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.

Please see Important Safety Information throughout this brochure and click here for full Prescribing Information, including Boxed WARNING, for JADENU (deferasirox).
INDICATION
Treatment of Chronic Iron Overload Due to Blood Transfusions
(Transfusional Iron Overload)
JADENU® (deferasirox) tablets is 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 throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
INDICATION
Treatment of Chronic Iron Overload Due to Blood Transfusions
(Transfusional Iron Overload)
JADENU® (deferasirox) tablets is indicated for the treatment of chronically elevated levels of iron in the blood caused by repeated blood transfusions (transfusional hemosiderosis) in patients 2 years of age and older.
- In these patients, deferasirox lowered the levels of iron in the blood (measured by serum ferritin levels) and liver (measured by liver iron concentration)
- There are ongoing studies to find out how JADENU works over a longer period of time

Limitations on the Use of JADENU
- It is not known if JADENU is safe or effective when taken with another therapy that lowers iron levels in the blood
- There are patients with a serious blood disorder known as myelodysplastic syndromes (MDS) that may take JADENU to treat chronically elevated levels of iron in the blood caused by repeated blood transfusions. The iron-lowering effects and safety of JADENU have not been studied in clinical trials specifically designed for just these patients with MDS

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
Chronic iron overload can affect important bodily organs\textsuperscript{2-4}

- Heart
- Liver

The body has no physiologic mechanism for removing iron\textsuperscript{2}

Transfusions overload the body with \( \geq 100 \times \) the normal daily iron intake\textsuperscript{2}

**IMPORTANT SAFETY INFORMATION** for JADENU\textsuperscript{®} (deferasirox) Tablets

**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 \( \times \) 10\(^9\)/L;
- Known hypersensitivity to deferasirox or any component of JADENU

Please see additional Important Safety Information throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
Iron can build up in your organs

Heart

Liver

IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets

What is the most important safety information to know about JADENU?

JADENU contains deferasirox, the same active ingredient in EXJADE® (deferasirox) tablets for oral suspension. Deferasirox may cause serious kidney problems, liver problems, and bleeding in the stomach or intestines. In some cases, these problems were fatal. Kidney problems occurred particularly in patients with multiple medical conditions and those who were very ill because of their disease. Bleeding in the stomach or intestines occurred more often in elderly patients. Liver problems were more likely to happen in patients older than 55 years.

Your doctor should check your kidneys with a blood test called serum creatinine and/or creatinine clearance:
- Before taking JADENU
- Monthly during treatment

If you already have a history of kidney problems or are at risk for kidney problems, your doctor should check your kidneys:
- Every week for the first month
- Monthly during treatment

Your doctor should check your liver with blood tests called serum transaminases and bilirubin:
- Before taking JADENU
- Every other week for the first month after starting JADENU
- Monthly during treatment

Please see additional Important Safety Information throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
The goal of chelation therapy is to achieve serum ferritin <1000 µg/L\(^5,6\)

- Serum ferritin levels must be monitored monthly during treatment\(^1\)
  — Ferritin is an iron-storage protein\(^4\)
- The dose of therapy may be adjusted as serum ferritin levels change\(^1\)

If the serum ferritin falls below 500 µg/L, consider temporarily interrupting therapy with JADENU since this result may increase JADENU toxicity\(^1\)

IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets (continued)

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 \(\beta\)-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 \(\beta\)-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 \(\beta\)-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

Please see additional Important Safety Information throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets (continued)

You should not take JADENU if you have:
• Certain kinds of kidney problems
• Pre-existing severe liver problems
• High-risk MDS
• Advanced cancer
• Low blood counts (low platelets)
• An allergy to JADENU or any ingredient of JADENU

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
JADENU® (deferasirox) tablets easily fit into your patient’s daily routine

• Single-step, once-daily administration with no mixing required¹
• Taken as oral tablets that are swallowed once daily with water or other liquid¹
• For patients who have difficulty swallowing whole tablets, JADENU tablets may be crushed and mixed with soft foods (eg, 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 use¹
• Taken with a light meal or on an empty stomach¹
  — The light meal should contain <7% fat content and <250 calories, such as 1 whole-wheat English muffin, 1 packet 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

