MultiHance has a significantly greater relaxivity, and provides statistically significant (p<0.0001) better contrast enhancement and diagnostic information in MRI of CNS lesions compared to Magnevist at an equivalent dose.\(^{(1),(2)}\)

MultiHance (gadobenate dimeglumine) injection, 529 mg/mL is the first extracellular fluid (ECF) contrast agent (CA) to possess a weak and transient interaction with plasma proteins, a characteristic that endows MultiHance with up to twice the in vivo relaxivity of all other ECF contrast agents.\(^{(3)}\) de Haen, 1999. This improved relaxation effect could potentially contribute to improved lesion visualization.

The MultiHance molecule, gadobenate, has a structure very similar to that of gadopentetate, except that MultiHance has a benzyloxymethyl group protruding from the molecule.\(^{(4)}\)

This lipophilic structure provides MultiHance with the ability to weakly and reversibly interact with plasma proteins and also to be taken up by functioning hepatocytes. MultiHance (gadobenate dimeglumine injection, 529 mg/mL) provides statistically significant (p<0.0001) better contrast enhancement and diagnostic information in MRI of CNS lesions compared with Magnevist (gadopentetate dimeglumine) at an equivalent dose.\(^{(5)}\)

Contact Us:
For more information about MultiHance®, please contact Bracco Professional Services at 1.800.257.5181 or email Bracco Customer Service at bracco.otc@diag.bracco.com.

Available in 5, 10, 15, and 20 mL single-dose vials, and 50 and 100 mL Multipack® (Pharmacy Bulk Packages)

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* Not for Direct Infusion.

For more information on MultiHance, visit www.multihanceUSA.com.
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For more information about Bracco products, visit www.bracco.com or call Bracco Customer Service at 1-877-Bracco-9 (1-877-272-2269).

**DESCRIPTION**

MULTIHANCE injection is supplied as a sterile, non-pyrogenic, clear, colorless aqueous solution intended for intravenous use only. Each mL of solution contains 150 mg gadobenate dimeglumine.

**CLINICAL PHARMACOLOGY**

**Gadobenate dimeglumine** is a paramagnetic agent and, as such, develops a magnetic moment when placed in a magnetic field. The large magnetic moment produced by the paramagnetic agent results in a large local magnetic field, which can enhance the relaxation rates of protons in its vicinity leading to an increase in signal intensity (both T1-weighted and T2-weighted imaging). Visualization of normal and pathological tissue depends on contrast enhancement or signal intensity changes that occur due to susceptibility or T2* effects. Changes in signal intensity observed in T1-weighted images are usually greater than those in T2-weighted images.

**Gadobenate dimeglumine** does not enhance normal brain or lesions that have a normal blood-brain barrier, e.g., cysts, mature tumors, or calcified lesions. It is not effective in the visualization of normal brain or normal brain structures that are not surrounded by a normal blood-brain barrier.

**CONTRAINdications**

• Hypersensitivity to any of the ingredients of MULTIHANCE

**WARNINGS**

Cerebral hemorrhage or stroke has been shown in vitro studies to alter anode permeability to a magnetic field. It may result in intra-cranial complications in vivo. The enhancement of magnetic resonance imaging (MRI) using MULTIHANCE may be used in patients with a history of cerebral hemorrhage or stroke who have not been previously evaluated and monitored. These patients should be carefully followed and treated as necessary if local reactions develop.

**PRECAUTIONS - General**

**Pharmacokinetics**

Three intravenous studies were conducted in 137 healthy male subjects to assess the pharmacokinetics of gadobenate dimeglumine. The doses administered in these studies ranged from 0.05 to 0.3 mmol/kg. Upon injection, the peak plasma and cerebrospinal fluid (CSF) gadobenate dimeglumine concentrations are essentially the same. This, therefore, is the basis on which the BID regimen is based in that the peak concentration is the same for plasma and CSF. The pharmacokinetic data from these in vivo investigations have not been described in a three-compartment model.

**Distribution:**

In heparinized human plasma, at 39°C.

**Metabolism:**

There was no detectable biotransformation of gadobenate dimeglumine. Dissipation of gadobenate dimeglumine in human plasma has been described for up to two hours after injection and was found to be reversible in human plasma.

**Pharmacodynamics**

**Analysis of studies that involved serial magnetic resonance imaging (MRI) for multiple indications showed that there are no significant differences in pharmacokinetic parameters among these studies. Therefore, the following summaries of pharmacokinetic data are: basal studies and 11 studies that involved serial MRI. The pharmacokinetic parameters for the 11 studies that involved serial MRI are based on a two-compartment model.**

**Pharmacokinetic parameters for the 11 studies that involved serial MRI are based on a two-compartment model.**

**Pharmacokinetic Parameters for the 11 Studies that Involved Serial MRI**

**Pharmacokinetic Parameters for the 11 Studies that Involved Serial MRI**

**Pharmacokinetics in Special Populations**

**Renal Impairment:**

A single intravenous dose of 0.2 mmol/kg of MULTIHANCE was administered to 20 subjects (5 males and 6 females) with end-stage renal disease requiring hemodialysis to determine the effects of renal impairment on the pharmacokinetics of MULTIHANCE. Mean estimates of the elimination half-life were 1.3 to 4.5 days. Since variations due to age and sex are small, these estimates may be used for patients with mild to moderate renal impairment.

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