Drug is indicated for the treatment of patients with cutaneous T-cell lymphoma (CTCL) who have received at least one prior systemic therapy.

**Approved Drugs:** Romidepsin for injection (Istodax)

**Indications**

Drug is indicated for the treatment of patients with cutaneous T-cell lymphoma (CTCL) who have received at least one prior systemic therapy.

**Mechanism of Action**
Romidepsin is a histone deacetylase (HDAC) inhibitor. Genes, like those that stop cancer growth (tumor suppressor genes) can be turned off if the DNA in the cell is wound too tightly. HDAC inhibitors block an enzyme that tightens the DNA coiling, so that the strand relaxes and the gene can be opened (expressed). This allows the gene to be copied, and the tumor suppressor protein made, so it can do its job to stop cancer growth.

**Metabolism**
Drug is extensively metabolized or broken down by the P450 microenzyme system in the liver—specifically the CYP3A4 system, and to a lesser degree CYP3A5, CYP1A1, CYP2B6, and CYP2C19. Mild hepatic impairment does not alter metabolism of drug.

**Drug Administration**
- 14 mg/m² administered IV over 4 hours on days 1, 8, and 15 of a 28-day cycle. Repeat cycles every 28 days if patient continues to derive benefit and tolerates drug.
- Drug should be interrupted or discontinued, with or without dose reduction to 10 mg/m², as needed to manage adverse drug events.
  - Dose reductions (hematologic side effects)
    - Grade 3/4 neutropenia or thrombocytopenia: hold drug until ANC 1,500/mm³ or platelet count is 75,000/mm³ or at baseline, then restart at full dose.
    - Grade 4 febrile (38.5°C or 101.3°F) neutropenia or thrombocytopenia requiring platelet transfusion: hold drug until labs return to Grade 1 or baseline, then dose should be permanently reduced to 10 mg/m².
  - Dose reductions (non-hematologic)
    - Grade 2 or 3 toxicity: hold drug until toxicity returns to Grade 1 or baseline, then resume drug at full dose. IF Grade 3 toxicity recurs, hold until toxicity returns to Grade 1 or baseline, then reduce dose permanently to 10 mg/m².
    - Grade 4 toxicity: hold drug until toxicity returns to Grade 1 or baseline, then reduce dose permanently to 10 mg/m².
    - Discontinue drug if Grade 3 or 4 toxicity recurs after dose reduction.

**Patient Education**
- Inform patient that drug is used to stop cancer cells from dividing and growing.
- Explain that drug can cause a fast or irregular heartbeat, or a condition known as QT prolongation, which is a lengthening of the time it takes heart muscle to pump blood from the heart to the blood.
vessels and then relax. Tell patient that, because low blood levels of potassium and magnesium can increase the risk of QT interval prolongation, blood levels of these electrolytes will be checked frequently; and the patient will need to have an EKG performed before receiving romidepsin. The EKG may be repeated during the course of therapy.

- Tell patient to disclose all medications, such as for a heart condition, or any anticoagulant therapy (eg, Coumadin [warfarin]). Patient should also tell the nurse or doctor if s/he is taking any medicines for tuberculosis, seizures, infections, HIV, or depression.
- Inform patient that drug has some interactions with other medicines, and that the pharmacist, nurse, and doctor will review the patient’s medication profile and advise on any potential interactions. Advise patient not to start any new medicine without talking to the doctor or nurse, including herbal preparations. The patient should NOT take St. John’s Wort while receiving romidepsin.
- Women of childbearing age should be advised not to become pregnant, as drug can harm the fetus. Drug may be passed in breast milk, so it is important that the patient not breastfeed while taking romidepsin.
- Drug may decrease the effectiveness of estrogen-based birth control medications (eg, birth control pills, patches, implants, IUDs). If the female patient is using an estrogen-based contraception, she should use a barrier contraception as well.
- Drug may increase risk of infection due to low white blood cell counts, so it is important for patients to tell the nurse or doctor right away if they get a fever (100.5°F or higher), or have signs or symptoms of infection (eg, a burning sensation when urinating, coughing up colored sputum) or chills. Drug may also increase the risk of bleeding (due to low numbers of platelets), so it is important for patients to avoid getting cuts or injuring themselves. Patients should report any bleeding or unusual bruising promptly. Patients may have low red cell counts, and so should try to alternate periods of rest and activity to avoid becoming fatigued. Patients should call nurse or doctor if they experience shortness of breath. Inform patients that their blood will be tested frequently to assess cell counts.
- Drug may cause nausea, vomiting, diarrhea, and/or loss of appetite. Patient should be instructed to call nurse or doctor right away if nausea, vomiting, or diarrhea occurs and does not stop after 24 hours with the medicines provided to prevent nausea/vomiting, as these conditions may cause a decrease in blood potassium levels.

