PATIENT INFORMATION LEAFLET

EMARAY Solution for Injection

For intravenous injection only

- ***Active substance:*** 1 ml of solution contains 469.01 mg dimeglumine salt of gadopentetic acid (equivalent to dimeglumine salt of gadopentetic acid).
- ***Excipients:*** Diethylenetriamine pentaacetic acid, meglumine, water for injections.

Before use this medicine, please read this PATIENT INFORMATION LEAFLET carefully, because it contains important information for you.

- *Keep this leaflet. You may need to read it again.*
- *If you have any further questions, consult your doctor or your pharmacist.*
- *This medicine has been prescribed for you personally; you should not pass it on to others.*
- *During use of this medicine please tell to your doctor that you use this medicine when you go to the doctor or hospital.*
- *Follow the information in the leaflet exactly. Do not use lower or higher dosages rather than recommended dosages regarding the medicine.*

In this leaflet:

1. What EMARAY is and what it is used for?

- EMARAY is a contrast agent which is administered intravenously for magnetic resonance imaging to provide diagnosis only. Magnetic resonance imaging is obtained by screening the motion of water molecules in normal and abnormal tissues.
- EMARAY contains 469,01 mg dimeglumin salt of gadopentatic acid in each ml.
- EMARAY is presented as clear solution with no particles in colorless glass vials and available in 10, 15 or 20 ml pack size.
- EMARAY is used for magnetic resonance imaging of head and spinal cord, vessels and whole body.

2. ***What you need to know before you use EMARAY***

Do not use EMARAY if

- you suffer from severe renal impairment
- you are about to have a liver transplant
- the patient is a newborn baby up to the age of 4 weeks

Take special care with EMARAY if

- you have a history of allergy to this kind of medicine
- you suffer from heart or blood circulation problems
- you suffer from moderate renal impairment
- you have seizures
- you have lesion in your brain
- the patient is newborn (over 4 years of age) or children
- you are premedicated with antihistaminics and/or glukocorticoids

EMARAY will only be used in newborns and infants up to 1 years of age, after careful consideration.

Please consult your doctor, even if these statements were applicable to you at any time in the past.

Use of EMARAY with food and drink

Nausea and vomiting are known side effects related to administration of contrast agents. Therefore, you should refrain from eating for 2 hours prior to investigation to avoid vomiting and reduce the aspiration risk of stomach contents during vomiting.

Pregnancy

Before use this medicine, consult your doctor or your pharmacist.

EMARAY should be used in pregnancy if only the benefit is more than the risk.

You must tell your doctor or your pharmacist if you become pregnant during treatment

Breast-feeding

Before use this medicine, consult your doctor or your pharmacist.

Very small amounts of EMARAY are excreted into breast milk. Breast-feeding should be discontinued for at least 24 hours after receipt of EMARAY.

Ability of drive and use machines

There is no known effect on ability of drive and use machines

Important information on excipients which are in contents of EMARAY

There is no warning.

Using with other medicines

There is no known interaction with other medicines.

Interaction with diagnostic tests

Because of diethylenetriamine pentaacetic acid (DTPA) content in solution of contrast substance, serum ferrum assay results obtained with complexometric methods (e.g. batophenanthroline) can be founded very low within 24 hour following administration.

If you are taking or have recently taken any other medicines, including medicines obtained without a prescription, please tell your doctor or your pharmacist

3. How to use EMARAY?

Instructions for use and for frequency of dosage/administration

Your doctor will determine the dose of based on your illness and administer to you.

Administration route and method:

EMARAY is administered by intravenous route. Your doctor will apply EMARAY.

Different age groups:

Children

Your doctor will determine the dose of medicine depends on his/her disease, age and body weight and then administer.

In newborns and infants (from 1 month up to 2 years of age) the required dose should be administered manually.

EMARAY should be only used after careful evaluation in newborns and infants up to 1 year of age. More than one dose should not be used during a scan. EMARAY injections should not be repeated unless the interval between injections is at least 7 days.

Use in elderly:

No dosage adjustment is needed. But caution should be exercised in elderly patients.

Special conditions:

Renal impairment

It should not be used in patient with severe renal impairment and before liver transplantation (See section 2).

If you think that the effect of EMARAY is too high or too low, please consult your doctor or your pharmacist.

If you receive more EMARAY than you should,

If you receive more EMARAY than you should, please consult a doctor or a pharmacist.

If you forget to use EMARAY,

Do not take a double dose to make up for a missed dose

Effects may be seen when treatment with EMERAY is stopped

EMARAY should be administered for once.

