

## 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 liver or kidney 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)
- are pregnant or plan to become pregnant. ISTODAX may harm your unborn baby. Talk to your doctor about the best way to prevent pregnancy while taking ISTODAX. Tell your doctor right away if you become pregnant while taking ISTODAX.
- are breastfeeding or plan to breastfeed. 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.

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.

## **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)
- 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)
  - bacterial infections (antibiotics such as erythromycin, clarithromycin, telithromycin, tacrolimus, moxifloxacin, levofloxacin, ciprofloxacin)
  - malaria (e.g. quinine, chloroquine)
  - fungal infections (e.g. ketoconazole, fluconazole, voriconazole)
  - 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.

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

Your doctor will decide how long you will receive treatment with ISTODAX.

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

ISTODAX may cause serious side effects, including:

- **Low blood cell counts:** Your doctor will regularly do blood tests to check your blood counts.
  - **Low platelets:** can cause unusual bleeding, or bruising under the skin. Talk to your doctor right away if this happens.

- **Low red blood cells:** may make you feel tired and you may get tired easily. You may look pale, and feel short of breath. Tell your doctor if you have these symptoms.

- **Low white blood cells:** can cause you to get infections, which may be serious. Your chance of life-threatening infections may be higher if you have received chemotherapy. Infection can also happen with normal white blood cell counts.

- Tell your doctor right away if you have any of these symptoms: fever, cough, flu-like symptoms, burning on urination, muscle aches, or worsening of skin problems.

- **Changes in the electrical activity of your heart seen on ECG (electrocardiogram).** Your doctor may check your ECG as needed for this problem. Tell your doctor if your feel an abnormal heart beat, chest pain or shortness of breath.

If you experience any symptoms of a possible heart rhythm disturbance, such as dizziness, palpitations, fainting, or seizures, you should seek immediate medical attention.

- **Tumor Lysis Syndrome (TLS).** TLS can occur during treatment as a complication of the rapid breakdown of cancer cells. Your doctor may do blood tests to check for TLS and may give you medicine to prevent or treat TLS.

Common side effects of ISTODAX include:

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

Tell your doctor if you have any side effect that bothers you or does not go away.

### 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	
Common	Fever/Neutropenia (low white blood cells)		✓	
Common	Tiredness/Anemia (low red blood cells)		✓	

Symptom / effect		Talk with your doctor or pharmacist		Stop taking drug and call your doctor or pharmacist
		Only if severe	In all cases	
Common	Bleeding from the gums or other sites or abnormal bleeding/Thrombocytopenia (low platelets that help with blood clotting)		✓	
Common	Signs of infection: fever, significant fatigue, shortness of breath, cough, burning on urination, flu-like symptoms, muscle aches, worsening skin problems		✓	
Uncommon	Vomiting		✓	
Rare	Irregular or abnormal heart beats			✓
Rare	Symptoms of tumor lysis syndrome: 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 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 [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect)
- 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 0701C  
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 [www.healthcanada.gc.ca/medeffect](http://www.healthcanada.gc.ca/medeffect).**

***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.

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