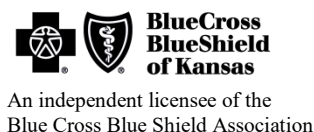


Medical Policy



Title: Plugs for Anal 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;
 December 14, 2015; May 10, 2017;
 December 20, 2017; February 27, 2019
 Current Effective Date: December 14, 2015

Institutional

Original Effective Date: December 11, 2009
 Revision Date(s): August 31, 2011;
 June 29, 2012; October 31, 2013;
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 Current Effective Date: December 14, 2015

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Populations	Interventions	Comparators	Outcomes
Individuals: • With anal fistula(s)	Interventions of interest are: • Placement of anal fistula plug(s)	Comparators of interest are: • Fistulotomy or fistulectomy • Endorectal/anal sliding flaps • Seton drains • Fibrin glue	Relevant outcomes include: • Symptoms • Change in disease status • Morbid events • Functional outcomes • Treatment-related morbidity

DESCRIPTION

Anal fistula plugs (AFP) are biosynthetic devices used to promote healing and prevent recurrence of anal fistula. They are proposed as an alternative to procedures including fistulotomy, endorectal advancement flaps, seton drain placement, and use of fibrin glue in the treatment of anal fistulas.

Objective

The objective of this evidence review is to evaluate whether the use of anal fistula plugs improves the net health outcome for anal fistulas compared with other approaches.

Background

ANAL FISTULAS

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, which are thought to arise from infection in the glands around the anal canal. When the abscess opens spontaneously into the anal canal (or has been opened surgically), a fistula may occur. Studies have reported that 26% to 37% of cases of perianal abscesses eventually form anal fistulas.¹

Other causes of fistulas include tuberculosis, cancer, prior radiotherapy, 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.

The most widely used classification of anal fistulas is the Parks classification system, which defines anal fistulas by their position relative to the anal sphincter as transsphincteric, intersphincteric, suprasphincteric, or extrasphincteric. More simply, anal fistulas are described as low (present distally and not extending up to the anorectal sling) or high (extending up to or beyond the anorectal sling). Repair of high fistula can be associated with incontinence. Diagnosis may involve fistula probe, anoscopy, fistulography, ultrasound, or magnetic resonance imaging.

Treatment

Treatment is aimed at repairing the fistula without compromising continence.

Surgical treatments for anal fistulas include fistulotomy or fistulectomy, endorectal or anal sliding flaps, ligation of the intersphincteric fistula tract (LIFT) technique, seton drain, and fibrin glue. Fistulotomy involves division of the tissue over the fistula and laying open of the fistula tract. Although fistulotomies are widely used for low fistulas, lay-open fistulotomy in high fistulas carries risk of incontinence. A seton is a thread placed through the fistula tract to drain fistula material and prevent the development of a perianal infection. Draining setons can control sepsis, but few patients heal after removal of the seton, and the procedure is poorly tolerated long-term. A "cutting seton" refers to the process of regular tightening of the seton to encourage gradual cutting of the sphincteric muscle with subsequent inflammation and fibrosis. Cutting setons can cause continence disturbances. Endorectal advancement flaps involve the advancement of a full or partial thickness flap of the proximal rectal wall over the internal (rectal) opening of

the fistula tract. The LIFT technique involves identifying the intersphincteric plane and then dividing the fistula tract; its use has been reported in small studies, but long-term follow-up is unavailable.² Fibrin glue is a combination of fibrinogen, thrombin, and calcium in a matrix, which is injected into the fistula track. The glue induces clot formation within the tract, which is then closed through overgrowth of new tissue.

Fistula Plugs

Fistula plugs are designed to provide a structure that acts as a scaffold for new tissue growth. The scaffold, which can be derived from animal (eg, porcine) tissue or a synthetic copolymer fiber, is degraded by hydrolytic or enzymatic pathways as healing progresses. The plug is pulled through the fistula tract and secured at the fistula's proximal opening; the fistula tract is left open at the distal opening to allow drainage. Several fistula plugs have been cleared for marketing by the U.S. Food and Drug Administration (see Regulatory Status section).

