PACKAGE LEAFLET: INFORMATION FOR THE USER

MultiHance 529 mg/ml solution for injection in pre-filled syringe
Gadobenate dimeglumine

Read all of this leaflet carefully before you start using this medicine because it contains important information for you.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your doctor
- This medicine has been prescribed for you. Do not pass it on to others. It may harm them, even if their symptoms are the same as yours.
- If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. See section 4.

What is in this leaflet:

1. What MultiHance is and what it is used for

MultiHance is a special dye (or contrast agent) which contains the rare earth metal gadolinium and improves images of the liver during MRI scans. It helps your doctor to identify any abnormalities of your liver.
This medicine is for diagnostic use only.

MultiHance is approved for use in children above two years of age.

2. What you need to know before you use MultiHance

MultiHance should only be given to you in a hospital or clinic where there are equipment and medically trained staff able to deal with allergic reactions.

Accumulation in the body
MultiHance works because it contains a metal called gadolinium. Studies have shown that small amounts of gadolinium can remain in the body, including the brain. No side effects have been seen due to gadolinium remaining in the brain.

Do not use MultiHance
• If you are allergic to gadobenate dimeglumine or any of the other ingredients of this medicine (listed in section 6)
• If you have had any allergic reaction (hypersensitivity reaction) in the past such as rash, itching, urticaria (hives) or difficulty in breathing following injection of any special dye or contrast agent for a MRI scan.
Tell your doctor if you think any of the points in this section apply to you

Children
MultiHance should not be given to children under two years of age.

Warnings and precautions
Talk to your doctor before using MultiHance if:
• you suffer from **a heart problem** or have **raised blood pressure**
• you have a history of epilepsy or brain lesions
• you have a **cardiac pacemaker**, or you are aware of the presence in your body of any other metallic objects such as clips, screws or plates as these might interfere with the magnet of the MRI scanner
• if you are allergic (hypersensitive) to benzyl alcohol, because small quantities of benzyl alcohol (a derivative of alcohol) can be released in the MultiHance solution during storage
• your kidneys do not work properly
• you have recently had, or soon expect to have, a liver transplant.

Your doctor may decide to take a blood test to check how well your kidneys are working before making the decision to use MultiHance, especially if you are 65 years of age or older.

Other medicines and MultiHance
There are no reports of reactions between MultiHance and other medicines.

Tell your doctor if you are taking or have recently taken any other medicines.

Pregnancy and breast-feeding
Ask your doctor for advice before being given this medicine.

Pregnancy
Gadobenic acid can cross the placenta. It is not known whether it affects the baby. You must tell your doctor if you think you are or might become pregnant or are planning to have a baby as MultiHance should not be used during pregnancy unless strictly necessary.

Breast-feeding
Tell your doctor if you are breast-feeding or about to start breast-feeding. Your doctor will discuss whether you should continue breast-feeding or interrupt breast-feeding for a period of 24 hours after you receive MultiHance.

Driving and using machines
There is no information about the effects of MultiHance on driving, or using tools or machines. Ask your doctor if you can drive and if it is safe for you to use any tools or machines.

3. How to use MultiHance

MultiHance is injected into a vein, usually in your arm just before the MRI scan. The amount in millilitre you will be injected depends on how much you weigh in kilogram of body weight.

The recommended dose is:
MRI of the liver: 0.1 ml per kilogram of body weight

The medical staff supervising your scan will administer your injection of MultiHance. They should ensure that the needle is correctly positioned: tell them if you feel pain or a burning sensation at the site of the injection while it is being administered.

You should remain in the hospital environment for one hour after the time of the injection.

Dosage in special patient groups

Impaired renal function

The use of MultiHance is not recommended in patients with severe kidney problems and patients who have recently had, or soon expect to have, a liver transplant. However if use is required you should only receive one dose of MultiHance during a scan and you should not receive a second scan for at least 7 days.

Elderly
It is not necessary to adjust your dose if you are 65 years of age or older but you may have a blood test to check how well your kidneys are working.

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

4. Possible side effects

Like all medicines, MultiHance can cause side effects, although not everybody gets them.
Most of the side effects that have been reported with MultiHance have been mild and were not prolonged, and spontaneously resolved without residual effects. However, severe and life-threatening reactions sometimes leading to death have been reported.

Possible side effects	
Common: (More than 1 out of 100 persons and less than 1 out of 10 persons)	- Headache - Nausea
Uncommon: (More than 1 out of 1,000 persons and less than 1 out of 100 persons)	- Dizziness, tingling, changes in taste - Changes in blood pressure, and in heart rate or rhythm, flushing - Vomiting, diarrhoea, dry mouth - Itching, skin rash, urticaria (hives) - Feeling hot, fever, local reactions where the injection was given such as: pain, burning, coldness or warmth feeling, redness, itching or discomfort at the injection site - Abnormal laboratory tests, such as: - abnormal electrocardiogram (a test that monitors changes in your heart beat) - changes in liver function tests - abnormal blood and urine tests
Rare: (More than 1 out of 10,000 persons and less than 1 out of 1,000 persons)	- Serious allergic reaction which causes difficulties in breathing or dizziness - Fainting, tremor, convulsion, strange smell - Reduced sensitivity to touch/pain/or other stimuli - Abnormal vision - Insufficient blood supply to the heart, slow heart beats - Fluid in the lungs (pulmonary oedema), shortness of breath, wheezing, tightness of the throat, swelling and irritation inside the nose, cough - Excessive salivation, abdominal pain - Swollen face, sweating - Pain in in muscles - Pain in the chest, feeling weak, chills, malaise - Change in laboratory blood tests
Not known (cannot be estimated from the available data)	- Chest pain, radiating to the neck or the left arm, which can be a sign of a potentially serious allergic reaction called Kounis syndrome - Serious allergic shock - Loss of consciousness

