

אפריל 2018

Multihance, solution for injection

צוות רפואי נכבד,

חברת דקסל בע"מ מבקשת להודיעכם על עדכון העלון לרופא של התכשיר מלטיהנס. בהודעה זו מפורטים העדכונים המהותיים בלבד. למידע מלא, יש לעיין בעלון.

העלון לרופא נשלח לפרסום במאגר התרופות שבאתר משרד הבריאות וניתן לקבלו מודפס ע"י פנייה לבעל הרישום: דקסל בע"מ, רח' דקסל 1, אור עקיבא 3060000, ישראל, טל': 04-6364000.

הרכב התכשיר:

1 ml of solution for injection contains: gadobenic acid 334 mg (0.5M) as the dimeglumine salt.

ההתוויות המאושרות:

MultiHance is a paramagnetic contrast agent for use in diagnostic magnetic resonance imaging (MRI) indicated for:

- MRI of the liver for the detection of focal liver lesions in patients with known or suspected primary liver cancer (eg. hepatocellular carcinoma) or metastatic disease.
- MRI of the brain and spine where it improves the detection of lesions and provides diagnostic information additional to that obtained with unenhanced MRI.
- Contrast-enhanced MR- angiography where it improves the diagnostic accuracy for detecting clinically significant steno-occlusive vascular disease in patients with suspected or known vascular disease of the abdominal or peripheral arteries.
- MRI of the breast, for the detection of malignant lesions in patients where breast cancer is known or suspected on the basis of previous mammography or ultrasound results

העלון לרופא עודכן ב-03/2018. להלן העדכונים המהותיים (מסומנים באדום):

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4.2 Posology and Method of Administration

The lowest dose that provides sufficient enhancement for diagnostic purposes should be used.

MRI of the liver: the recommended dose of MultiHance injection in adult patients is 0.05 mmol/kg body weight. This corresponds to 0.1 mL/kg of the 0.5 M solution .

MRI of the brain and spine: the recommended dose of MultiHance injection in adult and in paediatric patients greater than 2 years of age is 0.1 mmol/kg body weight. This corresponds to 0.2 mL/kg of the 0.5 M solution.

MRA: the recommended dose of MultiHance injection in adult patients is 0.1 mmol/kg body weight. This corresponds to 0.2 mL/kg of the 0.5 M solution.

MRI of the breast: the recommended dose of MultiHance in adult patients is 0.1 mmol/kg body weight. This corresponds to 0.2 mL/kg of the 0.5 M solution.

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4.4 Special warnings and special precautions for use

The use of diagnostic contrast media, such as MultiHance, should be restricted to hospitals or clinics staffed for intensive care emergencies and where cardiopulmonary resuscitation equipment is readily available.

Patients should be kept under close supervision for 15 minutes following the injection as the majority of severe reactions occur at this time. The patient should remain in the hospital environment for one hour after the time of injection.

The accepted general safety procedures for Magnetic Resonance Imaging, in particular the exclusion of ferromagnetic objects, for example cardiac pace-makers or aneurysm clips, are also applicable when MultiHance is used.

Caution is advised in patients with cardiovascular disease.

In patients suffering from epilepsy or brain lesions the likelihood of convulsions during the examination may be increased. Precautions are necessary when examining these patients (e.g. monitoring of the patient) and the equipment and medicinal products needed for the rapid treatment of possible convulsions should be available.

Hypersensitivity reactions

As with other gadolinium chelates, the possibility of a reaction, including serious, life-threatening, or fatal anaphylactic and anaphylactoid reactions involving one or more body systems, mostly respiratory, cardiovascular and/or mucocutaneous systems, should always be considered, especially in patients with a history of asthma or other allergic disorders.

Prior to MultiHance administration, ensure the availability of trained personnel and medications to treat hypersensitivity reactions.

Insignificant quantities of benzyl alcohol (<0.2%) may be released by gadobenate dimeglumine during storage. Nonetheless MultiHance should not be used in patients with a history of sensitivity to benzyl alcohol.

As with other gadolinium-chelates, a contrast-enhanced MRI should not be performed within 7 hours of a MultiHance-enhanced MRI examination to allow for clearance of MultiHance from the body.

Exercise caution to avoid local extravasation during intravenous administration of MultiHance. If extravasation occurs, evaluate and treat as necessary if local reactions develop (see section 4.8 Undesirable Effects).

Impaired renal function

Prior to administration of MultiHance, 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 ($GFR < 30 \text{ ml/min/1.73m}^2$).

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 MultiHance, it should therefore be avoided in patients with severe renal impairment and in patients in the perioperative liver transplantation period unless the diagnostic information is essential and not available with non-contrast enhanced MRI.

Haemodialysis shortly after MultiHance administration may be useful at removing MultiHance 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.

Elderly

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

Gadolinium retention

Gadolinium is retained for months or years in several organs. The highest concentrations (nanomoles per gram of tissue) have been identified in the bone, followed by other organs (e.g. brain, skin, kidney, liver, and spleen. The duration of retention also varies by tissue and is longest in bone. Linear GBCAs cause more retention than macrocyclic GBCAs.

The current evidence suggests that gadolinium may accumulate in the brain after multiple administrations of GBCAs. Increased signal intensity on non-contrast T1-weighted images of the brain has been observed after multiple administrations of GBCAs in patients with normal renal function. Gadolinium has been detected in brain tissue after multiple exposures to GBCAs, particularly in the dentate nucleus and Globus pallidus. The evidence suggests that the risk of gadolinium accumulation is higher after repeat administration of linear than after repeat administration of macrocyclic agents. The clinical significance of gadolinium accumulation in the brain is presently unknown; however, gadolinium accumulation may potentially interfere with the interpretation of MRI scans in the brain. In order to minimize potential risks associated with gadolinium accumulation in the brain, it is recommended to use the lowest effective dose and perform a careful benefit risk assessment before administering repeated doses.

While clinical consequences of gadolinium retention have not been established in patients with normal renal function, certain patients might be at higher risk. These include patients requiring multiple lifetime doses, pregnant and pediatric patients, and patients with inflammatory conditions. Consider the retention characteristics of the agent when choosing a GBCA for these patients. Minimize repetitive GBCA imaging studies, particularly closely spaced studies when possible.

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5.1 Pharmacodynamic properties

Pharmacotherapeutic group: paramagnetic contrast media, **linear gadolinium contrast agent**,
ATC code V08CA08

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