PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

LUTATHERA®

lutetium (^{177}Lu) oxodotreotide injection

Read this carefully before you start taking **LUTATHERA®** 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 **Lutathera**.

Serious Warnings and Precautions

- Lutathera should be used by health professionals who are appropriately trained in use of radiopharmaceuticals.
- Kidney impairment can occur in patients treated with Lutathera. Tell your physician about any kidney condition prior to receiving Lutathera.
- Secondary blood cancer (myelodysplastic syndrome or acute leukaemia) can rarely occur several years after you have completed Lutathera treatment.

What is Lutathera used for?

Lutathera is a radiopharmaceutical medicine used for

- The treatment of certain tumours (gastroenteropancreatic neuroendocrine tumours) that have somatostatin receptors, which cannot be completely removed from your body by surgery, have spread in your body (metastatic) and no longer responds to your current treatment.

How does Lutathera work?

The tumour needs to have certain proteins (somatostatin receptors) on the surface of its cells in order for the medicine to work. Lutathera binds to these receptors, delivering radioactivity directly to the tumour cells, causing their death.

The use of Lutathera involves exposure to amounts of radioactivity. Your doctor and the nuclear medicine doctor have considered that the clinical benefit that you will obtain from the procedure with the radiopharmaceuticals outweighs the risk due to radiation.

What are the ingredients in Lutathera?

Medicinal ingredient: lutetium (^{177}Lu) oxodotreotide.

Non-medicinal ingredients: acetic acid (to adjust acid content); ascorbic acid (for stability); diethylene triamine pentaacetic acid (DTPA) (removes unwanted chemical substances from the solution); gentisic acid (for stability); sodium acetate (to adjust acid content); sodium chloride (adjusts concentration of the substances in the product); sodium hydroxide; and water for injection (see Other warnings you should know about “Lutathera contains sodium”).

Lutathera comes in the following dosage forms:

Solution for Intravenous Injection, 370 MBq/mL. MBq is a measure of radioactivity.

Do not use Lutathera if:

- If you are allergic to lutetium (^{177}Lu) oxodotreotide or to any of the other ingredients in this medicine;
- If you are pregnant; and/or
- If your kidneys are seriously impaired.

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

- You are under 18 years of age.
- You are pregnant or plan to become pregnant. Exposure to radiation during pregnancy may harm your unborn baby. Women who are able to become pregnant should use effective contraception and avoid getting pregnant during treatment with Lutathera and for 7 months after your last dose of Lutathera.
- You are a male with a female partner of childbearing age. Male patients should use effective birth control during treatment and for at least 4 months after completing treatment.
- You are breastfeeding or plan to breastfeed. It is not known if Lutathera passes into your breast milk. Breast feeding must be stopped. If treatment with Lutathera during breast feeding is necessary, the child must be weaned.
- You have mild to moderate chronic kidney disease.
- You suffer from urinary incontinence (uncontrollable urination).
- You have a kidney or urinary tract abnormality, including urinary track obstruction.
- You have mildly altered blood cell counts. Lutathera can lead to a decrease in the number of your red blood cells (responsible for transporting the oxygen from the lungs to the different organs), platelets (cells that help the blood to clot), and other blood cells such as white blood cells (helps to fight infection). Before starting treatment and before each subsequent treatment, your doctor will perform blood tests. Depending on the results of these tests, your doctor will decide if the treatment can be started, can be continued, or needs to be adjusted, postponed or discontinued.
- You have altered liver function.
- You have a history of hyperkalemia.
- You have a history of heart disease.
- You previously received anti-cancer treatment (chemotherapy, radiation therapy)
- You have previously received any radionuclide therapy (therapy with a radioactive medicine)
- You had any other type of cancer within the last 5 years.

Other warnings you should know about:

Lutathera contains sodium.

This medicine contains 0.14 mmol (3.2 mg) of sodium per mL. To be taken into consideration by patients on controlled sodium diet.

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 Lutathera:

- Somatostatin analogues (drugs similar to Lutathera) – you may be asked to stop and/or adapt your treatment for a short period of time while receiving Lutathera.
- Corticosteroids – inform your physician if you are taking corticosteroids.

