BIODEGRADABLE STENTS FOR THE TREATMENT OF REFRACTORY OR RECURRENT BENIGN OESOPHAGEAL STENOSIS

Input from manufacturers, external reviewers and Strand B members on V 3.1 of the pilot rapid assessment

Assessment

Pilot ID: WP5-SB-14

CONTENT

STRAND B MEMBERS

Comments were received from:

Names	Agency
Zoltan Huszti Németh Bertalan Juhász Jácinta	OGYÉI, National Institute of Pharmacy and Nutrition Department of Health Technology Assessment, Hungary
Sylvana Magrin Sammut Isabell Zahra-Pulis	MEH, Directorate for Pharmaceutical Affairs, Ministry for Energy and Health, Malta
Renata Semeráková	Ministry of Health of the Czech Republic

Comment #	Comment received from	Page	Line number	Comment	Author's reply
Summary					
1	-	-	-	All agencies have reviewed the assessment and had no further comments	-

MANUFACTURES

Comments were received from:

Name	Company
Ivan Pohl	ELLA-CS s.r.o

Comment #	Page	Line	Comments	Character of comment • major ' =1 •'minor' = 2 •'linguistic' =3	Authors' reply
Summary					
1	5	90	Scope – no comments	---	---
2	6	127	The sentence does not end with terminal punctuation mark.	3	Changed
3	7	134	Oesophageal stents designed for relieving benign stenoses have been provided with covering primarily in order to prevent embedding of stent mesh in the mucosa, not to improve outcomes in general. Covering increased the risk of stent migration. I suggest to modify the present text.	2	Sentence modified
4	9	236	The word „analised" should be replaced by „analysed"	3	Changed
5	16	354	1 SCOPE (table) – Description (Population) – Project scope Present text: Rationale: Benign oesophageal stenosis (BOS) can be caused by a wide range of disorders such as the following: achalasia, anastomotic radiation, sclerotherapy, or medication induced strictures. Because of the fact that the main cause of BOS is corrosive effect of GE reflux (GERD) and imprecise formulation „anastomotic radiation" I propose to change the text as follows: Benign oesophageal stenosis (BOS) can be caused by a wide range of factors / disorders such as the following: acid peptic, autoimmune, infectious, caustic, congenital, iatrogenic,	1	Changed

			medication-induced, radiation-induced and achalasia.		
6	16	354	1 SCOPE (table) – Description (Intervention) – Project scope Present text: Oesophageal biodegradable stent (OBS).: The stent has been designed for oesophagus stenosis and is available in several sizes. I propose replace the formulation „oesophagus stenosis" by „oesophageal stenosis"	3	Changed
Health problem and current use of the technology					
7	20	418	I suggest to replace „as a sequel to gastroesophageal reflux disease" by „as a consequence of gastroesophageal reflux disease".	3	Changed
Description and technical characteristics of the technology					
8	28	694	Oesophageal stents designed for relieving benign stenoses have been provided with covering primarily in order to prevent embedding of stent mesh in the mucosa, not to improve outcomes in general. Covering increased the risk of stent migration. I suggest to modify the present text.	2	Changed
9	30	770	What kind of special premises are needed to use biodegradable oesophageal stents and the comparators? I suggest to complete the present text as follows: Because of material shape memory the biodegradable polydioxanone stent has to be loaded into the delivery system just before its implantation. This requires a training. SEPS requires the same procedure. SEMS are usually preloaded in the delivery system.	2	Sentence added
10	31	818	SX-ELLA Stent Esophageal Degradable BD (BD STENT) does not bear the trademark (TM).	2	Changed
Clinical effectiveness					
11	35	917 920 923	SX-ELLA Stent Esophageal Degradable BD (BD STENT) does not bear the trademark (TM).	2	Changed
Safety					
12	44	1204	SX-ELLA Stent Esophageal Degradable BD (BD STENT) does not bear the trademark (TM).	2	Changed
Appendix					
13	90	1677	Table 15: Summary table characterising the applicability of a		

			body of studies SX-ELLA Stent Esophageal Degradable BD (BD STENT) does not bear the trademark (TM).	2	Changed
General remarks/Other					
14			No general / Other remarks		