A fistula plug derived from autologous cartilage tissue has been investigated in a small (n=10) pilot study.³

Regulatory Status

Several plugs for fistula repair have been cleared for marketing by the U.S. Food and Drug Administration through the 510(k) process and are outlined in Table 1.

Table 1: Devices for Anal Fistula Repair

Device	Year	Description	Indication(s)	Predicate Device(s)	FDA Product Code
SIS Fistula Plug (Cook Biotech)	Mar 2005	<ul style="list-style-type: none"> Manufactured from porcine SIS 	<ul style="list-style-type: none"> Repair of anal, rectal, and enterocutaneous fistulas 	<ul style="list-style-type: none"> SURGISIS® Soft Tissue Graft (Cook Biotech) STRATASIS® Urethral Sling (Cook Biotech) 	FTM
Surgisis RVP Recto-Vaginal Fistula Plug (Cook Biotech)	Oct 2006	<ul style="list-style-type: none"> Manufactured from porcine SIS Tapered configuration with a button to increase plug retention and improve fistula blockage 	<ul style="list-style-type: none"> Reinforce soft tissue to repair rectovaginal fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM
Surgisis Biodesign Enterocutaneous Fistula Plug (Cook Biotech)	Feb 2009	<ul style="list-style-type: none"> Manufactured from porcine SIS Tapered configuration with flange to increase plug retention and improve fistula blockage 	<ul style="list-style-type: none"> Reinforce soft tissue to repair enterocutaneous fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM

Device	Year	Description	Indication(s)	Predicate Device(s)	FDA Product Code
Gore Bio-A Fistula Plug (W.L. Gore & Associates)	Mar 2009	<ul style="list-style-type: none"> Manufactured from bioabsorbable PGA:TMC copolymer Supplied in a 3-dimensional configuration of a disk with attached tubes 	<ul style="list-style-type: none"> Reinforce soft tissue to repair anorectal fistulas 	<ul style="list-style-type: none"> Gore Bioabsorbable Mesh (W.L. Gore & Associates) SIS Fistula Plug (Cook Biotech) 	FTL
Biodesign Anal Fistula Plug (Cook Biotech)	May 2016	<ul style="list-style-type: none"> Manufactured from porcine SIS Additional wash steps added in processing 	<ul style="list-style-type: none"> Reinforce soft tissue where a rolled configuration is required to repair anal, rectal, and enterocutaneous fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM

FDA: Food and Drug Administration; PGA:TMC: polyglycolide-co-trimethylene carbonate; SIS: small intestinal submucosa

POLICY

Biosynthetic fistula plugs, including plugs made of porcine small intestine submucosa or of synthetic material are considered **experimental / investigational** for the repair of anal fistulas.

RATIONALE

This evidence review has been updated with searches of the MEDLINE database. The most recent literature update was performed through September 6, 2018.

Evidence reviews assess the clinical evidence to determine whether the use of a technology improves the net health outcome. Broadly defined, health outcomes are length of life, quality of life, and ability to function—including benefits and harms. Every clinical condition has specific outcomes that are important to patients and to managing the course of that condition. Validated outcome measures are necessary to ascertain whether a condition improves or worsens; and whether the magnitude of that change is clinically significant. The net health outcome is a balance of benefits and harms.

To assess whether the evidence is sufficient to draw conclusions about the net health outcome of a technology, 2 domains are examined: the relevance and the quality and credibility. To be relevant, studies must represent one or more intended clinical use of the technology in the intended population and compare an effective and appropriate alternative at a comparable intensity. For some conditions, the alternative will be supportive care or surveillance. The quality and credibility of the evidence depend on study design and conduct, minimizing bias and confounding that can generate incorrect findings. The randomized controlled trial (RCT) is

preferred to assess efficacy; however, in some circumstances, nonrandomized studies may be adequate. RCTs are rarely large enough or long enough to capture less common adverse events and long-term effects. Other types of studies can be used for these purposes and to assess generalizability to broader clinical populations and settings of clinical practice.

Anal Fistula Repair

Clinical Context and Therapy Purpose

The purpose of placing anal fistula plugs (AFPs) in patients who have anal fistulas is to provide a treatment option that is an alternative to or an improvement on existing therapies.

