12.2021

CLARISCAN

קלריסקן

Active ingredient and strength:
GADOTERIC ACID 279.3 MG / 1 ML

חומר פעיל וכמותו:
חומצה גדוטרית 279.3 מ"ג/מ"ל

רופא/ה, רוקח/ת נכבד/ה,

- העלון לרופא של המוצר עודכן בנובמבר 2021.
- **בהודעה זו מתוארים רק השינויים העיקריים המהווים החמרה או תוספת מידע.** בעלון קיימים עדכונים נוספים.
- טקסט שנוסף מופיע על רקע אפור, טקסט שנמחק מופיע עם קו חוצה על רקע ~~אפור~~.
- החמרות מופיעות בצהוב, הקלות מופיעות ירוק.

להלן נוסח ההתוויה המאושר לתכשיר:

Enhancement of contrast in magnetic resonance imaging.
Encephalic and spinal pathologies: brain tumours, tumours of the spine and the surrounding tissue, intervertebral disk prolapse infectious diseases.
Abdominal pathologies: primary and secondary liver tumours.
Osteo-articular pathology: bone and soft tissue tumours synovial diseases.
Magnetic resonance imaging for angiography.

העדכונים העיקריים בעלון לרופא נעשו בסעיפים הבאים:

4.1. Therapeutic indications

- Enhancement of contrast in magnetic resonance imaging.
- ~~Ae~~Encephalic and spinal pathologies: brain tumors, tumors of the spine and the surrounding tissue, intervertebral disk prolapse infectious diseases.
- Abdominal pathologies: primary and secondary liver tumors.
- Osteo-articular pathology: bone and soft tissue tumors synovial diseases.
- Magnetic resonance imaging for angiography.

4.4. Special warnings and precautions for use

Do not use by intrathecal route. Take care to maintain strictly intravenous injection: extravasation may result in local intolerance reactions, requiring the usual local care. ~~Administer only by intravenous injection.~~

~~Ensure strict intravenous injection: in the event of extravasation, local intolerance reactions can occur, requiring standard local treatment.~~

~~Gadoteric acid must not be administered by subarachnoid (or epidural) injections.~~

~~There is always a risk of hypersensitivity regardless of the dose injected.~~

The usual precaution measures for MRI examination should be taken, such as exclusion of patients with pacemakers, ferromagnetic vascular clips, infusion pumps, nerve stimulators, cochlear implants, or suspected intracorporal metallic foreign bodies, particularly in the eye.

~~4.4.1 Special warnings~~ Hypersensitivity

- As with other gadolinium-containing contrast media, hypersensitivity reactions can occur, including life- threatening ones (see 4.8 "Undesirable effects"). ~~All MRI contrast agents can be responsible for minor or major, life-threatening hypersensitivity reactions.~~ Hypersensitivity reactions may be either allergic (described as anaphylactic reactions when serious) or non-allergic. They can be either immediate (less than 60 minutes), or delayed (up to 7 days). Anaphylactic reactions occur immediately and can be fatal. They are independent of the dose, can occur after even the first dose of the product, and are often unpredictable.
- There is always a risk of hypersensitivity, regardless of the dose injected.
- ~~Resuscitation equipment must be immediately at hand due to the risk of major reactions.~~

- Patients who have already experienced a reaction during previous administration of a gadolinium-containing MRI contrast agent present an increased risk of experiencing another reaction on subsequent administration of the same product, or possibly other products, and are therefore considered to be at high risk.
- The injection of gadoteric acid may aggravate symptoms of an existing asthma. In patients with asthma unbalanced by the treatment, the decision to use gadoteric acid must be made after careful evaluation of the risk/benefit ratio.
- As known from the use of iodinated contrast media, hypersensitivity reactions can be aggravated more difficult to treat in patients on beta-blockers, and particularly in the presence of bronchial asthma. These patients may be refractory to standard treatment of hypersensitivity reactions with beta-agonists.
- Before any contrast medium is injected, the patient should be questioned for ~~a 4.4.2 Precautions for use 4.4.2.1. Hypersensitivity to MRI contrast agents Before the examination~~: identify high-risk subjects by detailed clinical interview of the patient's history of allergy (e.g., seafood allergy, hay fever, hives), sensitivity to contrast media and bronchial asthma as the reported incidence of adverse reactions to contrast media is higher in patients with these conditions and premedication with antihistamines and/or glucocorticoids may be considered.
- During the examination, supervision by a physician is necessary. ~~ensure medical surveillance maintain an intravenous line~~ If hypersensitivity reactions occur, administration of the contrast medium must be discontinued immediately and - if necessary - specific therapy instituted. A venous access should thus be kept during the entire examination. To permit immediate emergency countermeasures, appropriate drugs (e.g., epinephrine and antihistamines), an endotracheal tube and a respirator should be ready at hand.

