PART III: CONSUMER INFORMATION

PRIMOVIST®

gadoxetate disodium injection

For Intravenous Use

For Professional Use Only

This leaflet is Part 3 of a three-part "Product Monograph" published when PRIMOVIST was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about PRIMOVIST. Contact your health professional if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

PRIMOVIST is a contrast medium for magnetic resonance imaging (MRI) of the liver. PRIMOVIST is used to help detect and diagnose changes that may be found in the liver. Abnormal signs within the liver can be better evaluated (as to the number, size, and distribution of liver lesions). PRIMOVIST can also help the doctor determine the nature of any abnormalities, thereby increasing the confidence one can have in the diagnosis. This medicine is for diagnostic use only.

MRI is a form of medical diagnostic imaging that forms pictures after water molecules have been detected in normal and abnormal tissues. This is done by a complex system of magnets and radiowaves.

What it does:

PRIMOVIST helps tissues viewed by MRI appear brighter to make it easier for the doctor to see any potential abnormalities.

When it should not be used:

If you have previously had a life-threatening allergic (hypersensitive) reaction to PRIMOVIST (see below).

What the medicinal ingredient is:

gadoxetate disodium

What the important nonmedicinal ingredients are:

caloxetate trisodium, hydrochloric acid, sodium hydroxide, trometamol, water for injection

What dosage forms it comes in:

PRIMOVIST is a ready-to-use solution for rapid injection into a vein. It is supplied in a strength of 181.43 milligrams of gadoxetate disodium per millilitre of solution (corresponding to 0.25 mmol/mL). It is packaged in glass vials.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Gadolinium-based contrast agents increase the risk of a rare disease called Nephrogenic Systemic Fibrosis (NSF) in patients with:

- **severe kidney disease, or acute kidney failure / acute kidney injury**

These patients should avoid the use of PRIMOVIST unless the healthcare professional believes the possible benefits outweigh the potential risks.

Your doctor will monitor your health before and after administration of PRIMOVIST if you are considered to be at risk for developing NSF (for details see Nephrogenic Systemic Fibrosis).

BEFORE you are given PRIMOVIST talk to your doctor if:

- You have a pacemaker for your heart or if you have another type of implant containing metal
- You have or have had a previous reaction to contrast media
- You suffer or have suffered from an allergy (eg, hay fever, hives) or asthma
- You have a severe disease of the heart and blood vessels
- You have very poor kidney function
- You have recently had, or shortly expect to have, a liver transplant
- You are pregnant, think you are or might become pregnant (even if you are not sure), since PRIMOVIST should not be used under such circumstances unless it is considered absolutely necessary.
- You are breastfeeding or intend to breastfeed, since PRIMOVIST should not be used under such circumstances unless it is considered absolutely necessary. You may discuss with your doctor whether stopping breastfeeding for 24 hours following PRIMOVIST administration is recommended.
- You are allergic (hypersensitive) to gadoxetate disodium or any of the other ingredients of PRIMOVIST

Allergy-like reactions may occur after use of PRIMOVIST. (see SIDE EFFECTS AND WHAT TO DO ABOUT THEM). Severe reactions are possible. Most of these reactions occur within 30 minutes after administration. Therefore, you will be observed for at least 30 minutes after the injection. Delayed reactions may occur (hours or even days later), (see SIDE EFFECTS AND WHAT TO DO ABOUT THEM).

The safety of PRIMOVIST in children under 18 has not yet been tested.

Accumulation of Gadolinium in the Brain

Recent information shows that gadolinium (as in **PRIMOVIST**) may build up in the brain after multiple uses and:

- The effect on the brain is unknown right now.
- Your doctor will:
  - Carefully consider whether to use repeated doses
  - Use the lowest dose

Nephrogenic Systemic Fibrosis

There have been postmarket reports of a rare disease called Nephrogenic Systemic Fibrosis (NSF) following gadolinium-based contrast agent (GBCA) use.

NSF is a rare condition which has only been observed so far in patients with severe kidney disease. At present, there is no evidence that other patient groups are at risk of developing the condition. Due to NSF, the skin becomes thickened, coarse, and hard, which sometimes makes bending of the joints difficult. NSF may spread to other organs and even cause death.

Before you receive PRIMOVIST, your doctor will screen you for the function of your kidneys. Your doctor will then decide whether the intended examination is possible or not.

Those who have already had an MR imaging procedure and who have any of the following symptoms, which may signal NSF, should seek medical attention as soon as possible:

- Swelling, hardening, and tightening of the skin
- Reddened or darkened patches on the skin
- Burning or itching of the skin
- Yellow spots on the whites of the eyes
- Stiffness in the joints, problems moving or straightening arms, hands, legs, or feet
- Pain deep in the hip bone or ribs
- Weakness of the muscles

Your doctor will monitor your health after administering PRIMOVIST, if you are considered to be at risk for developing NSF.

