MAGNETOL

Gadolinium (Gd) - DTPA 0.5 M Injection

Prescribing information

Magnetol is an injectable paramagnetic contrast medium for magnetic resonance imaging (MRI). The contrast enhancement is due to the paramagnetic properties of the gadolinium metal.
Magnetol enhancement provides improved lesion characterization and additional diagnostic information in a great number of abnormal cases, helping this interpretation. The Gd-DTPA complex is to be administered by intravenous injection and it is eliminated via the kidneys. Magnetol is available in a sterile, pyrogen-free, ready-to-use stable 0.5 molar solution.

COMPOSITION:
Gadopentetic acid, dimeglumine salt in aqueous solution - 469 mg/ml.

PRESENTATION:
Box containing 10 vials with 20 ml contrast medium each.

INDICATION AND USAGE:
Contrast-enhanced MRI for detection and localization of inflammatory and neoplastic (primary and metastatic) disease in either neuro imaging, body imaging and musculoskeletal imaging.

DOSAGE AND ADMINISTRATION:
The recommended dosage is 0.2 ml/kg (0.1 mmol/kg) administered intravenously, at a rate not to exceed 10 ml/minute. The maximum total dose is 20 ml. The drug must be injected immediately after it is withdrawn into a syringe. For injection use only disposable plastic syringes. Any unused portion must be discarded.
For optimal enhancement, the imaging following Magnetol injection must be timed according to the clinical objectives of the examination. For increasing the diagnostic yield of the examination a second injection equivalent to the original dose can be given. However, at least 30 minutes interval between the two injections is recommended in order to allow the clearing of the paramagnetic material.
Magnetol should not be drawn into the syringe until immediately before use. Any contrast agent solution not used in an examination session is to be discarded.

DOSAGE CHART

Body Weight (kg)	Dose (ml)	Approx. Duration of Injection (Seconds)
10	2.0	20
20	4.0	30
30	6.0	40
40	8.0	50
50	10.0	60
60	12.0	70
70	14.0	80
80	16.0	95
90	18.0	110
100	20.0	120

To ensure complete injection of the contrast medium, the injection should be followed by a 5 ml normal saline flush.
The imaging procedure should be completed within 1 hour of injection of Magnetol Injection.

OVERDOSAGE:
The LD_{50} of intravenously administered gadopentetate dimeglumine injection in mice is 5-12.5 mmol/kg and in rats it is 10-15 mmol/kg. The LD_{50} of intravenously administered Magnetol Injection in dogs is greater than 6 mmol/kg.
Clinical consequences of overdose with Magnetol Injection have not been reported.

CONTRAINDICATIONS:
None so far known.

TOLERANCE AND SIDE EFFECTS:
Care should be exercised in patients with a severe impairment of renal function, as gadolinium pentetate dimeglumine (Magnetol Injection) is eliminated from the body by renal glomerular filtration. The most commonly noted adverse experience is headache with an incidence of 8.7%. The majority of headaches are transient and of mild to moderate severity. In 42.3% of the cases it was felt that the headaches were not related to Magnetol Injection.
In a few patients the side effects may include a transient rise in serum iron levels, and a transient rise in serum bilirubin levels.
The effect of the drug on patients with hepatic disease has not been investigated, and caution is advised.
Patients receiving an injection of Magnetol should inform their physician if they have any disease that affects red blood cells or anemia.

PREGNANT WOMEN AND PEDIATRIC USE:
It has not been established that Magnetol can cause fetal harm when administered to pregnant women. Neither has been established safety in children under the age of 2 years. Magnetol should be given to pregnant women and children only if the expected benefits to be gained clearly outweigh the potential hazards.

NURSING MOTHERS:
C^{14} labeled gadopentetate dimeglumine was administered intravenously to lactating rats at a dose of 0.5 mmol/kg. Less than 0.2% of the total dose was transferred to the neonate via the milk during the 24-hour evaluation period. It is not known to what extent Magnetol Injection is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when the drug is administered to a nursing mother and consideration should be given to temporarily discontinuing nursing.

WARNINGS:

- Exposure to GBCAs (Gadolinium Based Contrast Agents) increases the risk for NSF in patients with impaired elimination of the drugs.
- Avoid use of GBCAs among these patients unless the diagnostic information is essential and not available with non-contrast enhanced MRI or other modalities. The GBCA-associated NSF risk appears highest for patients with chronic, severe kidney disease (GFR < 30 mL/min/1.73m^2) as well as patients with acute kidney injury. Do not administer MAGNETOL to these patients.
  The risk appears lower for patients with chronic, moderate kidney disease (GFR 30 - 59 mL/min/1.73m^2) and little, if any, for patients with chronic, mild kidney disease (GFR 60 - 89 mL/min/1.73m^2).
- Avoid use in patients with acute renal insufficiency of any severity due to the hepato-renal syndrome or in the perioperative liver transplantation period.
- NSF is a debilitating and sometimes fatal disease affecting the skin, muscle, and internal organs.
- Screen all patients for renal dysfunction by obtaining a history and/or laboratory tests.
- When administering a GBCA, do not exceed the dose recommended in product labeling. Allow sufficient time for elimination of the GBCA prior to any re-administration.

