

Pr**ISTODAX**[®]

Romidepsin for injection

PART III: CONSUMER INFORMATION

ISTODAX[®] (romidepsin is indicated for the treatment of patients with peripheral T-cell lymphoma (PTCL) who cannot receive a stem cell transplant and have disease which has come back after other attempted treatment by your physicians, pending the results of studies to verify its clinical benefit. For more information, patients are advised to contact their health care provider.

What is a Notice of Compliance with Conditions (NOC/c)?

An NOC/c is a form of market approval granted to a product on the basis of **promising** evidence of clinical effectiveness following review of the submission by Health Canada.

Products approved under Health Canada's NOC/c policy are intended for the treatment, prevention or diagnosis of a serious, life-threatening or severely debilitating illness. They have demonstrated promising benefit, are of high quality and possess an acceptable safety profile based on a benefit/risk assessment. In addition, they either respond to a serious unmet medical need in Canada or have demonstrated a significant improvement in the benefit/risk profile over existing therapies. Health Canada has provided access to this product on the condition that sponsors carry out additional clinical trials to verify the anticipated benefit within an agreed upon time frame.

Pr**ISTODAX**
romidepsin for injection

This leaflet is part III of a three-part "Product Monograph" published when ISTODAX was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ISTODAX. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

ISTODAX is a prescription medicine used to treat people with a type of blood cancer called peripheral T-cell lymphoma (PTCL) who cannot receive a stem cell transplant, after at least one other type of medicine by mouth or injection has been tried.

What is peripheral T-cell lymphoma:

Peripheral T-cell lymphoma (PTCL) is a disease in which certain cells of the lymph system called T-cells develop into cancer cells which develop and grow abnormally. The term "peripheral" means that this cancer develops in mature T-cells outside of the bone marrow such as lymph nodes, spleen, gastrointestinal tract, and skin. It is often not known why someone develops PTCL.

What it does:

ISTODAX belongs to a group of medicines called cytostatic drugs which work by preventing the growth of cancer cells.

When it should not be used:

Do not use ISTODAX if you are allergic to romidepsin or to any of the other ingredients of ISTODAX.

What the medicinal ingredient is:

romidepsin

What the important nonmedicinal ingredients are:

Povidone. The diluent contains 80% propylene glycol and 20% dehydrated alcohol.

What dosage forms it comes in:

ISTODAX is supplied as a sterile freeze-dried powder. Each vial delivers 10 mg of romidepsin.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

ISTODAX should only be prescribed by a doctor experienced in the use of anti-cancer drugs. Serious side effects may occur with the use of ISTODAX and could include:

- decrease in the production of blood cells resulting in very low levels of red blood cells, white blood cells, and platelets (pancytopenia)
- abnormal heart beat (**QTc prolongation**)
- life-threatening **infections** (including pneumonia and sepsis)
- **tumor lysis syndrome** due to rapid breakdown of cancer cells; this can result in damage to the kidneys, heart and liver
- birth defects or death of an unborn baby

ISTODAX has not been studied in patients with kidney disease.

ISTODAX is not recommended in patients with severe liver disease.

BEFORE you use ISTODAX talk to your doctor or pharmacist if you:

- have kidney problems
- have liver problems
- have nausea, vomiting, or diarrhea
- have any other medical conditions
- have any heart problems, including an irregular or fast heartbeat
- have **QT/QTc prolongation** or a family history of **QT/QTc prolongation**;
- have heart disease
- have a personal history of fainting spells
- have a family history of sudden cardiac death at <50 years
- have electrolyte disturbances (e.g., low blood potassium or magnesium levels) or conditions that could lead to electrolyte disturbances (e.g., vomiting, diarrhea, dehydration)
- have had previous viral infection (e.g. hepatitis B, cytomegalovirus (CMV), herpes, Epstein-Barr virus)

Female patients:

- if you are pregnant or plan to become pregnant, there are specific risks you should discuss with your doctor.
- Avoid becoming pregnant while receiving ISTODAX. It may harm your unborn baby or may cause you to lose the pregnancy. You should use effective methods of birth control while receiving ISTODAX. Keep using birth control for 8 weeks after your last dose of ISTODAX. Tell your doctor right away if you become pregnant while taking ISTODAX.
- **For women who can get pregnant:** a pregnancy test should be done before you start treatment with ISTODAX.
- It is not known if ISTODAX passes into your breast milk. You should not breast feed your baby if you are being treated with ISTODAX.

