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## Medical Policy



### Title: Plugs for Anal Fistula Repair

<b>Professional</b>	<b>Institutional</b>
Original Effective Date: December 11, 2009	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; February 24, 2021, January 13, 2022; December 29, 2022	Revision Date(s): August 31, 2011; June 29, 2012; October 31, 2013; December 14, 2015; May 10, 2017; December 20, 2017; February 27, 2019; February 24, 2021, January 13, 2022; December 29, 2022
Current Effective Date: December 14, 2015	Current Effective Date: December 14, 2015

**Archived Date: December 29, 2022**

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Populations	Interventions	Comparators	Outcomes
Individuals: <ul style="list-style-type: none"> <li>• With anal fistula(s)</li> </ul>	Interventions of interest are: <ul style="list-style-type: none"> <li>• Placement of anal fistula plug(s)</li> </ul>	Comparators of interest are: <ul style="list-style-type: none"> <li>• Fistulotomy or fistulectomy</li> <li>• Endorectal/anal sliding flaps</li> <li>• Seton drains</li> <li>• Fibrin glue</li> </ul>	Relevant outcomes include: <ul style="list-style-type: none"> <li>• Symptoms</li> <li>• Change in disease status</li> <li>• Morbid events</li> <li>• Functional outcomes</li> <li>• Treatment-related morbidity</li> </ul>

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## **DESCRIPTION**

Anal fistula plugs (AFPs) are biosynthetic devices used to promote healing and prevent the recurrence of anal fistulas. 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 determine 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 in 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.<sup>1</sup>

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). The repair of high fistulas can be associated with incontinence. Diagnosis may involve a 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 a division of the tissue over the fistula and laying open of the fistula tract. Although fistulotomies are widely used for low fistulas, lay-open fistulotomies in high fistulas carry the risk of incontinence. A seton is a thread placed through the fistula tract to drain fistula material and preventing the development of a perianal infection. Draining setons can control

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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 the 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 intersphincteric fistula tract 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.<sup>2</sup> Fibrin glue is a combination of fibrinogen, thrombin, and calcium in a matrix, which is injected into the fistula tract. The glue induces clot formation within the tract, which is then closed through the 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 (e.g., 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 (FDA) (see Regulatory Status section).

A fistula plug derived from autologous cartilage tissue has been investigated in a small (N=10) pilot study.<sup>3</sup>

### REGULATORY STATUS

Several plugs for anal fistula repair have been cleared for marketing by the FDA 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"> <li>Manufactured from porcine SIS</li> </ul>	<ul style="list-style-type: none"> <li>Repair of anal, rectal, and enterocutaneous fistulas</li> </ul>	<ul style="list-style-type: none"> <li>Surgisis® Soft Tissue Graft (Cook Biotech)</li> <li>Stratasis® Urethral Sling (Cook Biotech)</li> </ul>	FTM
Surgisis RVP Recto-Vaginal Fistula Plug (Cook Biotech)	Oct 2006	<ul style="list-style-type: none"> <li>Manufactured from porcine SIS</li> </ul>	<ul style="list-style-type: none"> <li>Reinforce soft tissue to repair rectovaginal fistulas</li> </ul>	<ul style="list-style-type: none"> <li>SIS Fistula Plug (Cook Biotech)</li> </ul>	FTM

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

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

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## **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.

**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.**

## **RATIONALE**

This evidence review has been updated regularly with searches of the PubMed database. The most recent literature update was performed through September 21, 2022.

Evidence reviews assess the clinical evidence to determine whether the use of technology improves the net health outcome. Broadly defined, health outcomes are the 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 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 technology, 2 domains are examined: the relevance, and quality and credibility. To be relevant, studies must represent 1 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. Randomized controlled trials 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 following PICO was used to select literature to inform this review.

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### ***Populations***

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 (e.g., abscess), and fistula recurrence.

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

### **Study Selection Criteria**

Methodologically credible studies were selected using the following principles:

- To assess efficacy outcomes, comparative controlled prospective trials were sought, with a preference for RCTs;
- In the absence of such trials, comparative observational studies were sought, with a preference for prospective studies.
- To assess long-term outcomes and adverse events, single-arm studies that capture longer periods of follow-up and/or larger populations were sought.
- Studies with duplicative or overlapping populations were excluded.

