17 Erin Street,
Richmond VIC 3144
Australia

APPLICATION TO THE MEDICAL SERVICES ADVISORY COMMITTEE

USE OF ARTIFICIAL DISC REPLACEMENT IN PATIENTS WITH CERVICAL DEGENERATIVE DISC DISEASE

January 2010

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List of abbreviations

ACD	Anterior cervical discectomy
ACDF	Anterior cervical discectomy and fusion
AIDR	Artificial intervertebral disc replacement
CDA	Cervical disc arthroplasty
CI	Confidence interval
CSM	Cervical Spondylotic Myelopathy
CT	Computed topography scan
DDD	Degenerative disc disease
MBS	Medicare Benefits Schedule
MRI	Magnetic resonance imaging
MSAC	Medical Services Advisory Committee
NA	Not applicable
NDI	Neck disability index
NHMRC	National Health and Medical Research Council
NSAID	Non-steroidal anti-inflammatory drug
RCT	Randomised controlled trial
TGA	Therapeutic Goods Administration

Submission background

In 2004, a Consortium including Medtronic Australia Pty Ltd, Taylor Bryant and Johnson & Johnson Medical (DePuy Spine) applied to the Medical Services Advisory Committee (MSAC) to list artificial intervertebral disc replacement (AIDR), specifically using the Bryan®, Prestige®, ProDisc C®, SB Charitè™ III and Prodisc, for the treatment of degenerative disc disease in the cervical and lumbar spine (MSAC application 1090).

Following the recommendation of the MSAC in March 2006, interim funding was approved for single level AIDR in patients with single level intra lumbar disc disease in the absence of osteoporosis and prior fusion at the same level who have failed conservative therapy. The use of AIDR in the lumbar indication is presently covered by MBS item numbers 48691, 48692 and 48693. Based on the absence of adequate evidence of clinical effectiveness at the time of the evaluation, MSAC recommended that public funding for AIDR in the cervical spine should not be supported.

This application seeks to expand the Medicare approved indications for AIDR to include patients with degenerative disc disease in the cervical spine. This indication is not currently covered by the existing MBS item numbers. To support this request, clinical evidence is presented in this application for cervical disc arthroplasty (CDA). CDA is the term used to refer to AIDR in cervical spine. For the purposes of the current application, therefore, the two are able to be used interchangeably. Since MSAC Assessment report 1090 was completed, new randomised head-to-head comparative evidence pertaining to AIDR in the cervical spine has been published. This evidence forms the basis of this submission.

Rationale for the evidence presented in the submission

Selection of studies demonstrating the efficacy and safety of CDA

This application considers four types of artificial disc that can be used for CDA; Prestige® and Bryan® Cervical Disc (Medtronic Australasia Pty Ltd); ProDisc-C (Synthes Australia Pty Ltd) and Discover™ disc (DePuy Spine).

- The Prestige® disc consists of two articulating metal plates that interface through a ball-and-trough mechanism

- The ProDisc-C® consists of two metal plates and a polyethylene inlay with a ball-and-socket/semi constrained design

- The Bryan® cervical disc system is a composite-type artificial disc comprising a closed unit with polyethylene articular surfaces, bonded to a titanium shell, enclosed in a polyurethane membrane

- The Discover™ Artificial Cervical Disc is comprised of a titanium alloy superior endplate that articulates with a polyethylene core that is mechanically fixed to the inferior titanium alloy endplate.

All CDA devices are currently TGA approved in Australia. A more detailed description of the devices can be found in **Appendix 1**.

A randomised controlled trial (RCT) has found that 24 months after surgery, patients treated with a cervical artificial disc had a statistically greater improvement in the primary outcome measures (neck disability index score and overall success), compared to those treated with cervical decompression and fusion (ACDF) (Heller *et al*, 2009). The recently published multi-institutional, phase III RCT by Heller *et al* (2009), randomised 582 patients to receive either CDA or anterior cervical plating and a bone allograft. Using a composite outcome measure, 'overall success', which comprised the primary effectiveness and safety measures, 82.6% of patients in the CDA group and 72.7% of patients in the ACDF group achieved overall success at 24 months follow-up ($P = 0.010$).

Only 1.7% of the CDA treated patients and 3.2% of the ACDF treated patients were determined to have experienced either implant-related or implant/surgical-procedure-related serious adverse events (SAEs) during the two year follow-up period. This difference was not statistically significant. Based on median return-to-work intervals, patients treated with CDA returned to work significantly sooner than patients treated with ACDF (48 days versus 61 days, respectively; $P = 0.015$). Importantly, safety data from the same trial, reported by Anderson *et al* (2008), indicated that after three years, patients treated with ACDF required significantly more re-operations than patients treated with CDA ($P = 0.045$).

