Package leaflet: Information for the user

Primovist 0.25 mmol/ml, solution for injection, pre-filled syringe

Gadoxetate, disodium

Read all of this leaflet carefully before you are given this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor giving you Primovist.

If you get any side effects talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet

1. What Primovist is and what it is used for

Primovist is a contrast medium for magnetic resonance imaging (MRI) of the liver. It 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 number, size, and distribution. Primovist can also help the doctor determine the nature of any abnormalities, thereby increasing the confidence in the diagnosis.
It is provided as a solution for intravenous injection. 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 using a complex system of magnets and radio waves.

2. What you need to know before you are given Primovist

Do not use Primovist
- if you are allergic to gadoxetate disodium or any of the other ingredients of this medicine (listed in section 6).

Warnings and precautions
Talk to your doctor before you are given Primovist if you have:
- or have had asthma or an allergy such as hay fever, nettle rash
- had a previous reaction to contrast media
- reduced kidney function.
  The use of some gadolinium-containing contrast agents in patients with these conditions has been associated with a disease called Nephrogenic Systemic Fibrosis (NSF). NSF is a disease involving thickening of the skin and connective tissues. NSF may result in debilitating joint immobility, muscle weakness or impairment of the function of internal organs which may potentially be life threatening.
- a serious disease of the heart and blood vessels
- low potassium levels

- or someone in your family, has had problems with the electrical rhythm of the heart called long QT syndrome
- had heart rhythm changes after taking medicines
- a heart pacemaker or if there are any implants or clips containing iron in your body

- Allergy-like reactions may occur after use of Primovist with delayed reactions after hours or days. See section 4.

Tell your doctor if:
- your kidneys do not work properly
- 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 Primovist, especially if you are 65 years of age or older.

Accumulation in the body
Primovist works because it contains a metal called gadolinium. Studies have shown that small amounts of gadolinium can remain in the body, including the brain. No side effects have been seen due to gadolinium remaining in the brain.

Children and adolescents
The safety and efficacy of Primovist have not been established in patients under 18 years as there is limited experience on its use. Further information is given at the end of the leaflet.

Other medicines and Primovist
Tell your doctor if you are taking, have recently taken or might take any other medicines. These include especially:
- betablockers, medicines to treat high blood pressure or other heart conditions
- medicines that change the rhythm or rate of your heartbeat such as amiodarone, sotalol
- rifampicin, medicine to treat tuberculosis or certain other infections

Pregnancy and breast-feeding

Pregnancy
You must tell your doctor if you think you are or might become pregnant, as Primovist should not be used during pregnancy unless strictly necessary.

Breast-feeding
Tell your doctor if you are breast-feeding or about to start breast-feeding. Your doctor will discuss whether you should continue breast-feeding or interrupt breast-feeding for a period of 24 hours after you receive Primovist.

Driving and using machines
Primovist has no influence on the ability to drive and use machines.

Primovist contains sodium
This medicine contains 82 mg sodium (main component of cooking/table salt) in each dose based on the amount given to a 70 kg person. This is equivalent to 4.1 % of the recommended maximum daily dietary intake of sodium for an adult.

3. How to use Primovist

Primovist is injected via a small needle into a vein. Primovist will be administered immediately before your MRI examination.
After the injection you will be observed for at least 30 minutes.

The recommended dose is
0.1 ml Primovist per kg body weight.

Dosage in special patient groups
The use of Primovist is not recommended in patients with severe kidney problems and patients who have recently had, or soon expect to have, a liver transplant. However if use is required you should only receive one dose of Primovist during a scan and you should not receive a second injection for at least 7 days.

Elderly
It is not necessary to adjust your dose if you are 65 years of age or older but you may have a blood test to check how well your kidneys are working.

If you receive more Primovist than you should

Overdosing is unlikely. If it does happen, the doctor will treat any symptoms that follow.

4. Possible side effects

Like all medicines, this medicine can cause side effects, although not everybody gets them.
Most of the side effects are mild to moderate.
If you get any side effects, talk to your doctor.