How to take Lutathera:

- Lutathera will be administered intravenously (into your arm) under the supervision of a healthcare professional who is experienced in the use of radiopharmaceuticals.
- There are strict laws on the use, handling and disposal of radiopharmaceutical products like Lutathera. It will only be used in special controlled areas. Your physician will inform you when you can leave the controlled area or hospital.

Usual dose:

The recommended dose to be administered is 7.4 GBq (gigabecquerel, the unit used to express radioactivity) of Lutathera in a single infusion into your vein, which is given at 4 times once every 8 weeks.

In addition to the Lutathera injection, an infusion with amino acids (substances present in many foods and in muscles) will be given to you in order to protect your kidneys. This might cause nausea and vomiting; you will also receive an injection before the start of treatment to reduce these symptoms.

Duration of the procedure:

Your physician will inform you about the usual duration of the procedure. The Lutathera infusion takes approximately 30 minutes; but the complete administration procedure will take approximately 5 hours.

Treatment monitoring:

Treatment with Lutathera can have an impact on blood cells, liver and kidneys. Your doctor will ask you to have regular blood tests in order to detect any side effects as early as possible. Based on the results, your physician may decide to delay or stop your treatment with this medicine.

After administration of Lutathera:

You will be requested to drink a sufficient amount of water (1 glass every hour) necessary to urinate every hour on the day of infusion and the day after. Try to defecate every day, use a laxative if necessary. These steps are needed to help remove the medicine from your body.

Because this medicine is radioactive, you will have to follow the instructions described below to minimize radiation exposure to others.

<u>General rule</u>

You must avoid close contact (less than 1 meter) with people who live with you and should try to keep a distance of at least one meter for 7 days after you receive Lutathera. When together for a prolonged period, a distance of 2 meters or more should be maintained.

<u>Use of toilets</u>

Toilets must be used in a seated position, even for men. It is absolutely necessary to use toilet paper each time. It is also important to wash your hands to avoid contaminating the door handles.

Contact with children and pregnant women

It is strongly recommended to limit close contact (less than 1 meter) with children and/or pregnant women to less than 15 minutes per day for 7 days after you receive each dose of Lutathera.

Contact with spouse and people in the family circle

During 7 days after Lutathera administration, sleep in separate bedroom from other people. For children and/or pregnant women, extend this time to 15 days.

People who need extra assistance

People who are confined to bed or have reduced mobility will preferably receive assistance by a care provider. It is recommended that when providing assistance in the bathroom, the care provider wears disposable gloves for 7 days after administration. In the case of the use of special medical equipment such as catheters, colostomy bags, bedpan, water nozzle, or anything that could be contaminated by your body fluids, these must be emptied immediately in the toilet and then cleaned. If anyone helps you clean up vomit, blood, urine, or stool they should wear plastic gloves. The gloves should then be disposed of in a specific trash plastic bag (according to "Trash recommendations" below).

Dishes and bathroom accessories

Take special precautions during the 7 days after treatment:

- Flush all wipes and/or toilet paper down the toilet immediately after use;
- Always wash your hands well after using the toilet;
- Take a shower every day;
- Flush any tissues or any other items that contain anything from your body, such as blood, urine and faeces down the toilet. Items that cannot be flushed down the toilet, such as menstrual pads and bandages, must be placed in specific trash plastic bags (according to "Trash recommendations" below); and
- Wash your underwear, pyjamas, sheets and any clothes that contain sweat, blood or urine separately from the laundry of other members of your household, using a standard washing cycle. You do not need to use bleach and do not need extra rinses.

Trash recommendations

Keep the specific plastic trash bags separated from the other trash. Keep the bags away from children and animals.

A member of the hospital staff will tell you how and when to get rid of these trash bags. You might be asked to bring the bags back to your treatment facility, or, after 70 days, the bags may be removed as the other household waste.

Hospitalisation and emergency care

If for any reason you require emergency medical assistance or an unplanned hospitalisation during the 3 months after your treatment, you should inform the medical providers that you have been treated with Lutathera. You should carry your discharge letter with you at all times, so that you can provide information on the reason for use, date and dose of Lutathera.

Travel

Keep your discharge letter with you whenever you are travelling for at least 3 months after treatment.

Other precautions

The nuclear medicine physician will inform you if you need to take any other special precautions after receiving this medicine. Contact your nuclear medicine physician if you have any questions.

