performed monthly. As needed, additional markers of renal tubular function (e.g. glycosuria in non-diabetics and low levels of serum potassium, phosphate, magnesium or urate, phosphaturia, aminoaciduria) may also be monitored. Dose reduction or interruption may be considered if there are abnormalities in levels of tubular markers and/or if clinically indicated. Renal tubulopathy has been mainly reported in children and adolescents with beta-thalassemia treated with EXJADE®.

If, despite dose reduction and interruption, the serum creatinine remains significantly elevated and there is also persistent abnormality in another marker of renal function (e.g. proteinuria, Fanconi's Syndrome), the patient should be referred to a renal specialist, and further specialized investigations (such as renal biopsy) may be considered.

HEPATIC SAFETY PROFILE

Liver function assessment[1]

Liver function test elevations have been observed in patients treated with EXJADE. Postmarketing cases of hepatic failure, sometimes fatal, have been reported in patients treated with EXJADE. Most reports of hepatic failure involved patients with significant morbidities including pre-existing liver cirrhosis. However, the role of EXJADE as a contributing or aggravating factor cannot be excluded.

It is recommended that serum transaminases, bilirubin and alkaline phosphatase be checked before the initiation of treatment, every 2 weeks during the first month and monthly thereafter. If there is a persistent and progressive increase in serum transaminase levels that cannot be attributed to other causes, EXJADE should be interrupted. Once the cause of the liver function test abnormalities has been clarified or after return to normal levels, cautious re-initiation of treatment at a lower dose followed by gradual dose escalation may be considered.

EXJADE is not recommended in patients with severe hepatic impairment (Child-Pugh Class C).

Recommendations in hepatic impairment[1]

EXJADE is not recommended in patients with severe hepatic impairment (Child-Pugh Class C). In patients with moderate hepatic impairment (Child-Pugh Class B), the dose should be considerably reduced followed by progressive increase up to a limit of 50%, and EXJADE must be used with caution in such patients. Hepatic function in all patients should be monitored before treatment, every 2 weeks during the first month and then every month.

The pharmacokinetics of deferasirox were not influenced by liver transaminase levels up to 5 times the upper limit of the normal range.

In a clinical study using single doses of 20 mg/kg deferasirox, the average exposure was increased by 16% in subjects with mild hepatic impairment (Child-Pugh Class A) and by 76% in subjects with moderate hepatic impairment (Child-Pugh Class B) compared to subjects with normal hepatic function. The average C_{max} of deferasirox in subjects with mild or moderate hepatic impairment was increased by 22%. Exposure was increased 2.8-fold in one subject with severe hepatic impairment (Child-Pugh Class C).

Other hepatic effects[1]

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 postmarketing experience, hepatic failure, sometimes fatal, has been reported with EXJADE, especially in patients with pre-existing liver cirrhosis. Serious acute pancreatitis may potentially occur as a complication of gallstones (and related biliary disorders). As with other iron chelator treatment, high-frequency hearing loss and lenticular opacities (early cataracts) have been uncommonly observed in patients treated with EXJADE.

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Monitoring recommendations[1]

	Baseline	In the first month after initiation of EXJADE®	Monthly	Every 3 months	Yearly
SF	✓		✓		
LIC[a]	✓			✓ (for pediatric patients only, if SF is <800 µg/l)	✓
Serum creatinine	2x	Weekly	✓		
Creatinine clearance		Weekly (or plasma cystatin C)	✓ (or plasma cystatin C)		
Proteinuria			✓		
Serum transaminases, bilirubin, alkaline phosphatase	✓	Every 2 weeks	✓		
Body weight, height, and sexual development (pediatric patients)					✓
Auditory/ophthalmic testing (including funduscopy)	✓				✓

[a]Liver iron concentration monitoring recommended for NTDT only

The results of the tests for serum creatinine, creatinine clearance, plasma cystatin C, proteinuria, serum ferritin, liver transaminases, bilirubin, and alkaline phosphatase should be recorded and regularly assessed for trends. The results should also be noted in the provided patient's booklet as well as in the patient's charts, along with pre-treatment baseline levels for all tests.

