MULTIHANCE (gadobenate dimeglumine), paramagnetic contrast agent

Minor improvement in treatment in terms of diagnostic performance in breast MRI when compared with MAGNEVIST.

Main points

- MULTIHANCE henceforth has Marketing Authorisation for MRI of the breast, for the detection of malignant lesions in patients with breast cancer that is known or suspected on the basis of the available results of mammography or ultrasonography.
- The use of gadolinium-based contrast agents can lead to the development of systemic nephrogenic fibrosis, a rare (400 to 700 cases worldwide in 2013), but potentially fatal, adverse effect. MULTIHANCE is a moderate-risk gadolinium chelate according to the European Medicines Agency classification; OMNISCAN and MAGNEVIST are high-risk and DOTAREM, GADOVIST and PROHANCE are low-risk.
- There are no data that would justify MRI in initial screening for breast lesions.

Pre-existing indication

MULTIHANCE already has Marketing Authorisation for MRI of the liver, head, and spinal cord and for magnetic resonance angiography.

This summary does not cover these indications.

Therapeutic use

Bilateral mammography is the reference examination for the detection of breast lesions. It may be combined with bilateral breast ultrasonography including examination of the axillary regions, and this is recommended in case of a suspicious mammographic image or in case of an abnormal breast examination with an uninformative mammography. There are insufficient data to justify the use of breast MRI in initial breast cancer screening. It is only possible to discuss whether it is indicated in certain special circumstances that should be weighed up in specialised facilities.

Role of the medicinal product in the therapeutic strategy

MULTIHANCE, like other gadolinium-based contrast media, is a first-line product when a MRI examination using contrast medium is necessary. Its position in relation to other contrast agents in the diagnostic strategy for breast cancer is not specified in the national and international guidelines.

Clinical data

- In a randomised, double-blind, phase III study carried out in 162 patients with a suspected or confirmed breast cancer lesion after examination by mammography and/or breast ultrasonography, MULTIHANCE was better than MAGNEVIST in terms of sensitivity (primary endpoint): 91.7% to 94.4% versus 79.9% to 83.3%, (p ≤ 0.003).
- In terms of safety, since 2009, all gadolinium-based contrast media have come under a European risk management plan focussing on systemic nephrogenic fibrosis. The risk of fibrosis led the European Medicines Agency to establish guidelines for the use of gadolinium-based contrast agents and to classify these products according to their level of risk. The proprietary medicinal products PROHANCE, GADOVIST and DOTAREM are classified as low risk, MULTIHANCE as moderate risk, and OMNISCAN and MAGNEVIST as high risk.
- The update of these data in 2013 confirms that no confirmed case of NSF has been reported with MULTIHANCE on its own.

Benefit of the medicinal product

© Haute Autorité de Santé 2015
The actual benefit* of MULTIHANCE is substantial in the indication “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 ultrasonography results”.

MULTIHANCE provides a clinical added value** (CAV IV, minor) in terms of diagnostic performance in breast MRI compared with MAGNEVIST.

Recommends inclusion on the list of reimbursable products for supply by pharmacists and for hospital use.

---

* The actual benefit (AB) of a proprietary medicinal product describes its benefit primarily in terms of its clinical efficacy and the seriousness of the condition being treated. The HAS Transparency Committee assesses the AB, which can be substantial, moderate, low or insufficient for reimbursement for hospital use.

** The clinical added value (CAV) describes the improvement in treatment provided by a medicinal product compared with existing treatments. The HAS Transparency Committee assesses the degree of CAV on a scale from I (major) to IV (minor). A level V CAV means “no clinical added value”.

---

* Haute Autorité de Santé 2015