OPINION ON MEDICINAL PRODUCTS

spheroids of human autologous matrix-associated chondrocytes

SPHEROX 10-70 spheroids/cm²,

suspension for implantation

New indication

Adopted by the Transparency Committee on 9 November 2022

SUMMARY

The legally binding text is the original French opinion version

Key points

Disapproval of reimbursement for the repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee (*International Cartilage Regeneration & Joint Preservation Society* [ICRS] grade III or IV) with defect sizes of up to 10 cm² in adolescents presenting with epiphyseal growth cartilage closure at the affected joint.

Role in therapeutic strategy?

The short- and medium-term therapeutic endpoints are to repair the damaged cartilage while obtaining functional neoformed tissue, improve functional performances and the patient's quality of life. The long-term objective is to prevent osteoarthritis of the knee.

There is a consensus to only envisage surgical treatment for unipolar (i.e. on a single face, which excludes symmetric osteoarthritis defects) symptomatic ICRS arthroscopic grade III and IV cartilage defects of the knee, with no associated ligamental defects and no unfavourable axis defect (valgus, varus), occurring in younger subjects where obesity is absent or controlled.

The choice of procedure depends on patient age, defect size, cartilage status and patient-related factors such as previous history of cartilage repair, BMI, and functional demand.

In France, the most commonly used procedures are microfracture procedures and osteochondral grafting (mosaicplasty). Mosaicplasty is the standard of care for defects < 2 cm². For these small defects, microfractures alone may also be used. The microfracture "plus" or "AMIC" procedure

(associated with membrane implantation) or autologous chondrocyte transplantation are envisaged for defects of 2 to 4 cm².

Extensive substance loss > 4 cm² is rare and can also be treated with microfracture “plus” procedures. However, in the case of very deep defects affecting the subchondral bone, they require an allogeneic graft salvage procedure, despite including immunological and pathogen transmission risks, or the mega-OATS procedure (posterior condyle osteochondral graft as per Imhoff) rarely used in France, as it is the only option to restore femoral condyle convexity.

Role of SPHEROX in the therapeutic strategy:

Considering:

- the purely descriptive data available from two observational studies, with a low level of evidence in the light of the following methodological limitations:
  - subjective medical practitioner assessment of the primary outcome measure in an open-label study,
  - small sample of patients with osteoarthritis dissecans (OCD) with epiphyseal growth cartilage closure in these two studies,
- the lack of comparative data with respect to standard surgical procedures used in France for defects ≤ 10 cm² (mosaicplasty, microfractures “plus”, allografts, mega-OATS) and supportive care (immobilisation, medicinal pain treatments, rehabilitation),
- the lack of usable quality-of-life data in view of the study methodologies,
- the limited follow-up in terms of efficacy and safety in the long term particularly for the prevention of osteoarthritis of the knee,
- the low level of evidence of the clinical benefit in adults.

the Committee deems that it is not possible to establish the role of SPHEROX 10-70 spheroids/cm², suspension for implantation, for the repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee with defect sizes of up to 10 cm² in adolescents presenting with epiphyseal growth cartilage closure at the affected joint.

Committee's conclusions

Clinical Benefit

- Symptomatic and deep cartilage defects of the knee (ICRS grade III and IV) may cause pain and joint function loss resulting in impairment and significant deterioration of quality of life. In the longer term, these defects may progress to osteoarthrosis.
- The proprietary medicinal product SPHEROX is a curative medicinal product for pain, and for improving functional capacities and patients' quality of life. SPHEROX could represent a preventive treatment by preventing the onset of osteoarthritis.
- The efficacy/adverse effect ratio of SPHEROX is poorly defined considering the lack of robust comparative data (2 non-comparative, open-label retrospective studies) and the low level of evidence of the clinical benefit in adults.
- Surgical alternatives are available for defects of up to 10 cm². The procedures used most commonly in France are microfracture procedures (with or without membrane cover), osteochondral grafting (mosaicplasty) and allogeneic osteochondral grafting.
- It is not possible to establish the role of SPHEROX for the repair of symptomatic articular cartilage defects of the femoral condyle and the patella of the knee with defect sizes of up to 10 cm² in adolescents presenting with epiphyseal growth cartilage closure at the affected joint.

Public health benefit

Considering:

- the impact of symptomatic and deep cartilage defects on patients' quality of life,
- the insufficiently met medical need and the need for surgical alternatives with sufficient evidence of efficacy, particularly on the onset of osteoarthritis,
- the lack of response of SPHEROX to the identified need on account of:
  - the lack of evidence of an additional impact on morbidity and on patients' quality of life
  - the benefits of this procedure, with respect to first- and second-generation ACI (autologous chondrocyte implantation) procedures, requiring no membrane, or fixing using fibrin glue, or growth factor (which is likely to reduce the operating time, post-surgical complications and improve the safety profile), but while the chondrocyte proliferation and differentiation mechanisms as well as the formation and fixing processes on the spheroids on the defect are apparently poorly defined, but the potentially negative impact on the delivery of care of the autologous chondrocyte implantation (ACI) procedures performed in 2 operative phases, with respect to microfracture procedures and mosaicplasty requiring a single hospital stay,

SPHEROX is not likely to have an additional impact on public health.

Considering all of these elements, the Committee deems that the actual clinical benefit of SPHEROX is significant in the marketing authorisation indication (including the claimed indication).

The Committee disapproves inclusion in the list of proprietary medicinal products approved for community use for the marketing authorisation indication (including the claimed indication) and at the marketing authorisation dosages.