The question addressed in this evidence review is: Does use of AFPs improve the net health outcome in those with anal fistulas?

The following PICOTS were used to select literature to inform this review.

Patients

The relevant population of interest is patients with anal fistulas.

Interventions

The therapy being considered is an AFP.

Comparators

The following therapies are currently being used to treat anal fistulas: fistulotomy or fistulectomy, endorectal or anal sliding flaps, seton drains, and fibrin glue.

Outcomes

The general outcomes of interest are fistula repair and healing, elimination of symptoms, treatment-related complications (eg, abscess), and fistula recurrence.

Timing

Short-term postsurgical follow-up can range between 2 and 12 weeks while longer term follow-up monitoring can range from weeks to months.

Setting

Anal plugs are placed by a surgeon under general anesthesia in an outpatient surgical center setting.

Systematic Reviews

Narang et al (2016) published a systematic review of the Gore Bio-A plug for anal fistulas, which included 6 studies (total N=221 patients) in a qualitative synthesis.⁴ Fistula healing rates ranged from 15.8% to 72.7%. Reviewers assessed the overall quality of the underlying studies as poor.

Nasseri et al (2016) reported on a systematic review of AFP for patients with Crohn disease and anal fistulas.⁵ Twelve studies were included: 8 nonrandomized prospective studies and 4 retrospective studies (total N=84 patients; range, 1-20 per study). Due to study heterogeneity, reviewers did not perform a weighted analysis with summary efficacy estimates. The total success rate of AFPs was 49 (58.3%) of 84 placed (95% confidence interval [CI], 47% to 69%).

Xu et al (2016) reported on a meta-analysis of 10 comparative studies of AFPs and mucosal advancement flaps (MAFs) for complex anal fistulas (total N=778 patients).⁶ Three studies were randomized trials; the remaining were observational studies or did not describe designs. In the pooled analysis, there were no significant differences in healing rates at the end of follow-up between the AFP and MAF groups (odds ratio [OR], 0.79; 95% CI, 0.36 to 1.73; $p=0.55$, $I^2=74\%$). None the 7 studies reporting on recurrence rates found significant differences in rates (OR=2.29; 95% CI, 0.59 to 8.88; $p=0.23$, $I^2=83\%$). However, conclusions were limited by shortcomings in the underlying evidence base.

Cirocchi et al (2013) published results of a systematic review and meta-analysis of studies that compared biologically derived products for fistula repair, including fibrin glue, AFPs, and acellular dermal matrix, with surgical therapy for fistula repair.⁷ Seven studies met eligibility criteria, four of which compared AFPs with surgery and two of which were RCTs (van Koperen et al [2011]⁸ and Ortiz et al [2009]⁹ are described in the Randomized Controlled Trials section). In the combined analysis, AFP placement did not differ significantly from surgical treatment on rates of healing (relative risk, 1.19; 95% CI, 0.51 to 2.76). Recurrence of anal fistulas did not differ significantly between patients treated with AFP and those treated with surgery, although the CI for the pooled analysis was very wide (OR=3.12; 95% CI, 0.52 to 18.83).

In 2012, 3 reviews compared AFP with conventional surgical treatment for anal fistulas.^{10,11,12} Pu et al (2012) undertook a meta-analysis of 5 studies (2 RCTs, 3 retrospective studies) published through April 2012. Treatment options in the conventional arm included endorectal or MAFs, fibrin glue, and seton drains.¹⁰ The 2 RCTs included van Koperen et al (2011)⁸ and Ortiz et al (2009).⁹ On combined analysis (5 studies, 428 patients), AFP patients had a higher recurrence rate (62%) than those undergoing conventional treatment options (47%; $p=0.004$) after 3-month follow-up (OR=1.91; 95% CI, 1.23 to 2.97).

