

PART III: CONSUMER INFORMATION

ATRIANCE, for use in adults and children who have a certain type of leukemia (T-cell acute lymphoblastic leukemia) or lymphoma (T-cell lymphoblastic lymphoma), has been approved with conditions, 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.

PrATRIANCE[®]
(nelarabine)

This leaflet is Part III of a three-part "Product Monograph" published when ATRIANCE (nelarabine) Injection was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about ATRIANCE. Read this information carefully before you or your child start taking ATRIANCE and read the information you get each time before you or your child get more ATRIANCE as there may be new information. This information does not take the place of talking with your or your child’s doctor about your/your child’s medical condition or treatment. If you have any questions about ATRIANCE, ask your/your child’s doctor. Your/your child’s doctor can determine if ATRIANCE is right for you or your child.

ABOUT THIS MEDICATION

What the medication is used for:

ATRIANCE is used to treat adults and children who have a certain type of leukemia (T-cell acute lymphoblastic leukemia) or lymphoma (T-cell lymphoblastic lymphoma).

What it does:

ATRIANCE damages cancer cells, causing their death.

When it should not be used:

You, or your child, should not take ATRIANCE if you/your child are allergic to the medicinal ingredient, nelarabine, or to any of the non-medicinal ingredients.

What the medicinal ingredient is:

ATRIANCE Injection contains nelarabine.

What the nonmedicinal ingredients are:

ATRIANCE Injection contains sodium chloride in Water for Injection, USP. Hydrochloric acid and sodium hydroxide may have been used to adjust the pH.

What dosage forms it comes in:

ATRIANCE is available as a sterile solution containing 5 mg of nelarabine per mL.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

ATRIANCE should be given under the supervision of a doctor experienced in the use of anti-cancer drugs.

ATRIANCE should only be given by injection into a vein.

ATRIANCE may cause brain or nervous system disorders which can be fatal. If you have pre-existing brain or nervous system disorders or have had chemotherapy injection into the area around the spinal cord or radiation to your head or spine, you may be at increased risk of more serious side effects.

Serious side effects include:

- Feel very sleepy or drowsy
- Less feeling. Tingling or numb fingers, hands, toes or feet
- Weak getting up from a chair or doing stairs
- Being confused
- Collapse, go unconscious or lack awareness
- Significant spinal cord damage that may be permanent and disabling
- Hard to speak and understand what people say
- Hard to remember
- Difficult to awaken
- Hard to control your eyes
- Seizures or coma
- Poor balance, unsteady or trips while walking
- Fine motor skills are hard to do such as doing up a button

Contact the doctor right away if any of the above occur.

The above symptoms may not go away, even when ATRIANCE is stopped.

Before you or your child receive treatment with ATRIANCE

tell your/your child's doctor:

- about any medical condition you or your child have, including liver or kidney problems, or if you or your child have had chemotherapy injection into the area around the spinal cord or radiation to your head or spine
- if you/your child or any of your close family/friends have recently been, or plan to be vaccinated with a live vaccine such as Polio, Varicella (chickenpox) or Typhoid

Decrease in red blood cells (severe anemia): **ATRIANCE can cause a decrease in red blood cells which can be life-threatening.** Your doctor will monitor you periodically. Signs that certain red cell counts are low may include:

- Severe lack of energy
- Pale skin
- Weakness
- Shortness of breath

Decrease in white blood cells (leukopenia and neutropenia): **ATRIANCE can cause a decrease in white blood cells that may lead to infection which can be life-threatening, or to unexpected bruising or bleeding.** Your doctor will monitor you periodically. Signs that certain white cell counts are low may include:

- Symptoms of infection (fever, chills, sore throat)
- Bruise or bleed easily
- Cold

Muscle or bone problems: **ATRIANCE may cause muscle pain or weakness that does not go away after you stop taking the drug.**

Liver problems: **ATRIANCE can cause problems with your liver which may develop into serious conditions such as hepatitis and liver failure, which may be fatal.** Signs that your liver may not be working properly may include:

- Loss of appetite
- Feeling sick (nausea)
- Being sick (vomiting)
- Pain in your stomach (abdomen)
- Yellowing of your skin or the whites of your eyes (jaundice)
- Dark-colored urine
- Itching of your skin

Pregnancy, Birth Control and Fertility for Men and Women, and Breastfeeding

ATRIANCE may harm or put an unborn baby at serious risk.

