

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

Pr**ISTODAX**®

romidepsin for injection

Read this carefully before you start taking **ISTODAX** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ISTODAX**.

Serious Warnings and Precautions

ISTODAX should only be prescribed by a healthcare professional experienced in the use of anti-cancer drugs. ISTODAX is only offered through the Restricted Access Program. A healthcare professional must register current patients under the program to receive ISTODAX. ISTODAX will be removed from the Canadian Market after the last patient ends treatment with ISTODAX. For more information on the Restricted Access Program, contact Medical Information Services at 1-866-463-6267 and medical.canada@bms.com.

Serious side effects may occur with the use of ISTODAX and could include:

- **QTc prolongation** (abnormal heart beat like rapid or pounding heart beat). This can also cause dizziness, fainting, seizures or death. Contact your healthcare professional right away if you experience these symptoms.
- **Pancytopenia** (decrease in red and white blood cells and platelets). Your healthcare professional will monitor your blood health before and during treatment;
- **Infections** that are life-threatening (including **pneumonia** and **sepsis**). ISTODAX can reactivate other viruses like Epstein Barr, hepatitis B, and cytomegalovirus (CMV);
- **Tumor lysis syndrome** (rapid breakdown of cancer cells); this can result in damage to the kidneys, heart and liver. Your healthcare professional will monitor and treat you as needed;
- **Birth defects** or **death** of an unborn baby;
- **Liver problems**. ISTODAX is not recommended if you have severe liver disease.

ISTODAX has not been studied in patients with kidney disease.

What is ISTODAX used for?

For the following indication ISTODAX has been approved with conditions (NOC/c). This means it has passed Health Canada's review and can be bought and sold in Canada, but the manufacturer has agreed to complete more studies to make sure the drug works the way it should. For more information, talk to your healthcare professional.

ISTODAX is used to treat adults with a type of blood cancer called peripheral T-cell lymphoma (PTCL) who:

- cannot receive a stem cell transplant, and
- have tried at least one other type of treatment by mouth or injection.

No additional studies are available to confirm if ISTODAX helps with survival or slowing down the disease. For more information, talk to your healthcare professional.

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

A Notice of Compliance with Conditions (NOC/c) is a type of approval to sell a drug in Canada.

Health Canada only gives an NOC/c to a drug that treats, prevents, or helps identify a serious or life-threatening illness. The drug must show promising proof that it works well, is of high quality, and is reasonably safe. Also, the drug must either respond to a serious medical need in Canada, or be much safer than existing treatments.

Drug makers must agree in writing to clearly state on the label that the drug was given an NOC/c, to complete more testing to make sure the drug works the way it should, to actively monitor the drug's performance after it has been sold, and to report their findings to Health Canada.

How does ISTODAX work?

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

What are the ingredients in ISTODAX?

Medicinal ingredients: romidepsin

Non-medicinal ingredients: dehydrated alcohol, povidone, propylene glycol

ISTODAX comes in the following dosage forms:

Sterile freeze-dried powder: 10 mg

Do not use ISTODAX if:

- You are allergic to romidepsin or to any of the other ingredients of ISTODAX

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ISTODAX. Talk about any health conditions or problems you may have, including if you:

- have kidney problems
- have liver problems

- have nausea, vomiting, or diarrhea
- have any other medical conditions
- have the following risks for abnormal heart beat:
 - you are female
 - you are 65 years old or older
 - have any heart problems, or a family history of heart problems
 - have a family history of sudden cardiac death at < 50 years
 - have or have a family history of irregular or fast heartbeat, including QT/QTc prolongation
 - have a personal history of fainting spells
 - have electrolyte problems (like low blood potassium or magnesium levels) or conditions that could lead to electrolyte disturbances (like vomiting, diarrhea, dehydration)
 - have diabetes
 - have nervous system or brain problems
- have had previous viral infection (e.g. hepatitis B, cytomegalovirus (CMV), herpes, Epstein-Barr virus)
- have bone marrow problems
- have a history of chemotherapy

Other warnings you should know about:

Pregnancy and breastfeeding:

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 non-hormone methods of birth control while receiving ISTODAX. Keep using birth control for 8 weeks after your last dose of ISTODAX. Tell your healthcare professional 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:

- You should father a child while you are receiving ISTODAX.
- You should use effective contraception to prevent pregnancy in your partner while you are receiving ISTODAX.
 - You should use a condom with spermicide even if you have had a vasectomy.
 - Keep using these birth control methods for 1 month after your last dose.
- ISTODAX may cause male infertility (low or no sperm count). This may affect your ability to father a child. Ask your healthcare professional for advice before starting treatment with ISTODAX.

