Reviewed date: October 3, 2006
Revised date: May 1, 2008
Revised date: October 1, 2010
Revised date: December 1, 2015
Revised date: September 1, 2016
Revised date: May 7, 2018
Revised date: June 10, 2019

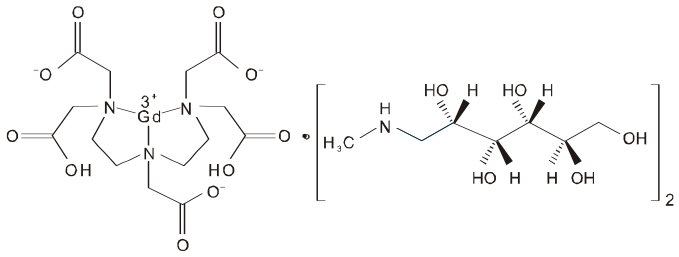
# Instructions for Gadopentetate Dimeglumine Injection

Please carefully read the package insert and use under the guidance of a physician.

**Gadolinium deposition**

**Both linear and macrocyclic gadolinium-containing contrast agents (GBCAs) will deposit trace amounts of gadolinium in the brain and other tissues. Animal experiments have shown that after repeated use of GBCAs, the deposition of linear GBCAs is higher than that of macrocyclics. This product is a linear GBCA.**

**[Drug Name]**
Generic name: Gadopentetate Dimeglumine Injection
English name: Gadopentetate Dimeglumine Injection
Chinese pinyin: Gapensuanpu'an Zhusheye
**[Ingredients]** Gadopentetate Dimeglumine
Chemical name: Diethylenetriaminepentaacetic acid gadolinium dimeglumine.
Chemical structural formula:



Molecular formula: $C_{14}H_{20}GdN_3O_{10} \cdot 2C_7H_{17}NO_5$
Molecular weight: 938.01
**[Excipients]** Diethylenetriaminepentaacetic acid, meglumine, water for injection.
**[Descriptions]** This product is a colorless to light yellow or yellowish green clear liquid.
**[Indication]**
Magnetic resonance imaging of the central nervous system (brain and spinal cord), abdomen, chest, pelvis, limbs and other human organs and tissues.
**[Strength]** (1) 10 ml: 4.69 g
(2) 12 ml: 5.63 g
(3) 15 ml: 7.04 g
(4) 20 ml: 9.38 g

**[Posology and method of administration]**

Intravenous injection. For adults and children over 2 years old, 0.2 ml/kg (or 0.1 mmol/kg) once as per body weight, and the maximum dosage is 0.4 ml/kg once as per body weight.

1. Magnetic resonance imaging of the brain and spinal cord: if necessary, the drug can be administered again within 30 minutes.

2. Whole body magnetic resonance imaging: in order to obtain sufficient enhancement, the drug can be administered 0.4 ml/kg once as per body weight. The best enhancement time is generally within 45 minutes after injection. In order to rule out adult lesion or tumor recurrence, the dosage can be increased to 0.6 ml/kg once as per body weight to increase the reliability of the diagnosis.

Use the lowest approved dose whenever possible.

**[Adverse reactions]** According to domestic and foreign literature reports

**Overview of the safety of this product**

The overall safety of this product is based on post-marketing monitoring data and clinical trial data of more than 11,000 patients. In the clinical trials of gadopentetate dimeglumine injection, the most frequently observed adverse drug reactions (≥0.4%) are:

- Various reactions at the injection site
- Headache
- Nausea
- Most of the adverse drug reactions in clinical trials are mild to moderate.

In general, the most serious adverse drug reactions in patients using gadopentetate dimeglumine injection are:

- Nephrogenic systemic fibrosis
- Anaphylactic reaction/anaphylactic shock

Delayed allergic reactions/anaphylactic reactions (after a few hours to a few days) are rare.

**List of adverse reactions**

According to the frequency of occurrence, the adverse drug reactions in clinical trials are classified. According to the following conventions, define frequency groups: uncommon ≥1/1000 to <1/100; rare: ≥1/10000 to <1/1000. Adverse drug reactions that are only found in post-marketing surveillance and whose frequency cannot be estimated are listed under 'unknown'.

