

## Medical Policy



### Title: Plugs for Fistula Repair

*See Also: Bio-Engineered Skin and Soft Tissue Substitutes*

#### **Professional**

Original Effective Date: December 11, 2009  
 Revision Date(s): August 31, 2011;  
 June 29, 2012; October 31, 2013  
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#### **Institutional**

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### **DESCRIPTION**

Anal fistula plugs (AFP) are biosynthetic devices used to promote healing and prevent recurrence of anal fistula (fistula-in-ano). The conical-shaped plug is anchored in the anal fistula and acts as a scaffold into which new tissue can grow to close the fistula. The plug is absorbed into the body in 6 to 8 weeks. The procedure may require 12–24 hours of observation postoperatively and can be repeated in case of failure.

### **Background**

An anal fistula is an abnormal communication between the interior of the anal canal or rectum and the skin surface. Rarer forms may communicate with the vagina or other pelvic structures, including the bowel. Most fistulas begin as anorectal abscesses. When

the abscess opens spontaneously into the anal canal (or has been opened surgically), a fistula may occur. Other causes of fistulas include tuberculosis, cancer, and inflammatory bowel disease. Fistulas may occur singly or in multiples. Symptoms include a purulent discharge and drainage of pus and/or stool near the anus, which can irritate the outer tissues causing itching and discomfort. Pain occurs when fistulas become blocked and abscesses recur. Flatus may also escape from the fistulous tract. Anal fistulas are described as low (present distally and not extending up to the ano-rectal sling) or high (extending up to or beyond the ano-rectal sling). High fistula can be associated with incontinence. Diagnosis may involve fistula probe, anoscopy, fistulography, ultrasound, or magnetic resonance imaging (MRI). Treatment is aimed at repairing the fistula without compromising continence. Treatments include fistulotomy/fistulectomy, endorectal/anal sliding flaps, seton drain, and fibrin glue. Lay-open fistulotomy in high fistulas carries risk of incontinence. Draining setons can control sepsis, but few patients heal after removal of the seton, and they are poorly tolerated long term. Cutting setons can cause continence disturbances.

The SIS Fistula Plug from Cook Biotech received 510(k) clearance from the U.S. Food and Drug Administration (FDA) in March 2005 based on similarity to predicate devices, including the SURGISIS® Soft Tissue Graft and the STRATASIS® Urethral Sling, both manufactured by Cook Biotech Incorporated. The SIS Fistula Plug is manufactured from porcine small intestinal submucosa (SIS) and is intended for repair of anal, rectal, and enterocutaneous fistulas. The modified SIS Fistula Plug, also manufactured from SIS, is supplied in a tapered configuration with a button to provide increased retention of the plug and improved blockage of the fistula. It received 510(k) clearance in October 2006. In March 2009, W.L. Gore & Associates received 510(k) clearance for the BIO-A® Fistula Plug intended for use in anorectal fistulas. The GORE BIO-A Fistula Plug device comprises a porous structure of synthetic bioabsorbable PGA/TMC copolymer fiber, degraded via a combination of hydrolytic and enzymatic pathways, using the same material, technology, and 3-dimensional disk with tubes mesh design as the predicate GORE Bioabsorbable Mesh hernia plug device. The indications for use and performance of the GORE BIO-A™ Fistula Plug are substantially equivalent to the predicate Cook SIS Fistula Plug.

## **POLICY**

Biosynthetic fistula plugs, including plugs made of porcine small intestine submucosa or of synthetic material are considered **experimental / investigational** for all indications including, but not limited to, repair of anal and rectal fistulas.

## **RATIONALE**

The most recent literature search was performed for March 2012 through August 28, 2013. Conventional treatments for anal fistulas include fistulotomy/fistulectomy, endorectal/anal sliding flaps, seton drains, and fibrin glue. Evidence for new treatments must allow comparison with conventional treatment on outcomes including safety, healing, fistula recurrence, and sphincter function.

There are limited published prospective, comparative data on outcomes of anal fistula plug (AFP) procedures. Searches of the MEDLINE database found 2 randomized controlled trials (RCTs) and several prospective case series and retrospective comparative studies.

### Systematic Reviews

At least 5 systematic reviews have been undertaken on AFP. In 2012, 3 reviews were published comparing AFP to conventional surgical treatment for anal fistulas. (1-3) Pu and colleagues undertook a meta-analysis of 5 studies (2 RCTs and 3 retrospective studies) published through April 2012. Treatment options in the conventional arm of this review included endorectal/mucosal advancement flaps, fibrin glue, and seton drains. (1) The 2 RCTs included in this analysis (Ortiz, 2009; van Koperen, 2011) are discussed below under randomized controlled trials. On combined analysis, AFP patients had a higher recurrence rate (62%) compared to those undergoing conventional treatment options (47%) after 3 months of follow-up (5 studies, 428 patients;  $p=0.004$ , odds ratio [OR]: 1.91; 95% confidence interval [CI]: 1.23-2.97).