Adverse reactions

• Safety profile is based on clinical trials conducted with EXJADE® (deferasirox) tablets for oral suspension¹
• In patients with transfusional iron overload, the most frequently occurring (>5%) adverse reactions are diarrhea, vomiting, nausea, abdominal pain, skin rashes, and increases in serum creatinine¹

IMPORTANT SAFETY INFORMATION for JADENU (continued)

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

Please see additional Important Safety Information throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
You have been prescribed JADENU® (deferasirox) tablets for your chronic iron overload

Taken as oral tablets that are swallowed once daily with water or other liquid

- If you have trouble swallowing whole tablets, JADENU 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.

Examples of a light meal (should contain <7% fat content and <250 calories)

- 1 whole-wheat English muffin, 1 packet jelly (0.5 ounce), and skim milk (8 fl ounces)
- A turkey sandwich (2 ounces turkey on whole-wheat bread with lettuce, tomato, and 1 packet mustard)¹

Be aware of common side effects from clinical trials of EXJADE® (deferasirox) tablets for oral suspension

- Safety profile is based on clinical trials conducted with EXJADE
- Gastrointestinal: nausea, vomiting, diarrhea, stomach pain
- Kidney: changes in kidney function
- Skin: rash

Talk with your doctor if you have any side effects

IMPORTANT SAFETY INFORMATION for JADENU (continued)

Additional Important Safety Information

Kidneys

- If you have a pre-existing kidney condition, are elderly, have multiple medical conditions, or are taking medicine that affects your kidneys, you are at increased risk of complications. Your doctor will give you a blood test (called serum creatinine and/or creatinine clearance) every week for the first month you are taking JADENU or if your dose has changed, and then every month after that. Your doctor may adjust your dose based on the results of these tests.
- Your doctor may also collect urine samples monthly.
- Some patients developed severe kidney problems while taking deferasirox, in some cases fatal, and in some cases requiring dialysis. Most of the fatalities occurred in patients who were very ill because of their disease.

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
Administration differences between JADENU® (deferasirox) tablets and EXJADE® (deferasirox) tablets for oral suspension

EXJADE®
ONE WEEK OF THERAPY
TABLETS FOR ORAL SUSPENSION

Once-daily oral suspension
Fasting for 30 minutes required
Multistep preparation requiring a glass, spoon, and liquid
Must be thoroughly mixed with water, orange juice, or apple juice until fine suspension is obtained

JADENU®
ONE WEEK OF THERAPY
FILM-COATED TABLETS

Once-daily, film-coated tablets
Taken with or without a light meala
No preparation required
No mixing required

aContains <7% fat content and <250 calories.1

IMPORTANT SAFETY INFORMATION for JADENU (continued)

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)

Please see additional Important Safety Information throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
JADENU® (deferasirox) tablets have the same active ingredient as EXJADE® (deferasirox) tablets for oral suspension

How is JADENU different from EXJADE?

- Taken as oral tablets that are swallowed whole once daily with water or other liquid
- Can be taken with or without a light meal
  - Less than 7% fat content and fewer than 250 calories
- No mixing or measuring required

JADENU tablet strengths

<table>
<thead>
<tr>
<th>Strength</th>
<th>Image</th>
</tr>
</thead>
<tbody>
<tr>
<td>90 mg</td>
<td><img src="90mg.png" alt="90mg Tablet" /></td>
</tr>
<tr>
<td>180 mg</td>
<td><img src="180mg.png" alt="180mg Tablet" /></td>
</tr>
<tr>
<td>360 mg</td>
<td><img src="360mg.png" alt="360mg Tablet" /></td>
</tr>
</tbody>
</table>

Remember to take exactly the number of tablets your doctor prescribes.

