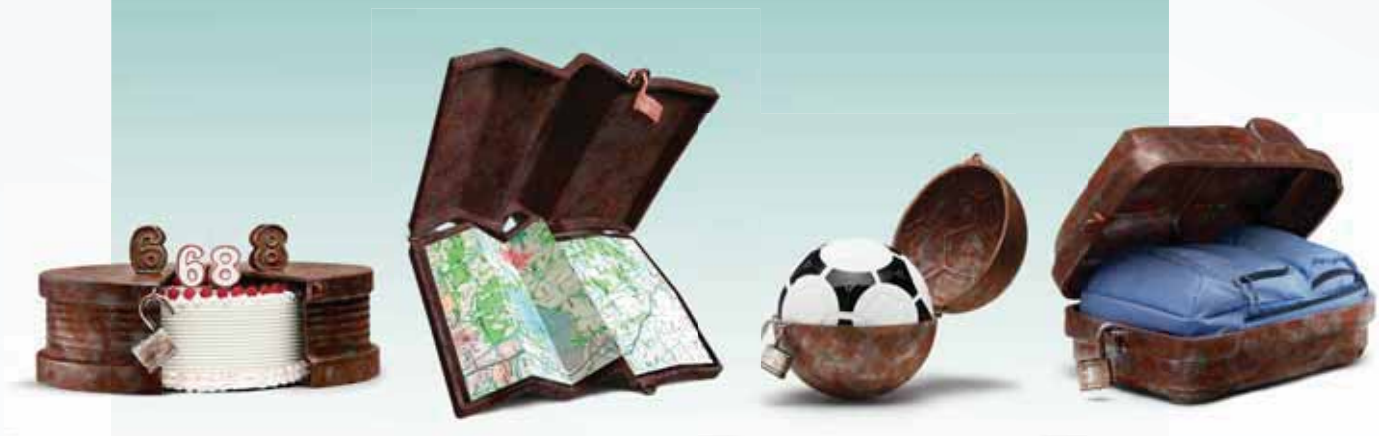
DOSING AND MONITORING GUIDELINES FOR EXJADE®



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 anemias 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.

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DOSING FOR PATIENTS WITH CHRONIC TRANSFUSIONAL IRON OVERLOAD

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.[1]

Starting dose and dose adjustment[1]

- The recommended initial daily dose of EXJADE® is 20 mg/kg body weight
- An initial daily dose of 30 mg/kg may be considered for patients who require reduction of elevated body iron levels and who are also receiving more than 14 ml/kg/month of packed red blood cells (approximately >4 units/month for an adult)
- An initial daily dose of 10 mg/kg may be considered for patients who do not require reduction of body iron levels and who are also receiving less than 7 ml/kg/month of packed red blood cells (approximately <2 units/month for an adult). The patient's response must be monitored and a dose increase should be considered if sufficient efficacy is not obtained
- For patients already well managed on treatment with deferoxamine, a starting dose of EXJADE that is numerically half that of the deferoxamine dose could be considered (e.g. a patient receiving 40 mg/kg/day of deferoxamine for 5 days per week (or equivalent) could be transferred to a starting daily dose of 20 mg/kg/day of EXJADE). When this results in a daily dose less than 20 mg/kg body weight, the patient's response must be monitored and a dose increase should be considered if sufficient efficacy is not obtained

Treatment Goal		Transfusion Frequency		Starting Dose
Reduction of body iron levels **NOT** required	AND	<7 ml/kg/month PRBC (~<2 U RBC/month for an adult)	=	10 mg/kg/day[a]
Reduction of body iron levels required	AND	<7 ml/kg/month PRBC (~<2 U RBC/month for an adult)	=	20 mg/kg/day
		<7-14 ml/kg/month PRBC (~<2-4 U RBC/month for an adult)	=	20 mg/kg/day
		>14 ml/kg/month PRBC (~<4 U RBC/month for an adult)	=	30 mg/kg/day

Doses >40 mg/kg/day are not recommended

Make dose adjustments in steps of 5 or 10 mg/kg/day and adjust to treatment goals (maintenance or reduction of body iron burden).

In patients not adequately controlled with doses of 30 mg/kg/day (ie, serum ferritin [SF] levels consistently >2500 µg/l and not showing a decreasing trend over time), doses ≤40 mg/kg/day may be considered.

If SF consistently falls ≤500 µg/l, consider temporarily interrupting treatment with EXJADE.

PRBCs, packed red blood cells; RBCs, red blood cells; U, units.

[a]Monitor patient response.