Selection of studies to support the indication

The proposed indication for CDA (using one of the four previously described artificial discs) is for the treatment of radiculopathy and/or myelopathy in patients with cervical degenerative disc disease (DDD). As noted in **Appendix 2**, the prevalence and incidence of cervical degenerative disc

and radiculopathy and/or myelopathy in the Australian setting is currently unclear. The number of individuals who may be eligible for CDA is, therefore, uncertain.

To support the application for the requested MBS listing, evidence of the effectiveness and safety of CDA in the treatment of cervical DDD will be presented. Limited data relating to CDA in the treatment of cervical DDD was presented in MSAC application 1090. Since then, however, significant evidence comprising an additional study of 463 patients has been published comparing outcomes for patients treated with Bryan® Cervical Artificial Disc with patients treated with ACDF. This pivotal study clearly demonstrates the effectiveness of CDA for the treatment of this disease. Additionally, data from studies of the Prestige® and Prodisc® discs reported in Mummaneni *et al* (2007) and Murrey *et al* (2009), respectively, are also used. These data are incorporated into an economic evaluation (See Appendix 5) which demonstrates that CDA is a cost-effective alternative to ACDF.

The pooling of these data into an economic evaluation is warranted on the grounds that, while there are differences in the discs themselves, they represent use of the same procedure in the same patient population and for the same purpose This is reflected in the consistent outcomes investigated across the studies and consistent results generated over equivalent follow-up. Furthermore, the relatively low patient numbers of each of the studies further justifies the pooling of the data in order to generate the most reliable estimates of efficacy.

Section 1 Applicant details

1.1 Name of applicant

Spine Society of Australia

1.2 Company or organisation contact person

Mr. Graeme Brazenor

Secretary

1.3 Physical address

17 Erin Street,

Richmond,

Victoria 3144

1.4 Postal address

17 Erin Street,

Richmond,

Victoria 3144

1.5 Contact numbers

Business hours: 03 9429 6262

Facsimile: 03 9429 6360

Mobile: 0418 318 451

1.6 E-mail address

spinetech@optusnet.com.au

1.7 Corporation/partnership details

Corporation name: N/A

ACN or BRN: 49 720 598 228

Business or trading name: Spine Society Australia

Registered office street address

The Adelaide Centre for Spinal Research

Institute of Medical and Veterinary Science

PO Box 14 Rundle Mall

Adelaide SA 5000

Postal address

17 Erin Street,

Richmond,

Victoria 3121

Partnership details (if the entity is a partnership, please list the names of all partners)

N/A

1.8 Preferred mode of contact

☐ Phone

✓ E-mail

☐ Fax

☐ Postal

☐ Other

Section 2 Description of service, and compliance with regulatory requirements

2.1 Service type

✓ A procedure

☐ A diagnostic test

☐ Other medical service

The proposed service is a surgical procedure for the implantation of a medical device used in the treatment and management of cervical DDD in patients who have failed to respond to conservative care. The procedure is known as CDA and involves surgical insertion of an artificial disc. Under general anaesthesia, the patient is placed in the supine position. The anterior cervical spine is exposed, and following standard discectomy and decompression of the neural elements, an artificial disc prosthesis is placed between the vertebrae.

This application considers the four artificial discs most commonly used, and best studied, for the treatment of cervical DDD in Australia: Medtronic's Prestige® and Bryan®, Synthes' ProDisc-C®, and DePuy Spine's Discover™ disc. Further information on the devices is provided in **Appendix 1**.

2.2 Name of service

The service is CDA for the treatment of cervical DDD in the absence of osteoporosis and prior fusion at the same level, who have failed conservative therapy. The proposed indication falls within the TGA approved indication for CDA (see Section 2.5.3).

2.3 Is the proposed service already covered under an existing MBS item?

☐ Yes

✓ No

Following the MSAC recommendation made in March 2006, AIDR was approved for interim funding for single level AIDR in patients with single level intra lumbar disc disease in the absence of osteoporosis and prior fusion at the same level, who have failed conservative therapy. The use of AIDR in the lumbar indication is presently covered by MBS item numbers 48691, 48692 and 48693. MSAC, however, recommended against public funding for AIDR in the cervical spine.

This application seeks to expand the Medicare approved indications for AIDR to include patients with DDD in the cervical spine on the basis of newly available clinical evidence.

2.3.1 If yes

What is the item number(s)?

How does the proposed service differ from the service(s) covered under this item number(s)?

REGULATORY REQUIREMENTS

2.4 Does the proposed service involve the use of a medical device or diagnostic test or pharmaceutical product (e.g. a radioactive tracer)?

✓ Yes

☐ No

2.4.1 If yes, please provide the name of the manufacturer and sponsor of the device/diagnostic test/pharmaceutical product.