Possible side effects	
	- Eyes inflammation - Cardiac arrest, blue discolouration of the skin and mucous membranes - Difficulties or suspension of breathing, swelling of the throat, lack of oxygen, difficulties in breathing or wheezing - Swelling inside the mouth - Serious allergic reaction which causes swelling of the face or throat - Swelling at the site of injection, blisters at injection site - Inflammation of the veins due to blood clots

There have been reports of nephrogenic systemic fibrosis (which causes hardening of the skin and may affect also soft tissue and internal organs) in patients who received MultiHance together with other gadolinium-containing contrast agents.

If you think you notice any side effects after receiving an injection of MultiHance, immediately tell the medical staff supervising your scan.
If you have any other questions not answered in this leaflet please ask the medical staff supervising your scan.

Reporting of side effects
If you get any side effects, talk to your doctor. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance - Website: www.hpra.ie.

By reporting side effects you can help provide more information on the safety of this medicine.

5. How to store MultiHance

• Keep out of the sight and reach of children.
• Do not use this medicine after the expiry date which is stated on the label. The expiry date refers to the last day of that month.
• Do not freeze.
• MultiHance should be administered to you immediately after opening.
• Do not use MultiHance if you notice that the container and closure have been damaged or the solution is discoloured or particulate matter is present.
• Do not throw away any medicines via wastewater or household waste. The hospital pharmacist will dispose any unused product or waste material. These measures will help to protect the environment.

6. Contents of the pack and other information

What MultiHance contains
- The active substance is gadobenic acid as gadobenate dimeglumine.
  1 ml of solution for injection contains: gadobenic acid 334 mg (0.5 mmol) as gadobenate dimeglumine (529 mg).
- The other ingredient (excipient) is water for injection.

What MultiHance looks like and contents of the pack
MultiHance is an aqueous solution for injection in pre-filled single dose syringe (clear, colourless to slightly yellow colour).
MultiHance is supplied in pre-filled syringes containing 10 ml, 15 ml, or 20 ml of solution for injection.
MultiHance is also supplied in kits with administration devices:

- 15 and 20 mL pre-filled syringe, 20 mL syringe (polypropylene), connector with 3-way stopcock (polycarbonate), spike (ABS/polypropylene), 20 G secured catheter
- 15 and 20 mL pre-filled syringe, syringe for magnetic resonance automatic injector ((115 mL syringe (polyethelene terephthalate/polycarbonate), connector (PVC/polycarbonate/polypropylene/silicone), spike (ABS)), 20 G secured catheter.

Not all pack sizes may be marketed.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Bracco Imaging s.p.a., Via E. Folli 50, Milan (Italy)

Manufacturer
Bracco Imaging spa, Via Ribes 5, Colleretto Giacosa (TO), Ivrea (Italy)

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The following information is intended for medical or healthcare professionals only.

Method of administration
MultiHance should be used immediately after opening and should not be diluted. Any unused product should be discarded and not be used for other MRI examinations.

To use the syringe, the threaded tip of the plunger rod clockwise should be screwed into the plunger and pushed forward a few millimetres to break any friction between the plunger and syringe barrel.

Whilst holding syringe erect (with the nozzle cap upwards), the nozzle cap should be removed aseptically from the tip of the syringe and either a sterile, disposable needle or 5/6 tubing with a compatible luer lock should be attached using a push-twist action.

While still holding the syringe erect, the plunger should be pushed forward until all the air is evacuated and the fluid either appears at the tip of the needle or the tubing is completely filled.

The injection should be completed following the usual aspiration procedure.

To minimise the potential risks of soft tissue extravasation of MultiHance, it is important to ensure that the i.v. needle or cannula is correctly inserted into a vein.

The product should be administered intravenously either as a bolus or slow injection (10 mL/min.), see table for post-contrast imaging acquisition.

The injection should be followed by a flush of sodium chloride 9 mg/ml (0.9%) solution for injection.

Post-contrast imaging acquisition:

Liver	Dynamic imaging:	Immediately following bolus injection.
	Delayed imaging:	between 40 and 120 minutes following the injection, depending on the individual imaging needs.

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 /1.73 m^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.

If use of MultiHance cannot be avoided, the dose should not exceed 0.05 mmol/kg body weight. Because of the lack of information on repeated administration, MultiHance injections should not be repeated unless the interval between injections is at least 7 days.

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

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.

MultiHance should not be used during pregnancy unless the clinical condition of the woman requires use of gadobenate dimeglumine.

Continuing or discontinuing breast feeding for a period of 24 hours after administration of MultiHance, should be at the discretion of the doctor and lactating mother.

The peel-off tracking label on the syringes should be stuck onto the patient record to enable accurate recording of the gadolinium contrast agent used. The dose used should also be recorded. If electronic patient records are used, the name of the product, the batch number and the dose should be entered into the patient record.