General safety profile[1]

Though this brochure is designed to explain the renal and hepatic profile in depth, it is important to be aware of other key adverse events.

The most frequent reactions reported during chronic treatment with EXJADE in adult and pediatric patients include gastrointestinal disturbances in about 26% of patients (mainly nausea, vomiting, diarrhea or abdominal pain) and skin rash in about 7% of patients. Diarrhea is reported more commonly in pediatric patients aged 2 to 5 years and in the elderly. These reactions are dose-dependent, mostly mild to moderate, generally transient and mostly resolve even if treatment is continued.

In patients with a short life expectancy (e.g. high-risk myelodysplastic syndromes), especially when co-morbidities could increase the risk of adverse events, the benefit of EXJADE might be limited and may be inferior to risks. As a consequence, treatment with EXJADE is not recommended in these patients.

Caution should be used in elderly patients due to a higher frequency of adverse reactions (in particular, diarrhea).

Auditory (decreased hearing) and ocular (lens opacities) disturbances have been reported. Auditory and ophthalmic testing (including fundoscopy) is recommended before the start of treatment and at regular intervals thereafter (every 12 months). If disturbances are noted during the treatment, dose reduction or interruption may be considered.

Cases of serious hypersensitivity reactions (such as anaphylaxis and angioedema) have been reported in patients receiving EXJADE, with the onset of the reaction occurring in the majority of cases within the first month of treatment. If such reactions occur, EXJADE should be discontinued and appropriate medical intervention instituted.

Skin rashes may appear during EXJADE treatment. The rashes resolve spontaneously in most cases. When interruption of treatment may be necessary, treatment may be reintroduced after resolution of the rash, at a lower dose followed by gradual dose escalation. In severe cases this reintroduction could be conducted in combination with a short period of oral steroid administration. Cases of Stevens-Johnson syndrome (SJS) have been reported post marketing. If SJS is suspected, EXJADE should be discontinued and should not be reintroduced.

There have been post-marketing reports of leukopenia, thrombocytopenia or pancytopenia (or aggravation of these cytopenias) and of aggravated anemias in patients treated with EXJADE. Most of these patients had pre-existing hematological disorders that are frequently associated with bone marrow failure. However, a contributory or aggravating role cannot be excluded. Interruption of treatment should be considered in patients who develop unexplained cytopenia.

Upper gastrointestinal ulceration and hemorrhage have been reported in patients, including children and adolescents, receiving EXJADE. Multiple ulcers have been observed in some patients. There have been reports of fatal gastrointestinal hemorrhages, especially in elderly patients who had hematological malignancies and/or low platelet counts. Physicians and patients should remain alert for signs and symptoms of gastrointestinal ulceration and hemorrhage during EXJADE therapy and promptly initiate additional evaluation and treatment if a serious gastrointestinal adverse reaction is suspected. Caution should be exercised in patients who are taking EXJADE in combination with substances that have known ulcerogenic potential, such as NSAIDs, corticosteroids, or oral bisphosphonates, in patients receiving anticoagulants and in patients with platelet counts below 50,000/mm^3 (50 x 10^9/l).

The concomitant administration of EXJADE with substances that have known ulcerogenic potential, such as NSAIDs (including acetylsalicylic acid at high dosage), corticosteroids or oral bisphosphonates may increase the risk of gastrointestinal toxicity. The concomitant administration of EXJADE with anticoagulants may also increase the risk of gastrointestinal hemorrhage. Close clinical monitoring is required when deferasirox is combined with these substances.

EXJADE deferasirox

EXJADE® (deferasirox)

EXJADE® dispersible tablets

▼ This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 of the SmPC for how to report adverse reactions.

PRESENTATION: dispersible tablets containing 250 mg or 500 mg deferasirox.

