BRIEF SUMMARY OF THE TRANSPARENCY COMMITTEE OPINION

INDUCTOS (dibotermín alfa), osteoinductive protein

Low actual benefit and no clinical benefit demonstrated in tibia fractures and lumbar degenerative disc disease with anterior lumbar interbody fusion

Main points

- INDUCTOS has Marketing Authorisation in the treatment of tibia fractures and as a substitute for autogenous bone grafts in lumbar interbody fusion (See below).
- In the treatment of tibia fractures, the use of INDUCTOS is marginal. The company was not able to perform the follow-up study requested in this indication in 2003.
- In the treatment of lumbar degenerative disc disease with anterior lumbar interbody fusion, its superiority compared with autogenous bone grafts has not been demonstrated with a rigorous methodology.

Indications

This brief summary only focuses on the indications which were reassessed by the Committee in May 2015:

- “INDUCTOS is indicated for single-level anterior lumbar interbody spine fusion (L4-S1) as a substitute for autogenous bone graft in adults with degenerative disc disease who have had at least 6 months of non-operative treatment for this condition.
- INDUCTOS is indicated for the treatment of acute tibia fractures in adults, as an adjunct to standard care using open fracture reduction and intramedullary unreamed nail fixation.”

The MA amendments made during the assessment (extension to all types of lumbar interbody fusion and not only the anterior approach and to any lumbar region and not only L4-S1) will be the subject of a future assessment that will result in updating of this brief summary.

Therapeutic use

- **Open tibia fractures**
  Therapeutic management of open tibia fractures differs depending on the characteristics of the fracture and the centres but intramedullary nail fixation is one of the most used techniques. INDUCTOS is an adjunct to standard care with intramedullary nail fixation.

- **Degenerative disc disease:**
  Management of lumbar pain involves identification of its cause and risk factors, on which the therapeutic approach is based. The physical treatment based on physiotherapy (stretching exercises, muscle strengthening, spinal stabilisation, cardiopulmonary training, etc.) associated with cognitive behavioural therapy forms the treatment cornerstone of common chronic lumbar pain. Analgesics (NSAIDs or others) can be used. If non-operative treatment fails after being used for a minimum of 2 years, interbody fusion can be considered. Its aim is to obtain a union between two or more lumbar vertebrae. If a lumbar interbody fusion is justified, the reference treatment is autologous bone grafts. Osteoinductive proteins, including INDUCTOS, are an alternative to autologous bone grafts. Other graft methods exist: allogenic bone grafts and bone substitutes. In some specific cases, disc replacement is also an alternative.

- **Role of the medicinal product in the therapeutic strategy**
  In the treatment of tibia fractures, the role of INDUCTOS is very marginal given that its use is not recommended in association with reamed nail fixation, the most commonly performed fixation technique.
In degenerative disc disease, INDUCTOS is an alternative to autogenous bone grafts from the iliac crest in the context of anterior lumbar interbody fusion.

Clinical data

- In the treatment of tibia fractures, the results of two meta-analyses confirm the efficacy of INDUCTOS in the treatment of tibia fractures with benefit compared with the standard treatment, subject to the methodological bias of the studies.
- In the treatment of degenerative disc disease with lumbar interbody fusion, a meta-analysis concluded that there was no clinical benefit demonstrated with INDUCTOS compared with autogenous bone grafts with a higher incidence of cancer (relative risk of 3.45 [1.98; 6]), subject to the methodological limits. In a second meta-analysis, the efficacy results from which are difficult to interpret given the considerable heterogeneity revealed for certain criteria, a higher incidence of cancer was also observed with INDUCTOS but no statistical difference was revealed (RR = 1.98 [0.86-4.54]).

Benefit of the medicinal product

- The actual benefit* of INDUCTOS is low.
- INDUCTOS does not provide clinical added value** (CAV V) in the treatment of its two MA indications (tibia fractures and lumbar interbody fusion for degenerative disc disease).
- Recommends continued inclusion on the list of reimbursable products for hospital use.

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1. ** 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.

2. ** 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”.

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