



# Louisiana

## Plugs for Anal Fistula Repair

**Policy #** 00598

**Original Effective Date:** 04/01/2018

**Current Effective Date:** 04/01/2018

*Applies to all products administered or underwritten by Blue Cross and Blue Shield of Louisiana and its subsidiary, HMO Louisiana, Inc. (collectively referred to as the "Company"), unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.*

### **Services Are Considered Investigational**

*Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.*

Based on review of available data, the Company considers biosynthetic fistula plugs, including plugs made of porcine small intestine submucosa or of synthetic material for the repair of anal fistulas to be **investigational**.\*

### **Background/Overview**

#### **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.

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 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 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 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 sepsis, but few patients heal after removal of the seton, and the

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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 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. 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 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 (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.

### **FDA or Other Governmental Regulatory Approval**

U.S. Food and Drug Administration (FDA)

Several plugs for fistula repair have been cleared for marketing by the U.S. 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> <li>Tapered configuration with a button to increase plug retention and improve fistula blockage</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
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

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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

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

### Centers for Medicare and Medicaid Services (CMS)

There is no national coverage determination. In the absence of a national coverage determination, coverage decisions are left to the discretion of local Medicare carriers.

### Rationale/Source

Assessment of efficacy for therapeutic intervention involves a determination of whether an intervention improves health outcomes. The optimal study design for this purpose is a randomized controlled trial (RCT) that includes clinically relevant measures of health outcomes. Intermediate outcome measures, also known as surrogate outcome measures, may also be adequate if there is an established link between the intermediate outcome and true health outcomes. Nonrandomized comparative studies and uncontrolled studies can sometimes provide useful information on health outcomes but are prone to biases such as noncomparability of treatment groups, placebo effect, and variable natural history of the condition.

### **ANAL FISTULA REPAIR**

Conventional treatments for anal fistulas include fistulotomy or fistulectomy, endorectal or anal sliding flaps, seton drains, and fibrin glue. Evidence for new treatments must allow comparison with conventional treatment on outcomes including symptoms, change in disease status, morbid events, functional outcomes (ie, sphincter function), and treatment-related morbidity (ie, fistula recurrence).

### **Systematic Reviews**

At least 9 systematic reviews have been undertaken on anal fistula plugs (AFPs).

In 2016, Narang et al 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. Fistula healing rates ranged from 15.8% to 72.7%. Reviewers assessed the overall quality of the underlying studies as poor.

In 2016, Nasserri et al reported on a systematic review of AFP for patients with Crohn disease and anal fistulas. 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

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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%).

Also in 2016, Xu et al reported on a meta-analysis of 10 comparative studies of AFPs and mucosal advancement flaps (MAFs) for complex anal fistulas (total N=778 patients). 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 recurrence 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.

In 2013, Cirocchi et al 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. Seven studies met eligibility criteria, four of which compared AFPs with surgery and two of which were RCTs (Ortiz et al [2009] and van Koperen et al [2011] are described in the Randomized Controlled Trials section). In the combined analysis, AFP placement did not differ significantly from surgical treatment regarding rates of healing (pooled 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 (pooled OR=3.12; 95% CI, 0.52 to 18.83).

In 2012, 3 reviews compared AFP with conventional surgical treatment for anal fistulas. Pu et al 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. The 2 RCTs included Ortiz et al (2009) and van Koperen et al (2011). 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. Two RCTs in this analysis were included by Pu et al (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). The risk of continence postoperatively (3 studies including 2 RCTs), however, 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 Ortiz and van Koperen) for patients with Crohn and non-Crohn-related anal fistulas. The follow-up period across studies ranged from 3 to 24.5 months. The pooled proportion of patients achieving fistula closure in those

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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 2010 systematic review reported a wide range of success rates. 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 of abscess formation and/or sepsis ranged from 4% to 29%, and plug extrusion rates ranged from 4% to 41%.

In a 2010 Cochrane review of surgical intervention for anorectal fistula, Jacob et al found few randomized trials comparing surgical repair procedures. 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**

In 2016, Senejoux et al 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. 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.

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. 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.

Van Koperen et al (2011) reported on a double-blinded, multicenter, randomized trial comparing AFP with MAF in 60 patients with high perianal fistulas. 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

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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.

### **Section Summary: Randomized Controlled Trials**

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. An additional RCT has compared AFP with seton drain removal alone for fistulizing Crohn disease, with no significant difference reported between groups.

### **Nonrandomized Comparative Studies**

A number of nonrandomized studies have compared AFP with alternative treatments for anal fistula. 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. 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.

Hall et al (2014) reported results from another larger multicenter registry study of prospectively collected data for 240 anal fistula surgeries, including those conducted with AFPs. 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%).

Several smaller or 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. 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.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

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. 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 in 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. The authors concluded 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 (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). 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. The authors concluded that a systematic randomized trial with long-term follow-up comparing advancement flaps with fistula plugs was needed, and they calculated that 112 patients would have to be randomized to detect a statistically significant difference in success rates for each procedure.

A 2009 retrospective study of 232 patients treated in Canada between 1997 and 2008 using various methods for high transsphincteric anal fistulas were reported by Chung et al. 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 authors concluded that closure of the primary fistula opening using an AFP and flap advancement resulted in similar fistula healing rates in 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 variability in 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.

