Australian Government

Department of Health

Application Form

(New and Amended

Requests for Public Funding)

(Version 2.4)

This application form is to be completed for new and amended requests for public funding (including but not limited to the Medicare Benefits Schedule (MBS)). It describes the detailed information that the Australian Government Department of Health requires in order to determine whether a proposed medical service is suitable.

Please use this template, along with the associated Application Form Guidelines to prepare your application. Please complete all questions that are applicable to the proposed service, providing relevant information only. Applications not completed in full will not be accepted.

Should you require any further assistance, departmental staff are available through the Health Technology Assessment Team (HTA Team) on the contact numbers and email below to discuss the application form, or any other component of the Medical Services Advisory Committee process.

Phone: +61 2 6289 7550
Fax: +61 2 6289 5540
Email: hta@health.gov.au
Website: www.msac.gov.au

PART 1 – APPLICANT DETAILS

1. Applicant details (primary and alternative contacts)

Corporation / partnership details (where relevant): Smith & Nephew Pty Ltd
Corporation name: REDACTED
ABN: REDACTED
Business trading name: REDACTED

Primary contact name: REDACTED

Primary contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

Alternative contact name: REDACTED

Alternative contact numbers
Business: REDACTED
Mobile: REDACTED
Email: REDACTED

2. (a) Are you a lobbyist acting on behalf of an Applicant?

☐ Yes
☒ No

(b) If yes, are you listed on the Register of Lobbyists?

☐ Yes
☐ No

PART 2 – INFORMATION ABOUT THE PROPOSED MEDICAL SERVICE

3. Application title

Chitosan-based cartilage biomatrix implant for articular cartilage repair

4. Provide a succinct description of the medical condition relevant to the proposed service (no more than 150 words – further information will be requested at Part F of the Application Form)

Articular cartilage provides a low-friction gliding service, acts as a shock absorber and minimises peak pressures on the subchondral bone in the joints (Bhosal 2008). Damage to the articular cartilage predominately follows acute traumatic injuries, however other causes of articular cartilage damage can include; prolonged periods of stress due to obesity or old age and long periods of inactivity (Cole 2009; Hjelle 2002). Typical symptoms of articular cartilage lesions include; swelling, local pain, locking and catching (Cole 2009). Articular cartilage lesions are relatively common, with an estimated prevalence of 60% found in patients undergoing knee arthroscopy (Aroen 2004; Curl 1997; Hjelle 2002) with lesions of the hip and ankle less common (Aurich 2014; Loken 2014).

5. Provide a succinct description of the proposed medical service (no more than 150 words – further information will be requested at Part 6 of the Application Form)

The proposed medical service is the application of a chitosan-based cartilage biomatrix implant in conjunction with the marrow stimulation technique (microfracture) for repair of focal cartilage defects. Using an arthroscopic awl, multiple holes or microfractures are made in the defect 3-4 mm apart. The chitosan-based biomatrix device is mixed with autologous whole blood and is applied to the microfractured cartilage lesion in which it physically stabilises the clot and guides and enhances marrow-derived repair to promote hyaline cartilage regeneration. Randomised controlled trial (RCT) evidence demonstrates superior lesion filling and superior repair tissue quality when the chitosan-based cartilage biomatrix implant is used in conjunction with microfracture compared with microfracture alone in the repair of focal cartilage defects of the knee (Stanish et al 2013).

6. (a) Is this a request for MBS funding?

☒ Yes
☐ No

REDACTED

In response to the above request by SOCAG/PLAC, this Application focuses on the repair of focal cartilage defects of the knee and the MBS item number 49561.

(b) If yes, is the medical service(s) proposed to be covered under an existing MBS item number(s) or is a new MBS item(s) being sought altogether?

☐ Amendment to existing MBS item(s)
☐ New MBS item(s)

REDACTED

The Applicant will work with the DoH in finalising a suitable item descriptor dependent on preferred approach.

(c) If an amendment to an existing item(s) is being sought, please list the relevant MBS item number(s) that are to be amended to include the proposed medical service:

N/A

(d) If an amendment to an existing item(s) is being sought, what is the nature of the amendment(s)?

i. ☐ An amendment to the way the service is clinically delivered under the existing item(s)
ii. ☐ An amendment to the patient population under the existing item(s)
iii. ☐ An amendment to the schedule fee of the existing item(s)
iv. ☐ An amendment to the time and complexity of an existing item(s)
v. ☐ Access to an existing item(s) by a different health practitioner group
vi. ☐ Minor amendments to the item descriptor that does not affect how the service is delivered
vii. ☐ An amendment to an existing specific single consultation item
viii. ☐ An amendment to an existing global consultation item(s)
ix. ☐ Other (please describe below):

N/A

REDACTED

CarGel is currently listed in the ARTG and used in cartilage repair of other joints than just the knee - including hip and ankle with associated relevant MBS item numbers.

The Applicant will work with the DoH in finalising a suitable item descriptor dependent on preferred approach (new MBS item code, amended MBS item code, or unchanged MBS item code).

(e) If a new item(s) is being requested, what is the nature of the change to the MBS being sought?

i. ☐ A new item which also seeks to allow access to the MBS for a specific health practitioner group
ii. ☐ A new item that is proposing a way of clinically delivering a service that is new to the MBS (in terms of new technology and / or population)
iii. ☐ A new item for a specific single consultation item
iv. ☐ A new item for a global consultation item(s)

See above comments relating to Q6A. The relevant medical service (MBS item number 49561) is currently in use in Australia, and as such, this is not an application for a new way of clinically delivering a service that is new to the MBS. This Application is lodged in response to the SOCAG / PLAC request as noted above.

(f) Is the proposed service seeking public funding other than the MBS?

☐ Yes
☒ No

(g) If yes, please advise:

N/A

7. What is the type of service:

☒ Therapeutic medical service
☐ Investigative medical service
☐ Single consultation medical service
☐ Global consultation medical service
☐ Allied health service
☐ Co-dependent technology
☐ Hybrid health technology

8. For investigative services, advise the specific purpose of performing the service *(which could be one or more of the following)*:

N/A

9. Does your service rely on another medical product to achieve or to enhance its intended effect?

☐ Pharmaceutical / Biological
☒ Prosthesis or device

☐ No

10. (a) If the proposed service has a pharmaceutical component to it, is it already covered under an existing Pharmaceutical Benefits Scheme (PBS) listing?

N/A

(b) If yes, please list the relevant PBS item code(s):

N/A

(c) If no, is an application (submission) in the process of being considered by the Pharmaceutical Benefits Advisory Committee (PBAC)?

N/A

(d) If you are seeking both MBS and PBS listing, what is the trade name and generic name of the pharmaceutical

Trade name: N/A
Generic name: N/A

11. (a) If the proposed service is dependent on the use of a prosthesis, is it already included on the Prostheses List?

☒ Yes
☐ No

(b) If yes, please provide the following information (where relevant):

Billing code(s): SL072
Trade name of prostheses: BST-CarGel
Clinical name of prostheses: chitosan-based liquid bioscaffold
Other device components delivered as part of the service: N/A

(c) If no, is an application in the process of being considered by a Clinical Advisory Group or the Prostheses List Advisory Committee (PLAC)?