Leng and Jin (2012) undertook a meta-analysis of 6 studies published through April 2011 (3 RCTs, 2 retrospective studies, 1 cohort study) involving 408 patients comparing AFP with MAF.¹¹ Two RCTs in this analysis were included in the Pu review (previously described); the third RCT was a Chinese trial of 90 patients comparing AFP (manufactured in China with design similar to the SURGISIS) with the MAF. On combined analysis, the differences in the overall success rates (6 studies) and incidence of fistula recurrence (4 studies including 3 RCTs) did not differ statistically significantly between AFP and MAF (risk difference, -0.12; 95% CI, -0.39 to 0.14; risk difference, 0.13; 95% CI, -0.18 to 0.43, respectively). However, the risk of continence postoperatively (3 studies including 2 RCTs) was reported to be lower with AFP (risk difference, -0.08; 95% CI, 0.15 to -0.02). In addition to the small numbers of controlled studies and limited follow-ups, the studies in this meta-analysis had significant heterogeneity.

O'Riordan et al (2012) conducted a systematic review of AFP (20 studies including the RCTs by van Koperen and Ortiz) for patients with Crohn and non-Crohn-related anal fistulas.¹² The follow-up period across studies ranged from 3 to 24.5 months. The pooled proportion of patients achieving fistula closure in those with non-Crohn anal fistula (0.54; 95% CI, 0.50 to 0.59) was similar to that in those with Crohn disease (0.55; 95% CI, 0.39 to 0.70). There were no reported cases of significant change in continence after AFP insertion in any study patients (total N=196 patients). Review findings were limited by the variability of operative technique and perioperative care across studies, which may have influenced the probability of success or failure associated with the AFP.

A systematic review by Garg et al (2010) reported a wide range of success rates.¹³ In the 12 case series selected, 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 rates for abscess formation and/or sepsis ranged from 4% to 29%, and plug extrusion rates ranged from 4% to 41%.

In a Cochrane review of surgical intervention for anorectal fistula, Jacob et al (2010) found few randomized trials comparing surgical repair procedures.¹⁴ The AFP procedure was noted as needing further study with randomized trials.

Section Summary: Systematic Reviews

Several systematic reviews of studies of AFP repair have demonstrated a wide range of success rates and heterogeneity in study results. The net benefit of a strategy using AFPs compared with open surgical repair is unknown given a lack of high-quality trials and uncertainty related to the tradeoffs between a less invasive procedure and a higher fistula recurrence rate.

Randomized Controlled Trials

Senejoux et al (2016) reported on an RCT comparing AFP with seton removal alone in 106 patients who had Crohn disease with non- or mildly active disease but at least 1 anoperitoneal fistula drained for at least 1 month.¹⁵ The trial was powered for the superiority of AFP, and analysis was intention-to-treat. At 12 weeks of follow-up, in the AFP group (n=54), the clinical remission rate was 31.5% compared with 23.1% in the control group (relative risk, 1.31; 95% CI, 0.59 to 4.02; p=0.19). Fistula tract healing rates on magnetic resonance imaging did not differ significantly between groups at 12 weeks.

Van Koperen et al (2011) reported on a double-blinded, multicenter, randomized trial comparing AFP with MAF in 60 patients with high perianal fistulas.⁸ At 11-month follow-up, trialists reported fistula recurrence in 22 (71%) patients in the AFP group and in 15 (52%) patients in the advancement flap group; these rates did not differ significantly (p=0.126). Postoperative pain scores, quality of life after surgery, and functional outcomes did not differ significantly between groups. Despite disappointing results, trialists indicated the plug might be considered as an initial treatment option because the procedure is simple and minimally invasive.

Ortiz et al (2009) compared the use of porcine submucosal (Surgisis) AFPs with an endorectal anal flap (ERAF) procedure in an RCT of 43 patients with high anal fistula.⁹ The primary end point 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 fistula recurrences in the fistula plug group led to the premature closure of the trial. After 1 year, fistula recurrence was seen in 12 of 15 patients treated with an AFP vs 2 of 16 patients who underwent the flap procedure (relative risk, 6.40; 95% CI, 1.70 to 23.97; p<0.001). A trend for more sphincter involvement and more women in the ERAF group was noted. Complications were not reported.