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

4. What are possible side effects?

Like all medicines, side effects can be observed in the patients who have sensitivity to the contents of EMARAY.

Below side effects involve the side effects which are obtained from clinical trials as well as from post marketing reports.

Below side effects are listed by frequency

Uncommon (may affect 1 to 10 users in 1000)

- Headache, dizziness, dysgeusia (disturbed sense of taste)
- Nausea, vomiting
- Pain, feeling hot, feeling cold
- Sensations or reactions at the injection site such as:
  Coldness, paresthesia (“pins and needles”), swelling, warmth, pain, irritation, hemorrhage (bleeding), erythema (reddish painful skin), discomfort.

Rare (may affect 1 to 10 users in 10000)

- Hypersensitivity (allergy)/ anaphylactoid (allergy-like) reactions, e.g. anaphylactoid shock (severe allergy-like reaction)
- Disorientation
- Convulsion (fits or seizures); paresthesia (numbness and tingling), burning sensation, tremor
- Problems with eyesight, watery eyes (lacrimation), pain in the eyes, infection in the eyes
- Increased and decreased heart rate, arrhythmia (irregular heart beat)
- Cardiac arrest (sudden stopping of the heart), bradycardia (decreased heart rate)
- Inflammation of a vein caused by or associated with a blood clot, flushing, widening of blood vessels (vasodilatation)
- Throat irritation/ throat tightness, pain or discomfort in the throat, coughing, difficulty in breathing, sneezing, wheezing
- Stopped breathing, difficulty in breathing, increased or decreased respiratory rate, bronchospasm, laryngospasm (voice box spasm), laryngeal oedema (voice box edema),

pharyngeal oedema (swelling of the throat), pulmonary oedema, cyanosis (blue lips), rhinitis (runny nose).
- Watery mouth (salivation)
- Stomach (abdominal) pain or discomfort, diarrhea, toothache, dry mouth, oral soft tissue pain and paresthesia (pains or numbness and tingling in the mouth)
- Shock, syncope, vasovagal reaction, hypotension, increased blood pressure
- Urticaria, pruritus, rash, erythema, swelling of the mouth, eyes and throat
- Problems with hearing; ear pain
- Pains in the arms, hands, legs and feet, back pain, arthralgia (joint pain)
- Chest pain, fever, swelling of the arms and legs, generally feeling unwell (malaise), tiredness (fatigue), thirst, weakness (asthenia).
- Kidney failure in patients who already have kidney problems, increased serum creatinine (blood marker for kidney function), loss of control of bladder (incontinence), urgent need to pass urine
- Chills, sweating, changes in body temperature
- Increased iron levels in blood
- Coma, somnolence (sleepiness), problems with speech, parosmia (disturbed sense of smell)
- Agitation, confusion
- Increased bilirubin (bile pigment), increased liver enzyme
- Sensations or reactions at the injection site such as:
  death of tissue (necrosis), inflammation of a vein caused by or associated with a blood clot (thrombophlebitis), inflammation of a vein (phlebitis), inflammation, bleeding into the tissue at the injection site (extravasation)

In patients with dialysis-dependent renal failure who received EMARAY, inflammatory-like reactions such as fever, chills and CRP (a test which shows inflammation) increase have been commonly observed. These patients had the MRI examination with EMARAY on the day before hemodialysis.

Cases of nephrogenic systemic fibrosis (NSF) have been reported.

If you notice any side effects not listed in this leaflet, please tell your doctor or your pharmacist.

5. Storage of EMARAY

Keep out of the sight and reach of children and store in the original pack.

Store at room temperature, below 25 °C. It should be stored in the outer cartoon because of light sensitivity.

Please use EMARAY in accordance with expiry date.

Do not use EMARAY after expiry date.

If you notice any visible signs of deterioration on product or pack, do not use EMARAY.

Registration holder:

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THE FOLLOWING INFORMATION IS INTENDED FOR MEDICAL OR HEALTHCARE PROFESSIONALS ONLY.

Any unused medicinal product or waste material should be disposed of in accordance with "Control of Medical Waste Regulations" and "Controls of Packaging Wastes Regulations".

EMARAY should only be drawn up into the syringe immediately before use. The rubber stopper should never be pierced more than once. Any contrast medium not used in one examination must be discarded.

Posology/ administration frequency and time:

Cranial and spinal MRI

Adults: In general, the administration of 0.2 ml EMARAY per kg body weight is sufficient for good enhancement and to answer the clinical question.