N/A

(d) Are there any other sponsor(s) and / or manufacturer(s) that have a similar prosthesis or device component in the Australian market place which this application is relevant to?

☐ Yes
☒ No

(e) If yes, please provide the name(s) of the sponsor(s) and / or manufacturer(s):

N/A

12. Please identify any single and / or multi-use consumables delivered as part of the service?

Single use consumables: (1) disposable 1.0 mL sterile syringe with a sterile needle; (2) disposable 5.0 mL sterile syringes; (1) sterile phlebotomy needle to be attached to a 5.0 mL syringe; (1) disposable 18G sterile needle; (2) disposable sterile dispensing pins vented with a 0.2 µm filter membrane

Multi-use consumables: N/A

PART 3 – INFORMATION ABOUT REGULATORY REQUIREMENTS

13. (a) If the proposed medical service involves the use of a medical device, in-vitro diagnostic test, pharmaceutical product, radioactive tracer or any other type of therapeutic good, please provide the following details:

Type of therapeutic good: Cartilage biomatrix implant

REDACTED

(b) Is the medical device classified by the TGA as either a Class III or Active Implantable Medical Device (AIMD) against the TGA regulatory scheme for devices?

☒ Class III
☐ AIMD
☐ N/A

14. (a) Is the therapeutic good to be used in the service exempt from the regulatory requirements of the *Therapeutic Goods Act 1989*?

☐ Yes (If yes, please provide supporting documentation as an attachment to this application form)
☒ No

(b) If no, has it been listed or registered or included in the Australian Register of Therapeutic Goods (ARTG) by the Therapeutic Goods Administration (TGA)?

☒ Yes (if yes, please provide details below)
☐ No

ARTG listing, registration or inclusion number: 298453, 252732
TGA approved indication(s), if applicable: N/A
TGA approved purpose(s), if applicable: "CarGel is a medical device intended to promote hyaline cartilage regeneration when used in conjunction with the bone marrow stimulation technique for the repair of focal articular cartilage lesions. Treatment with CarGel should be performed by an orthopaedic surgeon".

15. If the therapeutic good has not been listed, registered or included in the ARTG, is the therapeutic good in the process of being considered for inclusion by the TGA?

N/A

16. If the therapeutic good is not in the process of being considered for listing, registration or inclusion by the TGA, is an application to the TGA being prepared?

N/A

PART 4 – SUMMARY OF EVIDENCE

17. **Provide an overview of all key journal articles or research published in the public domain related to the proposed service that is for your application (limiting these to the English language only).** ***Please do not attach full text articles, this is just intended to be a summary.***

	Type of study design*	**Title of journal article or research project (including any trial identifier or study lead if relevant)**	**Short description of research (max 50 words)****	**Website link to journal article or research (if available)**	**Date of publication*****
1.	RCT, OL, MN, MC; Level II	Stanish et al., 2013. Novel Scaffold-Based BST-CarGel Treatment Results in Superior Cartilage Repair Compared with Microfracture in a Randomized Controlled Trial. J Bone Joint Surg Am. 2013;95:1640-50 NCT00314236	12 months Blinded quantitative MRI analysis demonstrated that, compared with microfracture treatment alone, BST-CarGel treatment met both primary end points by achieving statistical superiority for greater lesion filling (p = 0.011) and more hyaline cartilage-like T2 values (p = 0.033). Thus, BST-CarGel is superior to microfracture based on structural outcomes. WOMAC subscales for pain, stiffness, and function yielded equivalent improvement for both groups at twelve months, which were significant (p < 0.0001) from baseline. The safety of the procedures was considered comparable.	https://www.ncbi.nlm.nih.gov/pubmed/24048551	2013

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		Shive et al., 2015. BST-CarGel® Treatment Maintains Cartilage Repair Superiority over Microfracture at 5 Years in a Multicenter Randomized Controlled Trial. Cartilage Vol. 6(2) 62–72 NCT01246895	5 years Chitosan-based cartilage biomatrix implant maintained superior lesion outcomes over 5 years compared with microfracture alone (filling and cartilage-like T2 values). Chitosan-based cartilage biomatrix implant and microfracture groups showed highly significant improvement at 5 years from pre-treatment baseline for each WOMAC subscale ($P < 0.0001$); there were no differences between the treatment groups. Safety was comparable for both groups.	https://www.ncbi.nlm.nih.gov/pubmed/26069709	2015 (follow-up to Stanish et al 2013)

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
		Méthot et al., 2016. Osteochondral Biopsy Analysis Demonstrates That BST-CarGel Treatment Improves Structural and Cellular Characteristics of Cartilage Repair Tissue Compared With Microfracture. Cartilage 2016, Vol. 7(1) 16–28.	13 months Chitosan-based cartilage biomatrix implant is superior to microfracture with respect to ICRS macroscopic scores (better filling, integration and tissue appearance). Chitosan-based cartilage biomatrix implant is associated with significant improvement of structural and cellular parameters compared with microfracture alone.	https://www.ncbi.nlm.nih.gov/pubmed/26958314	2016 (follow-up to Stanish et al 2013)
2.	Retrospective case series; Level IV	Rhee et al., 2018. Safety Profile and Short-term Outcomes of BST-CarGel as an Adjunct to Microfracture for the Treatment of Chondral Lesions of the Hip. Orthop J Sports Med 6(8): 1–6.	Thirty-seven (n=37) patients who underwent microfracture and chitosan-based cartilage biomatrix implant to their hip were included in this case series. The minimum follow up was 12 months. Chitosan-based cartilage biomatrix implant resulted in statistically significant improvements in iHOT, HOS-ADL and HOS-SP scores relative to pre-operative scores. No major adverse events of DVT, blood vessel or nerve damage, hemarthrosis, arthralgia or device-related adverse events.	https://www.ncbi.nlm.nih.gov/pubmed/30116764	2018

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
3.	Prospective case series; Level IV	Tahoun et al., 2018. Arthroscopic Repair of Acetabular Cartilage Lesions by Chitosan-Based Scaffold: Clinical Evaluation at Minimum 2 Years Follow-up. Arthroscopy - Journal of Arthroscopic and Related Surgery. 2018;34(10):2821-8.	Twenty-three (n=23), nonarthritic nondysplastic FAI patients with full thickness acetabular chondral lesion (> 2 cm^2) were treated with microfracture and chitosan-based cartilage biomatrix implant. Significant improvement on patient reported outcomes were observed at 12 months relative to baseline (NAHS, iHOT33, HOS-ADL, HOS-SSS), 91% of patients meeting the MCID for these outcomes (82% for HOS-SSS). The improvements achieved during the first year were maintained through the endpoint of the study (mean 38.4 months, range 24-50 months).	https://www.ncbi.nlm.nih.gov/pubmed/30195954	2018

	Type of study design*	Title of journal article or research project (including any trial identifier or study lead if relevant)	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication***
4.	Prospective case series; Level IV	Tahoun et al., 2017. Results of arthroscopic treatment of chondral delamination in femoroacetabular impingement with bone marrow stimulation and BST-CarGel. SICOT J. 2017. 3:51.	Thirteen (n=13), nonarthritic nondysplastic patients with chondral lesion (> 2 cm^2) with cam- or mixed-type FAI were treated with microfracture and chitosan-based cartilage biomatrix implant. Patients were followed up for 24 months. Chitosan-based cartilage biomatrix implant led to statistically significant improvements in mean HOS for daily activities and for sports subscale compared to pre-operative scores.	https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5545970/	2017

Abbreviations: DVT, deep vein thrombosis; FAI, femoroacetabular impingement, HOS, Hip Outcome Score; HOS-ADL, Hip Outcome Score-Activities of Daily Living; HOS-SP, Hip Outcome Score-Sports Profile; ICRS, International Cartilage Repair Society; iHOT, international Hip Outcome Tool; MC, multicentre; MCID, minimally clinically important difference; MN, multinational; MRI, magnetic resonance imaging; OL, open label; RCT, randomised controlled trial; VAS, visual analogue scale; WOMAC=Western Ontario and McMaster Osteoarthritis Index.

