



Australian Government
Department of Health and Ageing



Horizon Scanning Technology Prioritising Summary SprayGel adhesion barrier system

May 2007



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



**Royal Australasian
College of Surgeons**

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The production of this Horizon scanning prioritising summary was overseen by the Health Policy Advisory Committee on Technology (HealthPACT), a sub-committee of the Medical Services Advisory Committee (MSAC). HealthPACT comprises representatives from health departments in all states and territories, the Australia and New Zealand governments; MSAC and ASERNIP-S. The Australian Health Ministers' Advisory Council (AHMAC) supports HealthPACT through funding.

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PRIORITISING SUMMARY

REGISTER ID: S000030

NAME OF TECHNOLOGY: SPRAYGEL ADHESION BARRIER SYSTEM
(CONFLUENT SURGICAL INC., WALTHAM, MA,
UNITED STATES)

PURPOSE AND TARGET GROUP: FOR THE PREVENTION OF ADHESION
FORMATION FOLLOWING GYNECOLOGICAL
SURGERY

STAGE OF DEVELOPMENT (IN AUSTRALIA):

- | | |
|--|--|
| <input type="checkbox"/> Yet to emerge | <input type="checkbox"/> Established |
| <input type="checkbox"/> Experimental | <input type="checkbox"/> Established <i>but</i> changed indication
or modification of technique |
| <input type="checkbox"/> Investigational | <input type="checkbox"/> Should be taken out of use |
| <input checked="" type="checkbox"/> Nearly established | |

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

- | | | |
|---|-------------|---------------|
| <input checked="" type="checkbox"/> Yes | ARTG number | 122805 |
| <input type="checkbox"/> No | | |
| <input type="checkbox"/> Not applicable | | |

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
Australia		✓	
Bahrain		✓	
Europe		✓	
Israel		✓	
Lebanon		✓	
New Zealand		✓	
Oman		✓	
Qatar		✓	
Saudi Arabia		✓	
South Africa		✓	
UAE		✓	
United States	✓		

IMPACT SUMMARY:

SprayGel® is a new adhesion prevention system developed for use intra-operatively. SprayGel has shown to provide some prevention in adhesion formation in ovarian surgery patients without major adverse events. The system is currently available in Australia and New Zealand.

Background

Adhesions (also called pelvic adhesions, intraperitoneal adhesions) are abnormal scar-like bands that form between two surfaces inside the body. Their formation can be a result of peritoneal damage, intra-abdominal ischemia or the presence of foreign materials in the abdominal cavity (e.g. surgical glove powder, micro-organisms, gauze lint, sutures and prosthetic mesh) (Mettler et al. 2002). Adhesions can range in severity from, thin film-like bands to thick fibrous bands. Although adhesions are not associated with specific symptoms, people with adhesions may experience pain (resulting from the pulling of nerves at the site of adhesions), intestinal obstruction, infertility and increased rate of complications during subsequent surgeries (Ellis et al. 1999).

Adhesions can occur anywhere within the peritoneal cavities. There are several causes of adhesion formation including endometriosis, attacks of appendicitis and pelvic inflammatory disease. However the most common cause of adhesion formation is surgery (Johns et al. 2003).

Treatment of adhesions involves the cutting or releasing of the adhesions through a process called adhesiolysis, a procedure which can be performed via laparoscopy or laparotomy (Szomstein et al. 2006). The surgery is performed to allow normal movement of the affected organs. Unfortunately, even after adhesiolysis has been performed up to two-thirds of patients will experience recurrence (Mettler et al. 2002).

Given that even adhesiolysis surgery can cause adhesion formation, surgeons use various surgical techniques in an attempt to prevent adhesion formation. These include: avoidance of the introduction of foreign bodies into the cavity (e.g. surgical glove powder), limiting unnecessary handling of organs, avoiding the use of dry sponges and irrigating the cavity during the surgical procedure, avoiding unnecessary damage to organs, tissues and blood vessels, and using the finest size suture thread appropriate to the surgery.

The SprayGel adhesion barrier system is designed to minimise adhesion formation and consists of two separate polyethylene glycol (PEG) based liquids that when mixed together (upon application) quickly cross-link to form a biocompatible flexible, absorbable hydrogel in situ. The SprayGel component liquids are sprayed onto the target tissue(s) with an air-assisted sprayer which can be used in either endoscopic or open procedures. SprayGel remains intact for five to seven days preventing fibrin deposition and fibrinolysis and after which it breaks down into water-soluble PEG components that undergo renal clearance.

