National Institute for Health and Care Excellence

IP1789 Laser lithotripsy for difficult-to-treat bile duct stones

IPAC date: 11 March 2021

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1 Company Boston Scientific	**1.1**	Thank you for the opportunity to respond to your consultation on GID-IPG10157 Laser lithotripsy for difficult-to- treat bile duct stones. We are disappointed and perplexed by the committee's decision to place this procedure in special arrangements. We would like to ask the committee to reconsider this decision. We believe the evidence base for laser lithotripsy and its position in the current patient pathway warrant a decision of standard arrangements. We believe that the use of advanced lithotripsy techniques (laser and electro-hydraulic) delivered via single-operator per-oral cholagioscope technology (SOPOC), in patients who have difficult to treat bile duct stones is considered established practice within the clinical community. This is reinforced by the fact that it is established as an intervention within NHS specialist centres and is specifically reserved to treat those patients who have had failed conventional ERCP procedures and have limited treatment alternatives.	Thank you for your comment. The committee has considered this comment but decided not to change the recommendation of special arrangements. The IP programme issues guidance on the procedure (laser lithotripsy for difficult-to-treat bile duct stones) rather than individual devices.
2	Consultee 1 Company Boston Scientific	**1.1**	As described in the draft IPG and recommended in CG188, conventional stone removal techniques involve accessing the patient's bile duct with an endoscope in a procedure known as endoscopic retrograde cholangiopancreatography (ERCP).	Thank you for your comment.

			Given that 65,000 ERCPs are conducted per annum in the UK(ref 1), and it has a well-recognised and accepted safety profile, we are confused as to why the recommendations suggest that that ERCP is unsafe in the opening statement. 'This procedure is also associated with the well-recognised complications of endoscopic retrograde cholangiopancreatography' Patients would be exposed to these risks either through repeat ERCP using conventional clearance techniques or ERCP with laser/EHL lithotripsy. We also believe this statement clouds the IPG's focus on laser lithotripsy, which we believe is the innovative element of this intervention.	The statement about ERCP has been removed from section 1.1.
3	Consultee 1 Company Boston Scientific		Boston Scientific supplies the single-operator per-oral cholagioscope technology (SOPOC -MIB 212); that allows the user to access the biliary system and directly visualise the ductal stones. The LL catheter is passed through the working channel of the SOPOC and enables the LL therapy to be administered. We believe the following information demonstrates the established position of this technology in the patient pathway. • Health Technology Wales assessed SOPOC via their HTA process in 2020 and endorsed it as a second line therapy after failed ERCP in both a diagnostic and therapeutic capacity.(ref 3) • Haute Autorité de santé assessed Spyglass DS (Brand name for SOPOC) in Oct 2020 and endorsed its use as second line therapy after failed ERCP in both a diagnostic and therapeutic capacity (ref 4) • ESGE recommends the use of cholangioscopy-assisted	Thank you for your comment. For referenced papers: see comment 8. Ref 3 has been added to the 'existing assessments' section of the overview. Ref 4 - non-English-language article - did not meet the inclusion criteria. Ref 5 and 6 were included in the 'existing assessments' section. NICE MIB21 (2005): There was 1 study (Maydeo et al. 2011) which was relevant to this procedure and was included in Veld (2018) in the main extraction table

			intraluminal lithotripsy (electrohydraulic or laser) as an effective and safe treatment of difficult bile duct stones (ref5) • The BSG 2017 guidelines recommend that cholangioscopy-guided EHL or LL be considered when other endoscopic treatment options fail to achieve duct clearance (ref 6) In addition • SOPOC is used by clinicians in approximately 35 centres in the UK • SOPOC is a recognised category on the High Cost Tariff Excluded Device list for over 10 years • SOPOC was subject of a NICE MIB in 2015 (ref1) In addition to these documents demonstrating SOPOC with LL/EHL, established position in the clinical pathway; extracts from three of these documents and relevant to the UK, highlight its strong safety profile. 1. Health Technology Wales concluded in section 7 of their evidence review document: Overall, the comparative studies showed similar or reduced adverse event rates with SOPOC compared to other modalities. (ref 3) 2. BSG guidelines stated: Cholangioscopy is safe but cholangitis has been reported to occur in up to 9% of patients, necessitating the use of prophylactic antibiotics. Otherwise complications are comparable to conventional ERCP. Cholangioscopy-guided lithotripsy is an important advance in the management of CBDS and is a useful strategy for patients in whom standard techniques fail. (ref 6) 3. ESGE: Cholangioscopy-assisted intraluminal lithotripsy	