Section Summary: Randomized Controlled Trials

An RCT has compared AFP with seton drain removal alone for fistulizing Crohn disease, with no significant difference reported between groups. Two relatively small RCTs have compared AFP

with surgical flap treatment for anal fistulas, one of which reported significantly higher rates of fistula recurrence with AFP while the other found similar rates of recurrence between AFP and surgical treatment. Larger RCTs are needed to determine the comparative efficacy of AFPs and surgical repair.

Nonrandomized Comparative Studies

Prospective Studies

Hall et al (2014) reported results from a larger multicenter registry study of prospectively collected data for 240 anal fistula surgeries, including those conducted with AFPs.¹⁶ Rates of utilization of fistulotomy, ligation of the intersphincteric fistula tract technique, advancement flap, AFP placement, draining seton, and cutting seton were 61%, 18%, 6.3%, 4.2%, 8.3%, and 0.83%, respectively. The healing rate for patients treated with AFPs was 20% (95% CI, 5% to 50%) compared with 95% after fistulotomy (95% CI, 89% to 97%), 79% after intersphincteric fistula tract technique (95% CI, 65% to 88%), 60% after advancement flap (95% CI, 33% to 77%), and 100% after cutting seton placement (95% CI, 34% to 100%).

In one of the larger, prospective studies, Hyman et al (2009) reported on outcomes data for various procedures to treat anal fistulas in 245 patients at 13 hospitals.¹⁷ Data were collected as part of a prospective, multicenter outcomes registry. 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 patients were listed as other or unrecorded. At 1 and 3 months, 19.5% and 63.2% of patients were healed, respectively. At 3 months, 32% of fistula plug patients had healed compared with 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 among patients. The 3-month results may also indicate longer healing times might be required.

Retrospective Studies

Several retrospective studies have also compared AFP with alternative treatments. Fisher et al (2015) retrospectively evaluated success rates after AFP (n=31) or endorectal advancement flap (n=40) in patients with anal fistula treated at a single institution from 2007 to 2012.¹⁸ For patients treated after May 2007; the Surgisis AFP was available. More patients treated with AFP had inflammatory bowel disease (IBD; 29.0% vs 5.0%; p=0.008). During follow-up, 12 (39%) patients treated with AFP and 17 (43%) treated with endorectal advancement flap had fistula recurrence (OR=0.94; 95% CI, 0.32 to 2.72; p=1.00). Rates of complications did not differ significantly between groups.

Christoforidis et al (2009) retrospectively analyzed patients from a U.S. center with transsphincteric fistulas treated with ERAF (n=43) or anal plug (Surgisis; n=37) between 1996 and 2007.¹⁹ Success was defined as a closed external opening in the absence of symptoms at minimal follow-up of 6 months. The success rate was 63% in the ERAF group and 32% in the AFP group after a mean follow-up of 56 months (range, 6-136 months) for ERAF and 14 months (range, 6-22 months) for AFP. After exclusion of patients with early AFP extrusion, which may be considered a technical failure, the ERAF advantage was not statistically significant (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 vs 6 of 7 in the AFP group. The lack of prospectively collected

incontinence scores before the procedure, and low response rate in the AFP group do not permit valid comparisons on functional outcomes. Complication rates were low in both groups; only 2 patients in the ERAF group required reoperation for bleeding.

Wang et al (2009) compared outcomes for patients who had transsphincteric fistulas treated using an AFP from 2005 to 2006 (n=29) with historical controls treated with ERAF (2001-2005) (n=26).²⁰ 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 additional treatments for failed initial procedures). Closure rates were 34% for plugs (mean follow-up, 279 days; range, 110-690 days) and 62% for flaps (median follow-up, 819 days; range, 93-1928 days; p=0.045). Complications were not reported.

A retrospective study of 232 patients treated in Canada between 1997 and 2008 using various methods for high transsphincteric anal fistulas was reported by Chung et al (2009).²¹ Postoperative healing rates at the 12-week follow-up for the fistula plug, fibrin glue, flap advancement, and seton drain groups were 59%, 39%, 60%, and 33%, respectively. The closure of the primary fistula opening using an AFP and flap advancement resulted in similar fistula healing rates in this patient group and that these strategies were superior to seton placement and fibrin glue. The 12-week follow-up in this study was likely too short to evaluate the durability of treatment.