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment, including providing the trial registration number to allow for tracking purposes.*

**** If the publication is a follow-up to an initial publication, please advise.*

18. Identify yet to be published research that may have results available in the near future that could be relevant in the consideration of your application by MSAC (limiting these to the English language only). *Please do not attach full text articles, this is just intended to be a summary.*

	Type of study design*	Title of research (including any trial identifier if relevant)	Short description of research (max 50 words)**	Website link to research (if available)	Date***
1.	RCT, MC, PG, SB	Randomized Evaluation of BST-CarGel Versus Microfracture Alone On Recovery From Distal Femoral Cartilage Lesions NCT02981355 (RECORD)	The RECORD trial is a MC, RCT designed to assess the impact of the chitosan-based cartilage biomatrix implant and microfracture versus microfracture alone on the clinical benefit. Approximately 158 participants with full thickness grade III and IV cartilage lesions will be randomised in a 1:1 ratio to receive one of the two treatments during an arthroscopic procedure and will be followed for up to 24 months to collect outcomes.	https://clinicaltrials.gov/ct2/show/NCT02981355?term=cargel&rank=1	Status: recruiting Estimated completion: December 2021
2.	NR, PG, SB	A Pilot Study for Efficacy of BST-CarGel as an Adjunct to Microfracture for the Treatment of Chondral Lesions of the Hip: a Case Control Study NCT02540200	The current study will collect data through standard of care practice when chitosan-based cartilage biomatrix implant in conjunction with a bone marrow stimulation technique is used for the treatment of focal cartilage lesions in the hip. In addition, these patients in the study group will be compared with the group of patients who undergo the bone marrow stimulation technique alone. Estimated enrolment is 50 participants.	https://clinicaltrials.gov/ct2/show/NCT02540200?term=cargel&rank=2	Status: unknown

** Categorise study design, for example meta-analysis, randomised trials, non-randomised trial or observational study, study of diagnostic accuracy, etc.*

***Provide high level information including population numbers and whether patients are being recruited or in post-recruitment.*

****Date of when results will be made available (to the best of your knowledge).*

Abbreviations: MC, multicentre; NR, non-randomised; PG, parallel group; RCT, randomised controlled trial; SB, single-blind

PART 5 – CLINICAL ENDORSEMENT AND CONSUMER INFORMATION

19. **List all appropriate professional bodies / organisations representing the group(s) of health professionals who provide the service (please attach a statement of clinical relevance from each group nominated):**

    Australian Orthopaedic Association (AOA)

    CarGel is currently listed in the ARTG and used in cartilage repair of joints including the knee, hip and ankle with associated, currently available relevant MBS item numbers.

    REDACTED

20. **List any professional bodies / organisations that may be impacted by this medical service (i.e. those who provide the comparator service):**

    Not applicable. The comparator service(s) are provided by the same health professionals, orthopaedic surgeons.

21. **List the relevant consumer organisations relevant to the proposed medical service (please attach a letter of support for each consumer organisation nominated):**

    None.

22. **List the relevant sponsor(s) and / or manufacturer(s) who produce similar products relevant to the proposed medical service:**

    There are no other relevant sponsor(s) and / or manufacturer(s) that produce similar products relevant to the proposed medical service.

23. **Nominate two experts who could be approached about the proposed medical service and the current clinical management of the service(s):**

    REDACTED

    Please note that the Department may also consult with other referrers, proceduralists and disease specialists to obtain their insight.

PART 6 – POPULATION (AND PRIOR TESTS), INDICATION, COMPARATOR, OUTCOME (PICO)

PART 6a – INFORMATION ABOUT THE PROPOSED POPULATION

24. Define the medical condition, including providing information on the natural history of the condition and a high level summary of associated burden of disease in terms of both morbidity and mortality:

Articular cartilage provides a low-friction gliding service, acts as a shock absorber and minimises peak pressures on the subchondral bone in joints (Bhosal 2008). Damage to the articular cartilage predominately follows acute traumatic injuries, however other causes of articular cartilage damage can include; prolonged periods of stress due to obesity or old age and long periods of inactivity (Cole 2009; Hjelle 2002).

Symptoms of articular cartilage injuries are predominant in weight-bearing joints such as the knee, hip and ankle (Loken 2014). Typical symptoms of articular cartilage lesions include; swelling, local pain, locking and limitation of function (Cole 2009; Merlkely 2018). Due to the complexity of the condition diagnostic measures such as magnetic resonance imaging (MRI) and arthroscopy are commonly used to identify cartilage lesions.

Hyaline cartilage lacks the ability to generate the vascular phase of repair response following an injury (Bhosale 2008). As this is the most vital determinant of healing, the reparative ability of cartilage is low (Bhosale 2008). If left untreated cartilage injuries can become degenerative and lead to pre-mature early arthritis and affect the activities of daily living (Bhosale 2008; Cole 2009). Although rarely fatal, articular cartilage lesions severely reduce quality of life, ability to perform daily activities and imposes major economic burdens on individuals and society (Evens 2009).

25. Specify any characteristics of patients with the medical condition, or suspected of, who are proposed to be eligible for the proposed medical service, including any details of how a patient would be investigated, managed and referred within the Australian health care system in the lead up to being considered eligible for the service:

Typically patients with focal articular cartilage lesions present to their general practitioner with activity related pain and swelling. However, there are no pathognomonic symptoms for cartilage defects, and it is not uncommon that these types of lesions coexist with other lesions of abnormalities such as meniscal or ligamental lesions of the joint. As such, imaging is imperative for diagnosis (Gomoll et al., 2010). Thus, to diagnose cartilage lesions physicians cannot rely on history and physical assessment alone. Patients with ongoing symptoms, despite conservative management should undergo diagnostic imaging, such as MRI, to formally diagnose cartilage defect. In patients who are contraindicated to MRI, a computed tomography arthrogram will be performed. Whilst x-rays do not directly explore cartilage damage unless there is coexisting damage of the bone, it helps to identify patients with degenerative disease and provides an assessment of joint alignment (Merkely et al., 2018). Patients with advanced osteoarthritis are generally not suitable for cartilage repair.

Patients with partial thickness cartilage defects (grade 1-2) are generally managed conservatively or using debridement (Lee 2010). Surgery is indicated for patients presenting with symptoms consistent with a full thickness (Grade 3 or 4) cartilage defect and mechanical symptoms despite an adequate trial of nonoperative management. The orthopaedic surgeon will determine treatment strategies for cartilage repair primarily based on the location and the size of the defect, with age and hence level of expected activity as important secondary considerations (Gomoll et al., 2010).

