JADENU® SPRINKLE (deferasirox) granules

One more option for simplified administration of deferasirox[1]

May be taken with or without a light meal (contains <7% fat content and <250 calories). JADENU Sprinkle is administered by sprinkling the full dose on soft food (eg, yogurt or applesauce) immediately prior to oral consumption.[1]

IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets and JADENU® Sprinkle (deferasirox) Granules

WARNING: RENAL FAILURE, HEPATIC FAILURE, AND GASTROINTESTINAL HEMORRHAGE

Renal Failure

- **JADENU can cause acute renal failure and death, particularly in patients with comorbidities and those who are in the advanced stages of their hematologic disorders**
- **Measure serum creatinine and determine creatinine clearance in duplicate prior to initiation of therapy, and monitor renal function at least monthly thereafter. For patients with baseline renal impairment or increased risk of acute renal failure, monitor creatinine weekly for the first month, then at least monthly. Consider dose reduction, interruption, or discontinuation based on increases in serum creatinine**

Hepatic Failure

- **JADENU 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 JADENU in patients with severe (Child-Pugh C) hepatic impairment, and reduce the dose in patients with moderate (Child-Pugh B) hepatic impairment**

Gastrointestinal Hemorrhage

- **JADENU 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 JADENU for suspected GI ulceration or hemorrhage**

INDICATION

Treatment of Chronic Iron Overload Due to Blood Transfusions (Transfusional Iron Overload)

JADENU® (deferasirox) tablets and JADENU® Sprinkle (deferasirox) granules are indicated for the treatment of chronic iron overload due to blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older.

- This indication is approved under accelerated approval based on a reduction of liver iron concentrations (LICs) and serum ferritin (SF) levels
- Continued approval for this indication may be contingent upon verification and description of clinical benefit in confirmatory trials

Limitations of Use

- Controlled clinical trials of JADENU in patients with myelodysplastic syndromes (MDS) and chronic iron overload due to blood transfusions have not been performed
- The safety and efficacy of JADENU when administered with other iron chelation therapy have not been established

Please see Important Safety Information for JADENU® (deferasirox) tablets and JADENU® Sprinkle (deferasirox) granules throughout, and accompanying full Prescribing Information, including Boxed WARNING.

JADENU®
Sprinkle (deferasirox) granules
90 mg, 180 mg, 360 mg

Introducing JADENU® SPRINKLE (deferasirox) granules

An additional administration alternative for patients taking EXJADE® (deferasirox) tablets for oral suspension or JADENU® (deferasirox) tablets[1]

- May be appropriate for patients 2 years of age and older with chronic iron overload who have difficulty swallowing whole JADENU tablets or are transitioning from EXJADE[1]
- Sprinkled on soft food (eg, yogurt or applesauce) immediately prior to use and administered orally[1]
- Contains the same active ingredient as EXJADE[1]

IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets and JADENU® Sprinkle (deferasirox) Granules

CONTRAINDICATIONS

JADENU is contraindicated in patients with:

- Serum creatinine >2 times the age-appropriate upper limit of normal or creatinine clearance <40 mL/min;
- Poor performance status;
- High-risk MDS;
- Advanced malignancies;
- Platelet counts less than 50 × 10^9/L;
- Known hypersensitivity to deferasirox or any component of JADENU

WARNINGS AND PRECAUTIONS

Renal Toxicity, Renal Failure, and Proteinuria

- JADENU can cause acute renal failure, fatal in some patients and requiring dialysis in others. Postmarketing experience showed that most fatalities occurred in patients with multiple comorbidities and who were in advanced stages of their hematologic disorders. In the clinical trials, deferasirox-treated patients experienced dose-dependent increases in serum creatinine. In patients with transfusional iron overload, these increases occurred at a greater frequency compared to deferoxamine-treated patients (38% vs 14%, respectively, in Study 1 [patients with β-thalassemia] and 36% vs 22%, respectively, in Study 3 [patients with sickle cell disease])
- Measure serum creatinine in duplicate (due to variations in measurements) and determine the creatinine clearance (estimated by the Cockcroft-Gault method) before initiating therapy in all patients in order to establish a reliable pretreatment baseline. Monitor serum creatinine weekly during the first month after initiation or modification of therapy, and at least monthly thereafter. Monitor serum creatinine and/or creatinine clearance more frequently if creatinine levels are increasing. Dose reduction, interruption, or discontinuation based on increases in serum creatinine may be necessary
- JADENU is contraindicated in patients with creatinine clearance <40 mL/min or serum creatinine >2 times the age-appropriate upper limit of normal
- Renal tubular damage, including Fanconi Syndrome, has been reported in patients treated with deferasirox, most commonly in children and adolescents with β-thalassemia and SF levels <1500 µg/L
- Intermittent proteinuria (urine protein/creatinine ratio >0.6 mg/mg) occurred in 18.6% of deferasirox-treated patients compared to 7.2% of deferoxamine-treated patients in Study 1 (patients with β-thalassemia). In clinical trials in patients with transfusional iron overload, deferasirox was temporarily withheld until the urine protein/creatinine ratio fell below 0.6 mg/mg. Monthly monitoring for proteinuria is recommended. The mechanism and clinical significance of the proteinuria are uncertain

Hepatic Toxicity and Failure

- Deferasirox can cause hepatic injury, fatal in some patients. In Study 1 (patients with β-thalassemia), 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 >55 years of age. Hepatic failure was more common in patients with significant comorbidities, including liver cirrhosis and multiorgan failure
- Measure transaminases (AST and 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 JADENU in patients with severe (Child-Pugh C) hepatic impairment. Reduce the starting dose in patients with moderate (Child-Pugh B) hepatic impairment. Patients with mild (Child-Pugh A) or moderate (Child-Pugh B) hepatic impairment may be at higher risk for hepatic toxicity