~~After the examination:~~

~~After administration of a contrast agent, the patient must be kept under observation for at least 30 minutes, as the majority of serious adverse reactions occur during this period.~~
~~The patient must be warned about the possibility of delayed reactions (for up to 7 days) (see section 4.8 Undesirable effects).~~

4.8. Undesirable effects

Side effects in association with the use of gadoteric acid are usually mild to moderate in intensity and transient in nature. Injection site reactions, nausea and headache are the most frequently observed reactions.

During clinical trials, nausea, headache, injection site reactions, feeling cold, hypotension, somnolence, dizziness, feeling hot, burning sensation, rash, asthenia, dysgeusia and hypertension were the most frequent, uncommon (≥1/1000 to <1/100) adverse reactions.

Post-marketing the most commonly reported adverse reactions following administration of gadoteric acid have been nausea, vomiting, pruritus and hypersensitivity reactions.

In hypersensitivity reactions, the reactions most frequently observed are skin reactions, which can be localised, extended or generalised. These reactions occur most often immediately (during the injection or within one hour after the start of injection) or sometimes delayed (one hour to several days after injection), presenting as skin reactions in this case.

Immediate reactions include one or more effects, which appear simultaneously or sequentially, and are most often cutaneous, respiratory, gastrointestinal, joint and/or cardiovascular reactions.

Each sign may be a warning sign of shock and may very rarely lead to death.

Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with gadoteric acid, most of which were in patients co-administered other gadolinium-containing contrast agents (see section 4.4).

The adverse reactions are listed in the table below by SOC (System Organ Class) and by frequency according to the following categories: very common (≥1/10), common (≥1/100 to 1<1/10), uncommon (≥1/1,000 to 1<1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), undetermined frequency (cannot be estimated on the basis of available data). The data presented are from clinical trials involving 2822 patients when available, or from a pool of observational studies involving 185,500 patients.

~~During clinical studies on 1,941 patients, 3.6% of patients experienced an adverse reaction related to administration of gadoteric acid, the most common being pain and coldness at the injection site and nausea.~~

~~Adverse reactions related to the use of gadoteric acid are generally mild to moderate, and transient.~~

~~During clinical trials, headache and paresthesia were very commonly observed (>1/10), and nausea, vomiting and skin reactions such as erythematous rash and pruritus were commonly observed (>1/100 - <1/10).~~

~~The adverse reactions most commonly reported during administration of gadoteric acid since marketing are nausea, vomiting, pruritus, and hypersensitivity reactions.~~

~~The effects most commonly observed during hypersensitivity reactions are skin rashes, which can be localized, extensive or generalized. These reactions are usually immediate (during the injection or over the hour following the start of the injection) or sometimes delayed (one hour to several days after the injection), and then appear in the form of adverse skin reactions.~~

~~Immediate reactions comprise one or several, successive or concomitant effects, usually including skin reactions, respiratory and/or cardiovascular disorders, which may be the first signs of shock, which can rarely be fatal.~~

~~Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with gadoteric acid, most of which were in patients co-administered other gadolinium-containing contrast agents (see section 4.4).~~

~~Adverse reactions are presented in the following table by system organ class and by frequency according to the following categories: very common (≥1/10), common (≥1/100 to 1<1/10), uncommon (≥1/1 000 to 1<1/100), rare (≥1/10 000 to <1/1,000), very rare (<1/10,000), undetermined frequency (cannot be estimated on the basis of available data). The frequencies presented are derived from the data of an observational study on 82,103 patients.~~

System Organ Class	**Frequency: adverse reaction**
Immune system disorders	Uncommon: hypersensitivity, ~~anaphylactic reaction, anaphylactoid reaction~~ Very rare: anaphylactic reaction, anaphylactoid reaction
Psychiatric disorders	Rare: anxiety Very rare: agitation, ~~anxiety~~
Nervous system disorders	Uncommon: headache, dysgeusia, dizziness, drowsiness, paraesthesia (including burning sensation) ~~Very common: paraesthesia, headache~~ Rare: presyncope, ~~taste perversion~~ Very rare: coma, convulsion, syncope, tremor, parosmia ~~seizure, syncope, faintness, dizziness, parosmia, tremor~~