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

Check-ups and Testing: You will have regular visits with your healthcare professional, before, during and at the end of your treatment. They will do:

- Blood tests to check your liver, blood and heart health
- Electrocardiograms (ECGs) to check your heart beat

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

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ISTODAX:

- Medicines used to treat:
 - abnormal heart beats, such as: quinidine, procainamide, disopyramide, amiodarone, sotalol, ibutilide, dronedarone, flecainide, propafenone;
 - schizophrenia and other mental disorders, such as: chlorpromazine, pimozide, haloperidol, droperidol, ziprasidone;
 - depression, such as: fluoxetine, citalopram, venlafaxine, amitriptyline, imipramine, maprotiline, nefazodone;
 - bacterial infections, such as: erythromycin, clarithromycin, telithromycin, tacrolimus, moxifloxacin, levofloxacin, ciprofloxacin, rifampin, rifabutin, rifapentine;
 - HIV infections, such as: atazanavir, indinavir, nelfinavir, ritonavir, saquinavir;
 - fungal infections, such as: ketoconazole, fluconazole, voriconazole, itraconazole;
 - seizures, such as: phenytoin, carbamazepine, phenobarbital;
 - malaria, such as: quinine, chloroquine;
 - nausea, such as: dolasetron, ondansetron
 - cancer, such as: vandetanib, sunitinib, nilotinib, lapatinib, vorinostat
 - asthma, such as: salmeterol, formoterol
- Blood thinner medicine, like warfarin sodium;
- Birth control that contains estrogen, like birth control “pills”, patches, implants, or intrauterine devices (IUDs);
- St. John’s Wort (*Hypericum perforatum*), an herbal treatment for depression
- Dexamethasone, a steroid used to treat different inflammatory conditions, allergic reactions, skin diseases, eye problems, breathing problems, bowel disorders, cancer, and immune system disorders;
- Domperidone, used to treat gastrointestinal problems;
- Methadone, an opioid used for chronic pain relief;
- Any medicine that cause imbalance in the electrolytes in your body:
 - diuretics (water pills)
 - laxatives and enemas, used to treat constipation
 - amphotericin B, used to treat fungal infections
 - high dose corticosteroids, used to treat inflammation

This list might not be all of the drugs that may cause side effects during treatment with ISTODAX.

How to take ISTODAX:

- ISTODAX will be given to you by a healthcare professional as an intravenous (IV) injection into your vein. It is usually over 4 hours.
- ISTODAX is usually given on Day 1, Day 8, and Day 15 of a 28 day cycle of treatment.
- Your healthcare professional will decide for how long you will receive treatment with ISTODAX.

Usual dose:

- **Adults:** Your healthcare professional will choose the starting dose of ISTODAX that is right for you.

Your healthcare professional may interrupt or stop your treatment or reduce your dose. This may happen if you:

- experience side effects, or
- your disease has gotten worse.

Overdose:

If you think you, or a person you are caring for, have taken too much ISTODAX, contact a healthcare professional, hospital emergency department, or regional Poison Control Centre immediately, even if there are no symptoms.

Missed Dose:

- ISTODAX needs to be given on fixed schedule. If you miss an appointment, call your healthcare professional for instructions.
- Your missed dose should be given as soon as possible unless it is within 5 days of the next dose.

What are possible side effects from using ISTODAX?

These are not all the possible side effects you may have when taking ISTODAX. If you experience any side effects not listed here, tell your healthcare professional.

Side effects include:

- nausea, diarrhea, constipation, and loss of appetite
- tiredness
- Swelling of your mouth, legs
- Stomach, mouth, joint, limb or back pain
- Decreased appetite
- Change in sense of taste
- Dehydration
- Night sweats
- Headache
- Dizziness
- Runny nose
- Weight loss
- Muscle spasms
- Anxiety, trouble sleeping, depression
- Dry skin, rash, itchy skin

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

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
VERY COMMON			
Pancytopenia, including neutropenia, leukopenia, anemia, thrombocytopenia (decreased red and white blood cells and platelets): low red blood cell count: paleness of the skin, fatigue, weakness, rapid heart rate, shortness of breath, pale skin; low white blood cell count: fever, and symptoms of infection such as cough, aches, pains and flu-like symptoms; low platelet count: bruising easily and bleeding from the gums or other sites, fatigue, weakness		✓	
Vomiting		✓	
COMMON			
Deep vein thrombosis or pulmonary embolism (blood clot in the deep veins of the leg or arm or lung): swelling, pain, arm or leg may be warm to the touch and may appear red, chest pain that may increase with deep breathing, cough, coughing up bloody sputum, shortness of breath		✓	
Electrocardiogram (ECG) changes (changes in the electrical activity of your heart seen on ECG) or QTc prolongation (heart rhythm condition), increased heart rate: Irregular or abnormal heart beats, chest pain, shortness of breath, dizziness, palpitations, fainting, seizures			✓
Infection, including pneumonia (lung infection), sepsis (blood infection), urinary tract infection: fever, significant fatigue, shortness of breath, cough, burning on urination, frequent urination, blood in urine, pain in the pelvis,		✓	

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
strong smelling urine, cloudy urine little to no urine, flu-like symptoms, muscle aches, worsening skin problems, sweating and shaking chills, confusion, nausea, vomiting, low blood pressure, high or low body temperature, thick white patches in the mouth, tongue or on the throat, sore throat			
Liver problems: yellowing of your skin and eyes (jaundice), right upper stomach area pain or swelling, nausea or vomiting, unusual dark urine, unusual tiredness		✓	
Tumor lysis syndrome (caused by the rapid breakdown of cancer cells): lack of urination, severe muscle weakness, heart rhythm disturbances, and seizures			✓

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (<https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html>) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- The healthcare professional will store at room temperature (15 to 30°C).
- Vials of ISTODAX and supplied diluent should be stored together in carton until use.
- Keep out of reach and sight of children.

If you want more information about ISTODAX:

- Talk to your healthcare professional
- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (<https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html>); the manufacturer's website www.bms.com/ca, or by calling 1-866-463-6267.

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