Manufacturer/Sponsor (device) name

Various: includes

1. Medtronic Sofamor Danek Australia Pty Ltd (Prestige® and Bryan® artificial discs)
2. Synthes Australia Pty Ltd (Prodisc-C® artificial disc)
3. DePuy Spine (Discover™ artificial disc)

2.5 Is the device or diagnostic test or pharmaceutical product used in the proposed procedure/test/service exempt from the regulatory requirements of the Therapeutic Goods Act 1989?

☐ Yes

✓ No

2.5.1 If yes, provide supporting documentation to this effect.

N/A

2.5.2 If no, has it been listed/registered on the Australian Register of Therapeutic Goods with the TGA?

✓ Yes, see 2.5.3

☐ No, see 2.5.4

2.5.3 If listed/registered, please provide the following details.

TGA listing/registration number

Medtronic: Bryan® (100706); Prestige® (100706)

Synthes: Prodisc-C (133399)

DePuy Spine (J & J): Discover™ (147793)

The indication (if registered)

Disc arthroplasty is indicated for:

- *Dynamic stabilisation of spine following total discectomy for treatment of axial pain or neurological compression*

The Discover™ Artificial Cervical Disc is specifically indicated for treatment of symptomatic cervical DDD at one or two adjacent levels between C3 and C7. Cervical DDD is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height.

The Bryan® Artificial Cervical Disc is specifically indicated for use in skeletally mature patients undergoing primary surgery for treatment of mechanically stable, degenerative disc disease of the cervical spine at any one level or two adjacent levels between C3 and C7, as demonstrated by signs and/or symptoms of radiculopathy and/or myelopathy associated with spondylotic foraminal or canal stenosis and/or disc herniations.

The Prodisc C™ Total Disc Replacement is indicated in sketally mature patients for reconstruction of the disc from C3 to C7 following single-level discectomy for intractable symptomatic cervical disc disease. Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging CT, MRI or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height.

The Prestige® Cervical Disc is generally indicated for use at any level from C2/C3 to C7/T1 for cervical degenerative discopathy and instability:

- in patients with adjacent levels either congenitally or surgically fused
- for primary surgery for degenerative discopathies or extensive anterior decompression
- revision surgery for failed disc operation, stenosis, post-operative instability
- pseudarthrosis or failed arthrodesis.

A copy of any relevant report (e.g. TGA evaluation report) or TGA correspondence relating to the approval

See attachments.

2.5.4 If not listed/registered, is listing/registration pending?

N/A

Section 3 Commercial-in-confidence material

The Department of Health and Ageing undertakes that it will treat this application and its contents as commercial-in-confidence if you so request. The application and/or its contents will only be released to those people who will consider it for the purpose of advising the Minister. Such people will be bound by deeds of confidentiality, which must be signed before receipt of any commercial-in-confidence material.

If your application needs to be treated as commercial-in-confidence, you should complete the information below to specify which data must be treated as commercial-in-confidence, sign on the following page, and return these pages to the MSAC Secretariat, either with your application, or as a separate document if you are lodging your application electronically. Commercial-in-confidence information will not be included in the final printed report.

Documents in the possession of the Department are subject to the requirements of the Freedom of Information Act 1982. This means that the Department may be required to grant access to documents in its possession. Even if a document is stamped commercial-in-confidence, this does not mean that access under this Act can be denied. However, the Department is required to consult with the author of the document when that document appears to contain commercial-in-confidence material, and take the author's views into account when deciding to grant/not grant access to documents.

Name of procedure/test/service

Cervical disc arthroplasty

Name of applicant

Spine Society of Australia

Is any part of the application commercial-in-confidence?

✓ Yes

☐ No

If yes, please specify the parts of the application and reasons.

The cost of each of the artificial discs is to be considered commercial-in-confidence. This extends to the product specific cost-effectiveness results presented in the Appendices. Finally, the utility weights used in the economic evaluation are to be treated as commercial-in-confidence until further notice.

I have read the above and I acknowledge and accept that this application and/or its contents will be made available to those people who will consider it for the purpose of advising the Minister for Health and Ageing.

Signature

Signed by: Graeme Brazenor

Secretary, Spine Society of Australia

Section 4 Indication for the service, and therapeutic claim

4.1 What are the proposed indications for the new procedure/ test/ service?

Cervical disc arthroplasty is indicated for:

- Dynamic stabilisation of spine following total discectomy for treatment of axial pain or neurological compression

The Discover™ Artificial Cervical Disc is specifically indicated for treatment of symptomatic cervical DDD defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height.

The Bryan® Artificial Cervical Disc is specifically indicated for use in skeletally mature patients undergoing primary surgery for treatment of mechanically stable, degenerative disc disease of the cervical spine at any one level or two adjacent levels between C3 and C7, as demonstrated by signs and/or symptoms of radiculopathy and/or myelopathy associated with spondylotic foraminal or canal stenosis and/or disc herniations.