Consistent with the clinical management pathway provided in Appendix A and discussed in Q.26, the proposed patient populations for the chitosan-based cartilage biomatrix implant with microfracture are as follows:

1. Patients aged 15-55 years with focal cartilage defect < 2 cm^2 without generalised arthritis.

2. Patients aged 15-55 years with focal cartilage defect ≥ 2 cm^2 with intact subchondral endplate and without generalised arthritis.

26. Define and summarise the current clinical management pathway *before* patients would be eligible for the proposed medical service (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway up to this point):

The International Cartilage Repair Society (ICRS) cartilage lesion classification system is provided in Table 1. Partial thickness focal cartilage defects (grade 1-2) are generally managed conservatively or through debridement. Conservative treatment includes activity modification, physical therapy and maintenance of body weight (Gomoll et al., 2010; Moyad et al., 2011). High impact activities are discouraged in favour of lower impact exercises (Moyad 2011). Oral nonsteroidal anti-inflammatory medications or creams can be used for temporary pain relief and to limit mild swelling and discomfort (Moyad 2011). Physical therapy includes patellofemoral strengthening and hip mobility programs (Gomoll et al., 2010). Older patients should undergo a trial of injection therapy with steroids and/or viscosupplementation (Gomoll et al., 2010).

Table 1 ICRS lesion classification system

Grade	Details
0	Normal
1	Nearly normal – superficial lesions. A) Soft indentation and/or B) superficial fissures and cracks
2	Abnormal – lesion extending down to < 50% of cartilage depth
3	Severely abnormal – cartilage defects extending down > 50% of cartilage depth (A) as well as down to calcified layer (B) and down to but not through the subchondral bone (C)
4	Severely abnormal – with penetration through subchondral plate

Source: Van der Meijder et al (2012)

Patients with ongoing mechanical symptoms despite conservative therapy with full thickness focal cartilage lesion are candidates for surgery (Lee et al 2010). Mechanical symptoms refer to pain when the joint is loaded, made unstable or catching and locking (key opinion leader [KOL] advice; Cole 2009). The goal of focal cartilage defect repair is for patients to return to normal activities or active lifestyle by improving joint function, providing pain relief and preventing osteoarthritis (Merkely et al., 2018).

There are a number of treatment options available including bone marrow stimulation (microfracture, abrasion, subchondral drilling), autologous grafting procedures (osteochondral autologous transplantation [OAT], i.e. mosaicplasty) and ACI. Microfracture is the most commonly used bone marrow stimulation technique (Bhosale 2008).

Microfracture involves penetration of the subchondral bone to elicit bleeding. Penetration of the subchondral bone plate disrupts the subchondral blood vessels and stimulates a repair response (Stanish 2013).

ACI is a technique that involves the cultivation of chondrocytes in-vitro, utilising a two-stage operative approach that is usually spread over approximately 8-12 weeks. The objective of the procedure is to replace damaged cartilage with hyaline cartilage. [The KOL advised that MACI, an alternate to ACI, has been removed from the market in Australia and is not considered further here].

OAT, more commonly referred to as mosaicplasty, is used in focal defects (ineffective in degenerative defects) and is optimal in young patients with medium-sized lesion (2.5-4 cm^2) (Falah et al 2010). In this technically demanding procedure, craters bored into the cartilage and bone of the damaged area are filled with cartilage and bone plugs removed from healthy, non-weight-bearing areas of the joint (Ozturk et al 2006).

No Australian clinical guidelines exist for the management of articular cartilage lesions. The assessment report for the MSAC application 1140 of ACI/MACI (December 2010) provides a clinical decision-making pathway for the management of cartilage lesions of the knee based on expert clinical advice (MSAC Application Assessment Report Figure 1 pg 7[1]). This algorithm was considered by KOLs. Minor amendments to this pathway were made based on advice from KOLs to represent current clinical management of focal cartilage lesions of the knee in Australia. The resultant algorithm is provided in Appendix A.

The treatment strategy for focal cartilage repair is primarily based on the location and the size of the defect, with age and hence level of expected activity as important secondary considerations (Gomoll et al., 2010). In patients with small focal lesions (< 2 cm^2), microfracture is the most commonly used surgical treatment option. An alternate treatment option in small lesions is ACI, however, given the lack of MBS funding of this treatment, utilisation in Australia is limited, particularly in the private setting. Chitosan-based cartilage biomatrix implant is currently used in conjunction with microfracture to treat focal cartilage lesions < 2 cm^2 in Australia.

In lesions that are ≥ 2 cm^2, the treatment decision is dependent on the status of the subchondral endplate, whether it is intact or not. In lesions with intact endplate, microfracture, ACI and mosaicplasty are potential treatment options. However, mosaicplasty is very rarely used in Australia because this is a technically difficult procedure to perform. Again, ACI is rarely used in the private setting due to the lack of MBS funding incurring large out of pocket expenses to patients. Microfracture alone is a treatment option in lesions ≥ 2 cm^2, as recognised in the 2018 NICE technology appraisal of ACI.

In lesions ≥ 2 cm^2 where the subchondral endplate is not intact the potential treatment options include ACI, mosaicplasty or fresh osteochondral allograft. Chitosan-based cartilage biomatrix implant in conjunction with microfracture is not used in these patients.

PART 6b – INFORMATION ABOUT THE INTERVENTION

27. Describe the key components and clinical steps involved in delivering the proposed medical service:

The proposed medical service is the application of a chitosan-based cartilage biomatrix implant after bone marrow stimulation technique, such as microfracture, for repair of hyaline cartilage. There is only one chitosan-based cartilage biomatrix implant available in Australia, CarGel, hence the details of the clinical steps of the interventions specifically refer to CarGel.

As suggested by the name, CarGel is a gel implant that promotes hyaline cartilage regeneration when used in conjunction with the bone marrow stimulation technique for the repair of focal articular cartilage lesions. The approved indication for CarGel is not limited to articular cartilage in specific locations.

Prior to surgery, patients are recommended to discontinue the use of aspirin, anti-inflammatory or anticoagulant medications at least 7 days prior to surgery to optimise clotting, and refrain from use for at least 24 hours post-surgery. Patients treated with anticoagulant therapy can resume treatment 6 hours post operation.

There are four main steps of the procedure

1. Preparation of cartilage biomatrix implant before blood collection – 0.3 mL of sterile disodium β-glycerophosphate solution is added drop by drop into the sterile chitosan polymer solution
2. Preparation of cartilage lesion:
    a. Routine arthroscopy and debridement of lesion is performed to form stable vertical cartilage margins, removing calcified cartilage layer
    b. Bone marrow stimulation procedure is performed, generating bone perforations 3-4 mm apart throughout the debrided lesion. Any loose fragments are cleaned, and the joint is drained. The prepared lesion is dried to enable delivery of chitosan-based cartilage biomatrix implant mixture.