Leng and Jin undertook a meta-analysis of 6 studies published through April 2011 (3 RCTs, 2 retrospective studies, and one cohort study) involving 408 patients comparing AFP with mucosal advancement flap (MAF). (2) Two of the RCTs in this analysis were included in the review by Pu and colleagues above; the third RCT was a Chinese trial of 90 patients comparing AFP (manufactured in China and similar in design to the SURGISIS®) to the MAF. On combined analysis, the differences in the overall success rates (6 studies) and incidence of fistula recurrence (4 studies including 3 RCTs) were not statistically significant between the AFP and MAF (risk difference [RD]: -0.12; 95% CI: -0.39 - 0.14; RD: 0.13; 95% CI: -0.18 - 0.43, respectively). (2) The risk of continence postoperatively (3 studies including 2 RCTs), however, was reported to be lower with AFP (RD: -0.08; 95% CI: 0.15 to -0.02). In addition to the small numbers of controlled studies and limited follow-up, the findings of this meta-analysis were further limited by significant heterogeneity across studies. (2)

O'Riordan and colleagues undertook a systematic review of AFP (20 studies including 2 RCTs by Ortiz and van Koperan) for patients with Crohn's and non-Crohn's-related anal fistulas. (3) The follow-up period across studies ranged from 3 months to 24.5 months. The pooled proportion of patients achieving fistula closure in patients with non-Crohn's anal fistula was 0.54 (95% CI: 0.50-0.59). The proportion achieving closure in patients with Crohn's disease was similar (0.55, 95% CI: 0.39-0.70). (3) There were no reported cases of any significant change in continence after AFP insertion in any of the study patients ( $n=196$ ). The findings of this systematic review are limited by the variability of operative technique and perioperative care across studies, which may influence the probability of success or failure associated with the AFP. (3)

A 2010 systematic review reports a wide range of success rates. (4) In the 12 case series included in the review, reported success rates for the AFP procedure ranged from 24% to 92%. Success rates in treating complex fistula-in-ano in the 8 prospective studies reviewed were 35% to 87%. The complications of abscess formation and/or sepsis ranged from 4% to 29%, and plug extrusion ranged from 4%-41%.

In a Cochrane review of surgical intervention for anorectal fistula, Jacob and colleagues found few randomized trials comparing procedures for surgical repair. (5) Anal fistula plug was one procedure noted as needing further study with randomized trials.

### Randomized controlled trials

Ortiz and colleagues, in a European trial, compared use of porcine submucosal (Surgisis) AFP with an endorectal anal flap (ERAF) procedure in an RCT with 43 patients with high anal fistula. (6) The primary endpoint was fistula healing. Recurrence was defined as the presence of an abscess in the same area or obvious evidence of fistulization. Five patients in the AFP group and 6 in the ERAF group did not receive the allocated intervention, leaving 32 patients. One patient in the AFP group was lost to follow-up. A large number of recurrences in the fistula plug group led to premature closure of the trial. After 1 year, fistula recurrence was seen in 12 of 15 patients treated with an AFP versus 2 of 16 patients who underwent the flap procedure (relative risk [RR]: 6.40; 95% confidence interval [CI]: 1.70-23.97];  $p < 0.001$ ). Fistulas recurred in 9 of 16 patients who had previously undergone fistula surgery; 8 of the 9 patients had an AFP. A trend for more sphincter involvement and more females in the ERAF group was noted. Complications were not reported in this paper.

Van Koperen and colleagues reported on a double-blinded, multicenter, randomized trial comparing AFP with mucosal advancement flap in 60 patients with high perianal fistulas. (7) At 11 months follow-up, the authors reported fistula recurrence in 22 patients (71%) in the AFP group and 15 patients (52%) in the advancement flap group; these rates were not significantly different ( $p = 0.126$ ). Postoperative pain scores, quality of life after surgery and functional outcomes were not significantly different between groups. Despite disappointing results, the authors indicated the plug might be considered as an initial treatment option because the plug procedure is simple and minimally invasive.