## **REVIEW OF EVIDENCE**

### **Systematic Reviews**

Cheung et al (2021) completed a systematic review and meta-analysis of all the available evidence (N=28 studies) on the surgical management of adults with non-Crohn-related perianal fistulas.<sup>4</sup> The primary outcomes were fistula recurrence and fecal incontinence. Since the included studies had a range of different comparison groups, pooling of data from all 28 studies was not possible. In the review, 2 studies (van Koperen et al [2011]<sup>5</sup> and Ortiz et al [2009]<sup>6</sup>, described in the Randomized Controlled Trials section) compared fistula plug with advancement flap, with an increased recurrence rate in the plug group. Pooled data analysis on recurrence revealed an odds ratio (OR) favoring the advancement flap (OR, 4.22; 95% confidence interval [CI], 1.76 to 10.13; p=.03). No difference in incontinence scores between groups was noted.

Narang et al (2016) published a systematic review of the Gore Bio-A plug for anal fistulas, which included 6 studies (N=221 ) in a qualitative synthesis.<sup>7</sup> Fistula healing rates ranged from 15.8% to 72.7%. Reviewers assessed the overall quality of the underlying studies as poor.



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Nasseri et al (2016) reported on a systematic review of AFP for patients with Crohn disease and anal fistulas.<sup>8</sup> Twelve studies were included: 8 nonrandomized prospective studies and 4 retrospective studies (N=84 ; range, 1 to 20 patients 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% 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 (N=778 ).<sup>9</sup> 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 (OR, 0.79; 95% CI, 0.36 to 1.73; p=.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=.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.<sup>10</sup> Seven studies met eligibility criteria, 4 of which compared AFPs with surgery and 2 of which were RCTs (van Koperen et al [2011]<sup>5</sup> and Ortiz et al [2009]<sup>6</sup> ). 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.<sup>11,12,13</sup> 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.<sup>11</sup> The 2 RCTs included van Koperen et al (2011)<sup>5</sup> and Ortiz et al (2009).<sup>6</sup> On combined analysis (5 studies, 428 patients), AFP patients had a higher recurrence rate (62%) than those undergoing conventional treatment options (47%; p=.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, and 1 cohort study) involving 408 patients comparing AFP with MAF.<sup>12</sup> Two RCTs in this analysis were included in the Pu et al (2012) review (previously described); the third RCT was a Chinese trial of 90 patients comparing an AFP (manufactured in China with a 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

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small number 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 et al [2011] and Ortiz et al [2009]) for patients with Crohn and non-Crohn-related anal fistulas.<sup>13</sup> 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 (N=196 ). 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.

### **Randomized Controlled Trials**

Jayne et al (2021) compared the use of porcine AFPs (Biodesign Surgisis) with surgeon's preference (advancement flap, cutting seton, fistulotomy, or Ligation of the Intersphincteric Fistula Tract [LIFT] procedure) in 304 patients with transsphincteric fistulas in the pragmatic, multicenter, randomized FIAT trial.<sup>14</sup> The primary outcome was fecal incontinence quality of life (FIQoL) at 12 months. Secondary outcome measures included fistula healing, incontinence rates, and complications. No significant differences were seen in FIQoL between groups at 12 months. Clinical fistula healing was reported in 66/122 (54%) of the AFP group and 66/119 (55%) of the surgeon's preference group at 12 months. Marginal improvement in fecal incontinence rates was observed in both groups. Frequent complications and reinterventions were observed, with significantly more complications in the AFP group at 6 weeks (49/142 (35%) vs. 25/137 (18%); p=.002).

Senejoux et al (2016) reported on a 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.<sup>15</sup> The trial was powered for the superiority of AFP, and the 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=.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-blind, multicenter, randomized trial comparing AFP with MAF in 60 patients with high perianal fistulas.<sup>5</sup> 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=.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.

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Ortiz et al (2009) compared the use of porcine submucosal (Surgisis) AFPs with an endorectal anal flap (ERAF) procedure in a RCT of 43 patients with high anal fistula.<sup>6</sup> 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 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 versus 2 of 16 patients who underwent the flap procedure (relative risk, 6.40; 95% CI, 1.70 to 23.97;  $p < .001$ ). A trend for more sphincter involvement and more women in the ERAF group was noted. Complications were not reported.

## 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.<sup>16</sup> Rates of the utilization of fistulotomy, LIFT 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 1 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.<sup>17</sup> 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.<sup>18</sup> For patients treated after May 2007; the Surgisis AFP was available. More patients treated with AFP had inflammatory bowel disease (29.0% vs. 5.0%;  $p=.008$ ). 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.

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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.<sup>19</sup> 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 to 136 months) for ERAF and 14 months (range, 6 to 22 months) for AFP. After the exclusion of patients with early AFP extrusion, which may be considered a technical failure, the ERAF advantage was not statistically significant (p=.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 before the procedure, and a low response rate in the AFP group does 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).<sup>20</sup> 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 to 690 days) and 62% for flaps (median follow-up, 819 days; range, 93 to 1928 days; p=.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).<sup>21</sup> 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 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 the treatment.