IMPORTANT SAFETY INFORMATION for JADENU (continued)

Additional Important Safety Information (continued)

Liver
- If you have a pre-existing severe liver problem, you should not use JADENU
- If you have mild or moderate liver problems, your doctor will give you blood tests called serum transaminases and bilirubin before starting treatment, every 2 weeks during the first month of treatment, and then monthly. Your doctor may adjust your dose based on the results of these tests
- Some patients developed severe liver problems, in some cases fatal, while taking deferasirox. Many of these patients were older than 55 years of age and/or had multiple medical conditions already affecting their liver

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
Many resources are available for patients receiving JADENU® (deferasirox) tablets

- JADENU Patient Starter Kit
- Financial: Patient Assistance Now Oncology (1-800-282-7630)
- Education: Novartis Clinical Educators (1-877-988-8812)

**IMPORTANT SAFETY INFORMATION for JADENU**

*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 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

Please see additional Important Safety Information throughout this brochure, including Boxed WARNING on cover, and click here for full Prescribing Information for JADENU (deferasirox).
Your JADENU® (deferasirox) tablets starter kit includes:

• An all-about-JADENU brochure
• Quick flash cards that explain
  — How eligible patients can save on JADENU co-pays
  — How JADENU can be delivered right to your home from a specialty pharmacy
  — How Clinical Educators are available to answer your questions about JADENU

Need help paying for JADENU?

• Novartis is committed to helping patients receive the medicines they need
• Call Patient Assistance Now Oncology at 1-800-282-7630

Have questions?

Novartis Clinical Educators are available face-to-face or over the phone to answer your questions about JADENU. Call 1-877-988-8812 today!

IMPORTANT SAFETY INFORMATION for JADENU (continued)

Additional Important Safety Information (continued)

Bleeding in the Stomach or Intestines
• Some patients developed stomach irritation or bleeds while taking deferasirox. In some cases, stomach bleeds were fatal, usually in patients who were elderly and had pre-existing blood cancers and/or low blood counts (low platelets)
• Talk to your doctor if you are taking other drugs that can also irritate your stomach or cause a stomach bleed (eg, pain relievers/anti-inflammatory drugs, corticosteroids, oral bisphosphonates, blood thinners)

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).
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
- 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. 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
IMPORTANT SAFETY INFORMATION for JADENU® (deferasirox) Tablets (continued)

Additional Important Safety Information (continued)

Blood Disorders
- Some patients developed severe blood disorders, in some cases fatal, while on deferasirox therapy. Having a pre-existing blood disorder may increase the risk
- Your doctor will give you a blood test to check your blood counts

Increased Risks When Used in Elderly Patients
- Since deferasirox has been on the market, there have been reports of serious reactions, sometimes leading to death. These serious reactions and deaths have happened most often when deferasirox was taken by elderly patients

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 you develop swelling of the throat, a severe rash, hearing problems, or vision disturbances, stop taking JADENU and contact your doctor immediately

Serious Skin Reactions
- Severe skin disorders that result in a very serious rash, called Stevens-Johnson syndrome (SJS), toxic epidermal necrolysis (TEN), and erythema multiforme, have been reported during treatment with deferasirox. Other skin reactions, including DRESS (drug reaction with eosinophilia and systemic symptoms), can also occur. If you develop a severe rash, stop taking JADENU and contact your doctor immediately
- Mild to moderate skin rashes may occur during treatment with deferasirox. Let your doctor know if the rash doesn’t go away on its own or gets worse. Your doctor may need to change your dose of JADENU

Hearing and Vision Changes
- Changes to hearing and vision have been reported in patients taking deferasirox. If you notice changes in your hearing or eyesight, contact your doctor immediately
- You may also receive a hearing or vision test prior to receiving JADENU and yearly thereafter. Your doctor may change your dose based on the results of these tests

Common Side Effects
- The most commonly reported side effects related to deferasirox in clinical trials were mainly nausea, vomiting, diarrhea, stomach pain, increases in kidney laboratory values, and skin rash
- Let your doctor know if you are experiencing any side effects. Your doctor may need to change your dose
- If you experience diarrhea or vomiting, you must continue to drink fluids
- You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088

Taking Other Medicines With JADENU
- If you are taking other medicines, such as birth control pills, diabetes drugs, seizure drugs, cholesterol-lowering drugs, or medicine for serious illnesses, talk to your doctor. JADENU may affect how these drugs work

Talk to your doctor to determine if prescription JADENU therapy is right for you.

Please see additional Important Safety Information, including Boxed WARNING, throughout this brochure and click here for full Prescribing Information for JADENU (deferasirox).