SEAMLESS TRANSITION FROM EXJADE TO JADENU[1]

	EXJADE		JADENU Tablets JADENU Sprinkle
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
DOSE STRENGTHS	125 mg 250 mg 500 mg		90 mg 180 mg 360 mg

The dose of JADENU should be about 30% lower than a patient's dose of EXJADE

- For patients already taking EXJADE, start JADENU at the nearest equivalent dose (eg, EXJADE 30 mg/kg/day = JADENU 21 mg/kg/day)[1]
- In patients not adequately controlled with JADENU 21 mg/kg/day, up to 28 mg/kg/day may be considered. Doses >28 mg/kg/day are not recommended[1]
- Dose may be increased or decreased every 3 to 6 months based on serum ferritin trends and individual patient's therapeutic goals and tolerability[1]
- If serum ferritin falls consistently below 500 µg/L, consider temporarily interrupting therapy with deferasirox[1]

Gastrointestinal (GI) Ulceration, Hemorrhage, and Perforation

- GI hemorrhages, including deaths, have 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 JADENU therapy, and promptly initiate additional evaluation and treatment if a serious GI adverse event is suspected
- The risk of GI hemorrhage may be increased when administering JADENU 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 gastrointestinal perforation (including fatal outcome)

Bone Marrow Suppression

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

Increased Risk of Toxicity in the Elderly

- Deferasirox has been associated with serious and fatal adverse reactions in the postmarketing setting, predominantly in elderly patients. Monitor elderly patients treated with JADENU more frequently for toxicity

Hypersensitivity

- JADENU 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 JADENU and institute appropriate medical intervention
- JADENU 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 skin reactions, including Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and erythema multiforme have been reported during deferasirox therapy. The risk of other skin reactions, including DRESS (drug reaction with eosinophilia and systemic symptoms), cannot be excluded. If severe skin reactions are suspected, discontinue JADENU immediately and do not reintroduce JADENU therapy

Skin Rash

- Rashes may occur during JADENU treatment. For rashes of mild to moderate severity, JADENU may be continued without dose adjustment since the rash often resolves spontaneously. In severe cases, interrupt treatment with JADENU. 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 <1% with deferasirox therapy in the clinical studies

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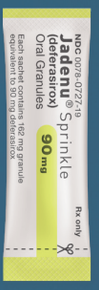
JADENU®
Sprinkle (deferasirox) granules
90 mg, 180 mg, 360 mg

SIMPLIFY YOUR PATIENTS' TREATMENT EXPERIENCE WITH JADENU® (deferasirox)[1]

Administration options for deferasirox[1,2]

	EXJADE® (deferasirox) tablets for oral suspension	JADENU® (deferasirox) tablets	JADENU® Sprinkle (deferasirox) granules
			
	Once-daily tablets for oral suspension • Contains lactose and sodium lauryl sulfate (SLS)	Once-daily film-coated tablets • Same active ingredient as EXJADE • Does not contain lactose or SLS	Once-daily granules in sachet • Same active ingredient as EXJADE • Does not contain lactose or SLS
Preparation	 Thoroughly mix in liquid until fine suspension is obtained, and swallow* Resuspend any residue in a small amount of liquid	 No preparation required	 Sprinkle on soft food (eg, yogurt or applesauce)
Meal Considerations	 Fasting for 30 minutes required	 Taken with or without a light meal†	 Taken with or without a light meal†

- JADENU and EXJADE must not be taken with aluminum-containing antacid products[1,2]

*Water, orange juice, or apple juice.[2]

†A light meal contains: <7% fat content and <250 calories; eg, 1 whole wheat English muffin, 1 packet of jelly (0.5 ounce), and skim milk (8 fl ounces) or a turkey sandwich (2 ounces turkey on whole wheat bread with lettuce, tomato, and 1 packet mustard).[1]

IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets and JADENU® Sprinkle (deferasirox) Granules (continued)

- Perform auditory and ophthalmic testing (including slit lamp examinations and dilated fundoscopy) before starting JADENU treatment and thereafter at regular intervals (every 12 months). If disturbances are noted, monitor more frequently. Consider dose reduction or interruption

Overchelation

- For patients with transfusional iron overload, measure SF monthly to assess for possible overchelation of iron. If the SF falls below 500 µg/L, consider temporarily interrupting therapy with JADENU since this result may increase JADENU toxicity

ADVERSE REACTIONS

- JADENU was evaluated in healthy subjects, and there are no clinical data in patients treated with JADENU tablets or JADENU Sprinkle granules. JADENU contains the same active ingredient, deferasirox, as EXJADE® tablets for oral suspension
- For patients with transfusional iron overload, the most common adverse reactions occurring in >5% of deferasirox-treated patients with β-thalassemia, patients with sickle cell disease, and patients with MDS were abdominal pain, nausea, vomiting, diarrhea, skin rashes, and increases in serum creatinine. Gastrointestinal symptoms, increases in serum creatinine, and skin rash were dose related

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References: 1. Jadenu [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2017. **2.** Exjade [prescribing information]. East Hanover, NJ: Novartis Pharmaceuticals Corp; 2016.

For more information about JADENU, please visit www.jadenu.com.

NOVARTIS

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90 mg, 180 mg, 360 mg

QR CODE FOR INTERNAL USE ONLY.

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Printed in USA 5/17 JAD-1157259