- Do not use ATRIANCE during pregnancy
- Do not take ATRIANCE if you are pregnant or plan to become pregnant
- If you get pregnant while you or your male partner are being treated with ATRIANCE, tell your doctor
- Men and women must use a highly effective method of

birth control while taking ATRIANCE. Discuss birth control options with your doctor, to be sure pregnancy is avoided

Women: Prevent pregnancy while taking ATRIANCE
Men: Inform female sexual partners that you are taking ATRIANCE. Tell them the serious risk of harm to an unborn baby. Prevent pregnancy in your partner while taking ATRIANCE.

- It is not known whether taking ATRIANCE could affect how well your birth control pills will work. This could result in pregnancy
- ATRIANCE may affect your ability to become pregnant or to father a child
- ATRIANCE may pass through breast milk. Do not breast feed while taking ATRIANCE
- Male patients with partners who are pregnant, possibly pregnant, or who could become pregnant should use condoms during sexual intercourse while receiving ATRIANCE and for 3 months following completion of therapy

BEFORE you use ATRIANCE also talk to your doctor if you:

- Have any past problems with muscles (pain, tenderness)
- Have low white blood cells
- Have low red blood cells
- Have had bleeding problems or blood clots
- Have any liver problems
- Have any kidney problems

Driving and using machines: Before you perform tasks which may require special attention, wait until you know how you respond to ATRIANCE. Some side effects such as sleepiness, dizziness, or **brain and nervous system disorders** can affect your ability to drive or use machines.

INTERACTIONS WITH THIS MEDICATION

Tell your/your child's doctor or pharmacist about any medications you/your child are taking, including prescription and non-prescription medicines, vitamins and natural health products.

It is not known whether taking ATRIANCE could affect how well your birth control pills will work. This could result in pregnancy.

PROPER USE OF THIS MEDICATION

Usual dose:

Adults: The recommended adult dose of ATRIANCE is 1,500 mg/m²/day administered intravenously (into a vein) over 2 hours on days 1, 3, and 5, repeated every 21 days.

Children: The recommended pediatric dose of ATRIANCE is 650 mg/m²/day administered intravenously over 1 hour on days 1 to 5, repeated every 21 days.

Missed dose:

If you or your child miss a scheduled dose of ATRIANCE, contact your/your child's doctor. Your/your child's doctor will advise you on what to do about the next dose.

Overdose:

If you think you (or your child) have been given ATRIANCE more frequently than you should, or at a higher dose, or 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.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Most patients taking ATRIANCE will experience side effects, although it is not always possible to tell whether such effects are caused by ATRIANCE, other medications you/your child may be taking, or the cancer itself. The occurrence of side effects has been reported to be different between adults and children. If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your/your child's doctor. Some possible side effects of ATRIANCE are listed below:

Adults:

Very common (may occur in more than 10 out of every 100 people):

- nervous system problems such as difficulty with sense of feeling in hands and/or feet, reduced sensitivity to light touch or pain, or abnormal sensation such as burning, prickling or sensations of something crawling on skin;
- infections (including pneumonia);
- blood problems including decreased blood counts, reduced resistance to infection, temporary anemia (which may make you feel tired or weak), bruising or bleeding;

- feeling sleepy or drowsy, headache, dizziness, build up of fluid around the lungs, shortness of breath, difficult or laboured breathing, cough, nausea (feeling sick), or being sick/throwing up, diarrhea, constipation, muscle pain, swelling due to accumulation of fluid, high body temperature or fever, tiredness, feeling weak/loss of strength.