INDICATIONS: Treatment of chronic iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) in patients with beta thalassaemia major aged 6 years and older. Treatment of chronic iron overload due to blood transfusions when deferoxamine therapy is contraindicated or inadequate in the following patient groups: in patients with beta thalassaemia major with iron overload due to frequent blood transfusions (≥7 ml/kg/month of packed red blood cells) aged 2 to 5 years, in patients with beta thalassaemia major with iron overload due to infrequent blood transfusions (<7 ml/kg/month of packed red blood cells) aged 2 years and older in patients with other anaemias aged 2 years and older. Treatment of chronic iron overload requiring chelation therapy when deferoxamine therapy is contraindicated or inadequate in patients with non-transfusion-dependant thalassaemia syndromes aged 10 years and older.

DOSAGE AND ADMINISTRATION: Transfusional iron overload ♦ Starting daily dose: Recommended initial daily dose is 20 mg/kg body weight; consider 30 mg/kg for patients receiving >14 ml/kg/month of packed red blood cells (>4 units/month for adults), and for whom the objective is reduction of iron overload; consider 10 mg/kg for patients receiving <7 ml/kg/month of packed red blood cells (<2 units/month for adults), and for whom the objective is maintenance of the body iron level; for patients already well-managed on treatment with deferoxamine, consider a starting dose of EXJADE® that is numerically half that of the deferoxamine dose. ♦ Monthly monitoring of serum ferritin for assessing patient's response to therapy ♦ **Dose adjustment:** to be adjusted if necessary every 3 to 6 months based on serum ferritin trends. Dose adjustments should be made in steps of 5 to 10 mg/kg. In patients not adequately controlled with doses of 30 mg/kg, doses of up to 40 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 5 to 10 mg/kg should be considered to maintain serum ferritin levels within the target range. EXJADE® should be interrupted if serum ferritin falls consistently below 500 micrograms/l. ♦ **Maximum daily dose** is 40 mg/kg body weight. **Paediatric patients:** dosing is the same as for adults. However change in weight of patients must be taken into account when calculating the dose. ♦ EXJADE® must be taken once daily on an empty stomach at least 30 minutes before food, preferably at the same time each day. ♦ EXJADE® tablets to be dispersed in water or apple or orange juice. Any residue is to be re-suspended in water or juice and swallowed. Tablets must not be chewed or swallowed whole. Dispersion in carbonated drinks or milk is not recommended due to foaming and slow dispersion respectively. It is not recommended in patients with severe hepatic impairment. **Non-transfusion-dependent thalassaemia syndromes.** Chelation 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 µg/l). LIC is the preferred method of iron overload determination and should be used wherever available. Caution should be taken during chelation therapy to minimise the risk of over-chelation in all patients. ♦ **Starting daily dose:** The recommended initial daily dose of EXJADE in patients with non-transfusion-dependent thalassaemia syndromes is 10 mg/kg body weight. ♦ **Dose adjustment:** It is recommended that serum ferritin be monitored every month. After every 3 to 6 months of treatment, a dose increase in increments of 5 to 10 mg/kg should be considered if the patient's LIC is ≥7 mg Fe/g dw, or if serum ferritin is consistently >2,000 µg/l and not showing a downward trend, and the patient is tolerating the medicinal product well. Doses above 20 mg/kg are not recommended because there is no experience with doses above this level in patients with non-transfusion-dependent thalassaemia syndromes. In patients in whom LIC was not assessed and serum ferritin is ≤2,000 µg/l, dosing should not exceed 10 mg/kg. For patients in whom the dose was increased to >10 mg/kg, dose reduction to 10 mg/kg or less is recommended when LIC is <7 mg Fe/g dw or serum ferritin is ≤2,000 µg/l. ♦ **Treatment cessation:** Once a satisfactory body iron level has been achieved (LIC <3 mg Fe/g dw or serum ferritin <300 µg/l), treatment should be stopped. There are no data available on the retreatment of patients who reaccumulate iron after having achieved a satisfactory body iron level and therefore retreatment cannot be recommended. ♦ **Paediatric patients:** In paediatric patients with non-transfusion-dependent thalassaemia syndromes, dosing should not exceed 10 mg/kg. In these patients, closer monitoring of LIC and serum ferritin is essential to avoid overchelation: in addition to monthly serum ferritin assessments, LIC should be monitored every three months when serum ferritin is ≤800 µg/l. Before treating heavily iron-overloaded children with non-transfusion-dependent thalassaemia with EXJADE, the physician should be aware that the consequences of long-term exposure in such patients are currently not known.**CONTRAINDICATIONS:** ♦Hypersensitivity to deferasirox or to any of the excipients. ♦Creatinine clearance <60 ml/min or serum creatinine >2 times the age-appropriate upper limit of normal. ♦Combination with other iron chelator therapies.