The Prodisc C™ Total Disc Replacement is indicated in sketally mature patients for reconstruction of the disc from C3 to C7 following single-level discectomy for intractable symptomatic cervical disc disease. Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging CT, MRI or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height.

The Prestige® Cervical Disc is generally indicated for use at any level from C2/C3 to C7/T1 for cervical degenerative discopathy and instability:

- in patients with adjacent levels either congenitally or surgically fused
- for primary surgery for degenerative discopathies or extensive anterior decompression
- revision surgery for failed disc operation, stenosis, post-operative instability
- pseudarthrosis or failed arthrodesis.

The proposed indication falls within the TGA approved indication for CDA (see Section 2.5.3).

4.2 State the therapeutic claim that you are making for this service (e.g. clinical benefit; relative safety).

There is strong evidence showing that CDA is clinically superior to ACDF. In the study by Heller *et al* (2009), patients in the Bryan® artificial disc group had a statistically greater improvement in the primary outcome variables: neck disability index score ($P = 0.025$) and overall success ($P = 0.010$), at 24 months after surgery, compared to patients treated with ACDF. Safety data indicate that there is no overall difference in adverse events between the two procedures. However, at three years follow-up, Anderson et al (2008), found patients treated with ACDF required significantly more re-operations than patients treated with CDA ($P = 0.045$).

Additionally, the study reported by Mummaneni *et al* (2007) observed a statistically significant improvement in overall success using the Prestige® disc relative to ACDF ($P = 0.0053$) at 24 months. The Murrey *et al* (2009) study reported similar results in terms of the Prodisc® disc with a significant difference ($P = 0.0105$) at 24 months.

Section 5 Clinical need, public health significance and patient selection

5.1 Provide a summary of information about the condition for which the proposed procedure/test/service is to be used.

See **Appendix 2** for further details.

Degenerative disease of the cervical spine is extremely common. A combination of advancing age and injury from single traumatic events or long periods of excessive loading combine to cause degeneration of the intervertebral discs. The radiological evidence of disc degeneration increases with age with patients in their fifties's experiencing about a 50% incidence. More often than not, however, the degeneration remains asymptomatic.

Degeneration can cause neck pain alone or it can be responsible for the development of cervical disc herniation, cervical spondylotic foraminal compression of nerve roots or cervical spondylotic myelopathy. The true incidence of neck pain in Australia is unknown. However, the one year prevalence has been shown to be 36% (95% CI 22-55%) in Scandinavia, 26% (95% CI 13-39%) in Europe and 13% (95% CI 0 – 58%) in Asia (Fejer *et al*, 2006). The vast majority of patients with neck pain do not require surgery. When nerve roots are compressed (radiculopathy) the symptom may present as arm pain and numbness.

The true incidence of radiculopathy in Australia is unknown. It is reported in Italy, however, that the reported incidence of radiculopathy due to cervical spondylotic radiculopathy is 3.5 cases per 1000 population (Salemi *et al*, 1996). In a population-based study in Rochester, Minnesota USA (Radhakrishnan *et al*, 1994), the annual incidence of documented cervical radiculopathy for men and women from all causes was 107.3 and 63.5 cases per 100,000 population, respectively.

When myelopathy is present, the compression is to the spinal cord and the symptoms are that of progressive, irreversible loss of function of the legs and/or arms by means of an incoordinated spastic gait or with difficulty performing fine motor tasks in the upper limb. Over time, myelopathy will eventually progress to partial or complete paraplegia or quadriplegia. The incidence of Cervical Spondylotic Myelopathy (CSM) is unknown, however 23.6% of 585 patients with tetraparesis or

paraparesis admitted to a United Kingdom regional neuroscience center had CSM (Moore *et al*, 1997).

The arm pain associated with cervical disc herniation has a good chance of spontaneous recovery within six-eight weeks, whereas about 50% of cases of arm pain due to Spondylotic radiculopathy recover to become intermittent and 25% become constant.

Time away from work due to persisting radiculopathy generates a substantial impact on the wider community through long term use of analgesics with possible addiction/tolerance, continued usage of conservative treatment (i.e. rest, pain medication, NSAIDs, anti-inflammatory and analgesic medication, physical therapy).

5.2 Please provide a copy of any data available to support the information described in 5.1 above.

A complete set of references is included with this application.

5.3 In which patients with the condition will the proposed service be used? What are the contraindications in this patient group?

The use of CDA will be limited to patients with the following indications:

1) Cervical disc herniation with radiculopathy (arm pain, numbness, weakness) with failure to respond to conservative treatment.

2) Cervical spondylotic radiculopathy with failure to respond to conservative treatment.

3) Cervical spondylotic myelopathy

Contraindications associated with each disc differ. These are outlined in the Product Information for each product.