**Drug Interactions**

- Patient should avoid drugs that are strong CYP3A4 inhibitors (ketoconazole, itraconazole, clarithromycin, atazanavir, indinavir, nefazodone, nelfinavir, ritonavir, saquinavir, telithromycin, voriconazole), as they may increase the drug levels of romidepsin (as its metabolism is reduced) and the risk of toxicity.
- Patients should also avoid drugs that are strong CYP3A4 inducers and which can increase the metabolism of romidepsin (eg, dexamethasone, carbamazepine, phenytoin, rifampin, rifabutin, rifapentine, phenobarbital), as they can decrease the serum level of romidepsin and the drug dose may need to be increased.
- Coumadin or Coumadin derivatives: may elevate INR (international normalized ratio) and prolong PT (prothrombin time). Patient INR and PT must be closely monitored and the Coumadin dosed according to these values.
- QT-prolonging drugs: may prolong the QTc interval and increase risk of cardiotoxicity.

**Special Considerations**

- Perform a baseline electrocardiogram (EKG) and document the QTc interval. Normal is 440 msec. If patient has a history of congenital prolonged QT interval or has significant cardiovascular disease, or is taking any QT-prolonging drugs (eg, methadone, haloperidol, amiodarone [Cordarone], sotalol [Betapace], certain serotonin receptor antagonists), the EKG and QTc should be monitored closely. If the QTc > 500 msec, the patient may develop torsades de pointes, a type of ventricular tachycardia that may rapidly become ventricular fibrillation. Risk is increased if the patient has hypokalemia and/or hypomagnesemia.
- Assess CBC/differential and electrolytes, including potassium and magnesium, prior to each treatment.
- Women of childbearing age should use effective contraception. Drug binds to estrogen receptors, so it may reduce the effectiveness of estrogen-based contraceptives. Teach patient to use an additional barrier contraception.
- Use caution in administering to patients with mild or severe hepatic dysfunction.
- Use caution in administering to patients with end-stage renal disease.

**Contraindications/Precautions**
- No contraindications.
- Serum potassium and magnesium must be normalized before administering the drug.
- Do not administer drug to pregnant or breastfeeding women.
- Patients on Coumadin or coumarin derivatives require close and frequent monitoring and dosing of Coumadin based on PT, INR.

Financial Disclosure: The author has no significant financial interest or other relationship with the manufacturers of any products or providers of any service mentioned in this article.

**Adverse Reactions to Romidepsin by Body System** (boldface type indicates more common events, with 20% or higher incidence)

**CNS**: Fatigue, asthenia  
**CV**: EKG ST-T wave changes, hypotension, QT prolongation, supraventricular rhythm, myocardial infarction, angina, cardiopulmonary failure  
**GI**: Nausea, vomiting, anorexia, hypomagnesemia, diarrhea, dysgeusia, constipation, hypokalemia, AST, ALT, hyperglycemia, hyponatremia, hypermagnesemia  
**Pulmonary**: Acute respiratory distress syndrome (ARDS)  
**GU**: Acute renal failure  
**Hematologic**: Anemia, thrombocytopenia, neutropenia, lymphopenia, infections, pyrexia, leucopenia, sepsis  
**Metabolic**: Hypocalcemia, hyperuricemia, hypophosphatemia  
**Reproductive**: Fetal harm (based on lab studies)  
**Skin**: Pruritis, dermatitis, exfoliative dermatitis

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