PART III: CONSUMER INFORMATION

GADOVIST® 1.0
gadobutrol injection

For Intravenous Use

For Professional Use Only

This leaflet is part III of a three-part "Product Monograph" published when GADOVIST 1.0 was approved for sale in Canada and is designed specifically for Consumers. This leaflet is a summary and will not tell you everything about GADOVIST 1.0. Contact your doctor or pharmacist if you have any questions about the drug.

ABOUT THIS MEDICATION

What the medication is used for:

GADOVIST 1.0 is a contrast medium for magnetic resonance imaging (MRI) of the brain, spine, blood vessels, breast and kidney.

MRI is a form of medical diagnostic imaging that delivers pictures using the behavior of water molecules in normal and abnormal tissues. This is done by a complex system of magnets and radiowaves.

What it does:

GADOVIST 1.0 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 are allergic (hypersensitive) to gadobutrol or to any of the other ingredients of GADOVIST 1.0 (see below), or if you have previously had a life-threatening reaction to GADOVIST 1.0.

What the medicinal ingredient is:

gadobutrol

What the important nonmedicinal ingredients are:

calcium sodium butrol, hydrochloric acid, trometamol, water for injection.

What dosage forms it comes in:

GADOVIST 1.0 is a ready-to-use solution for rapid injection into a vein. It is supplied as 604.72 milligrams of gadobutrol per milliliter of solution (corresponding to 1.0 mmol/mL). It is packaged in glass vials and in prefilled syringes.

WARNINGS AND PRECAUTIONS

Serious Warnings and Precautions

Gadolinium-based contrast agents (such as GADOVIST 1.0) 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 GADOVIST 1.0 unless the healthcare professional believes the possible benefits outweigh the potential risks.

Your doctor will monitor your health before and after administration of GADOVIST 1.0 if you are considered to be at risk for developing NSF (for details see Nephrogenic Systemic Fibrosis).

BEFORE you are given GADOVIST 1.0 talk to your doctor if any of the following situations apply to you. The doctor will decide whether the intended examination is possible or not:

- 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 suffer from brain conditions with seizures
- You are pregnant or could be pregnant (even if you are not sure), since GADOVIST 1.0 should not be used under such circumstances unless it is considered absolutely necessary
- You are breast-feeding or intend to breast-feed since breast-feeding should be stopped for at least 24 hours following GADOVIST 1.0 administration
- Allergy-like reactions, leading to heart problems, breathing difficulties, or skin reactions may occur with the use of GADOVIST 1.0. Severe reactions may occur. Most of these reactions occur within half an hour of administration. Therefore, postprocedure observation is recommended. Delayed reactions may occur hours or even days later

Accumulation of Gadolinium in the Brain

Recent information shows that gadolinium (as in **Gadovist 1.0**) 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

Kidneys/Liver

Tell your doctor if:

- You have very poor kidney function
- You have recently had, or soon expect to have, a liver transplant

Your doctor may decide to take a blood test to check how well your kidneys are working before making the decision to use GADOVIST.

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.

Patients with severe kidney disease should avoid the use of GADOVIST 1.0 unless the health care professional believes the possible benefits outweigh the potential risks.

Before you receive GADOVIST 1.0, your doctor will screen you for the function of your kidneys in order to 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 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 GADOVIST 1.0, if you are considered to be at risk for developing NSF.

If you have poor kidney function, your doctor will make sure that GADOVIST 1.0 has been eliminated from your body before you receive a second injection of GADOVIST 1.0.

GADOVIST 1.0 can be removed from the body by dialysis. If you have poor kidney function, your doctor will decide if you should receive dialysis after you have been given GADOVIST 1.0.

INTERACTIONS WITH THIS MEDICATION

Drug interaction studies have not been done for GADOVIST 1.0.

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

PROPER USE OF THIS MEDICATION

Usual dose:

GADOVIST 1.0 is injected into your vein using a small needle by a healthcare professional or MRI center staff. GADOVIST 1.0 will be administered immediately before your MRI examination.

The actual dose (volume) of GADOVIST 1.0 that is right for you will depend on your body weight and on the region being examined by MRI:

In adults, a single injection of 0.1 millilitre GADOVIST 1.0 per kg body weight is generally sufficient (this means for a person weighing 70 kg the dose would be 7 millilitres). A total amount of up to 0.3 millilitres GADOVIST 1.0 per kg body weight may be administered at maximum.

For magnetic resonance imaging of the brain or spine, a single injection of 0.1 millilitre per kg body weight GADOVIST 1.0 is generally sufficient.

For magnetic resonance imaging of the vessels, depending on the type of examination, a single injection of 7.5 to 15 mL (for a person weighing less than 75 kg) or of 10 to 20 mL (for a person weighing 75 kg or more) is recommended.

