National Institute for Health and Care Excellence

IP1797 Focal resurfacing implants to treat articular cartilage damage in the knee

IPAC date: 9 June 2022

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Episurf Company	Overview	In the Consultation overview document the Episealer implant is on a number of places referred to as being custom made. We would like to point out that that is an incorrect description, from a regulatory point of view. Custom made means that it is a special solution for each patient, and something you e.g. cannot CE-mark. The term customised is also used in the document, and that is a correct term. The Episealer is CE-marked and customised, which implies that it is individualised to each patient, within certain set parameters, while some measures of the implants have standard dimensions. In the draft IP guidance document, the word custom-adapted is used, which we consider as ok wording (even though customised is more commonly used).	Thank you for your comment. References to the Episealer device have been changed to 'customised' throughout the overview and guidance documents.
2	Consultee 2 Professor of public health medicine and health technology assessment	General	The NICE appraisal of focal resurfacing implant in the knee is based on a rapid review, which is the method used in IPG appraisals. The review team identifies the 6-8 most relevant studies and reports these in full in an evidence overview. Other relevant studies judged less relevant are summarised in an appendix. Coincidentally, a full systematic review of these procedures has been done, but not yet published,	Thank you for your comment. Consultee agrees with the main recommendation. Consultee summarises the findings of an as yet unpublished systematic review of focal resurfacing implants to treat articular cartilage damage in the knee.

			as part of the SCORE project reviewing surgery and comparators for early osteoarthritis. I was an author. HTA Project NIHR127398. The clinical effectiveness and cost effectiveness of surgery for early osteoarthritis of the hip and knee joint. The SCORE review of focal resurfacing (completed May 2021) covers two types of small area resurfacing interventions – synthetic forms designed to replace damaged chondral and subchondral areas, and forms such as MaioRegen, designed to allow native tissues to restore cartilage and bone defects. The IPG covers only the first of these but is more up to date. Despite the differences in methods, the conclusions of the NICE IPG rapid review and the SCORE project systematic review are similar. There are shortcomings in the evidence base due to an absence of randomised trials. Most studies are case series reporting before and after results. In general, I agree with the conclusions of the IPG review and the draft guidance and in particular with the statement in paragraph 1.1 of the draft guidance: “Evidence on the efficacy of focal resurfacing implants to treat articular cartilage damage in the knee is limited in quality and quantity.” Before and after case series tell us whether patients reported symptomatic improvements after focal resurfacing, but without control groups, we cannot quantify these improvements compared to conservative care (e.g. personalised physiotherapy) or other surgical interventions such	Consultee lists the following publication: • Mistry H, Metcalfe A, Smith N, Loveman E, Colquitt J, Royle P, Waugh N (2019). The cost-effectiveness of osteochondral allograft transplantation in the knee. KSSTA 27:1739-53 ○ This publication analyses the cost-effectiveness of osteochondral allograft transplantation and is therefore out of scope for the assessment of this procedure. The committee considered this comment and decided that no change to the guidance was necessary.

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			as osteochondral allograft transplantation. This makes cost-effectiveness analysis difficult. The IPG guidance did not look at other options such as osteochondral allograft transplantation which appears cost-effective. (See Mistry H, Metcalfe A, Smith N, Loveman E, Colquitt J, Royle P, Waugh N. The cost-effectiveness of osteochondral allograft transplantation in the knee. KSSTA 2019/27/1739-53.) Nor did it review the MaioRegen implant.	
3	Consultee 2 Professor of public health medicine and health technology assessment	General	**Age** These focal implants are often described as being most appropriate in the “gap years” – meaning in people older than considered suitable for biological treatments such as autologous chondrocyte implantation but too young for knee replacement. The draft guidance makes no recommendation for any age restriction and this seems correct, since there is no reason why older patients with focal defects but not generalised OA should not be included, since a focal implant would be a much lesser operation than joint replacement, and would provide better function. The ages of people having Hemicap implants in Australia range from 17 to 88. (Registry report 2020)	Thank you for your comment. Consultee agrees that recommendations on the age of patients in which this procedure can be used are not necessary. The committee considered this comment and decided that no change to the guidance was necessary.
4	Consultee 2 Professor of public health medicine and health technology assessment	General	**Choice of implant** One issue is whether the guidance should differentiate amongst the available implants.	Thank you for your comment. Consultee questions whether the guidance should differentiate between the implant types

