



Australian Government
Department of Health and Ageing



Horizon Scanning Technology Prioritising Summary

**DuraSeal™ Dural Sealant System for cerebral
spinal fluid leaks**

December 2005



**Australian
Safety
and Efficacy
Register
of New
Interventional
Procedures -
Surgical**



**Royal Australasian
College of Surgeons**

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Enquiries about the content of the report should be directed to:

HealthPACT Secretariat
Department of Health and Ageing
MDP 106
GPO Box 9848
Canberra ACT 2606
AUSTRALIA

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This Horizon scanning prioritising summary was prepared by staff from the Australian safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S).

Horizon Scanning Technology Prioritising Summary

Name of Technology:

DuraSeal™ Dural Sealant System (Confluent Surgical, Inc., in Waltham, [Massachusetts](#))

Purpose and Target Group:

DuraSeal™ Dural Sealant System is a synthetic gel used in cranial neurosurgical procedures, in particular dura mater surgery. It is designed to seal the sutured dura mater by forming a watertight closure that aids in the prevention of cerebrospinal fluid leakage. If the dura mater is not completely closed during surgery then the cerebrospinal fluid can leak which can cause persistent, often severe headache, meningitis or even death.

Stage of Development (in Australia):

- Experimental
- Investigational
- Nearly established
- Established
- Established but changed indication or modification of technique
- Should be taken out of use

The Duraseal™ Dural Sealant System is registered in the Australian Register of Therapeutic Goods (ARTG number: 106863).

International Utilisation:

| COUNTRY | LEVEL OF USE | | |
|--------------------------|-----------------|-------------|-----------------|
| | Trials underway | Limited use | Widely diffused |
| Netherlands | | | ✓ |
| South Africa | | | ✓ |
| United Arab Emirates | | | ✓ |
| United States of America | | | ✓ |

Impact Summary:

Background

One of the risks of brain surgery is that there is the potential for leakage of cerebrospinal fluid (CSF). This is because the dura mater which lines the inner surface of the skull and is the outermost tough fibrous membrane that surrounds the brain has to be cut open so the surgeon has access to the brain. At the end of brain surgery, the dura mater needs to

be sutured closed in an attempt to make it watertight and prevent any CSF from leaking. If CSF leaks after surgery, serious complications can arise such as severe headaches, infection and meningitis as the leakage can create a potential pathway for infection to reach the brain and spinal cord.

When the dura mater is closed during surgery, the surgeon will attempt to obtain a watertight closure, however the dura may dry out which results in small gaps remaining when the dura is sutured closed. Suturing can also produce small holes from where the needle passes through the dura which may result in tiny holes that may leak CSF. Despite meticulous attempts by surgeons to close the dura with no leaks, many patients experience symptoms that result from CSF leakage which can delay the healing of surrounding tissues.

This prioritising summary details the use of the DuraSeal™ Dural Sealant System which has been developed to provide a true watertight closure of the dura mater after cranial neurosurgical procedures. Following suturing, the surgeon is able to spray DuraSeal™ onto the excision, sealing the needle holes and other small gaps. The sealant sets within minutes and will stay in place, sealing the incision whilst healing occurs naturally underneath. Once the dura is healed, the DuraSeal™ will return to a liquid form and is absorbed naturally by the body.

The DuraSeal™ Dural Sealant System is the first and only FDA approved cranial dural sealant. It is designed to produce a watertight dural closure so that CSF does not leak and cause infection. The DuraSeal™ is a polyethylene glycol hydrogel sealant and consists of synthetic absorbable materials. It is packaged in a single use kit, with an applicator to apply the sealant to the incision site. It is stored at room temperature for convenience and quick preparation. The DuraSeal™ is composed of two solutions, a polyethylene glycol (PEG) ester solution and a trilycine amine solution (commonly referred to as the 'blue' and 'clear' precursors respectively) (Confluent Surgical 2005). The use of the colour blue makes the DuraSeal™ easy to visualise and aids in determining where it has been sprayed. When these two solutions mix together in the applicator, they form a sealant gel which has demonstrated a 98% seal which has been evaluated intra-operatively (FDA New Device Approval 2005). The sealant is not permanent and is absorbed approximately four to eight weeks after surgery which allows for enough time for healing to occur. DuraSeal™ is not to be used and applied to confined bony structures where nerves are present as neural compression could result in sealant gel swelling. This could result in the hydrogel swelling up to 50% of its original size.