Overdose:

An overdose is not expected because of how Lutathera is packaged and administered. However, in the case of an overdose, you will receive the appropriate treatment.

Should you have any further question on the use of this medicine, please ask the nuclear medicine doctor who supervises the procedure.

What are possible side effects from using Lutathera?

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

Very common side effects (may affect more than 1 in 10 people):

- Nausea, vomiting (usually during the first 24 hours)
- Abdominal pain, abdominal bloating (abdominal distension)
- Diarrhea
- Fatigue (possibly delayed for more than 24 hours after treatment)
- Decreased appetite
- Pain (including back pain, arms, legs, joints, chest, bone, side, muscles or neck)
- Headache
- Dizziness (vertigo)
- Fluid retention, swelling (usually in the legs)
- Flushing
- Increase in blood pressure (hypertension)
- Anxiety
- Hair loss (alopecia)
- Cough
- Trouble breathing (dyspnoea)
- Decrease in blood cell counts: red blood cells (anaemia), white blood cells (leukopenia or lymphopenia or neutropenia), platelets (thrombocytopenia), pancytopenia (decrease in multiple blood cell types)
- Change in blood test results: increased creatinine, increased or decreased blood sugar, decreased albumin, increased uric acid, increased or decreased calcium, increased or decreased sodium, increased or decreased potassium, increased liver enzyme levels, increased bilirubin

Common side effects (may affect between 1 in 100 and up to 1 in 10 people):

- Constipation
- Indigestion (dyspepsia), gas (flatulence)
- Sore mouth (stomatitis)
- Weakness, lack of energy (lethargy)
- Fever, chills, influenza-like illness
- Injection site pain, injection site reaction
- Allergic reaction (hypersensitivity)
- Muscle spasms, shaking (tremor)

- Tingling sensation (paraesthesia)
- Weight loss
- Dehydration, dry mouth
- Disturbed sense of taste, disturbed sense of smell
- Sleepiness (somnolence), trouble sleeping (insomnia)
- Fainting/loss of consciousness (syncope), falls
- Sprains, fractures
- Low blood pressure (hypotension)
- Hot flush
- Rash, skin itching and redness, dry skin
- Bruising (contusion)
- Wheezing or "high-pitched whistling sound"
- Change in voice (dysphonia)
- Depression
- Agitation
- Panic attack
- Double vision (diplopia)
- Ringing in the ears (tinnitus)
- Kidney stones
- Breast growth in men (gynecomastia)
- General decline in physical health
- General feeling of discomfort, illness, abnormal or uneasiness (malaise)
- Change in blood cell counts: increased lymphocyte count
- Change in blood test results: decreased magnesium, decreased vitamin D
- Difficulty swallowing (dysphagia)
- Death due to disease progression or underlying comorbidities

Uncommon side effects (may affect up to 1 in 100 people):

- Disturbance in walking
- Confusion (disorientation)
- Delirium
- Malnutrition

Not Known (frequency cannot be estimated from the available data):

- Facial/throat swelling and/or difficulty breathing (signs and symptoms of angioedema)

During Lutathera treatment, you may also have surgical/medical procedures

Common

- Blood transfusion

Uncommon

- To drain fluid from the peritoneal cavity, the space between the abdominal wall and organs (abdominal cavity drainage)
- To filter your blood to rid your body of harmful wastes, extra salt, and water (dialysis)
- To place a stent

- To drain abscess
- For gastrointestinal tube insertion
- To harvest (collect) stem cells from your bone marrow (bone marrow harvest)
- To remove polyps from the inside of the colon, also called large intestine (polypectomy)

Lutathera contributes to your overall long-term cumulative radiation exposure (the amounts of radiation that an individual typically receives from different sources over a longer period of time). Long-term cumulative radiation exposure may increase your risk for developing new cancers and increase the chances for your future children to have hereditary (from a parent) abnormalities. Lutathera has been associated with an increased risk for blood cancers.