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			The evidence base for HemiCap and Episealer is much greater than for Biopoly. Para 3.6 of the draft guidance states: "3.6 The committee was informed that there is more than 1 device available to use for this procedure and some of these devices may be adapted to individual people based on 3D imaging." The imaging refers to the Episealer device where MRI imaging is used to assess the dimensions of the chondral defect in order to tailor the implant to the defect. Ryd et al (Study 7 in IPG review) from the manufacturers, Episurf, report a series of 682 Episealer implants in 612 knees with a 7-year survival of 96%. Most failures occurred by 3 years and were attributed to incorrect selection of defects for the Episealer. Ryd et al argue that each defect is unique in area and depth, and that individually designed implants, using 3-dimensional MRI, are more successful. This sounds advantageous but there is as yet no published trial evidence comparing implants designed in this way with older forms.	due to the differences in the evidence bases and comments on the lack of comparative data. The committee considered this comment and decided that no change to the guidance was necessary. This was because the IP programme considers procedures and not devices.
5	Consultee 2 Professor of public health medicine and health technology assessment	General	**Case series versus routine care?** As noted in the IPG review, the evidence is mainly from case series. These come mainly from centres very experienced with these devices, and often report good results. However as noted in the IPG review, registry data may show poorer results. In particular, the Australian registry data (Study 2 in the IPG review) showed that by 12	Thank you for your comment. Consultee discusses the difference in outcomes between case series and registries. Consultee notes a news item that reports findings from a Danish registry. Full reference details are not provided. Note that Christensen,

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			years, about half of 220 Hemicap implants had been removed, with patients having knee replacements. A news item from the 2018 ESSKA conference reports a failure rate in the Danish registry of 47% at 6 years for all implants, with a 25% failure rate for the Hemicap at 5 years. The Australian registry data report a high failure rate of about half by 12 years, in routine care. However, in a group of patients with knee problems but who were mostly too young for knee replacement, by 12 years the implants had allowed half to postpone knee replacements and half to avoid them. In patients under 50-55, knee replacements are unlikely to last for life and second replacements are less successful and more expensive to the NHS. If focal implants can provide temporary relief from symptoms and allow return to activities, and postpone knee replacements, they would be expected to be cost-effective. The draft guidance notes that they "may reduce or delay the need for a later knee replacement" and I think that is correct.	2021 (Study 3 in the overview) is an analysis of a Danish registry. The committee considered this comment and decided that no change to the guidance was necessary.
6	Consultee 2 Professor of public health medicine and health technology assessment	General	**Biopoly data** The study by Nathwani and colleagues (London, Liverpool, Stanmore, Chester) is reported in the IPG review (Study 7) as a case series of 33 Biopoly implants but also provided a non-randomised comparison with results of microfracture from four previous studies. These were Saris 2014 (the SUMMIT trial), Saris 2008 (the 12-month TIGACT data) Rotterud 2016 (in	Thank you for your comment. Consultee comments on the evidence base of the BioPoly implant. The committee considered this comment and decided that no change to the guidance was necessary.

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			which microfracture gave poorer results than simple debridement or no treatment of the chondral defect, in people having ACL reconstruction) and Cole 2011 (a study comparing microfracture with a scaffold method, with only 9 patients having microfracture). No data are presented on the baseline characteristics of the microfracture groups. In the absence of RCTs, a historical comparison is better than nothing, if the baseline characteristics are similar. The evidence base for Biopoly is much smaller than for the other focal resurfacing implants, consisting of the two case series by Nathwani et al (33 cases) and Cepni et al (45 cases), and a few single case reports. An earlier report by Jermin 2015 of 20 cases is presumably superseded by Nathwani 2017. McNicholas, in a September 2019 article {#971} (for Orthopaedic Product News, a trade magazine http://www.opnews.com/2019/09/focal-resurfacing-implants-in-the-knee/15690) reports that there have been over 800 BioPoly implantations, a number which provides a rather stark contrast to the evidence from two case series with 33 and 45 patients and three single case reports. McNicholas argues that one advantage of focal implants compared to autologous chondrocyte implantation, is the short rehabilitation time, which may lead them to be preferred by some patients because of work requirements.	

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7	Consultee 2 Professor of public health medicine and health technology assessment	General	**Current research.** A randomised trial of the Episealer implant started in 2020. The Episealer Knee System IDE study aims to recruit 180 participants in USA, Canada, UK, Germany, and Denmark. NCT04000659 https://clinicaltrials.gov/ct2/show/NCT04000659?term=episurf&draw=2&rank=2 Participants will be randomised to focal implant or to microfracture. Results will not be available for some years.	Thank you for your comment. Consultee describes an ongoing trial. This trial is described in the overview. The committee considered this comment and decided that no change to the guidance was necessary.

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