

(701123)

Medical Benefit		Effective Date: 01/01/16	Next Review Date: 03/19
Preauthorization	No	Review Dates: 09/10, 07/11, 07/12, 07/13, 07/14, 07/15, 11/15, 11/16, 03/17, 03/18	

This protocol considers this test or procedure investigational. If the physician feels this service is medically necessary, preauthorization is recommended.

The following protocol contains medical necessity criteria that apply for this service. The criteria are also applicable to services provided in the local Medicare Advantage operating area for those members, unless separate Medicare Advantage criteria are indicated. If the criteria are not met, reimbursement will be denied and the patient cannot be billed. Please note that payment for covered services is subject to eligibility and the limitations noted in the patient's contract at the time the services are rendered.

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

Description

Anal fistula plugs (AFPs) are biosynthetic devices used to promote healing and prevent 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.

Summary of Evidence

For individuals who have anal fistula(s) who receive placement of AFP(s), the evidence includes three 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.

Policy

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

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.¹

Other causes of fistulas include tuberculosis, cancer, prior radiotherapy, and inflammatory bowel disease. Fistulas may occur singly or in multiples. Symptoms include a purulent discharge and drainage of pus and/or stool near the anus, which can irritate the outer tissues causing itching and discomfort. Pain occurs when fistulas become blocked, and abscesses recur. Flatus may also escape from the fistulous tract.

The most widely used classification of anal fistulas is the Parks classification system, which defines anal fistulas by their position relative to the anal sphincter as transsphincteric, intersphincteric, suprasphincteric, or extrasphincteric. More simply, anal fistulas are described as low (present distally and not extending up to the anorectal sling) or high (extending up to or beyond the anorectal sling). Repair of high 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 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.² Fibrin glue is a combination of fibrinogen, thrombin, and calcium in a matrix, which is injected into the fistula track. The glue induces clot formation within the tract, which is then closed through 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.³

Regulatory Status

Several plugs for 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"> Manufactured from porcine SIS 	<ul style="list-style-type: none"> Repair of anal, rectal, and enterocutaneous fistulas 	<ul style="list-style-type: none"> Surgisis® Soft Tissue Graft (Cook Biotech) Stratasis® Urethral Sling (Cook Biotech) 	FTM
Surgisis RVP Recto-Vaginal Fistula Plug (Cook Biotech)	Oct 2006	<ul style="list-style-type: none"> Manufactured from porcine SIS Tapered configuration with a button to increase plug retention and improve fistula blockage 	<ul style="list-style-type: none"> Reinforce soft tissue to repair rectovaginal fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM
Surgisis Biodesign Enterocutaneous Fistula Plug (Cook Biotech)	Feb 2009	<ul style="list-style-type: none"> Manufactured from porcine SIS Tapered configuration with flange to increase plug retention and improve fistula blockage 	<ul style="list-style-type: none"> Reinforce soft tissue to repair enterocutaneous fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM
Gore Bio-A Fistula Plug (W.L. Gore & Associates)	Mar 2009	<ul style="list-style-type: none"> Manufactured from bioabsorbable PGA:TMC copolymer Supplied in a 3-dimensional configuration of a disk with attached tubes 	<ul style="list-style-type: none"> Reinforce soft tissue to repair anorectal fistulas 	<ul style="list-style-type: none"> Gore Bioabsorbable Mesh (W.L. Gore & Associates) SIS Fistula Plug (Cook Biotech) 	FTL
Biodesign Anal Fistula Plug (Cook Biotech)	May 2016	<ul style="list-style-type: none"> Manufactured from porcine SIS Additional wash steps added in processing 	<ul style="list-style-type: none"> Reinforce soft tissue where a rolled configuration is required to repair anal, rectal, and enterocutaneous fistulas 	<ul style="list-style-type: none"> SIS Fistula Plug (Cook Biotech) 	FTM

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

Services that are the subject of a clinical trial do not meet our Technology Assessment Protocol criteria and are considered investigational. *For explanation of experimental and investigational, please refer to the Technology Assessment Protocol.*

It is expected that only appropriate and medically necessary services will be rendered. We reserve the right to conduct prepayment and postpayment reviews to assess the medical appropriateness of the above-referenced procedures. **Some of this protocol may not pertain to the patients you provide care to, as it may relate to products that are not available in your geographic area.**

References

We are not responsible for the continuing viability of web site addresses that may be listed in any references below.

1. Simpson JA, Banerjea 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):723-727. PMID 23816007
3. Ozturk E. Treatment of recurrent anal fistula using an autologous cartilage plug: a pilot study. *Tech Coloproctol*. May 2015; 19(5):301-307. PMID 25850629
4. 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
5. Nasserri 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
6. 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
7. 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
8. 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
9. 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
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*. Sep 2012; 33(9):962-966. PMID 22964807
11. 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
12. 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
13. 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
14. Jacob TJ, Perakath B, Keighley MR. Surgical intervention for anorectal fistula. *Cochrane Database Syst Rev*. May 12, 2010(5):CD006319. PMID 20464741
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):141-148. PMID 26351393
16. 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
17. 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
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):619-626. 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):692-697. 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):604-608. PMID 19393353
22. 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

23. 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
24. 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
25. 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.