No dosage adjustment is necessary for patients with poor kidney function, for patients with poor liver function, or for elderly patients (aged 65 or over).

In children of all ages including term newborns, a single injection of 0.1 millilitre per kg body weight GADOVIST 1.0 is recommended for all examinations.

Overdose:

No overdosing has so far been reported. In case you feel that you have been given too much GADOVIST 1.0, consult your doctor or healthcare practitioner administering the product in the procedure. If overdosing does occur, the doctor will treat any resulting symptoms and will check if your heart and kidneys are working normally.

If you have any further questions on the use of this product, ask your doctor or radiologist.

SIDE EFFECTS AND WHAT TO DO ABOUT THEM

Like all medicines, GADOVIST 1.0 can cause side effects, although not everybody gets them.

Most of the side effects are mild to moderate.

The most frequently observed side effects in patients receiving GADOVIST 1.0 (may affect 5 or more in 1,000 patients) are headache, nausea (feeling sick), and dizziness.

The most serious side effects (which have been fatal or life-threatening in some cases) are:

- Cardiac arrest (heart stops beating) and severe anaphylactoid (allergy-like) reactions.

In addition, for the following side effects, life-threatening or fatal outcomes have been observed in some cases:

- Dyspnea (shortness of breath) and loss of consciousness (fainting)

In rare cases, allergy-like reactions (hypersensitivity and anaphylaxis) may occur, including severe reactions (shock) that may need immediate medical intervention.

If you notice swelling of the face, lips, tongue, or throat, coughing, difficulty breathing, itching, runny nose, sneezing and 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.

Most hypersensitivity reactions occur within 30 minutes, but delayed reactions, several hours to several days after the administration of GADOVIST 1.0, have been observed in rare cases. If this should happen to you, tell your doctor or attending healthcare practitioner immediately if this occurs.

Possible side effects are listed below by how likely they are.

Common (may affect up to 1 in 10 people)
- headache
- nausea (feeling sick)

Uncommon (may affect up to 1 in 100 people)
- allergy-like (hypersensitivity/anaphylactoid) reaction (eg, hypotension (low blood pressure), urticaria (hives), face edema (swelling of the face), eyelid edema (swelling of the eyelid) and flushing
- dizziness, dysgeusia (disturbed sense of taste), parasthesia ("pins and needles")
- dyspnea (shortness of breath)
- vomiting
- erythema (redness of the skin)
- pruritus (including generalized pruritus) (itching)
- rash (including generalized rash, macular rash [small flat red spots], papular rash [small, raised, circumscribed lesions], pruritic rash [itchy rash])
- various kinds of injection site reactions (eg leakage into the surrounding tissue, burning, coldness, warmth, reddening, rash, pain or bruising)
- feeling hot

Rare (may affect up to 1 in 1000 people)
- loss of consciousness (fainting)
- convulsion
- parosmia (disturbed sense of smell)
- tachycardia (rapid heart beat)
- palpitations
- dry mouth
- malaise (generally feeling unwell)
- feeling cold

Not known (frequency cannot be estimated from the available data)

- cardiac arrest (heart stops beating)
- nephrogenic systemic fibrosis (NSF) (a disease mainly involving thickening of the skin and connective tissues. NSF may result in severe joint immobility, muscle weakness, or may affect the normal working of internal organs which may potentially be life-threatening)
- the following allergy-like reactions: anaphylactoid shock (a severe allergy-like reaction), circulatory collapse (shock), respiratory arrest (breathing stops), pulmonary edema (fluid in the lungs), bronchospasm (breathing difficulties), cyanosis (blueness of the lips), oropharyngeal swelling (swelling of the mouth and throat), laryngeal edema (swelling of the throat), increased blood pressure, chest pain, angioedema (eg, swelling of the face, throat, mouth, lips and/or tongue), conjunctivitis, hyperhidrosis (increased sweating), cough, sneezing, burning sensation, flushing and pallor (pale skin)

If you get any side effects, talk to your doctor or radiologist. This includes any possible side effects not listed in this leaflet.

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
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 GADOVIST 1.0, contact your doctor or pharmacist.

HOW TO STORE IT

GADOVIST 1.0 should be stored at temperatures between 15°C to 30°C. Do not freeze.

After the vial/bottle has been opened or the prefilled syringe has been prepared for use, GADOVIST 1.0 remains stable for 24 hours at 20°C to 25°C and must then be discarded.

REPORTING SUSPECTED SIDE EFFECTS

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 01908C
  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 health 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 by contacting the manufacturer at the above-mentioned phone number and email address

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