BlueCross BlueShield of Alabama

## Name of Policy:
# Plugs for Fistula Repair

Policy #: 399
Category: Surgical

Latest Review Date: November 2013
Policy Grade: A

## Background/Definitions:

*As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.*

*The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:*

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

*Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:*

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*


*Proprietary Information of Blue Cross and Blue Shield of Alabama*

## Description of Procedure or Service:

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

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

The SIS fistula Plug is manufactured from porcine small intestinal submucosa (SIS) and is intended for repair of anal, rectal, and enterocutaneous fistulas. The modified SIS Fistula Plug, also manufactured from porcine small intestinal submucosa, is supplied in the tapered configuration with a button to provide increased retention of the plug and improve blockage of the fistula. The GORE BIO-A Fistula Plug device is comprised of a porous structure of synthetic bioabsorbable PGA/TMC copolymer fiber, degraded via a combination of hydrolytic and enzymatic pathways, the same material, technology and three-dimensional disk with tubes mesh design as the predicate GORE Bioabsorbable Mesh hernia plug device. The indications for use and performance of the GORE BIO-A™ Fistula Plug are substantially equivalent to the predicate Cook SIS Fistula Plug.

## Policy:

**Biosynthetic fistula plugs**, including plugs made of porcine small intestine submucosa or of synthetic material **do not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational** for all indications including, but not limited to, repair of anal and rectal fistulas.

*Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the*

*members' contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.*

## Key Points:

This policy was created in 2009 and regularly updated with searches of the MEDLINE database. The most recent literature search was performed through August 2013.

Conventional treatments for anal fistulas include fistulotomy/fistulectomy, endorectal/anal sliding flaps, Seton drains, and fibrin glue. Evidence for new treatments must allow comparison with conventional treatment on outcomes including safety, healing, fistula recurrence, and sphincter function.

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

*Systematic Reviews*

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

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

O'Riordan and colleagues undertook a systematic review of AFP (20 studies including two RCTs by Ortiz and van Koperan) for patients with Crohn's and non-Crohn's-related anal fistulas. The follow-up period across studies ranged from three months to 24.5 months. The pooled proportion of patients achieving fistula closure in patients with non-Crohn's anal fistula was 0.54

(95% CI: 0.50-0.59). The proportion achieving closure in patients with Crohn's disease was similar (0.55, 95% CI: 0.39-0.70). There were no reported cases of any significant change in continence after AFP insertion in any of the study patients (n=196). The findings of this systematic review are limited by the variability of operative technique and perioperative care across studies, which may influence the probability of success or failure associated with the AFP.

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

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

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

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

*Non-randomized Comparative Studies*
Hyman et al. reported on prospective, multicenter registry outcomes data to compare a variety of procedures to treat anal fistulas in 245 patients at 13 hospitals. Data were collected as part of a prospective, multicenter outcomes registry created by colorectal surgeons in parts of New England. Fistulotomy was the most frequently performed procedure (n=120) followed by fistula plug (n=43), staged fistulotomy (n=36), Seton drain only (n=21), cutting Seton (n=13), fibrin glue (n=5), and advancement flap (n=4). Three other patients were listed as other or unrecorded.

At one month and three months, 19.5% and 63.2% of patients were healed, respectively. At three months, 32% of fistula plug patients were healed in comparison to 87% of fistulotomy, 50% of staged fistulotomy, and 5% of Seton drain-only patients. The authors noted limitations to this registry-based study including concerns about data entry, lack of standardized surgical procedures, and heterogeneity of patients. The three-months' results may also indicate longer healing times may be needed.

Christoforidis et al performed a retrospective analysis of patients from a U.S. center with transsphincteric fistulas treated with ERAF (n=43) or anal plug (Surgisis) (n=37) between January 1996 and April 2007. Success was defined as closed external opening in absence of symptoms at minimal follow-up of six months. The success rate was 63% in the ERAF group and 32% in the in AFP group after a mean follow-up of 56 (range, 6–136) months for ERAF and 14 (range, 6–22) months for AFP. After exclusion of patients with early AFP extrusion, which may be considered a technical failure, the ERAF advantage did not meet statistical significance (p=0.06). Twenty-three of 27 patients who had ERAF and seven 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 six of seven in the AFP group. The lack of prospectively collected incontinence scores prior to the procedure and low response rate in the AFP group prohibit valid comparisons on functional outcomes. Complication rates were low in both groups; two patients in the ERAF group required reoperation for bleeding. No serious complications occurred in the AFP group. The authors conclude that "randomized trials are needed to further elucidate the efficacy and potential functional benefit of AFP in the treatment of complex anal fistulas."