If a strong clinical suspicion of a lesion persists despite a normal contrast-enhanced MRI, a further injection of 0.2 or, in adults, even of 0.4 ml EMARAY per kg body weight within 30 minutes with immediately following MRI may increase the diagnostic yield of the examination.

For the exclusion of metastases or recurrent tumors in adults the injection of 0.6 ml EMARAY per kg body weight often leads to higher diagnostic confidence.

Children (including neonates and infants up to 2 years of age)

0.2 ml EMARAY/kg body weight is sufficient to provide diagnostically adequate contrast

EMARAY is contraindicated in neonates up to 4 weeks of age.

Due to immature renal function in infants up to 1 year of age, EMARAY should only be used in these patients after careful consideration at a dose not exceeding 0.2 ml/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, EMARAY injections should not be repeated unless the interval between injections is at least 7 days.

If a strong clinical suspicion of a lesion persists despite a normal contrast-enhanced MRI, a further injection of 0.2 ml EMARAY per kg body weight within 30 minutes with immediately following MRI in patients up to 1 year of age may increase the diagnostic yield of the examination.

In infants (from 1 month up to 2 years of age) the required dose should be administered manually.

Whole body MRI

Adults:

In general, the administration of 0.2 ml EMARAY per kg body weight is sufficient for good enhancement and to answer the clinical question.

In special cases (e.g. in lesions with poor vascularization and/or a small extracellular space) the administration of 0.4 ml EMARAY per kg body weight may be necessary for an adequate contrast effect especially on use of relatively slightly T1-weighted scanning sequences. For the exclusion of metastases or recurrent tumors in adults the injection of 0.6 ml EMARAY per kg body weight often leads to higher diagnostic confidence.

For the visualization of vessels, depending on the region to be investigated and the examination technique, in adults the injection of up to 0.6 ml per kg body weight may be required.

Children (over the 2 years of age)

In general, 0.2 ml EMARAY/kg body weight is sufficient to provide diagnostically adequate contrast.

In special cases (e.g. in lesions with poor vascularization and/or a small extracellular space) the administration of 0.4 ml EMARAY per kg body weight may be necessary for an adequate contrast effect especially on use of relatively slightly T1-weighted scanning sequences.

Neonates and infants below 2 years of age

EMARAY is contraindicated in neonates up to 4 weeks of age.

In children below two years of age, there are limited experiences. But this limited experiences show that the administration of 0.2 ml EMARAY per kg body weight can be used in this special population.

Due to immature renal function in infants up to 1 year of age, EMARAY should only be used in these patients after careful consideration at a dose not exceeding 0.2ml/kg body weight. More than one dose should not be used during a scan. Because of the lack of information on repeated administration, EMARAY injections should not be repeated unless the interval between injections is at least 7 days.

Method of administration:

EMARAY should only be drawn up into the syringe immediately before use. The rubber stopper should never be pierced more than once. Any contrast medium not used in one examination must be discarded.

The usual precautions for MRI (e.g. exclusion of cardiac pacemakers and ferromagnetic implants) must be observed.

Regardless of the field strength of the magnet, the recommended magnetic flux density for EMERAY is between 0.14 Tesla and 1.5 Tesla.

EMARAY should only be administered by intravenous administration. Contrast enhanced MRI may be initiated immediately after administration of the medium.

Dietary recommendations

Nausea and vomiting are known possible adverse reactions of all extracellular MRI contrast media. The patient should therefore refrain from eating for 2 hours prior to investigation to avoid aspiration.

Anxiety

Pronounced tension, anxiety or pain may increase the risk of undesirable effects or can aggravate the reactions caused by contrast agents. Sedatives may be given to these patients.

Special Populations:

Renal/Hepatic impairment

EMARAY is contraindicated in patients with severe renal impairment (GFR < 30 ml/min/1.73m^2) and in patients in the perioperative liver transplantation period. EMARAY should only be used after careful risk/benefit evaluation in patients with moderate renal impairment (GFR 30-59 ml/min/1.73m^2) at a dose not exceeding 0.2ml/kg body weight (=0.1 mmol/kg). More than one dose should not be used during a scan. Because of the lack of information on repeated administration, EMARAY injections should not be repeated unless the interval between injections is at least 7 days.

Pediatric population

See: Posology/ administration frequency and time.

Elderly (aged 65 years and above):

No dosage adjustment is considered necessary. Caution should be exercised in elderly patients.

Use of paramagnetic contrast agent can make difficult to be screened for lesions with unenhanced-MRI. It might be possible due to effects of paramagnetic contrast agents or screening parameters. Therefore, MRI scanning of EMARAY without accompanying unenhanced-MRI should be evaluated carefully.