The non product-specific contraindications to cervical disc arthroplasty associated with the conditions outlined above include:

- Osteoporosis (as indicated by a T-score < -2.5)
- Spondylolisthesis at the symptomatic level
- Previous attempted anterior or posterior fusion at the symptomatic level
- Previous laminectomy or foraminectomy at the symptomatic level
- Recent/current infection at the symptomatic level
- Moderate-severe facet arthropathy or iatrogenic facet injury at the symptomatic level
- Fracture of either adjacent vertebra, recent or past.

- Loss of disc height >50%
- Neck/arm pain of unknown aetiology
- Paget's disease, osteomalacia or other (non-osteoporotic) metabolic bone disease
- Allergy to cobalt, chromium, molybdenum, titanium or (with the Prodisc-C) polyethylene
- Sequestrated disc fragment lying dorsal to a vertebra in the spinal canal

5.4 Are there any particular considerations in relation to access to the proposed service which MSAC should consider when reviewing the application?

No

Section 6 Where the service will be performed, and who will perform it

6.1 How and where will the new service be used?

Cervical disc arthroplasty will be used by spinal surgeons (orthopaedic or neurosurgical) on a referral basis. It will be used as last line treatment only, once conservative treatment has failed and it is clear that further spontaneous recovery is not possible. Patients requiring surgery for this condition would currently be treated by anterior fusion and decompression of nerve roots with plate fixation (MBS Items 48660, 40330, 48684). It is the opinion of the Spine Society that approximately 30% of these procedures would be replaced by CDA.

6.2 Specify which group of professionals will provide the service.

Spinal surgeons (specialist orthopaedic surgeons or neurosurgeons) who are involved in the treatment of DDD will provide the service.

6.3 Specify what different or additional equipment and ancillary staff are required to perform the service compared to current services.

A slightly different set of surgical instruments is required than that used for fusion surgery. These instruments are supplied by the manufacturer of the disc. No additional staff are required, though it should be noted that the use of CDA is expected to require less resources per procedure relative to ACDF. Of particular note, autografts associated with ACDF would require an additional 20 minutes operating room time and anesthetist time. Clinical opinion sought also indicates that those undergoing ACDF may require additional days in hospital following surgery.

Section 7 Estimated utilisation

7.1 Estimate the likely annual number of patients who will use the proposed service

The full details of the calculations used to estimate the likely utilisation of CDA in Australia are presented in **Appendix 2**. Similarly, **Appendix 2** presents a number of sensitivity analyses illustrating the sensitivity of these estimates to changes in key assumptions.

In brief, it is estimated that the expected number of patients with cervical DDD to be treated with CDA will be 355 in 2011, increasing to 415 in 2013 (shown in **Table 1**). See **Appendix 5** for a more comprehensive assessment, including the likely annual financial implications to the Medicare budget.

Table 1 Total number of Australian patients with cervical DDD eligible for CDA.

Calendar year	2006	2007	2008	2009 [a]	2010 [b]	2011 [b]	2012 [b]	2013 [b]
Total number of patients treated with anterior fusion in lumbar, thoracic or cervical spine.	868	965	1,085	1,244	1,353	1,477	1,602	1,727
Estimated number of patients treated with anterior fusion in cervical spine	694	772	868	995	1,082	1,182	1,282	1,382
Estimated number of patients treated with CDA	N/A	N/A	N/A	N/A	N/A	355	385	415

Abbreviations: CDA = cervical disc arthroplasty; DDA = degenerative disc disease
Note: Analysis assumes CDA is granted reimbursement via the MBS from 2011 onwards
[a] 2009 figures were estimated based on MBS statistics for the first quarter.
[b] 2010-2012 figures are projected estimates

7.2 Estimate the change, if any, in the use of other services, especially the comparator identified in Section 8

The reduction in the number of cases of ACDF (ie, item number 48660) is expected to be equal in size to the CDA usage presented in **Table 1**. For example, in 2011 there will be 355 fewer cases resulting in approximately 827 ACDF's that year (**Table 2**). Note that all patients receiving CDA will be taken from the existing ACDF population.

Table 2 Total number of Australian patients with cervical DDD eligible for ACDF

Calendar year	2006	2007	2008	2009	2010	2011	2012	2013
Total number of patients treated with anterior fusion in lumbar, thoracic or cervical spine.	868	965	1,085	1,244	1,353	1,477	1,602	1,727
Estimated number of patients treated with anterior fusion in cervical spine	694	772	868	995	1,082	1,182	1,282	1,382
Net estimate of patients treated with ACDF after CDA inclusion	N/A	N/A	N/A	N/A	N/A	857	897	967

Abbreviations: ACDF = anterior cervical discectomy and fusion; CDA = cervical disc arthroplasty
Note: Analysis assumes CDA is granted reimbursement via the MBS from 2011 onwards

Section 8 Choice of comparator

8.1 What is the most commonly used diagnostic or therapeutic intervention for this condition at present? What is the appropriate comparator(s) for the proposed service?