EXTERNAL REVIEWERS

Comments were received from:

Name	Affiliation
Jesus Garcia-Cano	Spanish Society of Digestive Endoscopy, Virgen de la Luz Hospital, Spain
Stefan Müller-Lissner	Internal Medicine Department, Park-Klinik Weißensee, Germany

Comment #	Comment received from	Page	Line number	Comment	Character of comment • major ' =1 ; •'minor' = 2 ; •'linguistic' =3	Author's reply
1	Müller-Lissner	General		This is a very carefully done analysis of the available literature on the subject of biodegradable stents for benign esophageal stenosis	N/A	---
2	Müller-Lissner	General		Due to the widely used proton pump inhibitors reflux-induced strictures have become quite uncommon explaining the difficulties in patient recruitment	2	This is a comment to justify the below proposal for changing the quality rating. The answer to the proposal is below.
3	Müller-Lissner	General		Anastomotic strictures after (partial) esophageal resection with esophago-gastric anastomosis are becoming more prevalent. However, the pathophysiology of this kind of stenosis is different (ischemia) and the population is in a less favorable state of health	2	It is a comment to justify the below proposal of changing the quality rating. The answer to the proposal is below.
4	Müller-Lissner	8	206	The sentence is correct. However the study probably allows the conclusion that BOS are not superior to balloon dilation for strictures	2	The comment proposes to set a conclusion regarding a different population than it was stated in our

Comment #	Comment received from	Page	Line number	Comment	Character of comment • major ' =1 ; •'minor' = 2 ; •'linguistic' =3	Author's reply
				whether refractory or not		PICO question. Our population was refractory or recurrent BOS. However the comment is about a population that includes strictures whether refractory or not. Therefore it is possible to set that conclusion in our assessment.
5	Müller-Lissner	8	195	I consider the quality higher than the authors since I do not expect further research to affect the conclusion that BOS are advantageous over the comparators. For the above reasons the recruitment rates will be low also in upcoming trials. Hence quality assessment by GRADE should be at least "low" if not "moderate".	2	The difficulties to recruit patients not justify ignoring imprecision as quality criteria. The RCT was cancelled with 15 recruited patients when the minimum size was 25. According to GRADE methodology the risk of bias can be qualified as "no risk", "serious risk" or "very serious risk". We rated the RCT as "very serious risk" and the cohort studies as "serious risk". Although we would upgrade the RCT qualification to "serious risk" the final punctuation will remain as "very low quality" because there are other limitations which are described in the table 12.
6	Müller-Lissner	8	197	Also the risk of bias looks overstated to me. Tables 12 & 13 show that most relevant items are considered "low risk".	2	Several bias risks were identify and described in tables 12 and 13. Because of that we cannot classify the studies as "no risk". The other categories are "serious risk" or "very serious risk". Although we would upgrade to "serious risk"" the final

Comment #	Comment received from	Page	Line number	Comment	Character of comment • major ' =1 ; •'minor' = 2 ; •'linguistic' =3	Author's reply
						qualification would remain as "very low quality" because there are other GRADE criteria that are downgrading the quality (imprecision and design). The GRADE evaluations are described in tables 9-11.
7	Garcia-Cano	11	320	One major issue is the lack of consensus about refractory benign stricture definition	2	Agree. This has been highlighted in several sections of the assessment.
8	Garcia-Cano	11	322	Although this biodegradable stent cannot be recommended for general treatment of refractory benign strictures it does not prevent from any individualized use.	2	The conclusion of our assessment is that the available evidence does not allow recommending OBS for the treatment of RRBOS. Our scope population is those affected by RRBOS and therefore our assessment is not aimed to assess an individualized use of the technology.