			(electrohydraulic or laser) as an effective and safe treatment of difficult bile duct stones (ref 5)	
4	Consultee 1 Company Boston Scientific	**1.1**	Page 2 consultation summary We are pleased to see the recognition that the evidence of laser lithotripsy for difficult to treat bile duct stones is adequate. As explained in our general comments we are confused with the reference to the safety of ERCP procedures, particularly as NICE clinical guideline 188 clearly states that the "evidence reviewed for this guideline identified that intraoperative ERCP is both clinically and cost effective" We are uncertain about the committee's rationale for explicitly highlighting the risk of biliary stricture formation in the opening statement. To the best of our knowledge this is not a significant concern in the clinical community nor could we identify any additional evidence that suggests the rate of formation of biliary strictures following LL treatment is higher than other types of lithotripsy deployed in the biliary tree. We would ask the committee to revisit this inclusion, given that it is highlighted as a theoretical risk in the document.	Thank you for your comment. The statement about biliary stricture and ERCP has been removed from section 1.1.
5	Consultee 1 Company Boston Scientific	**Over view**	Page 44 Overview - Validity and generalisability of the studies section Concerning bullet point 6: Four randomised controlled trials were included but no trials that directly compared LL with EHL. We would like to highlight to the committee the meta-analysis by McCarty et al (2020) conducted a sub-group analysis considering this topic. It reported overall fragmentation success rate was not statistically different and there was no difference in the rate of adverse events.	Thank you for your comment. McCarty et al. (2020) has been added to the main extraction table. Of the 35 studies included in McCarty et al. (2020), there are 3 RCTs (Bang et al. 2020; Buxbaum et al. 2018; Neuhaus et al. 1998) which were included in the main extraction table and none of which directly compared LL with EHL.

			McCarty T, Gulati R, Rustagi T. Efficacy and Safety of Per-Oral Cholangioscopy with Intraductal Lithotripsy for Difficult Biliary Stones: A Systematic Review and Meta-Analysis. Endoscopy. 2020 Jun 16	
6	Consultee 1 Company Boston Scientific	**1.1**	Interpretation of existing data We believe none of the papers included in the review demonstrate any concerning safety signals. In the 3 RCT's for example, that reflect current UK standard of care (LL via SOPOC), the safety profile was comparable between LL and the considered comparator. Furthermore in one of the considered RCT's (Ang et al 2019) the authors reported a higher percentage of patients requiring more than one ERCP session in the non-LL group (0% in LL vs 18.8% in non LL) and in another RCT (Bang et al 2020) there was a substantial difference in treatment success between LL and LBS; 93.9% and 72.7% respectively. We believe this helps demonstrate the value of the intervention and the potential risk reduction by exposing patients to fewer repeat ERCP procedures through more effective single session management. We also would like to highlight the fact that due to the age of the publications some of the papers considered do not assess technologies that are the current UK standard of care. Neuhaus et al 1998, Jakobs et al 2007 and Jiang et al 2012; assessed LL via mother and baby technique an earlier version of visualising the biliary duct. Whilst we acknowledge these results can be considered within this review, we believe the age and relative disadvantages of	Thank you for your comment. The committee felt that it was important to establish the long-term safety of laser lithotripsy. Therefore, the safety statement in section 1.1 has been changed to *'evidence on its long-term safety is limited in quantity'*. Additional wording has been added to section 3.5 to reflect different techniques resulting in different outcomes: 'The committee was informed that the technique is evolving *and different techniques may have different efficacy and safety profiles*.' Ang et al. (2019) was included in the appendix. Bang et al. (2020) was included in the main extraction table. McCarty et al. (2020) has been added to the main extraction table.

			these studies justify further consideration of the more recent papers highlighted below. Newly published evidence A recent meta-analysis published after the literature search was concluded by NICE, helps exemplify how the technology has evolved since its inception and shows some of the limitations of the older papers currently within the overview. McCarty T, Gulati R, Rustagi T. Efficacy and Safety of Per-Oral Cholangioscopy with Intraductal Lithotripsy for Difficult Biliary Stones: A Systematic Review and Meta-Analysis. Endoscopy. 2020 Jun 16 Within this analysis the authors assessed efficacy (via overall fragmentation and single session fragmentation) and adverse events of different per-oral cholangioscopy technologies. As stated earlier; LL is delivered under direct visualisation. Originally this was achieved using a mother-daughter system, this was superseded by single operator cholangioscopy and more recently by a second generation of this technology called Spyglass DS, which is now the standard of care in the UK, for delivering EHL & LL therapy. The improvement in pooled rates of both efficacy and safety published in this meta-analysis are reported and highlighted below. It clearly demonstrates how efficacy and safety have improved as the technology has evolved. We encourage the committee to consider this article as we believe it is a significant publication presenting new evidence that directly relates to the concerns raised on the draft consultation. Data below extracted from table 2 in McCarty et al (2020): Efficacy and safety of peroral cholangioscopy: data of individual techniques for peroral cholangioscopy. Presented as a pooled rate (95% CI)	