The accepted safety considerations and procedures that are required for magnetic resonance imaging are applicable when Magnetol Injection is used for contrast enhancement. In addition deoxygenated sickle erythrocytes have been shown in *in vitro* studies to align perpendicular to a magnetic field which may result in vaso-occlusive complications *in vivo*. The enhancement of magnetic moment by gadopentetate dimeglumine may possibly potentiate sickle erythrocyte alignment. Magnetol Injection in patients with sickle-cell anemia and other hemoglobinopathies has not been studied.
Patients with other hemolytic anemias have not been adequately evaluated following administration of Magnetol Injection to exclude the possibility of increased hemolysis.
Hypotension may occur in some patients after injection of Magnetol Injection. In clinical trials two cases were reported and in addition, there was one case of a vasovagal reaction and two cases of pallor with dizziness, sweating and nausea in one and substernal pain and flushing in the other. These were reported within 25 to 85 minutes after injection except for the vasovagal reaction which was described as mild by the patient and occurred after 6.5 hours. In a study in normal volunteers one subject experienced syncope after arising from a sitting position two hours after administration of the drug. Although the relationship of gadopentetate dimeglumine to these events is uncertain, patients should be observed for several hours after drug administration.

- Among the factors that may increase the risk for NSF are repeated or higher than recommended doses of a GBCA.
- For patients receiving hemodialysis, healthcare professionals may consider prompt hemodialysis following GBCA administration in order to enhance the contrast agent's elimination. However, it is unknown if hemodialysis prevents NSF.
- Determine the renal function of patients by obtaining a medical history or conducting laboratory tests that measure renal function prior to using a GBCA.
- Post-marketing reports have identified the development of NSF following single and multiple administrations of GBCAs. These reports have not always identified a specific agent. Where a specific agent was identified, the most commonly reported agent was Omniscan, followed by Magnevist/ Magnetol and OptiMARK. NSF has also developed following the sequential administration of Omniscan and MultiHance and Omniscan and ProHance. The distribution of the number of reports for the individual GBCAs may relate to multiple factors, including more limited use of some GBCAs, under-reporting of NSF, characteristics of the agent and a lack of patients' complete GBCA exposure history.

PRECAUTIONS GENERAL:
Diagnostic procedures that involve the use of contrast agents should be carried out under direction of a physician with the prerequisite training and a thorough knowledge of the procedure to be performed.
In a patient with a history of grand mal seizures, Magnetol Injection was reported to induce such a seizure.
Since gadopentetate dimeglumine is cleared from the body by glomerular filtration, caution should be exercised in patients with severely impaired renal function.
The possibility of a reaction, including serious life-threatening, fatal, anaphylactoid or cardiovascular reactions or other idiosyncratic reactions should always be considered, especially in those patients with a known clinical hypersensitivity or a history of asthma or other allergic respiratory disorders.
Animal studies suggest that gadopentetate dimeglumine may alter red cell membrane morphology resulting in a slight degree of extravascular (splenic) hemolysis. In clinical trials 15-30% of the patients experienced an asymptomatic transient rise in serum iron. Serum bilirubin levels were slightly elevated in approximately 3.4% of patients. Levels generally returned to baseline within 24 to 48 hours. Hematocrit and red-blood cell count were unaffected and liver enzymes were not elevated in these patients. While the effects of gadopentetate dimeglumine on serum iron and bilirubin have not been associated with clinical manifestation, the effect of the drug in patients with hepatic disease is not known and caution is therefore advised.
When Magnetol Injection is to be injected using plastic disposable syringes, the contrast medium should be drawn into the syringe and used immediately. If nondisposable equipment is used, scrupulous care should be drawn to prevent residual contamination with traces of cleansing agents.
Repeat procedures: If in the clinical judgment of the physician sequential of repeat examinations are required, a suitable interval of time between administrations should be observed to allow for normal clearance of the drug from the body.

INFORMATION FOR PATIENTS:
Patients receiving Magnetol Injection should be instructed to:
1. Inform your physician if you are pregnant or breastfeeding.
2. Inform your physician if you have an anemia of any disease that affects red blood cells.
3. Inform your physician if you have asthma or other allergic respiratory disorders.
4. Inform your physician if you suffer from advanced kidney failure.

GBCAs increase the risk of NSF among patients with impaired elimination of drugs. To counsel patients at risk of NSF:
- Describe the clinical manifestation of NSF.
- Describe procedures to screen for the detection of renal impairment.
- Instruct the patients to contact their physician if they develop signs or symptoms of NSF following Magnetol administration, such as burning, itching, swelling, scaling, hardening and tightening of the skin; red or dark patches on the skin; stiffness in joints with trouble moving, bending or straightening the arms, hands, legs or feet; pain in the hip bones or ribs; or muscle weakness.

STORAGE:
Magnetol Injection should be stored below 25°C and protected from light.
Do not freeze. Prior to use check the vial for particulate matter.

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