Clinical Need and Burden of Disease

Conventional techniques of preventing CSF leaks are often insufficient and do not stop CSF leaks completely. Duraseal™ Dural Sealant System was designed to be used in any type of surgery that would require watertight closure of the dura mater to stop CSF leaks.

Therefore, if proven to be safe and effective, Duraseal™ may fill this need of a reliable and safe method of stopping and preventing CSF leakage.

Estimated Speed, Geographic and Practitioner Use, Patterns of Diffusion in the Health System

According to the Food and Drug Association report (Summary of Safety and Effectiveness Data), the DuraSeal™ Dural Sealant System has been approved for commercial sale in the European Economic Area (EEA) since June 2003, in South Africa since January 2004, in the United Emirates since March 2004 and in Australia since August 2004 (ARTG Number 106863, Class III). DuraSeal™ is currently been applied in a centre in Perth where it is being used as a barrier for serious skin burns as well as cardiac and thoracic applications [personal communication, Confluent Surgical Representative 2005].

The DuraSeal™ System has not been withdrawn from any country due to reasons related to safety and effectiveness of the device.

Existing Comparators

At present surgeons are using a variety of methods to insure that the surgical incision site does not leak cerebrospinal fluid. Some surgeons used the method called “oversew” which results in surgeons sewing the stitches closer together in the tissue immediately overlying the surgical site. Other methods include surgeons packing the area with other tissues from the patient, such as fat, muscle or connective tissue.

There are a few dural substitutes on the market. They either fall into one of two categories - absorbable and permanent. There are few commercially available absorbable dural substitutes however there are a large number of products in the permanent category, including various synthetic materials and processed allograft and xenograft tissues from various anatomic sites. BioGlue® and Tisseal® are two completely synthetic glues which are made of animal and human products which provide sealants in neurosurgical procedures.

Estimated Cost Impact

DuraSeal™ is currently available in Australia for \$499.00 for one 5ml kit [M. Bryant, personal communication, Confluent Surgical Representative 2005]. This kit is designed to be used on one patient only.

Efficacy and Safety Issues

List of Studies Found

| | |
|-------------------------|---|
| Total number of studies | 2 |
| Case series | 2 |

The studies included in this summary are highlighted in bold in the reference list. These studies were chosen as they represent the body of evidence currently available on Duraseal™.

The Duraseal™ US pivotal trial was a prospective, multi-centre, non-randomised, single arm clinical investigation to determine the safety and efficacy of Duraseal™ which enrolled 111 patients. Two patients were lost to follow-up while another two died (unrelated to study treatment), leaving 107 patients which completed the 3 month follow-up screening. Of the 111 patients enrolled into this study, 67 patients (60.4%) experienced spontaneous CSF leakage intra-operatively while 44 patients (39.6%) had CSF leakage after the Valsalva manoeuvre. Duraseal™ successfully stopped CSF leakage in all patients during the intra-operative assessment. Freedom from CSF leakages at 135 days post-surgery was 95.5% (Kaplan-Meier estimate), the time to first endpoint CSF leakage ranged from 7 to 29 days post-surgery (Duraseal Dural Sealant System, Summary of Safety and Effectiveness Data, FDA 2005).

The prospective, non-randomised, single centre clinical trial conducted by Boogaarts *et al.* (2004) evaluated the safety and performance of Duraseal™ in preventing CSF leakage. A total of 49 patients undergoing a variety of intradural, cranial or spinal procedures were enrolled into this study. Spontaneous CSF leakage was observed in 34 patients (69%) while a further 12 patients with CSF leakage were identified after a Valsalva manoeuvre to 20cm H₂O which resulted in all 46 of these patients being treated using Duraseal™. Three patients did not exhibit spontaneous CSF leakage and thus did not require treatment with Duraseal™. The sealant was successful in stopping spontaneous CSF leakage in all 46 patients who received it. Forty two patients completed the one month follow-up but two patients refused to return while another two patients died (One due to basilar artery thrombosis and the other due to hematoma). A total of 41 patients completed the three month end-of-study follow-up, one patient died due to sepsis after a diverticulitis resulting in sigmoid resection. Two patients (4.9%) were identified to have a CSF leak at the three month follow-up screening. The first patient has a midline-suboccipital craniotomy for a high-grade glioma. One month post-surgery a pseudomeningocele was found, but it was asymptomatic. The second patient was treated for a temporal arachnoid cyst. At the one-month follow-up visit the patient presented with rhinorrhea which was treated with an external lumbar drain, bed rest and oxygen for five days. The patient presented again at three months with rhinorrhea, which was successfully operated (Boogaarts *et al.* 2004).