As with other contrast media, in rare cases allergy-like reactions may occur. Delayed reactions hours to days after the administration of Primovist may occur.
The most serious side effect in patients receiving Primovist is anaphylactoid shock (a severe allergy-like reaction).
Inform your doctor immediately if you experience any of the following signs or have difficulty in breathing:
- low blood pressure
- swelling in the tongue, throat or face.
- runny nose, sneezing, cough
- red, watery and itchy eyes
- stomach pain
- nettle rash
- reduced feeling or sensitivity in the skin, itching, pale skin

The following further side effects may occur:
Common: may affect up to 1 in 10 people
- headache
- nausea

Uncommon: may affect up to 1 in 100 people

- dizziness
- numbness and tingling
- problems with sense of taste or smell
- flushing
- high blood pressure
- breathing difficulties
- vomiting
- dry mouth
- skin rash
- severe itching, affecting the whole body or the eye
- back pain, chest pain
- injection site reactions, such as
  - burning, coldness, irritation, pain
- feeling hot
- chills
- tiredness
- feeling abnormal

Rare: may affect up to 1 in 1000 people
- incapability to sit or stand still
- uncontrollable shaking
- feeling of increased heart rate
- irregular heartbeat (signs of heart block)
- discomfort of the mouth
- increased production of saliva
- red skin rash with pimpoles or spots
- increased sweating
- feeling of discomfort, generally feeling unwell

Not known: frequency cannot be estimated from the available data
- fast heartbeat
- restlessness

Changed laboratory values may occur shortly after you have been given Primovist. Inform your healthcare professional if you have recently been administered Primovist if giving blood or urine samples.

There have been reports of nephrogenic systemic fibrosis (which causes hardening of the skin and may affect also soft tissue and internal organs) associated with use of other gadolinium-containing contrast agents.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store Primovist

Keep this medicine out of the sight and reach of children.

Do not use this medicine after the expiry date which is stated on the syringe and outer carton after EXP. The expiry date refers to the last day of that month.

This medicine does not require any special storage conditions.

This medicine should be used immediately after opening.

It should be visually inspected before use. This medicine should not be used in case of severe discoloration, the occurrence of particulate matter or a defective container.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. Contents of the pack and other information

What Primovist contains

- The active substance is gadoxetate disodium. Each ml of solution for injection contains 0.25 mmol gadoxetate disodium (equivalent to 181.43 mg gadoxetate disodium)
- The other ingredients are caloxetate trisodium, trometamol, sodium hydroxide and hydrochloric acid (both for pH adjustment), water for injections.

1 pre-filled syringe with 5.0 ml contains 907 mg gadoxetate disodium,
1 pre-filled syringe with 7.5 ml contains 1361 mg gadoxetate disodium,
1 pre-filled syringe with 10.0 ml contains 1814 mg gadoxetate disodium.

What Primovist looks like and contents of the pack

Primovist is a clear, colourless to pale yellow solution free from visible particles. The contents of the packs are 1, 5 or 10 pre-filled syringes with:

5.0 ml solution for injection (in 10-ml glass prefilled syringes)
7.5 ml solution for injection (in 10-ml glass prefilled syringes)
10.0 ml solution for injection (in 10-ml glass prefilled syringes)

Not all pack sizes may be marketed.

Marketing Authorisation Holder

Bayer Limited, 1st Floor, The Grange Offices, The Grange, Brewery Road, Stillorgan, Co. Dublin, A94 H2K7, Ireland

Manufacturer

Bayer AG
Müllerstrasse 178
13353 Berlin, Germany

This leaflet was last revised in September 2022

The following information is intended for healthcare professionals only:

- **Renal impairment**

Prior to administration of Primovist, it is recommended that all patients are screened for renal dysfunction by obtaining laboratory tests.

There have been reports of nephrogenic systemic fibrosis (NSF) associated with use of some gadolinium-containing contrast agents in patients with acute or chronic severe renal impairment (GFR< 30ml/min /1.73 m^2). Patients undergoing liver transplantation are at particular risk since the incidence of acute renal failure is high in this group. As there is a possibility that NSF may occur with Primovist, it should be avoided

- in patients with severe renal impairment
- in the perioperative liver transplantation period

unless the diagnostic information is essential and not available with non-contrast enhanced MRI. If use of Primovist cannot be avoided, the dose should not exceed 0.025 mmol/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, Primovist injections should not be repeated unless the interval between injections is at least 7 days.

As the renal clearance of gadoxetate may be impaired in the elderly, it is particularly important to screen patients aged 65 years and older for renal dysfunction.

Haemodialysis shortly after Primovist administration may be useful at removing Primovist from the body. There is no evidence to support the initiation of haemodialysis for prevention or treatment of NSF in patients not already undergoing haemodialysis.

- **Pregnancy and breast-feeding**

Primovist should not be used during pregnancy unless the clinical condition of the woman requires use of gadoxetate.