WARNINGS/PRECAUTIONS: ♦ This medicinal product is subject to additional monitoring. ♦ There have been post-marketing reports of leukopenia, thrombocytopenia or pancytopenia (or aggravation of these cytopenias) and of aggravated anaemia in patients treated with Exjade. ♦ Caution in elderly patients due to a higher frequency of adverse reactions. ♦ EXJADE® has not been studied in patients with renal and hepatic impairment and should be used with caution in such patients. ♦ Due to chances of metabolic acidiosis, in patients where acid-base imbalance is a known complication like diarrhea, renal impairment or renal tubulopathy (Fanconi's syndrome), acid-base balance should be monitored ♦Creatinine clearance, serum creatinine and proteinuria should be monitored weekly in first month after initiation or modification of therapy with EXJADE® and monthly thereafter: dose reduction may be needed in some cases of non-progressive increase in serum creatinine. More frequent creatinine monitoring recommended in patients with an increased risk of renal complications. Dose may be reduced if it is seen in two consecutive visits that serum creatinine rises by >33% above the average of the pre-treatment measurements in adults (and above the age-appropriate upper limit of normal in paediatric patients) and estimated creatinine clearance decreases below the lower limit of the normal range (<90 ml/min). EXJADE® should be interrupted if serum creatinine shows a progressive rise beyond the age-appropriate upper limit of normal. Rare reports of acute renal failure, some of which required dialysis. Reports of renal tubulopathy mainly in children and adoloscents with betathalassaemia and serum ferritin levels <1,500 microgram/L. Caution in patients who are receiving medicinal products that depress renal function and those receiving high doses of EXJADE® and/or low rates of transfusion. ♦ Monthly monitoring of serum ferritin is recommended to assess patient's response to therapy. ♦ Postmarketing cases of hepatic failure have been reported. 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. Not recommended in patients with severe hepatic impairment. ♦ Maintain adequate hydration in patients who develop diarrhoea or vomiting. ♦ Not recommended in patients with short life expectancy (e.g. high risk myelodysplastic syndrome) especially when co-morbidities could increase the risk of adverse events. ♦ Monitor cardiac function in patients with severe iron overload during long term treatment with EXJADE®. ♦ As a general precaution, in paediatric patients with transfusional iron overload, monitor body weight, height and sexual development. ♦ Gastrointestinal irritation may occur. Upper gastrointestinal ulceration and haemorrhage have been reported in patients, including children and adolescents. Multiple ulcers have been observed in some patients. There have been rare reports of fatal GI haemorrhages, especially in elderly patients who had advanced hematologic malignancies and/or low platelet counts. Caution in patients with platelet counts <50 x 10^9/L. ♦ Skin rashes: EXJADE® should be interrupted if severe rash develops. ♦ Discontinue if severe hypersensitivity reaction occurs. ♦ Recommended ophthalmological/audiological testing before start of treatment and annually. ♦ In patients who develop unexplained cytopenia consider interruption of treatment. ♦ Should not be used during pregnancy unless clearly necessary.♦ Not recommended when breast-feeding. ♦ Caution when driving or operating machinery.♦ Product contains lactose. ♦ Exjade may decrease the efficacy of hormonal contraceptives.