The following table reports the adverse drug reactions reported in clinical studies or post-marketing surveillance among patients treated with this product

| System Organ Classification (MedDRA) | Uncommon | Rare | Unknown |
|---|---|---|---|
| Blood and lymphatic system | | | Elevated serum iron* |
| Immune system | | Hypersensitivity/anaphylactic reactions (eg: anaphylactic shock*, anaphylactoid reaction§*, hypersensitivity reaction§*, shock§*, hypotension§*, conjunctivitis, loss of consciousness§*, throat tightness*, sneezing, hives, itching, rash, erythema, dyspnea*, respiratory arrest§*, bronchospasm§*, asthma, | |

| | | | |
|---|---|---|---|
| | | laryngospasm §*, laryngeal edema §*, pharyngeal edema §*, cyanosis §*, rhinitis § , angioedema §*, facial edema*, reflex tachycardia §) | |
| Mental system | | Disorientation | Anxiety<br>Confusion |
| Nervous system | Dizziness<br>Headache<br>Taste disorders | Convulsions*<br>Paraesthesia<br>Burning sensation<br>Tremor | Coma*<br>Drowsiness*<br>Speech disorder<br>Abnormal smell |
| Eye | | | Visual disorder<br>Eye pain<br>Tears |
| Ears and labyrinth | | | Hearing impaired<br>Ear pain |
| Heart | | Tachycardia*<br>Arrhythmia | Cardiac arrest*<br>Decreased heart rate/ |
| Blood vessel | | Thrombophlebitis<br>Facial flushing<br>Vasodilation | Syncope*<br>Vasovagal response<br>Elevated blood pressure |
| Respiratory tract, chest and mediastinum | | Throat irritation/sore throat<br>Pharynx discomfort<br>Cough | Respiratory distress<br>Increased or decreased respiratory rate<br>Pulmonary Edema* |
| Gastrointestinal tract | Vomiting<br>Nausea | Abdominal pain<br>Stomach upset<br>Diarrhea<br>Toothache<br>Dry mouth<br>Oral soft tissue pain and paresthesia | Salivation |
| Liver and gallbladder | | | Elevated blood bilirubin<br>Elevated liver enzymes |
| Skin and subcutaneous tissue | | | Nephrogenic Systemic Fibrosis (NSF)* |
| Musculoskeletal, connective tissue | | Pain in extremities | Backache<br>Arthralgia |
| Kidney and urinary system | | | Acute renal failure*, **Elevated serum creatinine**<br>Urinary incontinence<br>Urgency urination |
| General disease and administration site | Pain<br>Heat feelings<br>Cold feelings | Chest pain, fever<br>Peripheral edema<br>Discomfort | Chill<br>Sweating<br>Increased or decreased |

| | | | |
|---|---|---|---|
| | Injection site reactions (such as: cold feelings, paresthesia, swelling, fever, pain, edema, inflammation, bleeding, erythema, discomfort, necrosis §, thrombophlebitis §, phlebitis §, inflammation §, extravasation § at the injection site) | Fatigue<br>Thirst<br>Weakness | body temperature |

*Reported life-threatening and/or fatal cases

**Appears in patients with pre-existing renal impairment

§Reactions identified only in post-marketing surveillance (frequency unknown)

**Description of specific adverse reactions**

After receiving this product in patients with dialysis-dependent renal failure, delayed and transient inflammatory-like reactions are common, such as fever, chills, and increased C-reactive protein. These patients should use this product for MRI examination on the day before dialysis.

**[Contraindications]**

People who are allergic to this product are contraindicated.