Common (may occur in 1 to 10 out of every 100 people):

- loss of muscle coordination, convulsions, weight loss and loss of appetite, difficulty with memory/feeling disoriented, blurred vision, increases in blood levels of liver enzymes;
- tremors;
- pain in the joints, back or extremities;
- chest pain;
- stomach pain;
- nausea and vomiting, shortness of breath, irregular heartbeat, clouding of urine, lethargy and/or joint discomfort (tumour lysis syndrome);
- low blood pressure;
- taste disturbance or loss of taste;
- dehydration.

Children:

Very common (may occur in more than 10 out of every 100 people):

- difficulty with sense of feeling in hands and/or feet;
- blood problems including decreased blood counts, reduced resistance to infection, temporary anemia (which may make you feel tired or weak), bruising or bleeding;
- abnormally low levels of potassium in the blood (which may make you feel weak), being sick/throwing up, headache, increases in blood levels of liver enzymes.

Common (may occur in 1 to 10 out of every 100 people):

- infection (including pneumonia);
- convulsions, reduced sensitivity to light touch or pain, abnormal sensation such as burning, prickling or sensations of something crawling on skin;
- loss of muscle coordination or balance;
- tremors;
- feeling drowsy or sleepy;
- abnormally low glucose in the blood (which may cause symptoms like feeling sick, sweating, weakness, faintness, confusion or hallucinations); abnormally low levels of calcium in the blood which may cause symptoms like muscle cramps, abdominal cramps or spasms); abnormally low levels of magnesium in the blood; increase in creatinine (a substance produced by the kidneys) in the blood;
- high body temperature/fever, feeling weak/loss of strength.

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor		Stop taking ATRIANCE and call your doctor immediately
		Only if severe	In all cases	
Common/ very common	Brain or nervous system disorders including headache, sleepiness, tingling or numbness in fingers, hands, toes or feet; collapse or periods of unconsciousness or lack of awareness, or seizures.		✓	
Very common	Low white blood cells which may give you a greater chance of infection, which may be life threatening. Symptoms of infection may include: fever; serious deterioration of general condition; fever with local symptoms such as sore throat/mouth or urinary problems.		✓	
Very common	Low platelets which may give you a greater chance for bleeding. Symptoms may include easy bruising or unusual bleeding while brushing teeth or from other sources.		✓	
Common	Stroke: Speech difficulty, weak on one side of the body, dizziness, poor balance		✓	
Uncommon	Blindness		✓	
Uncommon	Hallucinations: See or hear things that are not there		✓	
Uncommon	Sudden or very bad headache		✓	

SERIOUS SIDE EFFECTS, HOW OFTEN THEY HAPPEN AND WHAT TO DO ABOUT THEM				
Symptom / effect		Talk with your doctor		Stop taking ATRIANCE and call your doctor immediately
		Only if severe	In all cases	
In post marketing experience				
	Cases of spinal cord disorders including a block of blood supply to, or inflammation of, the spinal cord have been reported. Symptoms may include leg weakness, numbness, paralysis of arms and legs, fecal and/or urinary incontinence.		✓	
	Abnormal breakdown of muscle tissue (rhabdomyolysis). Symptoms may include abnormal urine colour, muscle aching, weakness of affected muscles.		✓	
	Cases of acute liver failure have been reported. Symptoms may include yellowing of skin and eyes, stomach pain, nausea and/or vomiting.			✓

This is not a complete list of side effects. For any unexpected effects while taking ATRIANCE, contact your/your child's doctor or pharmacist.

HOW TO STORE IT

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

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
- 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 0701D
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.

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

This leaflet summarizes important information about ATRIANCE. If you have questions or problems, talk with your/your child's doctor or other healthcare provider immediately. You can ask your/your child's doctor or pharmacist for information about ATRIANCE that is written for healthcare providers.

This document plus the full product monograph, prepared for health professionals can be found at:

<http://www.novartis.ca> or by contacting the sponsor,

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