1 http://www.msac.gov.au/internet/msac/publishing.nsf/Content/E72BFBEC5447F91FCA25801000123B6D/$File/1140_Report_Final040211.pdf (accessed 31 October 2018)

3. Preparation of chitosan-based cartilage biomatrix implant after blood collection – 0.3 mL of fresh, untreated whole blood from the patient is mixed with the prepared chitosan-based cartilage biomatrix implant.
4. Chitosan-based cartilage biomatrix implant delivery and closure – using a syringe, the chitosan-based cartilage biomatrix implant mixture is applied to the area drop by drop immediately, whilst maintaining the lesion motionless and horizontal for at least 15 minutes whilst the implant solidifies. Incisions are then sutured, and the area is kept motionless for 10 minutes prior to gently extending the joint and application of standard dressing and wrapping. A post-operative brace may be worn for the first 24 hours.

Following the procedure, standard pain management measures should be undertaken. Cartilage repair specific physiotherapy should commence ideally before day three postoperatively. The patient should refrain from load bearing on the treated joint for 6-8 weeks.

28. Does the proposed medical service include a registered trademark component with characteristics that distinguishes it from other similar health components?

The proposed medical service, chitosan-based cartilage biomatrix implant in conjunction with microfracture does include a registered trademark component. CarGel, which is a chitosan-based biomatrix implant available in Australia has a registered trademark.

29. If the proposed medical service has a prosthesis or device component to it, does it involve a new approach towards managing a particular sub-group of the population with the specific medical condition?

The proposed medical service has a prosthesis component to it, however, does not involve a new approach towards managing a particular sub-group of patients. The chitosan-based cartilage biomatrix implant CarGel has been listed on the PL since August 2015 and the procedure has been performed and reimbursed via the appropriate MBS item number since then.

30. If applicable, are there any limitations on the provision of the proposed medical service delivered to the patient (i.e. accessibility, dosage, quantity, duration or frequency):

The medical service, chitosan-based cartilage biomatrix implant in conjunction with microfracture, is intended to be performed once. There are no current limitations on the provision of the proposed medical service with respect to accessibility.

31. If applicable, identify any healthcare resources or other medical services that would need to be delivered <u>at the same time</u> as the proposed medical service:

The healthcare resources required at the same time as the proposed medical service include administration of anaesthesia (patients are under general anaesthesia) and hospitalisation.

32. If applicable, advise which health professionals will primarily deliver the proposed service:

The procedure is performed by orthopaedic surgeons.

33. If applicable, specify any proposed limitations on who might deliver the proposed medical service, or who might provide a referral for it:

Only orthopaedic surgeons perform the procedure.

34. If applicable, advise what type of training or qualifications would be required to perform the proposed service as well as any accreditation requirements to support service delivery:

The procedure is performed by orthopaedic surgeons. No additional training is required to apply the chitosan-based cartilage biomatrix implant in conjunction with microfracture.

35. If applicable, advise whether the proposed medical service could be delegated or referred to another professional for delivery:

N/A

36. (a) Indicate the proposed setting(s) in which the proposed medical service will be delivered (select all relevant settings):

- ☒ Inpatient private hospital
- ☒ Inpatient public hospital
- ☐ Outpatient clinic
- ☐ Emergency Department
- ☐ Consulting rooms
- ☒ Day surgery centre
- ☐ Residential aged care facility
- ☐ Patient's home
- ☐ Laboratory
- ☐ Other – please specify below

(b) Where the proposed medical service is provided in more than one setting, please describe the rationale related to each:

The vast majority of procedures are performed in the hospital inpatient setting (private and public) with patients staying overnight, with a small number performed in the day surgery centre setting.

37. Is the proposed medical service intended to be entirely rendered in Australia?

- ☒ Yes
- ☐ No – please specify below

PART 6c – INFORMATION ABOUT THE COMPARATOR(S)

38. Nominate the appropriate comparator(s) for the proposed medical service, i.e. how is the proposed population currently managed in the absence of the proposed medical service being available in the Australian health care system (including identifying health care resources that are needed to be delivered at the same time as the comparator service):

The proposed comparators for chitosan-based cartilage biomatrix implant used in conjunction with microfracture, consistent with current clinical management of patients and utilisation of services are as follows:

1. Patients aged 15-55 years with focal cartilage defect < 2 cm^2 without generalised arthritis. Comparator: microfracture alone
2. Patients aged 15-55 years with focal cartilage defect ≥ 2 cm^2, with intact subchondral endplate and without generalised arthritis. Comparator: microfracture alone

There are several potential MBS item codes that may be used for cartilage repair of the knee (Table 2). Also, the inclusion of several procedures in the one item descriptor makes utilisation data for any particular intervention difficult to interpret. As per the MSAC evaluation of MACI/ACI in 2009 / 2010, the primary code for microfracture was 49561 (MSAC Application 1140 PSD). MBS item 49561 is the primary code used for the microfracture procedure with chitosan-based cartilage biomatrix implant. As explained in Q.6A, in their request for an MSAC application for CarGel the SOCAG / PLAC specifically nominated MBS item 49561

As shown in Table 2 below, MBS item 49561 is the most commonly utilised code in 2017 relating to cartilage repair of the knee, with 34,566 services claimed in 2017. It is not clear what proportion of this service is directly relevant to microfracture.

In population 1, microfracture alone is the most appropriate comparator given this is the most commonly used treatment option in small defects (< 2 cm^2).

In population 2, microfracture alone is also the most commonly used treatment option and thus selected as the appropriate comparator for repair of defects ≥ 2 cm^2. REDACTED, mosaicplasty is very rarely used in Australia given it is a technically challenging procedure to perform, and as such is not considered an appropriate comparator. As previously noted, ACI is not reimbursed on the MBS and the utilisation of this procedure is limited in Australia. Thus, the most prevalent procedure in this population is microfracture alone and is the nominated comparator in this population.

Table 2 MBS item codes relating to cartilage repair of the knee

MBS item #	Descriptor	Fee	Services 2017 (Jan-Dec)
49500	KNEE, arthrotomy of, involving 1 or more of; capsular release, biopsy or lavage, or removal of loose body or foreign body	$376.55	1,419
41512	MEATOPLASTY involving removal of cartilage or bone or both cartilage and bone, not being a service to which item 41515 applies	$585.90	564
49557	KNEE, diagnostic arthroscopy of (including biopsy, simple trimming of meniscal margin or plica) - not being a service associated with autologous chondrocyte implantation or matrix-induced autologous chondrocyte implantation or any other arthroscopic procedure of the knee region	$272.95	479
49558	KNEE, arthroscopic surgery of, involving 1 or more of: debridement, osteoplasty or chondroplasty - not associated with any other arthroscopic procedure of the knee region	$272.95	710
49559	KNEE, arthroscopic surgery of, involving chondroplasty	$408.70	71