Anterior cervical fusion (48660)

Nerve root decompression (40330)

Segmental fixation (48684)

8.2 Will the proposed procedure/test/service be used in addition to, or instead of, the comparator(s) identified in 8.1 above?

Cervical disc arthroplasty will be used instead of approximately 30% of anterior cervical disc fusions.

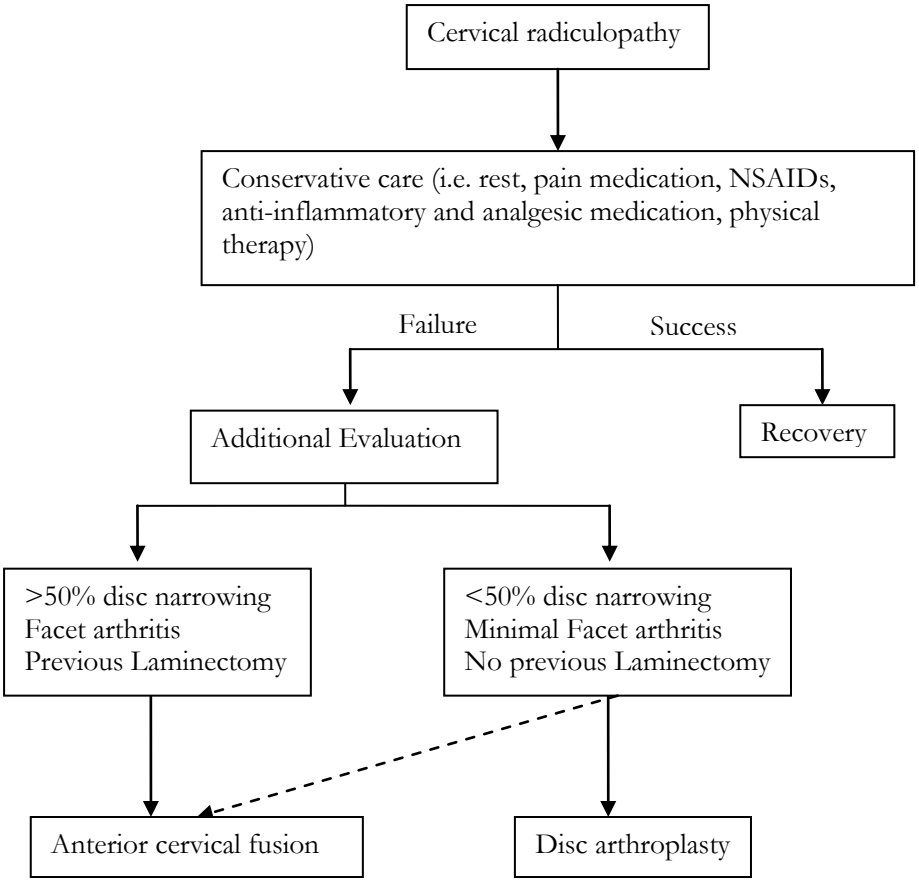
8.3 How does the proposed procedure/test/service differ from the comparator(s)?

Both procedures are performed with the primary aim of decompressing the spinal cord or nerve roots. This procedure requires removal of the disc to gain access to the neural structures. At the end of the procedure, the disc space needs to be reconstructed. In the past, the only procedure available was to fuse the disc space with a bone graft (eliminating motion). Disc arthroplasty is now available to reconstruct the disc space while maintaining movement. The maintenance of movement has important theoretical advantages in potentially reducing the incidence of degeneration at adjacent segments. It is predicted that this may result in lower long-term morbidity that would be reflected by a reduced need for further surgery or non operative medical treatment.

8.4 Provide a clinical flowchart to illustrate any differences in the clinical pathway linking the procedure/test/service with patient outcomes with that of the comparator service(s).

A clinical flowchart describing the basic procedures required for the delivery of CDA for the treatment of cervical DDD is presented in Figure 1.

Figure 1 Clinical flowchart for CDA in cervical DDD



Section 9 Summary of the literature search

9.1 Provide a copy of the literature search which has been undertaken to identify evidence in support of the safety and effectiveness of the proposed service.

A full review of the literature was undertaken in order to identify all clinical studies in humans (ie, randomised trials, non-randomised comparative studies, and case series) and systematic reviews examining the safety and efficacy of CDA, using the Prestige®, Bryan®, Prodisc-C® or Discover™ disc, in the treatment of cervical DDD. The literature review included searching the grey literature to uncover research performed by Health Technology Assessment agencies in other geographies.

Please refer to **Appendix 3** for a copy of the full literature search and results.

9.2 If there are other sources of evidence which support the proposed use of the service, please list them and provide copies.

