מאי 2015

Multihance 334 mg/ml, Solution for Injection

צוות רפואי נכבד,

חברת דקסל פארמה מבקשת להודיעכם על עדכון בעלון לצרכן של התכשירים:

מלטיהנס
Multihance

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

הרכב:

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

התוויות מאושרות:

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.

העלון לרופא עודכן באפריל 2015, העדכון הינו בסעיפים באים:

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4.4 Special warnings and special precautions for use

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.

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.

Small quantities of benzyl alcohol (<0.2%) may be released by gadobenate dimeglumine during storage. Thus 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.

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

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<30ml/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.

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4.8 Undesirable effects

The following adverse events were seen during the clinical development of MultiHance among 2637 adult subjects. There were no adverse reactions with a frequency greater than 2%.

System organ classes	Common (≥1/100, <1/10)	Uncommon (≥1/1,000, <1/100)	Rare (≥1/10,000, <1/1,000)
Infections and infestations		Nasopharyngitis	
Nervous system disorders	Headache	Paraesthesia, dizziness, syncope, parosmia	Hyperaesthesia, tremor,intracranial hypertension, hemiplegia, convulsion
Eye disorders			Conjunctivitis
Ear and labyrinth disorders			Tinnitus
Cardiac disorders		Tachycardia, atrial fibrillation, first-degree atrioventricular block, ventricular extrasystoles, sinus bradycardia,	Arrhythmia, myocardial ischaemia, prolonged PR interval
Vascular disorders		Hypertension, hypotension	
Respiratory, thoracic and mediastinal disorders		Rhinitis,	Dyspnoea N.O.S., laryngospasm, wheezing, pulmonary congestion, pulmonary oedema
Gastrointestinal disorders	Nausea	Dry mouth, taste perversion, diarrhoea, vomiting, dyspepsia, salivation, abdominal pain	Constipation, faecal incontinence, necrotising pancreatitis

Skin & subcutaneous tissue disorders		Pruritus, rash, face oedema, urticaria, sweating	
Musculoskeletal, connective tissue and bone disorders		Back pain, myalgia	
Renal and urinary disorders			Urinary incontinence, urinary urgency
General disorders and administration site conditions	Injection Site Reaction, feeling hot	Asthenia, fever, chills, chest pain, pain, injection site pain, injection site extravasation	injection site inflammation
Investigations		Abnormal laboratory tests, abnormal ECG, prolonged QT	

Laboratory abnormalities cited above include hypochromic anaemia, leukocytosis, leukopenia, basophilia, hypoproteinaemia, hypocalcaemia, hyperkalaemia, hyperglycaemia or hypoglycaemia, albuminuria, glycosuria, haematuria, hyperlipidaemia, hyperbilirubinaemia, serum iron increased, and increases in serum transaminases, alkaline phosphatase, lactic dehydrogenase, and in serum creatinine and were reported in equal or less than 0.4% of patients following the administration of MultiHance. However these findings were mostly seen in patients with evidence of pre-existing impairment of hepatic function or pre-existing metabolic disease.

The majority of these events were non-serious, transient and spontaneously resolved without residual effects. There was no evidence of any correlation with age, gender or dose administered.

<u>paediatric</u>

In paediatric patients enrolled in clinical trials the most commonly reported adverse reactions included vomiting (1.4 %), pyrexia (0.9%) and hyperhydrosis (0.9%). The frequency and nature of adverse reactions was similar to that in adults.

In marketed use, adverse reactions were reported in fewer than 0.1 % of patients.

Most commonly reported were: nausea, vomiting, signs and symptoms of hypersensitivity reactions including anaphylactic shock, anaphylactoid reactions, angioedema, laryngeal spasm and rash.

Injection site reactions due to extravasation of the contrast medium leading to local pain or burning sensations, swelling blistering and, in rare cases when localised swelling is severe, necrosis have been reported.

Localised thrombophlebitis has also been rarely reported.

Isolated cases of nephrogenic systemic fibrosis (NSF) have been reported with MultiHance in patients co-administered other gadolinium-containing contrast agents (see Section 4.4).

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