CLINICAL NEED AND BURDEN OF DISEASE

It has been reported that adhesions occur in 68% to 100% of patients who have undergone one or more laparotomies (Ellis 1997, Luijendijk et al. 1996, Menzies and Ellis 1990). Previous abdominal surgery has been described as the single most important predictive factor of adhesion formation (Szomstein et al. 2006).

Adhesions can have severe implications for sufferers. Sufferers of abdominal adhesions can suffer chronic abdominal pain as well as develop small bowel obstructions. Female sufferers of pelvic adhesions (involving the uterus, ovaries, fallopian tubes or bladder) may develop reproductive complications including infertility and ectopic pregnancy. Finally, sufferers of heart adhesions may suffer from decreased heart efficiency.

Unfortunately, the majority of adhesion barriers and agents used for prevention of adhesion formation are difficult to use in open surgery settings and even more difficult under laparoscopic surgery settings (Mettler et al. 2002).

DIFFUSION

The SprayGel adhesion barrier is currently not approved for sale in the United States. The barrier has received CE Mark and is available in the European community. The system is also available in Australia, New Zealand, South Africa, UAE, Oman, Qatar, Bahrain, Israel, Saudi Arabia and Lebanon.

The extent of diffusion of the SprayGel adhesion barrier in Australia was not revealed in the searches conducted.

COMPARATORS

Various barriers have been evaluated to reduce or prevent adhesion formation. However, many are difficult apply under laparoscopic conditions, have unsuitable absorption times or are associated with increased adverse events (Mettler et al. 2004).

Other adhesion barriers suitable for abdominal and ovarian surgery include:

- Gynecare Interceed (TC7) Absorbable Adhesion Barrier (Ethicon, Inc.)
- Seprafilm Adhesion Barrier (Genzyme Corporation)
- ADEPT (ML Laboratories)

SAFETY AND EFFECTIVENESS ISSUES

The first clinical evaluation of SprayGel was conducted as a multi-centre study investigating the safety and effectiveness of the barrier in women undergoing open or laparoscopic myomectomy procedures. Three publications reporting results from the same study were retrieved in the literature search (Mettler et al. 2003a, Mettler et al. 2003b, Mettler et al. 2004). Only results from the most recent, detailed study are presented (Mettler et al. 2004).

In this prospective, randomised, controlled phase III study, patients undergoing open or laparoscopic surgery for leiomyoma or leiomyomatous uteri were assigned to receive the SprayGel adhesion barrier plus optimal surgical technique (treatment group) or optimal surgical technique alone (control group). Following myomectomy, patients were randomly allocated to either the treatment or control group. At each site, the first eligible patient was not randomised but instead received treatment with SprayGel to familiarise the investigators with its use (these patients were followed-up for safety analysis only). All patients who received application of the SprayGel barrier had suture lines and all potentially adhesiogenic surfaces on the uterus and adjacent structures coated to a thickness of approximately 0.5 mm to 1.0 mm.

Of the 69 women enrolled, five did not proceed to randomisation (two training patients and three study withdrawals). Therefore, 64 were included in the efficacy evaluation (34 treatment and 30 control group patients) and 66 in the safety evaluation (including the two training patients). The uterine myomectomy procedure and thus application of the SprayGel barrier was performed laparoscopically in 28 (82.4%) of treatment and 23 (76.7%) of control patients. The authors noted that application of the SprayGel barrier was easy in both laparoscopic and open procedures with mean time of application of 3.7 minutes and average requirement of 1.9 kits per treatment patient. There were no adverse events related to the use of the SprayGel barrier.

The primary efficacy outcomes were incidence¹, severity² and extent³ of adhesions measured at the second look laparoscopy (SLL), which was performed between three and 16 weeks after surgery. Twenty-two (64.7%) treatment and 18 (60%) control group patients returned for SLL. Despite the high attrition rates, no significant differences between patients who returned and those who did not were found. Prior to surgery, patients in both groups had similar incidence, severity and extent of adhesions. At the SLL there were no significant differences between groups in regards to extent of adhesions with both groups having similar median areas of the uterus covered with adhesions ($p > 0.1$). Although treatment patients experienced lower incidence than control patients (31.8% versus 11.1% adhesion free, respectively), no statistically significant difference was observed. Treatment group patients experienced significantly lower severity as shown by a lower mean tenacity score than the control group (1.0 versus 1.9, $p = 0.002$). In terms of recurrent adhesions, no statistical difference between the two groups was reported.

Comparison of SLL to initial myomectomy values revealed patients who did not receive SprayGel were at an increased risk of forming adhesions compared to patients in the treatment group, demonstrated by increased incidence of adhesions (0.64 for treatment versus 1.22 for control, $p = 0.035$). Similarly, severity at the SLL was significantly lower for treatment group patients than at the initial surgery compared to control group patients (0.6 for treatment versus 1.7 for control, $p = 0.001$). No statistically significant difference in the extent of adhesion was noted with both groups having similar increase in the adhesion area from initial surgery to SLL (4.5 cm² for treatment versus 7.2 cm² for control, $p > 0.1$).