Eye disorders	Rare: eyelid oedema Very rare: conjunctivitis, ocular hyperaemia, blurred vision, ~~increased lacrimal secretion~~ excess tears ~~eyelid oedema~~
Cardiac disorders	Rare: palpitations Very rare: tachycardia, cardiac arrest, arrhythmia, bradycardia. ~~palpitations~~
Vascular disorders	Uncommon: hypotension, hypertension Very rare: : ~~hypotension, hypertension~~ pallor, vasodilatation
Respiratory, thoracic and mediastinal disorders	Rare: sneezing Very rare: respiratory arrest, pulmonary oedema, bronchospasm, laryngospasm, pharyngeal oedema, dyspnoea, nasal congestion, ~~sneezing~~, cough, dry throat
Gastrointestinal disorders	~~Common~~ Uncommon: nausea, abdominal pain ~~vomiting~~ Very rare: vomiting, diarrhoea, ~~abdominal pain~~, ~~excessive salivary hypersecretion~~
Skin and subcutaneous tissue disorders	Uncommon: rash ~~Common: pruritus, erythema~~, ~~rash~~ Rare: urticaria, pruritus, hyperhidrosis Very rare: erythema, angioedema, eczema ~~Undetermined frequency~~ Not known: nephrogenic systemic fibrosis
Musculoskeletal and connective tissue disorders	Very rare: muscle ~~contractures~~ cramps, muscleular weakness, back pain
General disorders and administration site conditions	~~Common~~ Uncommon: feeling hot, feeling cold, asthenia, injection site reactions (extravasation, pain, discomfort, oedema, inflammation, coldness) Rare: chest pain, chills Very rare: malaise~~, chest pain,~~ chest discomfort, pyrexia, face oedema ~~fever, rigors, facial oedema, asthenia, coldness,~~ injection site ~~discomfort~~ necrosis (in case of extravasation), ~~injection site pain~~, ~~injection site reaction, injection site oedema, extravasation at injection site, injection site inflammation following extravasation, injection site necrosis following extravasation, superficial~~ phlebitis superficial
Investigations	Very rare: decreased oxygen saturation

The following adverse reactions have been reported with other intravenous contrast agents for MRI: ~~and may therefore occur after administration of Clariscan:~~

System Organ Class	Adverse reaction
Blood and lymphatic system disorders	Haemolysis
Psychiatric disorders	Confusion
Eye disorders	~~Transient b~~Blindness transient, eye pain
Ear and labyrinth disorders	Tinnitus, ear pain
Respiratory, thoracic and mediastinal disorders	Asthma
Gastrointestinal disorders	Dry mouth
Skin and subcutaneous tissue disorders	~~Bullous d~~Dermatitis bullous
Renal and urinary disorders	Urinary incontinence, renal tubular necrosis, acute renal failure
Investigations	Electrocardiogram PR prolongation, blood iron increased, blood bilirubin increased, serum ferritin increased, liver function test abnormal ~~Prolonged PR on electrocardiogram, elevated serum iron, elevated serum bilirubin, elevated serum ferritin, abnormal liver function tests.~~

Adverse reactions in children

Safety of paediatric patients was considered in clinical trials and post-marketing studies. As compared to adults, the safety profile of gadoteric acid did not show any specificity in children. The most common reactions are gastrointestinal symptoms or signs of hypersensitivity.

6.5. Nature and contents of container

(...)

Poly-propylene bottles

Polypropylene bottles of 50 ml (filled to 50 ml) or 100 ml (filled with 100 ml), closed with rubber stopper and a screw cap.

Packed in outer box of 1 and 10 units

- העלון לרופא נשלח למשרד הבריאות לצורך העלאתו למאגר התרופות שבאתר משרד הבריאות.
- ניתן לקבל עלון זה מודפס על ידי פניה ישירה לבעל הרישום:
אלדן ציוד אלקטרוני בע"מ, רח' השילוח 6, ת.ד. 7641, פתח תקווה 4917001, טלפון: 03-9371111.

בברכה, עוז וולך,
רוקח ממונה עבור בעל הרישום אלדן ציוד אלקטרוני בע"מ