INTERACTIONS: ♦ Should not be taken with aluminium-containing antacids or with other iron chelator therapies. ♦Caution when combined with drugs metabolised through CYP3A4 (e.g. ciclosporin, simvastatin, bepridil, ergotamine, hormonal contraceptive agents). ♦Increases in the dose of EXJADE® should be considered when concomitantly used with potent UGT inducers (e.g. rifampicin, phenytoin, phenobarbital, carbamazepine, ritonavir). ♦Concomitant use with repaglinide should be avoided. If combination is necessary, careful monitoring of glucose levels should be performed. An interaction between EXJADE® and other CYP2C8 substrates like paclitaxel cannot be excluded. ♦Caution when combined with drugs with ulcerogenic potential (e.g. NSAIDS, corticosteroids, oral bisphosphonates) or with anticoagulants.

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ADVERSE REACTIONS: ♦ **Very common**: blood creatinine increased ♦ **Common:** headache, proteinuria, transaminases increased, rash, pruritus, diarrhoea, constipation, vomiting, nausea, abdominal pain, abdominal distension, dyspepsia ♦ **Uncommon:** anxiety, sleep disorder, dizziness, early cataract, maculopathy, hearing loss, pharyngolaryngeal pain, gastrointestinal haemorrhage, gastric ulcer (including multiple ulcers), duodenal ulcer, gastritis, hepatitis, cholelithiasis, pigmentation disorder, pyrexia, oedema, fatigue, renal tubulopathy (acquired Fanconi's syndrome), glycosuria ♦ **Rare:** oesophagitis, optic neuritis ♦ Not known: metabolic acidosis, neutropenia, gastrointestinal perforation, nephrolithiasis, renal tubular necrosis**,** anaemia aggravated,pancytopenia, thrombocytopenia, hypersensitivity reactions (including anaphylaxis and angioedema), acute renal failure, Stevens-Johnson syndrome leukocytoclastic vasculitis, urticaria, erythema multiforme, alopecia, hepatic failure, tubulointerstitial nephritis

LEGAL CATEGORY: POM

PACK SIZES: Packs of 28 dispersible tablets

MARKETING AUTHORISATION HOLDER: Novartis Europharm Limited, Frimley Business Park, Camberley, GU16 7SR, United Kingdom.

MARKETING AUHORISATION NUMBER: EU/1/06/356/003 and 005

Please refer to Summary of Product Characteristics (SmPC) before prescribing. Full prescribing information is available on request from Novartis Pharma Services Inc., Representative Office Malta, P.O. Box 4, Marsa, MRS 1000, Malta. Tel: +356 21222872

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Any suspected adverse reactions and medication errors with the use of Exjade, can be reported via the national Adverse Drug Reactions (ADRs) reporting system.

Report forms can be downloaded from http://www.medicinesauthority.gov.mt/adrportal and posted to Medicines Authority Post-licensing directorate, 203, Level 3, Rue D'Argens, Gzira, GZR 1368, MALTA or sent by email to postlicensing.medicinesauthority@gov.mt

Healthcare professionals may also report any adverse events suspected to be associated with the use of Exjade to Novartis Pharma Services Inc. Representative Office Malta by phone on 21222872, by fax on 22487219 or e-mail at drug_safety.malta@novartis.com

References: 1. EXJADE® (deferasirox) dispersible tablets: EU Summary of Product Characteristics. Novartis; 2. Data on file. Novartis Pharmaceuticals Corp. 3. Cockcroft DW, Gault MH. Nephron. 1976;16(1):31-41. 4. Earley A, Miskulin D, Lamb EJ, Levey AS, Uhlig K. Ann Intern Med. 2012;156(11):785-795. 5. Levey AS, Stevens LA, Schmid CH, et al; for the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI). Ann Intern Med. 2009;150(9):604-612. 6. Schwartz GJ, Brion LP, Spitzer A. Pediatr Clin North Am. 1987;34(3):571-590.

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