**[Precautions]**

1. Use with caution in patients with severe kidney damage, epilepsy, hypotension, asthma and other allergic respiratory diseases and those with allergic tendencies.
2. Take care to avoid the extravasation of the liquid during injection to prevent tissue pain.
3. The serum iron and bilirubin levels of some patients will increase slightly after medication, but they are asymptomatic and can return to normal within 24 hours.
4. Pregnant women and breast-feeding women should use it with caution. Animal experiments show that a small amount of medicine liquid enters the milk.
5. The effective enhancement time of this product is 45 minutes. MRI examination should be performed immediately after intravenous injection.
6. The remaining medicine liquid after one examination should not be used again.
7. When applying this product, follow the relevant safety regulations in the magnetic resonance imaging.
8. GBCAs should be used with caution. When plain scan MRI cannot obtain the corresponding vital diagnostic information, GBCAs can be used, and the lowest approved dose is used as much as possible.
9. Gadolinium deposition

Current evidence shows that after repeated use of GBCAs, trace amounts of gadolinium can remain in the brain and other body tissues. Research reports have shown that multiple use of GBCAs can increase the intensity of brain signals, especially in the dentate nucleus and globus pallidus. Currently, there are more reports about linear GBCAs and fewer reports about macrocyclic GBCAs. Animal experiments have shown that the amount of gadolinium deposited after repeated use of linear GBCAs is higher than that of repeated use of macrocyclics.

The clinical significance of brain gadolinium deposition is unclear.

In order to minimize the potential risks associated with gadolinium deposition in the brain, it must be used in strict accordance with the indications and approved doses. It is recommended to use the lowest approved dose

that meets the requirement of diagnosis and perform careful benefit risk assessment and patient informed communication before repeated administration.

**[Use in Pregnant and Lactating Women]**

Animal experiments have shown that there are slight signs of delaying fetal development with gadopentetate dimeglumine. Whether it is safe for pregnant women to use the drug has not yet been proved by sufficient study results, so unless the doctor considers it necessary, try to avoid using it.

Whether the drug is secreted in human milk is not yet clear, but considering that many drugs will be excreted through breast milk, special care should be taken when using this product in breastfeeding women.

**[Pediatric Use]**

Children from 2 to 16 years old can use this product for magnetic resonance imaging of central nervous system, extracranial tissue and body.

Because this product is mainly eliminated by the kidneys, and the renal function of infants and young children is not yet mature, and the pharmacokinetics of this product in infants and young children has not been studied, the safety and effectiveness of this product for children under 2 years of age have not been confirmed.

**[Geriatric Use]**

So far in clinical study, there is no specific problem for the elderly.

**[Drug Interactions]** Unknown.

**[Overdose]** Unknown.

**[Pharmacology and Toxicology]**

Pharmacological effects: this product is a paramagnetic contrast agent used for magnetic resonance imaging. After entering the body, it can shorten the T1 and T2 relaxation time of protons in the tissues, thereby enhancing the clarity and contrast of the image.

**[Pharmacokinetics]**

This product is rapidly distributed in the extracellular fluid after intravenous injection, and the concentration in blood and tissues has reached the peak in about 1 minute.

The elimination half-life is about 20-100 minutes, and about 90% of it is excreted in urine in its unchanged form within 24 hours. Hemodialysis can excrete this product from the body.

**[Storage]** Keep away from light and airtight.

**[Package]** Glass bottle with chlorinated butyl rubber stopper. According to the order of [Strengths]

(1) 10 ml/vial: 1 bottle/box; 10 bottles/box (2) 12 ml/vial: 1 bottle/box; 10 bottles/box

(3) 15 ml/vial: 1 bottle/box; 10 bottles/box (4) 20 ml/vial: 1 bottle/box; 10 bottles/box

**[Shelf Life]** 36 months.

**[Executive Standard]** 2015 Edition of *Chinese Pharmacopoeia II*

**[Approval number]** (1) 10 ml NMPA License No. H10860002

(2) 12 ml NMPA License No. H20013088

(3) 15 ml NMPA License No. H10860001

(4) 20 ml NMPA License No. H10960045

**[Manufacturer]**

Enterprise name: Beijing Beilu Pharmaceutical Co., Ltd.

Production address: Industrial Development Zone, Miyun District, Beijing

Postcode: 101500

Telephone: (010) 82626932

Fax: (010) 82626933