### Non-randomized comparative studies

Hyman et al. reported on prospective, multicenter registry outcomes data to compare a variety of procedures to treat anal fistulas in 245 patients at 13 hospitals. (8) Data were collected as part of a prospective, multicenter outcomes registry created by colorectal surgeons in parts of New England. Fistulotomy was the most frequently performed procedure ( $n = 120$ ) followed by fistula plug ( $n = 43$ ), staged fistulotomy ( $n = 36$ ), seton drain only ( $n = 21$ ), cutting seton ( $n = 13$ ), fibrin glue ( $n = 5$ ), and advancement flap ( $n = 4$ ). Three other patients were listed as other or unrecorded. At 1 month and 3 months, 19.5% and 63.2% of patients were healed, respectively. At 3 months, 32% of fistula plug patients were healed in comparison to 87% of fistulotomy, 50% of staged fistulotomy, and 5% of seton drain-only patients. The authors noted limitations to this registry-based study including concerns about data entry, lack of standardized surgical procedures, and heterogeneity of patients. The 3-months' results may also indicate longer healing times may be needed.

Christoforidis et al. performed a retrospective analysis of patients from a U.S. center with transsphincteric fistulas treated with ERAF ( $n = 43$ ) or anal plug (Surgisis) ( $n = 37$ ) between January 1996 and April 2007. (9) Success was defined as closed external opening in absence of symptoms at minimal follow-up of 6 months. The success rate was 63% in the ERAF group and 32% in the in AFP group after a mean follow-up of 56 (range, 6–136) months for ERAF and 14 (range, 6–22) months for AFP. After exclusion of patients with early AFP extrusion, which may be considered a technical failure, the ERAF advantage did not meet statistical significance ( $p = 0.06$ ). Twenty-three of 27 patients who had ERAF and 7 of 12 patients who had AFP responded to a questionnaire addressing functional outcomes. In the ERAF group, 11 of 23 patients had no continence disturbance versus 6 of 7 in the AFP group. The lack of prospectively collected incontinence scores prior to the procedure and low response rate in the AFP group prohibit valid

comparisons on functional outcomes. Complication rates were low in both groups; 2 patients in the ERAF group required reoperation for bleeding. No serious complications occurred in the AFP group. The authors conclude that “randomized trials are needed to further elucidate the efficacy and potential functional benefit of AFP in the treatment of complex anal fistulas.”

Wang et al. compared outcomes of all patients with transsphincteric fistulas treated with AFP from July 2005 to December 2006 (n=29) and compared them with historical controls treated with ERAF (2001–2005) (n=26). (10) Of 26 initial flap procedures, 10 failed and 16 healed. Of 29 initial plug procedures, 19 failed and 10 healed. In total, 30 advancement flaps and 34 plug procedures were performed (including the additional treatments for failed initial procedures). Closure rates were 34% for plugs (mean follow-up 279 days [range, 110–690]) and 62% for flaps (median follow-up 819 days [range, 93–1,928]; p=0.045). Complications were not reported. The authors conclude that a systematic randomized trial with long-term follow-up comparing advancement flaps with fistula plugs is needed, and they calculate that 112 patients would need to be randomized to detect a statistically significant difference in success rates for each procedure. Because the fistula plugs are costly, the authors recommend that cost-benefit analysis be performed.

A retrospective study of 232 patients treated in Canada between 1997 and 2008 by a variety of methods for high transsphincteric anal fistulas was reported by Chung et al. (11) Postoperative healing rates at the 12-week follow-up for the fistula plug, fibrin glue, flap advancement, and seton drain groups were 59.3%, 39.1%, 60.4%, and 32.6%, respectively. They conclude that closure of the primary fistula opening using a biologic AFP and anal flap advancement result in similar fistula healing rates in patients with high transsphincteric fistulas and that these strategies are superior to seton placement and fibrin glue. “Given the low morbidity and relative simplicity of the procedure, the anal fistula plug is a viable alternative treatment for patients with high transsphincteric anal fistulas.” The 12-week follow-up time in this study is likely too short to evaluate the durability of treatment.

Other papers report treatment of very small numbers of patients with rectovaginal fistulas, endoscopic treatment of postoperative enterocutaneous fistulas after bariatric surgery, a colocolocutaneous fistula, and a recurrent tracheoesophageal fistula treated with fistula plug.

### **Clinical Input Received through Physician Specialty Societies and Academic Medical Centers**

While the various physician specialty societies and academic medical centers may collaborate with and make recommendations during this process through the provision of appropriate reviewers, input received does not represent an endorsement or position statement by the physician specialty societies or academic medical centers, unless otherwise noted.

In response to requests, input was received from 3 physician specialty societies and 5 academic medical centers in 2013. The clinical input was mixed with three reviewers in agreement that biosynthetic fistula plugs are considered investigational for all indications, and four reviewers considered its use as both investigational and medically necessary. One reviewer disagreed with the policy statement but noted that the success rates of all of the procedures (including AFPs) are widely varied, as reflected by our review of the literature.