Johns and colleagues conducted another randomised controlled trial of the SprayGel adhesion barrier to investigate its impact on frequency of adhesion formation and reformation after ovarian surgery (Johns et al. 2003). In this study 14 women undergoing laparoscopic ovarian surgery were randomised to have one ovary treated with SprayGel and the other with good surgical technique only. Patients who received the SprayGel treatment had the barrier applied to the entire surface of the relevant ovary and immediately adjacent structures with the air-assisted applicator. No SprayGel was applied to any contralateral structures.

At the SLL treated ovaries demonstrated a reduction in adhesion formation of 21.4% (p value not reported) and a significantly lower extent of adhesion cover over the treated ovary (control mean extent surface area 52.0%, treated mean extent surface area 29.6%, $p = 0.0298$). Additionally the mean severity score was lower for the treated ovaries (mean 2.1) than for the control (mean 2.7) ovaries although statistical significance was not reported. The frequency and extent of adhesion formation on ovaries, fallopian tubes and pelvic side walls were also evaluated by an independent reviewer who determined that the change in both frequency and extent between the initial surgery and the SLL were significantly lower in the treated ovary side compared to the control side ($p = 0.0488$ for frequency and $p = 0.0494$ for extent). The frequency in the treated sides increased from 3.21 (initial surgery) to 4.21 (SLL) compared to 2.57 (initial surgery) and 6.07 (SLL) for the control side. Similarly extent of adhesions increased from 5.46 cm² at the initial surgery to 10.97 cm² at the SLL. No adverse events related to the use of the SprayGel barrier were reported.

COST IMPACT

A search of the published literature and website of the manufacturer of SprayGel (Confluent Surgical Inc., Massachusetts, United States) did not reveal the cost of SprayGel.

¹ Incidence: defined as mean number of sites adherent to the uterus

² Severity: defined as mean adhesion tenacity score, ranging from 0 to 3: 0 = no adhesions, 1 = filmy or vascular adhesions, 2 = vascular and/or dense adhesions, 3 = cohesive adhesions

³ Extent: defined as mean area of uterus covered by adhesions, cm²

The Medicare Benefits Schedule reimbursement fees for procedures related to the treatment of adhesions are listed in Table 1:

Table 1: Medical Benefits Schedule of fees for procedures related to the treatment of adhesions (Department of Health and Ageing 2007)

Category	Item Number	Benefit (AUD)	Number of Claims (July 2005 to June 2006)
Laparotomy for the division of peritoneal adhesions	30376	\$460.55	456
Laparotomy involving division of adhesions in conjunction with another intra-abdominal procedure where time to divide adhesions is between 45 minutes and 2 hours	30378	\$462.70	4,381
Laparotomy with division of extensive adhesions (duration greater than 2 hours)	30379	\$820.15	1,195
Laparoscopic division of adhesions in association with another intra-abdominal procedure where time taken to divide adhesions exceeds 45 minutes	30393	\$462.70	4,686
Laparoscopic division of adhesions, as independent procedure lasting 1 hour or less	31450	\$359.35	284
Laparoscopic division of adhesions, as an independent procedure lasting more than 1 hour	31452	\$628.70	248
Thoracotomy or sternotomy involving division of adhesions where time taken exceeds 45 minutes	38643	\$943.15	559
Thoracotomy or sternotomy involving division of adhesions where time taken exceeds 2 hours	38647	\$1,886.15	489

ETHICAL, CULTURAL OR RELIGIOUS CONSIDERATIONS

No issues were identified from the retrieved material.

OTHER ISSUES

No issues were identified from the retrieved material.

HEALTHPACT CONCLUSION

Adhesions present major complications for sufferers. Although adhesiolysis is performed to divide any adhesions present, the technique itself can lead to further adhesion formation. Various surgical techniques and adhesion barriers are available to reduce adhesion formation. Though the evidence suggests that SprayGel is somewhat effective in reducing adhesion formation, there is a lack of studies comparing SprayGel to other adhesion barriers as well as documenting the long term effects of this adhesion barrier. It is recommended that SprayGel be archived in view of the limited evidence and the alternative barriers currently available.

SOURCES OF FURTHER INFORMATION

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LIST OF STUDIES INCLUDED

Total number of studies 2
Level II intervention evidence

SEARCH CRITERIA TO BE USED

Adhesion\$
Barrier
SprayGel
Hydrogel
Pelvic adhesion\$
Abdominal adhesion\$

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