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional**	
	Only if severe	**In all cases**
VERY COMMON		
Anaemia (marked by weakness, paleness, shortness of breath, headaches, dizziness, heart palpitations, decreased red blood cell test results)		X
Thrombocytopenia, lymphopenia, neutropenia, leukopenia, pancytopenia (marked by unusual bruising, more bleeding than usual after injury, fever, catching infections more frequently)		X
Kidney problems including renal failure (marked by changes in urine output, changes in urine colour, changes in blood test results)		X
Liver changes (marked by changes in liver enzyme levels in the blood)		X
COMMON		
Heart problems including atrial fibrillation, palpitations (marked by irregular heart beat, shortness of breath, chest pain), angina pectoris, myocardial infarction (marked by chest pain, pain in arms, neck, jaw, shoulder, shortness of breath, sweating), cardiac failure (marked by shortness of breath, swelling in legs, ankles, and feet, cough, wheezing)		X
Stomach and gastrointestinal problems including gastritis (marked by abdominal pain or bloating, vomiting, indigestion), ascites (fluid buildup in the abdomen), intestinal obstruction (marked by constipation, cramps, vomiting), rectal bleeding, diverticulitis (inflammation of the intestine marked by abdominal pain, fever, nausea), clostridium difficile infection (marked by watery diarrhea and fever)		X
Liver, gall bladder, and bile duct problems including cholestasis (reduced bile flow), cholecystitis (inflamed gallbladder marked by upper abdominal pain), gallstones (marked by upper abdominal pain), jaundice (yellowing of eyes and skin)		X

Serious side effects and what to do about them		
Symptom / effect	**Talk to your healthcare professional**	
	Only if severe	**In all cases**
Urinary problems including infection (marked by frequent urination, urgency), blood in the urine, incontinence		X
Kidney problems: kidney swelling		X
Respiratory problems including nasopharyngitis (marked by stuffy nose, sore throat, fever, aches), bronchitis (marked by cough, fever, aches), lower respiratory tract infection, pneumonia (marked by chest pain, fever, cough); pleural effusion (marked by shortness of breath, chest pain when breathing deeply)		X
Thyroid problems including hypothyroidism, secondary hypothyroidism (marked by weakness, fatigue, changes in thyroid blood tests)		X
Diabetes mellitus (marked by increased blood sugar levels)		X
Cancer progression and other cancers including blood cancers, myelodysplastic syndrome, acute leukaemia (marked by feeling tired, dizzy, weak, shortness of breath, pale skin, infections and abnormal bleeding)		X
Neuroendocrine hormonal crisis, carcinoid syndrome (marked by flushing, diarrhea, low blood pressure, difficulty breathing usually within 24 hours of Lutathera dose)		X
UNCOMMON		
Other gastrointestinal problems including gastrointestinal tract tears, bleeding, lower abdominal pain, inguinal hernia (marked by a painful bulge on either side of pelvic bone), blood in stools, vomiting or coughing blood, ileus (slowed intestinal movement marked by cramping, feeling full, constipation), inflamed pancreas (marked by abdominal pain that radiates into the back, nausea, vomiting, and fever)		X
Other liver problems including liver failure (marked by jaundice -yellowing of skin and eyeballs, upper abdominal pain, nausea), hemorrhagic ascites (build up of fluid containing blood in the abdomen)		X
Blood clotting problems including clots in a vein (marked by pain, swelling), lungs (marked by shortness of breath, chest pain, cough), clotting or bleeding in the brain (stroke)		X
Other heart problems including heart valve problems, heart muscle problems (marked by fatigue, swelling in the abdomen, legs, shortness of breath)		X
Herpes zoster (marked by a painful rash)		X
Spinal cord compression (marked by pain, numbness, or weakness in arms, hands, legs or feet)		X
Tumour compression		X
Impaired wound healing		X

Serious side effects and what to do about them		
Symptom / effect	Talk to your healthcare professional	
	Only if severe	In all cases
Collapsed lung (marked by sudden chest pain and shortness of breath)		X
Weakening of umbilical cord		X
NOT KNOWN		
Facial/throat swelling and/or difficulty breathing (signs and symptoms of angioedema)		X

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:

You will not have to store this medicine. This medicine is stored under the responsibility of the specialist in appropriate premises. Storage of radiopharmaceuticals will be in accordance with national regulation on radioactive materials.

If you want more information about Lutathera:

- 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 https://www.novartis.ca or by calling 1-800-363-8883.

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