### Ongoing Clinical Trials

A search of online site [clinicaltrials.gov](http://clinicaltrials.gov) identified at least 5 randomized controlled trials on anal fistula plugs. In NCT00830661, a biodegradable porcine anal fistula plug will be compared to ligation of the intersphincteric fistula tract (LIFT) procedure (LIFT vs. PLUG) in 124 randomized patients at 4 North American institutions. The estimated completion date of this trial was March 2012; however, its recruitment status is presently unknown because the information has not been verified as of May 2009. In another RCT, the SURGISIS® anal fistula plug will be compared to the advancement flap procedure in 86 randomized patients in Germany (NCT 00545441). This trial is completed, but not recruiting participants; study results have not been published.

The University of California, Los Angeles is conducting a trial to compare the SURGISIS® plug to cutting seton drain in 300 patients (NCT00450671). The estimated completion date of this trial was February 2012; however, its recruitment status is presently unknown because the information has not been verified as of March 2007. In NCT 01021774, an unspecified collagen plug will be compared to advancement flap in 100 randomized patients in Sweden. This trial is currently recruiting participants with an estimated completion date of December 2013. And finally, the LIFT procedure will be compared to LIFT combined with the anal fistula plug in China in 240 patients (NCT01478139). The estimated completion date of this trial was February 2013; however, its recruitment status is presently unknown because the information has not been verified as of November 2011.

### Summary

Anal fistula plugs are biosynthetic devices used to promote healing and prevent recurrence of anal fistula. Evidence of efficacy of anal fistula plug treatment is quite limited. Available evidence reports a wide range of results and does not demonstrate that anal fistula plugs improve healing rates or reduce recurrence of anal fistulas. Randomized controlled trials that have sufficient numbers of patients with at least six months of follow-up, and that report healing, recurrence rates, and sphincter function before and after the procedure are required. In light of the limited data available and inconsistent outcomes reported, the impact on net health outcome is not known, and the use of anal fistula plugs is considered investigational.

### Practice Guidelines and Position Statements

The 2011 Practice Parameters for the Treatment of Perianal Abscess and Fistula-in-Ano from the American Society of Colon and Rectal Surgeons gives treatment with an anal fistula plug for complex anal fistulas a weak recommendation. The guidelines note the available evidence is of moderate quality with success rates of less than 50% in the majority of studies. (12)

The National Institute for Health and Care Excellence (NICE) published an updated guidance on the suturable bioprosthetic plug in November 2011. (13) NICE determined that while there are no major safety concerns, evidence on the efficacy of the procedure is not adequate for it to be used without special arrangements for consent and for audit or research. Further, clinicians wishing to perform the procedure are encouraged to enroll patients into the Fistula-In-Ano Trial (FIAT) (Available online at: <http://www.birmingham.ac.uk/research/activity/mds/trials/bctu/trials/coloproctology/flat/index.aspx>). If the clinician chooses to perform the procedure outside of a clinical trial, the clinician should inform the clinical governance leads in their Trust, ensure that patients understand the uncertainty about the procedure's efficacy and provide patients with clear written information

(NICE recommends the information it developed for patients be provided) and audit and review clinical outcomes.

## **CODING**

**The following codes for treatment and procedures applicable to this policy are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.**

### **CPT/HCPCS**

43305	Esophagoplasty (plastic repair or reconstruction), cervical approach; with repair of tracheoesophageal fistula
43312	Esophagoplasty (plastic repair or reconstruction), thoracic approach; with repair of tracheoesophageal fistula
44640	Closure of intestinal cutaneous fistula
46707	Repair of anorectal fistula with plug (e.g., porcine small intestine mucosa [SIS])
57300	Closure of rectovaginal fistula; vaginal or transanal approach
57305	Closure of rectovaginal fistula; abdominal approach
57307	Closure of rectovaginal fistula; abdominal approach, with concomitant colostomy
57308	Closure of rectovaginal fistula; transperineal approach, with perineal body reconstruction, with or without levator plication

- There is a specific CPT code for use of these plugs in repair of an anorectal fistula: 46707.

### **DIAGNOSIS**

Experimental / investigational for all diagnoses related to this policy.

### **REVISIONS**

08-31-2011	Policy added to the bcbsks.com web site.
06-29-2012	Description section updated.
	Rationale section added.
	References section updated.
10-31-2013	In Header: Revised the See Also titled policy from "Wound Care: Skin Substitutes and Growth Factors" to " Bio-Engineered Skin and Soft Tissue Substitutes"
	Description section updated
	Rationale section updated
	References updated

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