INTERACTIONS WITH THIS MEDICATION

Drugs that may interact with PRIMOVIST include:

- rifampicin or rifamycin (medicines used to treat infections, such as tuberculosis)

Tell your doctor if you are taking or have recently taken any other medicines, including medicines obtained without a prescription.

Slightly elevated laboratory values (eg, for serum iron) may occur for a short period after you have been given PRIMOVIST. Therefore, if you need to have blood samples taken, inform the health professionals that you have recently undergone an examination with PRIMOVIST.

See also **ABOUT THIS MEDICATION - When it should not be used**, and **SIDE EFFECTS AND WHAT TO DO ABOUT THEM.**

PROPER USE OF THIS MEDICATION

PRIMOVIST is injected by a doctor or healthcare professional via a needle or catheter into your vein. Your MRI examination can start immediately.

Usual dose

The actual dosage of PRIMOVIST that is right for you will depend on your body weight:

In adults, a single injection of 0.1 mL of PRIMOVIST per kg body weight is generally sufficient (this means, for a person weighing 70 kg the dose would be 7 mL).

PRIMOVIST is not recommended for use in children below 18 years.

Overdose

No overdosing has been reported so far. If it does happen, the doctor will treat any symptoms and will check whether your kidneys are working normally. If necessary, PRIMOVIST can be removed from the body by hemodialysis.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, PRIMOVIST can cause side effects, although not everybody gets them.

Most of the side effects are mild to moderate.

The most serious side effect in patients receiving PRIMOVIST is anaphylactoid shock (a severe allergy-like reaction).

In rare cases allergy-like reactions may occur, including severe reactions (shock) that may need immediate medical intervention. If you notice mild swelling of the face, lips, tongue or throat, coughing or sneezing, difficulty in breathing, itching, runny nose and/or hives (nettle-type rash) tell the MRI department staff immediately. These may be the first signs that a severe reaction is happening. Your investigation may need to be stopped and you may need further treatment. Delayed allergy-like reactions, hours to several days after the administration of PRIMOVIST, have been observed in rare cases. If this should happen to you, tell your doctor or radiologist.

Uncommon side effects observed in clinical trials affects 1 to 10 users in 1,000):

- headache, dizziness, disturbed sense of taste (dysgeusia), pins and needles (paresthesia), disturbed sense of smell, sensation of whirling (vertigo)
- high blood pressure, flushing
- breathing difficulties (dyspnea, respiratory distress)
- vomiting, nausea (feeling sick), dry mouth
- rash, severe itching of the skin or eyes (pruritus)
- back pain
- chest pain
- various kinds of injection site reactions (including involuntary leakage of the contrast agent (extravasation) and bleeding, burning, coldness, irritation, pain)
- chills, feeling hot
- feeling abnormal, tiredness (fatigue)

Rare side effects observed in clinical trials (less than 1 in every 1,000 patients is likely to get these):

- tremor, restlessness (akathisia)
- heart block (bundle branch block), irregular, rapid beating or pulsation of the heart (palpitation)
- discomfort of the mouth, increased production of saliva (salivary hypersecretion)
- measle-like rash (rash maculopapular), excessive sweating
- discomfort, generally feeling unwell

Side effects reported from postmarketing experience:

- hypersensitivity/anaphylactoid (allergy-like) reaction (eg shock, hypotension (low blood pressure), swelling in the tongue or throat (pharyngeal edema, laryngeal edema), hives or nettle-type rash (urticaria), swelling of the face (face edema), runny nose (rhinitis), redness of the eyes (conjunctivitis), stomach pain, reduced feeling or sensitivity in the skin (hypoesthesia), sneezing, cough, pale skin (pallor)),
- fast heart beat (tachycardia)
- restlessness

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or radiologist.

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

Symptom / Effect		Talk with your doctor	
		Only if severe	In all cases
Very Rare	Serious allergic reactions, sometimes fatal, with symptoms such as swelling of the mouth and throat, difficulty in breathing, rash.		✓

This is not a complete list of side effects. For any unexpected effects while taking PRIMOVIST, contact your health professional.

HOW TO STORE IT

PRIMOVIST should be stored at temperatures between 15°C to 30°C.

REPORTING SUSPECTED SIDE EFFECTS

To monitor drug safety, Health Canada through the Canada Vigilance Program collects information on serious and unexpected side effects of drugs. If you suspect you have had a serious or unexpected reaction to this drug you may notify Canada Vigilance:

Canada Vigilance Program:

You can report any suspected adverse reactions associated with the use of heath 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 0701E
  Ottawa, ON 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, please contact your health professional. The Canada Vigilance Program does not provide medical advice.

MORE INFORMATION

For more information, please contact your healthcare professional or pharmacist first, or Bayer Medical Information at 1-800-265-7382 or Canada.medinfo@bayer.com.

This document plus the full product monograph, prepared for health professionals can be found at: http://www.bayer.ca or obtained by contacting the manufacturer at the above mentioned phone number and email address.

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