	Yes	Partly (please specify)	No (please specify)	Other (please specify)
Part I: Methods (see appendix 1 of the pilot assessment)				
Are inclusion/exclusion criteria for selection of the studies described in appropriate detail?	2X			
1. Are the quality appraisal tools appropriate?	X	See		

		comment 5 & 6		
2. Is the type/presentation of evidence (e.g. Meta analysis, qualitative synthesis, GRADE) appropriate for this analysis?	2X			
3. Is the risk of bias sufficiently assessed, both on study level and on an outcome level?	X	See comment 5 & 6		
4. Is the choice of study types appropriate to the population, intervention(s), comparison(s) and outcome(s)?	2X			
5. Are the types of studies to be included (randomised trials, quasi-randomised trials or other designs) described?	2X			
6. If it was relevant to include data from indirect comparisons, is this step justified and the methods of indirect comparisons sufficiently described?	2X			
7. Are appropriate methods of measuring each outcome and appropriate time points for measurement identified?	2X			

8. Details on sources of information and literature search strategies provided?

Search strategy	Databases	Year range	Language restriction	Primary data	Other kind of information resources
2x	2x	1x	2x	2x	2x

Comments
OBS are very new, therefore definition of a year range is not necessary.
Published sources have been appropriately included

9. Information on basis for the assessment and interpretation of selected data and information?

Method of data extraction described?	Critical appraisal method (for quality assessment of the literature) described?	Method of data synthesis described?
2x	2x	1x

Comments
Due to paucity of available data synthesis is not really possible
Published sources have been appropriately included

	Yes	**Partly (please specify)**	**No (please specify)**	**Other (please specify)**
Part II: Results (See Domain Reports)				
Health problem and current use of the technology				
1. Does the section describe the health issue including incidence and prevalence, how it occurs, who is affected (including high-risk groups,	2X			

vulnerable/disadvantaged populations, where it occurs, how it is diagnosed, symptoms and consequences)?				
2. Are the supporting references current and do they provide an international picture of the problem?	2X			
Description and technical characteristics of the technology				
3. Does the section describe the intervention under review including how it works and how it may have an impact on potential recipients?	1X	Potential advantages of BOS should be discussed and weighted		
4. Does the section describe the comparator(s) under review including how it works and how it may have an impact on potential recipients?	2X			
5. Are the supporting references current and do they provide an international picture of the problem?	2X			
Safety and effectiveness				
6. Is the risk of bias clearly reported?	1X	Overstated		
7. Is quality of data sufficiently evaluated?	2X			
8. Are both relative and absolute effect measures presented for each dichotomous outcome?	1X, 1 N/A			
9. Are continuous data reported according to appropriate statistics (e.g. 'standardised mean difference' or 'weighted mean difference')?	1X, 1 N/A			
10. In case of time-to event analysis, are hazard ratios (HR) and ratios of medians presented?	1X, 1N/A			
11. Are measures of the precision of the effect estimates presented or, in case of absence of this essential information, is this fact reported?	1X			
12. Is frequency of adverse events, frequency of occurrence, relative risk or number needed to harm (NNH) presented for the safety data?	X			
13. In cases where adverse events are incorporated in utility values of quality of life, is the source of quantification accessible?	1X, 1N/A			
14. Was the transformation of the surrogate outcomes into patient-relevant final outcomes considered (if relevant)?	1X, 1N/A			

General				
15. Do you agree that the data extracted are relevant to the research questions formulated in the beginning and that analysed and synthesised data still answer the question?	2X			
16. Can the results be applied to the intended population?	2X			
17. Is the assessment sufficiently transparent and evidence ('facts') distinguished from judgements (including values and preferences)?	2X			
Part III: Summary of Relative Effectiveness				
1. Does the summary present a balanced representation of the content of the report?	2X			
2. Does the discussion of the summary clearly address the uncertainty in the available evidence, the evidence gaps and the applicability of the evidence?	2X			
Part IV: Other Considerations				
1. Have all relevant ethical, organisational, social and legal aspects been considered? (See Appendix 3 of the Pilot assessment)	2X			