Male patients:

- Your partner should not become pregnant while you are receiving ISTODAX.

- You should use effective contraception to prevent pregnancy in your partner while you are receiving ISTODAX. Keep using these birth control methods for 1 month after your last dose.
- You should use a condom with spermicide even if you have had a vasectomy.

It is not known if ISTODAX is safe and effective in children under 18 years of age.

ISTODAX has an effect on the electrical activity of the heart known as **QT/QTc prolongation**. This effect can be measured as a change in the electrocardiogram (ECG). In very rare cases, drugs with this effect on the ECG can lead to disturbances in heart rhythm (arrhythmias/dysrhythmias) that could result in dizziness, palpitations (sensation of rapid, pounding, or irregular heart beat), fainting or death. These heart rhythm disturbances are more likely in patients with risk factors, such as heart disease, or in the presence of certain interacting drugs. In general, females and people more than 65 years in age are at higher risk. It is important to follow the instructions of your doctor with regard to dosing or any special tests. If you experience any symptoms of a possible heart rhythm disturbance, such as dizziness, palpitations (sensation of rapid, pounding, or irregular heart beat), fainting, or seizures, you should seek immediate medical attention.

Electrocardiograms (ECGs) and blood tests may be required periodically to monitor the risk of potentially serious side effects during treatment with ISTODAX.

Driving cars and using machines: ISTODAX is known to cause fatigue and weakness. Avoid driving, using machines or performing hazardous tasks if you experience these side effects.

INTERACTIONS WITH THIS MEDICATION

Tell your doctor about all of the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements.

Some medicines may affect how ISTODAX works, or ISTODAX may affect how your other medicines work.

Drugs that may interact with ISTODAX include:

- Blood thinner medicine (e.g. warfarin sodium). Ask your doctor if you are not sure if you are taking a blood thinner. Your doctor may want to test your blood more often.
- Drugs to treat abnormal heart beats (e.g. quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dronedarone, flecainide, propafenone).

- Drugs to treat schizophrenia and other psychiatric disease (e.g. chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone)
- Drugs to treat HIV infections (e.g. atazanavir, indinavir, nelfinavir, ritonavir, saquinavir)
- Drugs to treat seizures (e.g. phenytoin, carbamazepine, phenobarbital)
- Birth control that contains estrogen, such as the “pills”, patches, implants, or Intrauterine devices (IUDs). ISTODAX may reduce the effectiveness of estrogen-containing contraceptives. You may become pregnant.
- St. John’s Wort (*Hypericum perforatum*), an herbal treatment for depression
- Domperidone, used to treat gastrointestinal disorder.
- Methadone (an opioid)
- Medicine for:
 - depression (e.g. fluoxetine, citalopram, venlafaxine, amitriptyline, imipramine, maprotiline, nefazodone)
 - bacterial infections (antibiotics such as erythromycin, clarithromycin, telithromycin, tacrolimus, moxifloxacin, levofloxacin, ciprofloxacin, rifampin, rifabutin, rifapentine)
 - malaria (e.g. quinine, chloroquine)
 - fungal infections (e.g. ketoconazole, fluconazole, voriconazole, itraconazole)
 - nausea (e.g. dolasetron, ondansetron)
 - cancer (e.g. vandetanib, sunitinib, nilotinib, lapatinib, vorinostat)
 - asthma (e.g. salmeterol, formoterol)

Any medicine that cause imbalance in the electrolytes in your body:

- diuretics (water pills)
- laxatives and enemas
- amphotericin B
- high dose corticosteroids

This list includes some, but not all, of the drugs that may increase the risk of side effects while receiving ISTODAX.