Dose adjustments should be based on the monthly monitoring of serum ferritin according to the following guidelines:[1]

- It is recommended that serum ferritin be monitored every month and that the dose of EXJADE be adjusted, if necessary, every 3 to 6 months based on the trends in serum ferritin. Dose adjustments may be made in steps of 5 to 10 mg/kg and are to be tailored to the individual patient's response and therapeutic goals (maintenance or reduction of iron burden)
- In patients not adequately controlled with doses of 30 mg/kg (e.g. serum ferritin levels persistently above 2,500 µg/l and not showing a decreasing trend over time), doses of up to 40 mg/kg may be considered. The availability of long-term efficacy and safety data with EXJADE used at doses above 30 mg/kg is currently limited (264 patients followed for an average of 1 year after dose escalation)
- If only very poor hemosiderosis control is achieved at doses up to 30 mg/kg, a further increase (to a maximum of 40 mg/kg) may not achieve satisfactory control, and alternative treatment options may be considered. If no satisfactory control is achieved at doses above 30 mg/kg, treatment at such doses should not be maintained and alternative treatment options should be considered whenever possible. Doses above 40 mg/kg are not recommended because there is only limited experience with doses above this level
- In patients treated with doses greater than 30 mg/kg, dose reductions in steps of 5 to 10 mg/kg should be considered when control has been achieved (e.g. serum ferritin levels persistently below 2,500 µg/l and showing a decreasing trend over time). In patients whose serum ferritin level has reached the target (usually between 500 and 1,000 µg/l), dose reductions in steps of 5 to 10 mg/kg should be considered to maintain serum ferritin levels within the target range. If serum ferritin falls consistently below 500 µg/l, an interruption of treatment should be considered
- The dosing recommendations for pediatric patients aged 2 to 17 years with transfusional iron overload are the same as for adult patients. Changes in weight of pediatric patients over time must be taken into account when calculating the dose
- In children with transfusional iron overload aged between 2 and 5 years, exposure is lower than in adults. This age group may therefore require higher doses than are necessary in adults. However, the initial dose should be the same as in adults, followed by individual titration

EXJADE deferasirox

DOSING FOR PATIENTS WITH NON–TRANSFUSION-DEPENDENT THALASSEMIA

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.[1]

Starting dose and dose adjustment[1]

- The recommended initial daily dose of EXJADE® in patients with non-transfusion-dependent thalassemia syndromes is 10 mg/kg body weight

INITIATE	UP-TITRATE	DOWN-TITRATE	INTERRUPT
chelation therapy 10 mg/kg/day Monitor monthly	to achieve goal when necessary Increase in increments when necessary 5 to 10 mg/kg/day up to 20 mg/kg/day	to avoid overchelation Decrease dose to 10 mg/kg/day	once goal achieved
LIC ≥5 mg Fe/g dw OR **SF >800 µg/l**	**LIC ≥7** mg Fe/g dw OR **SF >2000 µg/l**	**LIC <7** mg Fe/g dw OR **SF ≤2000 µg/l**	GOAL **LIC <3** mg Fe/g dw OR **SF <300 µg/l**

dw, dry weight; LIC, liver iron concentration; SF, serum ferritin.

- Doses >20 mg/kg/day are not recommended
- Liver magnetic resonance imaging should be used with SF measurements to most accurately determine iron overload in NTDT patients

Dose adjustments should be based on the yearly monitoring of LIC and monthly monitoring of serum ferritin according to the following guidelines:

- 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 thalassemia syndromes
- In patients in whom LIC was not assessed and serum ferritin is ≤2,000 µg/l, dosing should not exceed 10 mg/kg
- In pediatric patients with non-transfusion-dependent thalassemia 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
- 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[1]

- 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

Monitoring recommendations

For patients with chronic transfusional iron overload or with non-transfusion-dependent thalassemia[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)	✓				✓

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

[a]Liver iron concentration monitoring recommended for NTDT only.

EXJADE deferasirox

Hepatic[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
- 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

Renal[1]

- 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
- 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
- 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

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[2]
The Cockcroft–Gault formula employs creatinine measurements and the patient's weight to predict creatinine clearance.

The formula states creatinine clearance in ml/min.

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

The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation[3,4]
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 x $\min(\text{Scr}/\kappa, 1)^{\alpha}$ x $\max(\text{Scr}/\kappa, 1)^{-1.209}$ × 0.993^{Age} × 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[5]

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

[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.

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.

EXJADE deferasirox

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.** Cockcroft DW, Gault MH. Nephron. 1976;16(1):31-41. **3.** Earley A, Miskulin D, Lamb EJ, Levey AS, Uhlig K. Ann Intern Med. 2012;156(11):785-795. **4.** 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. **5.** Schwartz GJ, Brion LP, Spitzer A. Pediatr Clin North Am. 1987;34(3):571-590.

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