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

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

transsphincteric anal fistulas." The 12-week follow-up time in this study is likely too short to evaluate the durability of treatment.

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

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

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

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

## Key Words:
Biosynthetic fistula plugs, SIS Fistula Plug, modified SIS Fistula Plug, GORE BIO-A Fistula Plug, porcine small intestine submucosa plugs, synthetic fistula plug, suturable bioprosthetic plug, anal fistula plug, fistula plug

## Approved by Governing Bodies:
The SIS Fistula Plug from Cook Biotech received 510(k) clearance from the FDG March 2005. The modified SIS Fistula Plug received FDA 510(k) clearance in October 2006.

The GORE BIO-A Fistula Plug received FDA 510(k) clearance in March 2009.

## Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.

ITS: Home Policy provisions apply
FEP: FEP does not consider investigational if FDA approved. Will be reviewed for medical necessity.
Pre-certification requirements: Not applicable

## Coding:

CPT Codes: **46707** Repair of anorectal fistula with plug (e.g. porcine small intestine mucosa [SIS])

## References:


1. 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 2009;52(1):18-22.
2. 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 2009;197(5):604-8.
3. Garg P, Song J, Bhatia A, et al. The efficacy of anal fistula plug in fistula-in-ano: a systematic review. Colorectal Dis 2009 April 29. [Epub ahead of print]
4. Hyman N, O'Brien S, Osler T. Outcomes after fistulotomy: results of a prospective, multicenter regional study. Dis Colon Rectum 2009; 52(12):2022-7.
5. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. Cochrane Database Syst Rev 2010; (5):CD006319.
6. Leng Q, Jin HY. Anal fistula plug vs mucosa advancement flap in complex fistula-in-ano: a meta-analysis. World J Gastrointest Surg 2012;4(11):256-61.
7. National Institutes for health and Clinical Excellence (NICE). Closure of anal fistula using a suturable bioprosthetic plug. June 2007. Accessible at www.nice.org.uk/nicemedia/pdf/boardmeeting/IPG221guidance.pdf
8. 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 2012;55(3):351-8.
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. Brit J Surg 2009;96(6):608-12.
10. 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 2012;33(9):962-6.
11. Steele Sr, Kumar R, Feingold DL et al. Practice parameters fro the management of perianal abscess and fistula-in-ano. Dis Colon Rectum 2011;54(12):1465-74.

12. 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 2011; 54(4):387-93.
13. Wang JY, Garcia-Aguilar J, Sternberg JA, et al. Treatment of transsphincteric anal fistulas: are fistula plugs an acceptable alternative? Dis Colon Rectum 2009;52(4):692-97.
14. Whiteford MH, Kilkenny J 3rd, Hyman N et al. Standards Practice Task Force; American Society of Colon and rectal Surgeons. Practice parameters for the treatment of perianal abscess and fistula-in-ano (revised). Dis Colon rectum 2005;48(7):1337-42. Accessible at www.fascrs.org/files/pp_0705.pdf

## Policy History:

Medical Policy Group, December 2009 **(2)**
Medical Policy Administration Committee, January 2010
Available for comment January 26-March 11, 2010
Medical Policy Group, January 2012 **(2)**: Key Points & References
Medical Policy Panel, May 2012
Medical Policy Group, June 2012 **(2):** Updated Key Points and References
Medical Policy Panel, September 2013
Medical Policy Group, November 2013 **(2):** No change to policy statement. Key Points and References updated based on literature search through August 2013.

*This medical policy is not an authorization, certification, explanation of benefits, or a contract. Eligibility and benefits are determined on a case-by-case basis according to the terms of the member's plan in effect as of the date services are rendered. All medical policies are based on (i) research of current medical literature and (ii) review of common medical practices in the treatment and diagnosis of disease as of the date hereof. Physicians and other providers are solely responsible for all aspects of medical care and treatment, including the type, quality, and levels of care and treatment.*

*This policy is intended to be used for adjudication of claims (including pre-admission certification, pre-determinations, and pre-procedure review) in Blue Cross and Blue Shield's administration of plan contracts.*