			We would specifically like to highlight the reported adverse events of the legacy mother daughter approach and second-generation direct visualisation single operator cholagioscope (UK standard of care) which were 13.5% and 4.6% respectively. Mother – Daughter system Overall Fragmentation: 89.3% (81.5-94.1) Single session Fragmentation: 66.8% (54.0–77.5) Adverse events: 13.5% (8.5–20.7) First Generation direct visualisation single-operator cholangioscope Overall Fragmentation: 90.1% (82.1-94.6) Single session Fragmentation: 80.6% (65.5-90.1) Adverse events: 9.8% (6.5-14.4) Second Generation direct visualisation single-operator cholangioscope Overall Fragmentation: 95.0% (92.2-96.8) Single session Fragmentation: 82% (74.9-87.5) Adverse events: 4.6% (3.1-6.9)	
7	Consultee 1 Company Boston Scientific	**Overview**	We note that the following 2 papers were not included in NICE's evidence overview. We ask the committee would look again at this evidence as we feel it makes a positive	Thank you for your comment.

			contribution to demonstrating the safety of laser lithotripsy. 1. Jin Z, Wei Y, Tang X, Shen S, Yang J, Jin H, Zhang X. Single-operator peroral cholangioscope in treating difficult biliary stones: A systematic review and meta-analysis. Digestive Endoscopy. 2019 May;31(3):256-69. Rationale: This analysis included sub-group analysis of LL delivered via SOPOC. It reported a pooled AE rate of 8.1% (95% CI 3.6 - 13.7%) 2. Maydeo AP, Rerknimitr R, Lau JY, Aljebreen A, Niaz SK, Itoi T, Ang TL, Reichenberger J, Seo DW, Ramchandani MK, Devereaux BM. Correction: Cholangioscopy-guided lithotripsy for difficult bile duct stone clearance in a single session of ERCP: results from a large multinational registry demonstrate high success rates. Endoscopy. 2019 Oct;51(10):C4. Rationale: Whilst the design is not RCT it is a relevant paper for the following reasons. Contains 117 patients treated with LL via SOPOC. Reports on procedure related AE's for the entire cohort: 1.9%.	Jin et al. (2019) and Maydeo et al. (2019) have been added to the main extraction table.
8	Consultee 1 Company Boston Scientific	**1.1**	Closing remarks We would ask that the committee reviews its proposal to recommend that Laser lithotripsy for difficult-to- treat bile duct stones should be given special measures status. We would like to re-emphasie our rationale for this request with the following points. Laser Lithotripsy with Single Operator Per Oral cholagioscopy is an established procedure in difficult to treat bile duct stones and it offers patients with limited therapy options an effective alternative to surgery.	Thank you for your comment. The committee has considered this comment but decided not to change the recommendation of special arrangements. The statement about biliary stricture and ERCP has been removed from section 1.1. The committee felt that it was important to establish the long-term safety of laser lithotripsy. Therefore, the safety statement in section 1.1 has been changed to *'evidence on its long-term safety is limited in quantity'*.

			1. The risks associated with ERCP are known and accepted and we therefore question the need to include them explicitly in the opening statement as they cloud the focus of the IPG 2. We do not see the rationale for highlighting the risk of bile duct stenosis 3. We believe the procedure has a good evidence base that demonstrates no concerning safety signals and in fact demonstrates benefits such as fewer repeat procedures which may lessen patient risk and burden on the system. References 1. Shenbagaraj L et al. Endoscopy in 2017: a national survey of practice in the UK. Frontline gastroenterology. 2019 Jan 1;10(1):7-15 2. NICE MIB21 2005: The SpyGlass direct visualisation system for diagnostic and therapeutic procedures during endoscopy of the biliary system 3. Health Technology Wales 2020. Evidence Appraisal Report. Single-operator per-oral cholangioscopy for the evaluation and treatment of hepato-biliary-pancreatic disorders 4. HAS-Saute HTA 2020: Spyscope. Access and administration catheter for single-use operator cholangiopancreatoscope : https://www.has-sante.fr/jcms/p_3169456/fr/spyscope-ds 5. Manes G, Paspatis G, Aabakken L, Anderloni A, Arvanitakis M, Ah-Soune P, Barthet M, Domagk D, Dumonceau JM, Gigot JF, Hritz I. Endoscopic management of common bile duct stones: European Society of Gastrointestinal Endoscopy (ESGE) guideline. Endoscopy. 2019 May;51(05):472-91.	Ref 1: This study reported the results from a national survey of endoscopic practice in the UK. It did not meet the inclusion criteria. Ref 2: There was 1 study (Maydeo et al. 2011) which was relevant to this procedure and was included in Veld (2018) in the main extraction table. Ref 3 has been added to the ‘existing assessments’ section of the overview. Ref 4 - non-English-language article - did not meet the inclusion criteria. Ref 5 and 6 were included in the ‘existing assessments’ section.

			6. Williams E, Beckingham I, El Sayed G, Gurusamy K, Sturgess R, Webster G, Young T. Updated guideline on the management of common bile duct stones (CBDS). Gut. 2017 May 1;66(5):765-82.	

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