### **Summary of Evidence**

For individuals who have anal fistula(s) who receive placement of AFP(s), the evidence includes 4 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: 1 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. An RCT comparing AFP with surgeon's preference reported significantly higher complication rates with AFP. Systematic reviews of AFP repair have demonstrated a wide range of success rates and heterogeneity in study results. Nonrandomized studies have also reported

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conflicting results. The evidence is insufficient to determine that the technology results in an improvement in the net health outcome.

### **SUPPLEMENTAL INFORMATION**

The purpose of the following information is to provide reference material. Inclusion does not imply endorsement or alignment with the evidence review conclusions.

#### **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.

#### **2013 Input**

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**

Guidelines or position statements will be considered for inclusion in 'Supplemental Information' if they were issued by, or jointly by, a US professional society, an international society with US representation, or National Institute for Health and Care Excellence (NICE). Priority will be given to guidelines that are informed by a systematic review, include strength of evidence ratings, and include a description of management of conflict of interest.

#### **American Society of Colon and Rectal Surgeons**

The 2022 practice guideline on the treatment of anorectal abscess, fistula-in-ano, and rectovaginal fistula from the Society provided a strong recommendation based on moderate-quality evidence that anal fistula plug and fibrin glue are relatively ineffective treatments for fistula-in-ano.<sup>22</sup>

#### **National Institute for Health and Care Excellence**

In 2019, the National Institute for Health and Care Excellence updated its guidance on the suturable bioprosthetic plug.<sup>23</sup> The Institute determined that "evidence on the safety and efficacy of bioprosthetic plug insertion for anal fistula is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent, and audit." Though, it was noted that "the procedure should only be done by a surgeon experienced in managing anal fistulas."

#### **U.S. Preventive Services Task Force Recommendations**

Not applicable.

**No review or update is scheduled on this Medical Policy as it is unlikely that further published literature would change the policy position. If there are questions about coverage of this service, please contact Blue Cross and Blue Shield of Kansas customer service, your professional or institutional relations representative, or submit a predetermination request.**

### **Ongoing and Unpublished Clinical Trials**

There are currently no relevant ongoing clinical trials of plugs for anal fistula repair in ClinicalTrials.gov through September 21, 2022.

**No review or update is scheduled on this Medical Policy as it is unlikely that further published literature would change the policy position. If there are questions about coverage of this service, please contact Blue Cross and Blue Shield of Kansas customer service, your professional or institutional relations representative, or submit a predetermination request.**

## CODING

The following codes for treatment and procedures applicable to this policy are included below for informational purposes. This may not be a comprehensive list of procedure codes applicable to this policy.

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.

The code(s) listed below are medically necessary ONLY if the procedure is performed according to the "Policy" section of this document.

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

ICD-10 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"> <li>▪ 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."</li> </ul>
	Rationale section updated
	In Coding section: <ul style="list-style-type: none"> <li>▪ Removed CPT codes: 43305, 43312, 44640, 57300, 57305, 57307, 57308</li> </ul>
References updated	

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<b>REVISIONS</b>	
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
02-24-2021	Updated Description section
	Updated Rationale section
	Updated Reference section
01-13-2022	Updated Description Section
	Updated Rationale Section
	Updated References Section
12-29-2022	Updated Description Section
	Updated Rationale Section
	Updated References Section
12-29-2022	Archived

## REFERENCES

1. Simpson JA, Banerjee A, Scholefield JH. Management of anal fistula. *BMJ*. Oct 15 2012; 345: e6705. PMID 23069597
2. Campbell ML, Abboud EC, Dolberg ME, et al. Treatment of refractory perianal fistulas with ligation of the intersphincteric fistula tract: preliminary results. *Am Surg*. Jul 2013; 79(7): 723-7. PMID 23816007
3. Ozturk E. Treatment of recurrent anal fistula using an autologous cartilage plug: a pilot study. *Tech Coloproctol*. May 2015; 19(5): 301-7. PMID 25850629
4. Cheung XC, Fahey T, Rogers AC, et al. Surgical Management of Idiopathic Perianal Fistulas: A Systematic Review and Meta-Analysis. *Dig Surg*. 2021; 38(2): 104-119. PMID 33503621
5. van Koperen PJ, Bemelman WA, Gerhards MF, et al. The anal fistula plug treatment compared with the mucosal advancement flap for cryptoglandular high transsphincteric perianal fistula: a double-blinded multicenter randomized trial. *Dis Colon Rectum*. Apr 2011; 54(4): 387-93. PMID 21383557
6. Ortiz H, Marzo J, Ciga MA, et al. Randomized clinical trial of anal fistula plug versus endorectal advancement flap for the treatment of high cryptoglandular fistula in ano. *Br J Surg*. Jun 2009; 96(6): 608-12. PMID 19402190
7. Narang SK, Jones C, Alam NN, et al. Delayed absorbable synthetic plug (GORE(R) BIO-A(R)) for the treatment of fistula-in-ano: a systematic review. *Colorectal Dis*. Jan 2016; 18(1): 37-44. PMID 26542191