Continuing or discontinuing breast feeding for a period of 24 hours after administration of Primovist, should be at the discretion of the doctor and lactating mother.

- **Paediatric population**

An observational study was performed in 52 paediatric patients aged over 2 months and less than 18 years. Patients were referred for Primovist enhanced liver MRI to evaluate suspected or known focal liver lesions. Additional diagnostic information was obtained when combined unenhanced and enhanced liver MRI were compared with unenhanced MRI alone. Serious adverse events were reported, however none were assessed by the investigator to be related to Primovist. Due to the retrospective nature and small sample size of this study, no definitive conclusion can be made regarding efficacy and safety in this population.

- **Before injection**

Primovist is a clear, colourless to pale yellow solution free from visible particles. The contrast medium should be inspected visually before use. Contrast media should not be used in case of severe discoloration, the occurrence of particulate matter or a defective container.

- **Administration**

Primovist is to be administered undiluted as an intravenous bolus injection at a flow rate of about 2 ml/sec. After the injection the intravenous cannula/ line should be flushed using physiological saline solution (9 mg/ml).

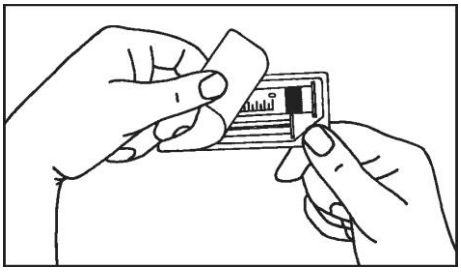
- Patient should be observed for at least 30 minutes after the injection.

- Primovist must not be mixed with other medicinal products.
- Intramuscular injection must be strictly avoided.

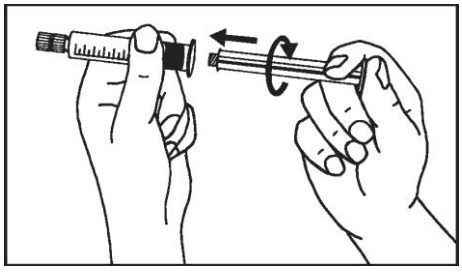
- **Handling**

Primovist is ready to use.
The pre-filled syringe should be prepared for the injection immediately before the examination. The tip cap should be removed from the pre-filled syringe immediately before use.
Any solution not used in one examination is to be discarded in accordance with local requirements.

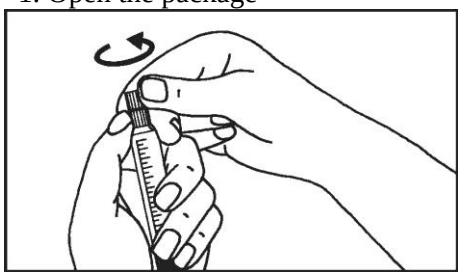
The peel-off tracking label on the syringes should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded.
If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record.



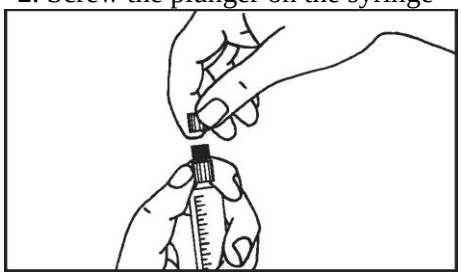
1. Open the package



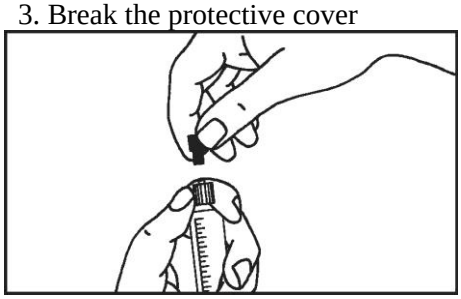
2. Screw the plunger on the syringe



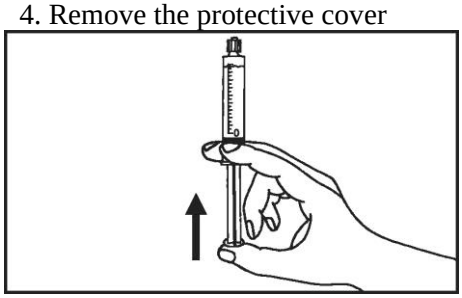
3. Break the protective cover



4. Remove the protective cover



5. Remove the rubber stopper



6. Remove the air in the syringe