MBS item #	Descriptor	Fee	Services 2017 (Jan-Dec)
	requiring multiple drilling or carbon fibre (or similar) implant; including any associated debridement or oestoplasty - not associated with any other arthroscopic procedure of the knee region		
49560	KNEE, arthroscopic surgery of, involving 1 or more of: partial or total meniscectomy, removal of loose body or lateral release - not being a service associated with any other arthroscopic procedure of the knee region	$551.60	2,616
49561	KNEE, ARTHROSCOPIC SURGERY OF, involving 1 or more of: partial or total meniscectomy, removal of loose body or lateral release; where the procedure includes associated debridement, osteoplasty or chondroplasty - not associated with any other arthroscopic procedure of the knee region	$674.00	34,566
49562	KNEE, ARTHROSCOPIC SURGERY OF, involving 1 or more of: partial or total meniscectomy, removal of loose body or lateral release; where the procedure includes chondroplasty requiring multiple drilling or carbon fibre (or similar) implant and associated debridement or osteoplasty - not associated with any other arthroscopic procedure of the knee region	$735.50	3,278
49563	KNEE, arthroscopic surgery of, involving 1 or more of: meniscus repair; osteochondral graft; or chondral graft (excluding autologous chondrocyte implantation or matrix-induced autologous chondrocyte implantation) - not associated with any other arthroscopic procedure of the knee region	$796.70	1,492
49503	KNEE, partial or total meniscectomy of, repair of collateral or cruciate ligament, patellectomy of, chondroplasty of, osteoplasty of, patellofemoral stabilisation or single transfer of ligament or tendon (not being a service to which another item in this Group applies) - any 1 procedure	$489.55	210
49506	KNEE, partial or total meniscectomy of, repair of collateral or cruciate ligament, patellectomy of, chondroplasty of, osteoplasty of, patellofemoral stabilisation or single transfer of ligament or tendon (not being a service to which another item in this Group applies) - any 2 or more procedures	$734.40	330

Source: MBS online (accessed 31 Oct 2018).

39. Does the medical service that has been nominated as the comparator have an existing MBS item number(s)?

☒ Yes (please provide all relevant MBS item numbers below)
☐ No

Several MBS item numbers are used for repair of cartilage repair of the knee with many descriptors being non-specific to any one intervention (Table 2). The primary MBS item code used for microfracture is 49561, the primary code which is also used for chitosan-based cartilage biomatrix implant in conjunction with microfracture (refer to Table 2).

40. Define and summarise the current clinical management pathways that patients may follow *after* they receive the medical service that has been nominated as the comparator (supplement this summary with an easy to follow flowchart [as an attachment to the Application Form] depicting the current clinical management pathway that patients may follow from the point of receiving the comparator onwards including health care resources):

Following chondral surgery, clinicians should assess for impairments in range of motion, motor control, strength and endurance of the limb associated with cartilage defect (American Physical Therapy Association [APTA] 2018). The APTA (2018) guidelines recommend rehabilitation strategies to assist in the clinical management of cartilage repair following knee surgery. These include; progressive motion, progressive weight-bearing, progressive return to activity, therapeutic exercises and neuromuscular electrical stimulation (APTA 2018). Patients should be re-evaluated post rehabilitation management to ensure success of treatment and rehabilitation (APTA 2018).

REDACTED the majority of patients report improvements in symptoms post-surgery and continue on with their life. However, on the rare occasion that symptoms persist and are troublesome enough for the patient to seek further specialist opinion, re-operation with the same procedure is not performed. Rather, these patients would undergo realignment osteotomy or partial or complete joint replacement surgery.

41. (a) Will the proposed medical service be used in addition to, or instead of, the nominated comparator(s)?

☒ Yes
☐ No

(b) If yes, please outline the extent of which the current service/comparator is expected to be substituted:

The proposed medical service is performed in addition to the proposed comparator, microfracture. CarGel, a chitosan-based cartilage biomatrix implant, has been available on the PL since August 2015 and its use in Australia is well established. Given the procedure is currently reimbursed through the MBS in the proposed populations, current utilisation of the comparator service is not expected to change as a result of this application. Refer to Q.49 for current utilisation.

42. Define and summarise how current clinical management pathways (from the point of service delivery onwards) are expected to change as a consequence of introducing the proposed medical service including variation in health care resources (Refer to Question 39 as baseline):

Given the procedure is currently reimbursed through the MBS in the proposed populations, current utilisation, the healthcare resources from the point of service delivery is not expected to change relative to microfracture alone as a consequence of the proposed medical service. Patients who have received chitosan-based cartilage biomatrix implant in conjunction with microfracture require a knee brace for a short time to immobilise the joint immediately after the procedure to prevent the gel from being displaced. Patients undergoing microfracture alone do not require a knee brace.

PART 6d – INFORMATION ABOUT THE CLINICAL OUTCOME

43. Summarise the clinical claims for the proposed medical service against the appropriate comparator(s), in terms of consequences for health outcomes (comparative benefits and harms):

Compared with microfracture alone, the application of chitosan-based cartilage biomatrix implantation in conjunction with microfracture results in superior outcomes (Stanish et al 2013).

44. Please advise if the overall clinical claim is for:

☒ Superiority
☐ Non-inferiority

45. Below, list the key health outcomes (major and minor – prioritising major key health outcomes first) that will need to be specifically measured in assessing the clinical claim of the proposed medical service versus the comparator:

Safety Outcomes:
Procedural complications/device-related adverse events
Long-term safety
Failure/retreatment rate
Clinical Effectiveness Outcomes:
Structural cartilage repair tissue quantity (degree of lesion filling)
Structural cartilage repair tissue quality (T2 relaxation time)
International Cartilage Repair Society [ICRS] score
Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)
Lysholm score
Tegner score
Quality of life
Resource utilisation

PART 7 – INFORMATION ABOUT ESTIMATED UTILISATION

46. Estimate the prevalence and/or incidence of the proposed population:

Articular cartilage lesions of the knee are relatively common, with an estimated prevalence of 60% found in patients undergoing knee arthroscopy (Aroen 2004; Curl 1997; Hjelle 2002). Lesions in the hip and ankle are less common, full thickness acetabular lesions are seen in around 10% of hips treated for femoroacetabular impingement (FAI) (Loken 2014). Cartilage lesions of the ankle are often non-symptomatic, as such the prevalence is unclear (Loken 2014). A retrospective analysis of medical records from patients undergoing arthroscopy of the knee or ankle found that high grade (ICRS grade 3 and 4) cartilage defects were significantly more prevalent in the knee (49.47%) compared to the ankle (26.31%) (Aurich 2014).

The ICRS provide a grading system consisting of five grading levels, from grade 0 (normal cartilage without notable defects) to grade 4 (severely abnormal, full thickness osteochondral injury). Localised full thickness cartilage lesions are more severe and graded >3 using ICRS grading system. The prevalence of grade 3-4 lesions varies; localised full thickness cartilage lesions (grade 3-4) were found in 11% of patients undergoing knee arthroscopy (Areon 2004). APTA (2018) report that grade 3-4 lesions make up 30% to 60% of all articular cartilage lesions. With a growing percentage of the population that is overweight, the ageing population and a more active society, the prevalence of articular cartilage damage is increasing (Evans 2009).

47. Estimate the number of times the proposed medical service(s) would be delivered to a patient per year:

The proposed medical service is intended to be delivered once only.

48. How many years would the proposed medical service(s) be required for the patient?

As stated in Q.47, the proposed medical service is to be a once off service.