Both studies did not observe any unanticipated adverse effects due to the use of Duraseal™. The US pivotal study reported two patient deaths (discharged from hospital)

which were attributed to their prior condition and the surgical procedure undertaken. A total of 32 /111 (29%) patients suffered 54 serious adverse events, 78% of these incidents were determined to be non-Duraseal™ related while the relation to Duraseal™ was ‘undetermined’ for the other 22% of serious adverse events. The patients who had serious adverse events in the ‘undetermined’ group, included six patients with deep surgical site infection, three patients with cerebrospinal fluid leaks and one patient with headaches that did not respond to standard treatment. These serious adverse events are comparable to expected outcomes of intracranial surgery (Duraseal Dural Sealant System, Summary of Safety and Effectiveness Data 2005).

The US pivotal study reported an overall rate of surgical wound infection of 9/111 (8.1%) with a 7.2% rate of deep surgical infection, which all required repeat surgery. The overall CSF leak in this study was 5/111 (4.5%) (Duraseal Dural Sealant System, Summary of Safety and Effectiveness Data, FDA 2005). In the trial by Boogaarts *et al* (2004), there were 51 adverse events with 30 neurological events. The neurological adverse events were related to the disease or operation; none were related to the dural sealant. Boogaarts *et al.* (2004) stated that there was no relation between any of the adverse events and the DuraSeal™ Dural Sealant System.

Ethical Issues

No issues were identified from the retrieved material.

Cultural or Religious Considerations

No issues were identified from the retrieved material.

Other Issues

No issues were identified from the retrieved material.

Recommendation:

A small amount of evidence exists on the safety and efficacy of DuraSeal™ Dural Sealant System. Long-term safety and efficacy data from randomised controlled trials will be required before this procedure can be widely accepted. Due to the small number of trials available about this procedure, it is recommended that the following be conducted:

- | | |
|--|--|
| <input type="checkbox"/> Horizon Scanning Report | <input type="checkbox"/> Full Health Technology Assessment |
| <input checked="" type="checkbox"/> Monitor | <input type="checkbox"/> Archive |

References:

Australian Government Department of Health and Ageing. Australian Government Department of Health and Ageing. Medicare Benefits Schedule. Last updated November 2004. <http://www7.health.gov.au/pubs/mbs/mbsnov04/index.html> [Accessed November 2005].

Boogaarts JD, Grotenhuis JA, Bartels RH, Beems T. Use of a novel absorbable hydrogel for augmentation of dural repair: Results of a preliminary clinical study. *Operative Neurosurgery* 2005; 57 (1): 146-151.

Confluent Surgical. DuraSeal™ Dural Sealant System. Last updated 2005. <http://www.confluenturgical.com/index.htm> [Accessed October 2005]

DuraSeal Dural Sealant System. Summary of safety and effectiveness data. FDA. Last updated 2005. <http://www.fda.gov/cdrh/PDF4/p040034b.pdf> [Accessed October 2005]

Food and Drug Administration (FDA). New Device Approval – DuraSeal Dural Sealant System – P040034. Last updated May 2005. <http://www.fda.gov/cdrh/mda/docs/p040034.html> [Accessed October 2005]

Personal Correspondence with Michael Bryant, Confluent Surgical Representative. 14th November 2005.

Search Criteria:

A search of MEDLINE, PubMed and Cochrane Library, Current Controlled Trials metaRegister, UK National Research Register, International Network for Agencies for Health Technology Assessments, relevant online journals and the Internet was conducted in October 2005.

Search terms used were:

DuraSeal, 'Dura Sealant', 'Confluent Surgical', 'Dura Mater Sealant'

This Horizon Scanning Prioritising Summary was prepared by Miss Catherine Easterbrook from the NET-S Project, ASERNIP-S for the Health Policy Advisory Committee on Technology (Health PACT), on behalf of the Medical Services Advisory Committee (MSAC) and the Australian Health Ministers' Advisory Council (AHMAC).