Tell your doctor or pharmacist if you are taking these or any other medicines even those not prescribed (including any over the counter drugs, vitamins, or herbal medicines).

PROPER USE OF THIS MEDICATION

Usual dose:

ISTODAX will be given to you by a healthcare provider as an intravenous (IV) injection into your vein usually over 4 hours. Your doctor will choose the starting dose of

ISTODAX that is right for you. This will be based on how well your liver is working.

ISTODAX is usually given on Day 1, Day 8, and Day 15 of a 28 day cycle of treatment.

Your doctor will decide for how long you will receive treatment with ISTODAX. Your doctor may interrupt or stop your treatment or reduce your dose. This will depend on how you are feeling or if your disease has gotten worse.

Your doctor will check your blood cell counts and will perform other blood tests regularly during your treatment with ISTODAX. Your doctor may decide to do further tests to check your health as needed.

Overdose:

In case of drug overdose, contact a health care practitioner, hospital emergency department or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

This medicine needs to be given on fixed schedule. If you miss an appointment, call your doctor for instructions.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

These are not all the possible side effects you may feel while receiving ISTODAX. If you experience any side effects not listed here or if you have any side effect that bothers you or does not go away, contact your healthcare professional

Side effects include:

- nausea, diarrhea, constipation, and loss of appetite
- tiredness

ISTODAX may cause abnormal blood test results. Your doctor will decide when to perform blood tests and will interpret the results.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Very Common	Vomiting		✓	
	Neutropenia (low level of white blood cells): fever, infections, fatigue, aches, pains and flu-like symptoms		✓	

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Very Common	Anemia (low level of red blood cells): fatigue, tiredness, weakness, shortness of breath, pale skin		✓	
	Thrombocytopenia (low level of platelets, which help with blood clotting): bruising, bleeding from the gums or other sites, fatigue, weakness		✓	
Common	Infection: fever, significant fatigue, shortness of breath, cough, burning on urination, flu-like symptoms, muscle aches, worsening skin problems		✓	
	Electrocardiogram (ECG) changes (changes in the electrical activity of your heart seen on ECG) or increased heart rate: Irregular or abnormal heart beats, chest pain, shortness of breath, dizziness, palpitations, fainting, seizures			✓
	Tumor lysis syndrome (caused by the rapid breakdown of cancer cells): lack of urination, severe muscle weakness, heart rhythm disturbances, and seizures			✓

This is not a complete list of side effects. For any unexpected effects while taking ISTODAX, contact your doctor or pharmacist.

HOW TO STORE IT

Store at room temperature (15 to 30°C). Keep out of reach and sight of children.

REPORTING SUSPECTED SIDE EFFECTS

You can report any suspected adverse reactions associated with the use of health products to the Canada Vigilance Program by one of the following 3 ways:

- Report online at <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>
- Call toll-free at 1-866-234-2345
- Complete a Canada Vigilance Reporting Form and:
 - Fax toll-free to 1-866-678-6789, or
 - Mail to: **Canada Vigilance Program
Health Canada
Postal Locator 1908C
Ottawa, Ontario
K1A 0K9**

Postage paid labels, Canada Vigilance Reporting Form and the adverse reaction reporting guidelines are available on the MedEffect™ Canada Web site at <https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada/adverse-reaction-reporting.html>

NOTE: Should you require information related to the management of side effects, contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

The information in this document is current as of the last revision date shown below. The most current information can be found at: <http://www.celgenecanada.net> or by contacting the sponsor, Celgene Inc. at: 1-888-712-2353.

This leaflet was prepared by Celgene Inc.

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