

**National Institute for Health and Care Excellence**  
**IP1704 Collagen paste for closing an anal fistula**  
**IPAC 14 February 2019**

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 NHS Professional	General	<p>Overall I found the documents well written and detailed. The review of the relatively limited evidence on this relatively new procedure is comprehensive and well laid down. I could not identified any inaccuracy or other potential concerns within the documents.</p> <p><b>Disclosure -</b></p> <p>I was the chief investigator for the largest multicentre study on this technique. The study was funded by the manufacturer Medtronic. I still have on going professional relationship with Medtronic working with them as trainer and as advisor.</p>	Thank you for your comment.
2	Consultee 2 Company Medtronic Ltd	General	Medtronic would like to thank NICE for the opportunity to comment on this draft guidance. We are happy for any information contained within our response to be in the public domain.	Thank you for your comment.
3	Consultee 2 Company Medtronic Ltd	General	We would like the committee to note that for patients with an increased risk of faecal incontinence, Permacol Paste provides a less invasive treatment option that balances overall success rate for maximum preservation of continence.	Thank you for your comment. Section 2.5 of the draft guidance states: 'It is a less invasive procedure than traditional surgery and the aim is to allow the fistula to heal whilst preserving sphincter function.'
4	Consultee 2	General	██████ regards the use of Permacol Paste for closure of an anal fistula as being both safe and effective. He believes that it is an	Thank you for your comment.

	Company Medtronic Ltd		<p>option which should be presented to patients and he is happy to be contacted on [REDACTED]</p> <p>In addition, [REDACTED] is also happy to be contacted [REDACTED] he believes that this should be a treatment option, especially in younger demographics.</p>	NICE approached the relevant professional organisations for the names of specialist advisers and sought the opinions of those identified advisers.
5	Consultee 2 Company Medtronic Ltd	1.1	We do not agree that this procedure should only be used in the context of research. We believe that the evidence base supports that this procedure should be used with "standard arrangements".	Thank you for your comment. The Committee discussed your comment but decided not to change the recommendation.
6	Consultee 2 Company Medtronic Ltd	2.2	<p>We agree that the current treatment for closing an anal fistula usually involves surgery. However, we would like the committee to note that the surgical interventions also have various degrees of success and unlike Permacol, Collagen paste carry a high risk of continence disorders. It is our understanding from the literature that a Fistulotomy carries a has 7% - 52% of continence disorders<sup>1,2,3,4,5</sup>, Cutting Seton up to 57%<sup>4,6</sup>, Advancement Flap 13%<sup>7</sup> and a LIFT 6%<sup>8,9</sup>.</p> <p>1. Rosa G et al. Fistula in ano: anatomoclinical aspects, surgical therapy and results in 844 patients. Tech Coloproctol 2006;10:215-221.</p> <p>2. Toyonaga T et al. Factors affecting continence after fistulotomy for intersphincteric fistula-in-ano Int J Colorectal Dis 2007;22:1071-5.</p> <p>3. van Koperen PJ, et al. Long-term functional outcome and risk factors for recurrence after surgical treatment for low and high perianal fistulas of cryptoglandular origin. Dis Colon Rectum 2008;51:1474-1481.</p> <p>4. van Tets WF and Kuijpers HC. Continence disorders after anal fistulotomy. Dis Colon Rectum. 1994;37(12):1194-7.</p>	<p>Thank you for your comment.</p> <p>It is not within the remit of the IP programme to assess the efficacy and safety of comparator interventions.</p>

			<p>5. Holzheimer RG and Siebeck M. Treatment procedures for anal fistulous cryptoglandular abscess – how to get the best results. Eur J Med Res 2006;11:501-515.</p> <p>6. Vial M et al. Faecal incontinence after seton treatment for anal fistulae with and without surgical division of internal anal sphincter: a systematic review. Colorect Dis 2010;12:172-178.</p> <p>7. Soltani A and Kaiser AM. Endorectal advancement flap for cryptoglandular or Crohn’s fistula-in-ano. Dis Colon Rectum 2010;53:486-495.</p> <p>8. Alasari S and Kim NK. Overview of anal fistula and systematic review of ligation of the intersphincteric fistula tract (LIFT). Tech Coloproctol 2014;18:13-22</p> <p>9. Yassin NA et al. Ligation of the intersphincteric fistula tract in the management of anal fistula. A systematic review. Colorectal Dis 2013;15:527-535.</p>	
7	Consultee 2 Company Medtronic Ltd	2.4	<p>“The paste fills the exact shape of the tract, which is intended to reduce the risk of it being expelled from the body when defaecating”</p> <p>We ask the committee to consider rewording this paragraph to “As an injectable collagen paste, it conforms to the shape of the anal fistula tract, which is intended to reduce the risk of it being expelled from the body when defaecating, differentiating it from other more rigid or liquid implant materials”</p>	<p>Thank you for your comment.</p> <p>The committee decided not to change the wording in section 2.4 of the draft guidance.</p>
8	Consultee 2 Company Medtronic Ltd	2	<p>We would also like the committee to note that “The use of Permacol, does not impact upon future treatment options”</p>	<p>Thank you for your comment.</p> <p>A committee comment was added to section 3.6 of the guidance as follows:</p>

				<i>The committee was informed that having this procedure does not affect future treatment options.</i>
9	Consultee 2 Company Medtronic Ltd	3.1	We would like the committee to note that in the case series of 100 patients, there was “no reported impact on faecal incontinence” .	Thank you for your comment. The cited study (study 1 in overview) states the following: ‘The mean CCF-FI scores at all patients’ last visit, including scores for those 24 patients who exited the study early, was not significantly different from baseline.’ This has been added to the outcomes in table 2 of the overview for this study.
10	Consultee 2 Company Medtronic Ltd	3.1	We would like the committee to note that in the case series of 21 patients “no significant differences were observed in the FISl scores before and after surgery” .	Thank you for your comment. Table 2 of the overview includes the FISl scores before surgery and at 12 months follow-up for the cited study and it notes that no patients reported a worsening in their continence status.
11	Consultee 2 Company Medtronic Ltd	3.1	We would also like to bring the following articles to the committee’s attention: 10. Schiano di Visconte, M. et al. (2018) “Permacol Collagen Paste Injection for Treatment of Complex Cryptoglandular Anal Fistulas: An Observational Cohort Study With a 2-Year Follow-up”, Surgical Innovation, p. 155335061880812. doi: 10.1177/1553350618808120.  11. Schiano di Visconte, M. and Bellio, G. (2018) “Comparison of porcine collagen paste injection and rectal advancement flap for the treatment of complex cryptoglandular anal fistulas: a 2-year follow-up study”, International Journal of Colorectal Disease, 33(12), pp. 1723–1731. doi: 10.1007/s00384-018-3154-z.	Thank you for your comment.  The cited articles were identified in the updated literature search and have been added to table 2 of the overview.

12	Consultee 2 Company Medtronic Ltd	3.1	We would also like to bring to the attention of the committee, a Medtronic funded cohort study on the use of Permacol paste in perianal fistullising Crohn's Disease, due for completion October 2020 - NCT03776825	<p>Thank you for your comment.</p> <p>The cited study is an observational prospective cohort study of 20 patients with perianal Crohn's disease, with a start date of January 2019 and expected completion date of October 2020.</p> <p>The IP guidance may be updated should new data concerning the safety and efficacy of the procedure be published.</p>
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