FDA reports on:

1) Prestige® cervical artificial disc

2) Bryan® cervical artificial disc

3) Prodisc-C® cervical artificial disc

4) Discover™ cervical artificial disc

Section 10 Summary of the evidence

10.1 From the literature search described in Section 9.1, provide a list of the studies which support the use of the service for the proposed indication(s).

Please refer to **Appendix 4**.

10.2 Classify the studies in 10.1 according to hierarchy of evidence as set out in Part 2 (Application Guidelines)

Please refer to **Appendix 4.**

10.3 Provide a summary of the evidence for the effectiveness and safety of the service based on the studies in 10.1.

Though a summary of the evidence is provided below, please refer to **Appendix 4** for full details.

In total, 18 publications examining the safety and efficacy of disc arthroplasty for the treatment of cervical DDD are included in this submission. These 18 publications referred to 8 different studies. Of these eight studies, six were RCTs, one was a prospective comparative cohort study, and one was a retrospective pilot study. They were generally considered to be of good quality with five studies assessed as level II evidence according to the NHMRC levels of evidence. These studies represent a significant body of evidence and experience in the use of artificial discs to treat cervical DDD.

10.4 Based on the studies, assess the effectiveness and safety of the new service compared with that of the comparator identified in Section 8.

Comparative efficacy

Since the initial MSAC application for artificial disc replacement (Application 1090), there has been a significant increase in the body of evidence published on the efficacy and safety of cervical artificial disc. Three large, prospective, RCT's have been conducted as part of FDA-approved IDE studies for the Bryan®, Prestige® and Prodisc-C® artificial cervical disc. The primary outcome in each trial, 'overall success', included both efficacy and safety results. This outcome was consistently achieved by significantly more patients treated with cervical artificial disc when compared to ACDF.

According to in Heller *et al* (2009), overall success was achieved in 82.6% (95% CI: 77.1%–87.3%) of the patients in the Bryan® artificial disc group and 72.7% (95% CI: 65.8%–78.8%) of patients in the ACDF group at 24 months follow up. This difference of 9.9% (95% CI: 2.0%–17.9%) was statistically significant ($P = 0.010$). In Mummanemi *et al* (2007), overall success rates for the Prestige artificial disc group were significantly higher than the ACDF group at 24 months following surgery (79.3% versus 67.8%, respectively; $P = 0.005$). In Murrey *et al* (2009), the overall success rate was 72.3% for the Prodisc-C® group and 68.3% for the ACDF group at 24-months follow-up (P = 0.0105).

Comparative safety

The main difference of note between artificial cervical disc and ACDF observed in these studies was the number of re-operations required. In Anderson *et al* (2008), re-operations on the cervical spine (at all levels) at three-year follow-up occurred in 5.4% of patients treated with Bryan® artificial disc and 7.7% of patients treated with ACDF ($P = 0.045$). The total number of cervical spine re-operation at all levels was also statistically greater in the ACDF group compared with the artificial disc group (21 versus 14, respectively; *P* value not reported). Overall re-operations were performed at the index level 12 times and at the adjacent level 11 times in the ACDF group, compared with 7 and 8 times in the Bryan® artificial cervical disc group, respectively. Four patients in the ACDF and one in the Bryan® artificial disc group had more than one re-operation. In the study by Mummaneni *et al* (2007), the Prestige® artificial disc group had a significantly lower re-operation rate at the adjacent segment level compared with ACDF (3 versus 9 patients, respectively; $P = 0.0492$) at two years of follow-up. In the study by Murrey *et al* (2009), it was observed that, at two years of follow-up, one patient in the ACDF group required a re-operation and three a supplemental fixation. In the Prodisc-C® group, no re-operations or supplemental fixations were required.

For the complete set of efficacy and safety data for CDA in the treatment of cervical DDD, please read **Appendix 4**.

Section 11 Economic information

11.1 Provide a list of all economic studies of the service identified in your literature search.

The economic literature sourced and used in this application is discussed in **Appendix 5**.

11.2 Make an assessment of the quality of the studies and their relevance to the Australian setting.

Appendix 5 provides a comprehensive discussion of the studies and their relevance to the current application.

11.3 List the components of the service and their respective costs as well as the source(s) of information used to derive the costs.

The costs of each of the discs considered in this application are presented in **Table 3**.

Table 3 Costs of artificial discs

Artificial disc	Acquisition cost
Bryan® disc	[redacted]
Prestige® disc	[redacted]
Prodisc-C® disc	[redacted]
Discover™ disc	[redacted]

A full description of the methods and results of the formal economic evaluation are presented in **Appendix 5**.

11.4 State the proposed fee for the service and the reasons why this fee is deemed appropriate.

The proposed fee is equivalent to the MBS fee for lumbar AIDR total disc replacement (MBS item number 48691). That is, a fee of $1695.20 is requested and assumed throughout this application. Given that the requested procedure is based on the same technology, with equivalent resources required, this is appropriate.