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8. Nasser Y, Cassella L, Berns M, et al. The anal fistula plug in Crohn's disease patients with fistula-in-ano: a systematic review. *Colorectal Dis.* Apr 2016; 18(4): 351-6. PMID 26749385
9. Xu Y, Tang W. Comparison of an anal fistula plug and mucosa advancement flap for complex anal fistulas: a meta-analysis. *ANZ J Surg.* Dec 2016; 86(12): 978-982. PMID 27680894
10. Cirocchi R, Trastulli S, Morelli U, et al. The treatment of anal fistulas with biologically derived products: is innovation better than conventional surgical treatment? An update. *Tech Coloproctol.* Jun 2013; 17(3): 259-73. PMID 23207714
11. Pu YW, Xing CG, Khan I, et al. Fistula plug versus conventional surgical treatment for anal fistulas. A system review and meta-analysis. *Saudi Med J.* Sep 2012; 33(9): 962-6. PMID 22964807
12. Leng Q, Jin HY. Anal fistula plug vs mucosa advancement flap in complex fistula-in-ano: A meta-analysis. *World J Gastrointest Surg.* Nov 27 2012; 4(11): 256-61. PMID 23494149
13. O'Riordan JM, Datta I, Johnston C, et al. A systematic review of the anal fistula plug for patients with Crohn's and non-Crohn's related fistula-in-ano. *Dis Colon Rectum.* Mar 2012; 55(3): 351-8. PMID 22469804
14. Jayne DG, Scholefield J, Tolan D, et al. A Multicenter Randomized Controlled Trial Comparing Safety, Efficacy, and Cost-effectiveness of the Surgisis Anal Fistula Plug Versus Surgeon's Preference for Transsphincteric Fistula-in-Ano: The FIAT Trial. *Ann Surg.* Mar 01 2021; 273(3): 433-441. PMID 32516229
15. Senejoux A, Siproudhis L, Abramowitz L, et al. Fistula Plug in Fistulising Ano-Perineal Crohn's Disease: a Randomised Controlled Trial. *J Crohns Colitis.* Feb 2016; 10(2): 141-8. PMID 26351393
16. Hall JF, Bordeianou L, Hyman N, et al. Outcomes after operations for anal fistula: results of a prospective, multicenter, regional study. *Dis Colon Rectum.* Nov 2014; 57(11): 1304-8. PMID 25285698
17. Hyman N, O'Brien S, Osler T. Outcomes after fistulotomy: results of a prospective, multicenter regional study. *Dis Colon Rectum.* Dec 2009; 52(12): 2022-7. PMID 19934925
18. Fisher OM, Raptis DA, Vetter D, et al. An outcome and cost analysis of anal fistula plug insertion vs endorectal advancement flap for complex anal fistulae. *Colorectal Dis.* Jul 2015; 17(7): 619-26. PMID 25641401
19. Christoforidis D, Pieh MC, Madoff RD, et al. Treatment of transsphincteric anal fistulas by endorectal advancement flap or collagen fistula plug: a comparative study. *Dis Colon Rectum.* Jan 2009; 52(1): 18-22. PMID 19273951
20. Wang JY, Garcia-Aguilar J, Sternberg JA, et al. Treatment of transsphincteric anal fistulas: are fistula plugs an acceptable alternative?. *Dis Colon Rectum.* Apr 2009; 52(4): 692-7. PMID 19404076
21. Chung W, Kazemi P, Ko D, et al. Anal fistula plug and fibrin glue versus conventional treatment in repair of complex anal fistulas. *Am J Surg.* May 2009; 197(5): 604-8. PMID 19393353
22. Gaertner WB, Burgess PL, Davids JS, et al. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Anorectal Abscess, Fistula-in-

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Ano, and Rectovaginal Fistula. *Dis Colon Rectum*. Aug 01 2022; 65(8): 964-985. PMID 35732009

23. National Institute for Health and Care Excellence (NICE). Bioprosthetic plug insertion for anal fistula [IPG662]. September 25, 2019; <https://www.nice.org.uk/guidance/ipg662>. Accessed September 21, 2022.