Section Summary: Nonrandomized Comparative Studies

Nonrandomized comparative studies have reported variable rates of healing after AFP compared with other fistula closure methods. These studies are limited by patient heterogeneity and relatively short-term follow-up durations.

Summary of Evidence

For individuals who have anal fistula(s) who receive placement of AFP(s), the evidence includes 3 RCTs, a number of comparative and noncomparative nonrandomized studies, and systematic reviews of these studies. Relevant outcomes are symptoms, change in disease status, morbid events, functional outcomes, and treatment-related morbidity. Two RCTs comparing AFP with surgical flap treatment have reported disparate findings: one found significantly higher rates of fistula recurrence with AFP; the other found similar rates of recurrence for AFP and surgical treatment. Another RCT that compared AFP with seton drain removal alone for patients with fistulizing Crohn disease, found no significant difference in healing rates at 12 weeks between groups. Systematic reviews of AFP repair have demonstrated a wide range of success rates and heterogeneity in study results. Nonrandomized studies have also reported conflicting results. The evidence is insufficient to determine the effects of the technology on health outcomes.

Clinical Input From 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 while this policy was under review in 2013. Input was mixed, with 3 reviewers agreeing that biosynthetic fistula plugs are considered investigational for all indications while 4

reviewers considered their use as both investigational and medically necessary. One reviewer disagreed with the policy statement but noted that the success rates of all procedures (including anal fistula plugs) vary widely, as reflected by BCBSA's review of the literature.

Practice Guidelines and Position Statements American Society of Colon and Rectal Surgeons

The 2017 practice guidelines on management of anal fistulas from the American Society of Colon and Rectal Surgeons did not evaluate use of plugs for anal fistula repair.²²

The 2016 practice guidelines on the treatment of anorectal abscess, fistula-in-ano, and rectovaginal fistula from the Society provided a weak recommendation with moderate-quality evidence.²³ With recent evidence of success rates of less than 50% in most studies for the treatment of complex anal fistulas with an anal fistula plug, the guidelines concluded that the fistula plug is relatively ineffective in the treatment of fistula-in-ano.

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence updated its guidance on the suturable bioprosthetic plug in 2011.²⁴ The Institute determined that while there are no major safety concerns, evidence on the efficacy of the procedure was inadequate for it to be used without special arrangements.

U.S. Preventive Services Task Force Recommendations

Not applicable.

Ongoing and Unpublished Clinical Trials

Some currently unpublished trials that might influence this review are listed in Table 2.

Table 2. Summary of Key Trials

NCT No.	Trial Name	Planned Enrollment	Completion Date
Unpublished			
ISRCTN78352529	Surgisis® anal fistula plug versus surgeon's preference (advancement flap, fistulotomy, cutting seton) for transsphincteric fistula-in-ano: a multicentre phase III randomised controlled trial	306	May 2017 (completed)
NCT01478139	Ligation of Intersphincteric Fistula Tract (LIFT) Versus LIFT-plug Procedure for Anal Fistula Repair: a Multicenter, Randomized, Open-label, Parallel Controlled Trial	240	Nov 2013 (unknown)

NCT: national clinical trial.

^a Denotes industry-sponsored or cosponsored trial.

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

46707 Repair of anorectal fistula with plug (e.g., porcine small intestine mucosa [SIS])

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
12-14-2015	Policy published 12-04-2015. Policy effective 12-14-2015.
	Titled changed from "Plugs for Fistula Repair" to "Plugs for Anal Fistula Repair"
	Description section updated
	In Policy section: <ul style="list-style-type: none"> ▪ Removed "all indications including, but not limited to," and "and rectal" to read, "Biosynthetic fistula plugs, including plugs made of porcine small intestine submucosa or of synthetic material are considered experimental / investigational for the repair of anal fistulas."
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> ▪ Removed CPT codes: 43305, 43312, 44640, 57300, 57305, 57307, 57308
	References updated
05-10-2017	Description section updated
	Rationale section updated
	References updated
12-20-2017	Description section updated
	Rationale section updated
	References updated
02-27-2019	Description section updated
	Rationale section updated
	References updated

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