49. Estimate the projected number of patients who will utilise the proposed medical service(s) for the first full year:

CarGel, a chitosan-based cartilage biomatrix implant, has been listed on the PL since August 2015 and has been reimbursed through the MBS since 2016 primarily utilising MBS item code 49561 for repair of cartilage defects of the knee. The utilisation of MBS item code 49561 over time is provided in Figure 1. The graph suggests that the introduction of chitosan-based cartilage biomatrix implant in 2015, has not resulted in an increased utilisation for MBS item code 49561. In contrast, number of services claimed for this item code has decreased from 49,278 in 2014 to 34,566 in 2017. However, given the MBS item descriptor for code 49561 is not limited to microfracture, it is unclear what proportion of utilisation of this code is directly relevant for microfracture making interpretation of MBS utilisation data difficult.

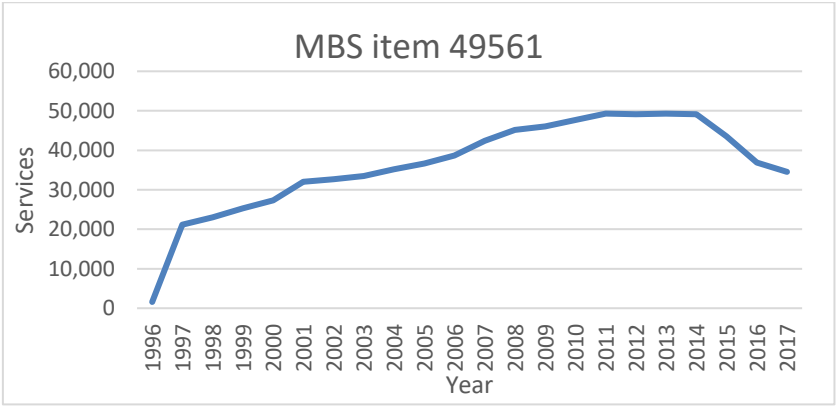

Figure 1 Utilisation of MBS item code 49561 over time (1996-2017)

Source: MBS statistics online, 1996-2017.

REDACTED

Table 3 Chitosan-based cartilage biomatrix implant units sold over time in Australia (private hospital and private patients in public hospitals)

REDACTED

50. Estimate the anticipated uptake of the proposed medical service over the next three years factoring in any constraints in the health system in meeting the needs of the proposed population (such as supply and demand factors) as well as provide commentary on risk of 'leakage' to populations not targeted by the service:

Given chitosan-based cartilage biomatrix implant used in conjunction with microfracture has been used on the MBS since 2016, this Application is not expected to result in any change to the utilisation in terms of substitutions (chitosan-based cartilage biomatrix implant is used in addition to microfracture, not instead of). The market for repair of cartilage of the knee on the MBS is well established and given the modest use of chitosan-based cartilage biomatrix implant in the currently reimbursed setting, this Application is unlikely to result in any market growth. Any growth in the market as a consequence of chitosan-based cartilage biomatrix implant would already have taken place.

REDACTED

Table 4 Estimated utilisation of chitosan-based cartilage biomatrix implant in Years 2 to 4 (2020-22)

	Year 2	**Year 3**	**Year 4**
Actual utilisation of chitosan-based cartilage biomatrix implant (Private hospital)	REDACTED	REDACTED	REDACTED

PART 8 – COST INFORMATION

51. Indicate the likely cost of providing the proposed medical service. Where possible, please provide overall cost and breakdown:

The provision of the proposed medical service, chitosan-based cartilage biomatrix implantation in conjunction with microfracture for articular cartilage repair of the knee, is estimated to cost $6,898. Cost estimates are comprised of: chitosan-based implant, the procedure itself (MBS 49561) and anaesthesia. The cost of consumables, including syringes, needles and pins (Q.12), is not included, however is expected to be small given these consumables are standard equipment REDACTED Table 5 provides breakdown of estimated procedure costs associated with chitosan-based cartilage biomatrix implantation in conjunction with microfracture. These estimates will be confirmed in an SBA.

Table 5 Costs associated with providing chitosan-based cartilage biomatrix implantation in conjunction with microfracture for cartilage defect repair of the knee

Row	Parameters	Cost	Source/calculation
A	Chitosan-based cartilage biomatrix implant (CarGel)	$6,022	Prosthesis list SL072
B	Pre-anaesthesia consultation	$43.65	MBS item 17610
C	Initiation anaesthesia	$79.20	MBS item 21382
D	Arthroscopic surgery including application of chitosan-based cartilage biomatrix implant	$674.00	MBS item 49561
E	Anaesthesia	$79.20	MBS item 21382
F	Total	$6,898	A+B+C+D+E

52. Specify how long the proposed medical service typically takes to perform:

REDACTED the average duration of microfracture surgery is 20-25 min. An additional 30 minutes is required for the chitosan-based cartilage biomatrix implant to be prepared and insert due to the gel setting time.

53. If public funding is sought through the MBS, please draft a proposed MBS item descriptor to define the population and medical service usage characteristics that would define eligibility for MBS funding.

As previously stated in Q.6A, the lodging of this MSAC Application is in response to the SOCAG of PLAC request. CarGel has been listed on the PL since August 2015. REDACTED an MSAC application was requested to help clarify the appropriateness of the existing MBS item number 49561.

The proposed populations in the MSAC Application refers to the populations currently treated with chitosan-based cartilage biomatrix implant in conjunction with microfracture.

As stated previously, the Applicant will work with the DoH in finalising a suitable item descriptor dependent on preferred approach (new MBS item code, amended MBS item code, unchanged MBS item code).