11.5 State the fee for the comparator.

The comparator procedure, cervical fusion, is reimbursed at a fee of $1023.25. It is worth noting, however, that additional procedures are required to be performed in conjunction with the comparator that are not required in the case of CDA (ie, decompression and bone graft). These are covered in more detail in the economic evaluation presented in Appendix 5.

11.6 Provide a formal economic evaluation if required.

A formal economic evaluation is presented in **Appendix 5**.

Section 12 Diagnostic tests

12.1 Assessing the evidence for the clinical impact of the test

12.1.1 Is the test to be used for screening for a disease/condition (ie in asymptomatic subjects) or for diagnosis and /or management of a disease / condition in subjects who are known to have the disease?

12.1.2 Provide evidence of the effective management of the disease / condition being diagnosed / managed by the test.

12.1.3 Provide any available evidence that the use of the test influences clinical decision making or health outcomes

12.2 Assessing the evidence for the performance of the test.

12.2.1 Reports on the performance of the test

12.2.2 Validity, accuracy, reliability and applicability

Section 13 Additional clinical opinion

This section asks applicants to identify clinical experts who can be invited to provide advice.

If you want to identify more than three people, provide additional details as an attachment. Applicants are asked to provide details of a clinical expert(s) who can be contacted by MSAC for clinical advice during the assessment process (this may be the applicant).

Please note that nominated experts will need to declare any potential conflict of interest in any submission or advice to MSAC.

First clinical expert

Dr Peter McCombe

Orthopaedic Surgeon

Level 9 Watkins Medical Centre

225 Wickham Terrace

Brisbane Qld 4000

Ph: 07 38317039

Email: pmccombe@bigspine.net

Second clinical expert (if desired)

Dr William Sears

Neurosurgeon

26 Stanhope Rd

Killara NSW 2071

Ph: 02 9880 2446

Email: william.sears@mac.com

Third clinical expert (if desired)

Dr Matthew Scott Young

Orthopaedic Surgeon

PO Box 8295

Gold Coast mail centre

Qld 9726

Ph: 07 5528 6477

Email: syortho@ozdoc.com.au

CHECKLIST

Make sure you have:

- ☐ **Provided contact details (Section 1)**
- ☐ **Identified commercial-in-confidence information (Section 3) and signed the relevant box)**

For a diagnostic test

- ☐ **Completed Section 12 (and not Sections 9 or 10)**

For other services

- ☐ **Provided full details of the literature search (Section 9)**
- ☐ **Provided a table classifying studies according to the level of evidence (Section 10.2)**
- ☐ **Provided a summary of the evidence for the effectiveness and safety of the service (Section 10.3)**
- ☐ **Compared the proposed new service to the appropriate comparator (Section 10.4)**

For all services

- ☐ **Provided relevant costing information (Section 11)**
- ☐ **Attached all supporting documents/articles**

Reference list

Anderson PA, Sasso RC, and Riew KD. (2008) Comparison of adverse events between the Bryan artificial cervical disc and anterior cervical arthrodesis. *Spine* 33:1305-1312.

Fejer R, Kyvik KO, and Hartvigsen J. (2006) The prevalence of neck pain in the world population: A systematic critical review of the literature. *European Spine Journal* 15:834-848.

Heller JG, Sasso RC, Papadopoulos SM, Anderson PA, Fessler RG, Hacker RJ, Coric D, Cauthen JC, and Riew DK. (2009) Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled, clinical trial. *Spine* 34:101-107.

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Moore PA and Blumhardt LD. (1997) A prospective survey of the causes of non-traumatic spastic paraparesis and tetraparesis in 585 patients. *Nature* 35(6):361-367

Mummaneni PV, Burkus JK, Haid RW, Traynelis VC, and Zdeblick TA. (2007) Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: A randomized controlled clinical trial. *Journal of Neurosurgery: Spine* 6:198-209.

Murrey D, Janssen M, Delamarter R, Goldstein J, Zigler J, Tay B, and Darden B. (2009) Results of the prospective, randomized, controlled multicenter Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. *Spine Journal* 9:275-286.

Radhakrishnan K, Litchy WJ, O'Fallon WM, and Kurland LT. (1994) Epidemiology of cervical radiculopathy: A population-based study from Rochester, Minnesota, 1976 through 1990. *Brain* 117:325-335.

Salemi G, Savettieri G, Meneghini F, Di Benedetto ME, Ragonese P, Morgante L, Reggio A, Patti F, Grigoletto F, and Di Perri R. (1996) Prevalence of cervical spondylotic radiculopathy: A door-to-door survey in a Sicilian municipality. *Acta Neurologica Scandinavica* 93:184-188.