### **Noncomparative Studies**

Retrospective and prospective studies have reported on outcomes after AFP placement. Two larger noncomparative studies are by Stamos et al and Blom et al. Stamos et al (2015) prospectively evaluated healing rates after treatment with a bioabsorbable AFP among 93 patients with complex transsphincteric anal fistulas. Seventy-three (78%) patients also received draining setons preoperatively at the surgeon's

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

discretion. Over the 1-year follow-up, 13 patients were lost, and 21 patients withdrew, most often for an alternative treatment. Of the 66 patients examined 6 months after plug implantation, 30 had a healed fistula. Of the 55 patients examined 12 months after plug implantation, 36 had a healed fistula, but plug implantation failed in 18 patients before the 12-month visit. Overall continence scores improved from presurgery baseline to 6 months postsurgery.

Blom et al (2014) retrospectively analyzed outcomes after AFP placement (with the Biodesign plug) at 4 hospitals. They identified 126 patients who underwent AFP placement and were followed for a median of 13 months (range, 1-7 months). At the last assessment, 30 (24%) of 126 patients had no symptoms indicative of fistula (pain at the fistula site or drainage). Anterior fistulas were less likely to have successful closure (12%) than posterior (32%) or lateral (41%) fistulas.

Other studies have reported treatment of very small numbers of patients with rectovaginal fistulas, endoscopic treatment of postoperative enterocutaneous fistulas after bariatric surgery, colocolic fistulas, and recurrent tracheoesophageal fistulas treated with a fistula plug.

### **Section Summary: Noncomparative Studies**

Noncomparative studies evaluating outcomes after AFP have demonstrated a range of fistula recurrence rates postprocedure. These types of studies provide limited information on the relative performance of AFP compared with standard treatments for anal fistulas.

### **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, which 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.

### **References**

1. Blue Cross and Blue Shield Association, *Medical Policy Reference Manual*, "Plugs for Anal Fistula Repair", 7.01.123, 11:2017.
2. Simpson JA, Banerjee A, Scholefield JH. Management of anal fistula. *BMJ*. Oct 15 2012;345:e6705. PMID 23069597
3. 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):723-727. PMID 23816007
4. Ozturk E. Treatment of recurrent anal fistula using an autologous cartilage plug: a pilot study. *Tech Coloproctol*. May 2015;19(5):301-307. PMID 25850629
5. 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
6. 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):351-356. PMID 26749385

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.





# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

7. 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
8. 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):259-273. PMID 23207714
9. 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):608-612. PMID 19402190
10. 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):387-393. PMID 21383557
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):962-966. 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):256-261. 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):351-358. PMID 22469804
14. Garg P, Song J, Bhatia A, et al. The efficacy of anal fistula plug in fistula-in-ano: a systematic review. *Colorectal Dis.* Oct 2010;12(10):965-970. PMID 19438881
15. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. *Cochrane Database Syst Rev.* May 12 2010(5):CD006319. PMID 20464741
16. 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):141-148. PMID 26351393
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):2022-2027. PMID 19934925
18. 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):1304-1308. PMID 25285698
19. 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):619-626. PMID 25641401
20. 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
21. 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):692-697. PMID 19404076
22. 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):604-608. PMID 19393353
23. Stamos MJ, Snyder M, Robb BW, et al. Prospective multicenter study of a synthetic bioabsorbable anal fistula plug to treat cryptoglandular transsphincteric anal fistulas. *Dis Colon Rectum.* Mar 2015;58(3):344-351. PMID 25664714
24. Blom J, Husberg-Sellberg B, Lindelius A, et al. Results of collagen plug occlusion of anal fistula: a multicentre study of 126 patients. *Colorectal Dis.* Aug 2014;16(8):626-630. PMID 24506192
25. Vogel JD, Johnson EK, Morris AM, et al. Clinical practice guideline for the management of anorectal abscess, fistula-in-ano, and rectovaginal fistula. *Dis Colon Rectum.* Dec 2016;59(12):1117-1133. PMID 27824697
26. National Institute for Health and Care Excellence (NICE). Closure of anal fistula using a suturable bioprosthetic plug [IPG 410]. 2011; <http://www.nice.org.uk/guidance/IPG410>. Accessed September 19, 2017.

### Policy History

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

01/04/2018 Medical Policy Committee review

01/17/2018 Medical Policy Implementation Committee approval. New policy.

Next Scheduled Review Date: 01/2019

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.



# Louisiana

## Plugs for Anal Fistula Repair

Policy # 00598

Original Effective Date: 04/01/2018

Current Effective Date: 04/01/2018

### Coding

The five character codes included in the Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT)<sup>®†</sup>, copyright 2017 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physician.

The responsibility for the content of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines is with Blue Cross and Blue Shield of Louisiana and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of Blue Cross Blue Shield of Louisiana Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

CPT is a registered trademark of the American Medical Association.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	46707
HCPCS	No codes
ICD-10 Diagnosis	K60.0-K60.5

\*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

- A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. FDA and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
- B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
  - 1. Consultation with the Blue Cross and Blue Shield Association technology assessment program (TEC) or other nonaffiliated technology evaluation center(s);
  - 2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
  - 3. Reference to federal regulations.

† Indicated trademarks are the registered trademarks of their respective owners.

**NOTICE:** Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Company recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

©2018 Blue Cross and Blue Shield of Louisiana

Blue Cross and Blue Shield of Louisiana is an independent licensee of the Blue Cross and Blue Shield Association and incorporated as Louisiana Health Service & Indemnity Company.

No part of this publication may be reproduced, stored in a retrieval system, or transmitted, in any form or by any means, electronic, mechanical, photocopying, or otherwise, without permission from Blue Cross and Blue Shield of Louisiana.