Appendix A

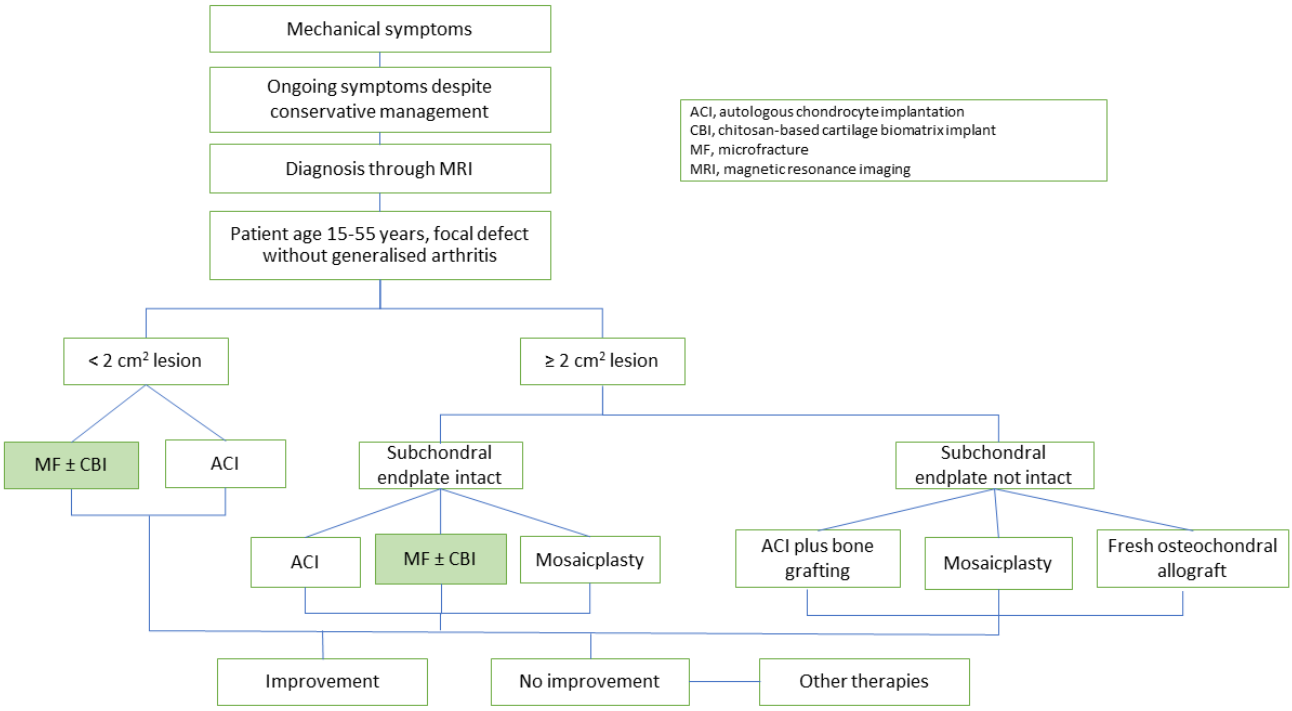

Figure 2 Clinical algorithm of the management of focal cartilage defects

References

Aroen A, Loken S, Heir S, et al. Articular cartilage lesions in 993 consecutive knee arthroscopies. American journal of Sports Medicine. 2004;32(1):211-215.

Asik M, Ciftci F, Sen C, Erdil M, Atalar A (2008) The microfracture technique for the treatment of full-thickness articular cartilage lesions of the knee: midterm results. Arthroscopy 24:1214–1220

Aurich M, hofmann G, Rolauffs B, et al. Differences in injury pattern and prevalence of cartilage lesions in knee and ankle joints: a retrospective cohort study. Orthopedic Reviews. 2014;6(5611):164-167.

Bhosale A, Richardson J. Articular cartilage: structure, injuries and review of management. British Medical Bulletin. 2008;87:77-95.

Cole B, Pascual-Garrido C, Grumet R. Surgical management of articular cartilage defects in the knee. The Journal of Bone and Joint Surfer. 2009;91:1778-1790.

Curl W, Krome J, Gordon E, et al. Cartilage injuries: a review of 31,516 knee arthroscopies. Arthroscopy. 1997;13(4):456-460.

Evans C, Ghivizzani S, Robbins P. Orthopedic gene therapy in 2008. Molecular Therapy. 2009;17(2):231-244.

Falah M, Nierenberg G, Soudry M, et al. Treatment of articular cartilage lesions of the knee. Int Orthop. 2010;34(5):621-630.

Gomoll A, Farr J, Gollogly S, et al. Surgical management of articular cartilage defects of knee. The Journal of Bone and Joint Surgery. 2010;92(14):2470-2490.

Gudas R, Kalesinskas RJ, Kimtys V, Stankevicius E, Toliusis V, Bernotavicius G, Smailys A (2005) A prospective randomized clinical study of mosaic osteochondral autologous transplantation transplantation versus microfracture for the treatment of osteochondral defects in the knee joint in young athletes. Arthroscopy 21(9):1066–1075

Gudas R, Stankevicius E, Monastyreckiene E, Pranys D, Kalesinskas RJ (2006) Osteochondral autologous transplantation versus microfracture for the treatment of articular cartilage defects in the knee joint in athletes. Knee Surg Sports Traumatol Arthrosc 14:834–842

Hjelle K, Solheim E, Strand T, et al. Articular cartilage defects in 1,000 knee arthroscopies. Arthroscopy. 2002;18(7):730-4.

Lee, S, Jee, WH, Kim, S, et al. Differentiation between grade 3 and grade 4 articular cartilage defects of the knee: Fat surpressed proton density-wegithed versus fat-supressed three dimensional gradient-echo MRI. Acta Radiologica. 2010;4:455-461.

Logerstedt D, Scalzitti D, Bennell K, et al. Knee pain and mobility impairments: meniscal and articular cartilage lesions revision 2018. American Physical Therapy Association (APTA). J Orthop Sports Phys Ther. 2018;48(2)A1-A50.

Loken S, Granan L, Sivertsen E, et al. Epidemiology of cartilage injuries. Sports Injuries. 2014:1-12.

Merkely G, Ackermann J, Lattermann C. Articular cartilage defect: Incidence, diagnosis and natural history. Oper Tech Sports Med. 2018;26:156-161.

Méthot et al., 2016. Osteochondral Biopsy Analysis Demonstrates That BST-CarGel Treatment Improves Structural and Cellular Characteristics of Cartilage Repair Tissue Compared With Microfracture. Cartilage 2016, Vol. 7(1) 16–28

Mithoefer K, Williams RJ 3rd, Warren RF , et al: High-impact athletics after knee articular cartilage repair: A prospective evaluation of the microfracture technique. Am J Sports Med 34:1413-1418,2006.

Moyad T. Cartilage injuries in the adult knee; Evaluation and management. Cartilage. 2011:2(3):226-236

Ozturk A, Ozdemir M, Ozkan Y. Osteochondral autografting (masaicplasty) in grade IV cartilage defects in the knee joint: 1 to 7 year results. Int Orthop. 2006;30(3):200-204.

Rhee et al 2018. Safety Profile and Short-term Outcomes of BST-CarGel as an Adjunct to Microfracture for the Treatment of Chondral Lesions of the Hip. Orthop J Sports Med 6(8): 1–6.

Shive et al., 2015. BST-CarGel® Treatment Maintains Cartilage Repair Superiority over Microfracture at 5 Years in a Multicenter Randomized Controlled Trial. Cartilage Vol. 6(2) 62–72

Stanish W, McCormack R, Forriol F, et al. Novel Scaffold-based BST-CarGel treatment results in superior cartilage repair compared with microfracture in a randomized controlled trial. J Bone Joint Surg Am. 2013;95:1640-50.

Tahoun. 2017. Results of arthroscopic treatment of chondral delamination in femoroacetabular impingement with bone marrow stimulation and BST-CarGel. SICOT J. 2017. 3:51

Tahoun et al 2018. Arthroscopic Repair of Acetabular Cartilage Lesions by Chitosan-Based Scaffold: Clinical Evaluation at Minimum 2 Years Follow-up. Arthroscopy - Journal of Arthroscopic and Related Surgery. 2018;34(10):2821-8

Van der Meijden OA, Gaskill TR, Millett PJ. Glenohumeral joint preservation: A review of management options for young, active patients with osteoarthritis. Adv Orthop. 2012;2012:160923

PART 9 – FEEDBACK

The Department is interested in your feedback.

54. How long did it take to complete the Application Form?

Insert approximate duration here

55. (a) Was the Application Form clear and easy to complete?

☐ Yes
☐ No

(b) If no, provide areas of concern:

Describe areas of concern here

56. (a) Are the associated Guidelines to the Application Form useful?

☐ Yes
☐ No

(b) If no, what areas did you find not to be useful?

Insert feedback here

57. (a) Is there any information that the Department should consider in the future relating to the questions within the Application Form that is not contained in the Application Form?

☐ Yes
☐ No

(b) If yes, please advise:

Insert feedback here