National Institute for Health and Care Excellence

IP885/2 Personalised external aortic root support (PEARS) using mesh to prevent aortic root expansion and aortic dissection in people with Marfan syndrome

IPAC date: 10 February 2022

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 1	**2.3**	It has specifically been identified that redo surgery on the aortic valve may be required after valve-sparing aortic root replacement. This is true. But there is also a risk that redo surgery on the aortic valve is required after the PEARS procedure, and if it is, this is likely to be a complex procedure. The risk cannot be mentioned against one approach and not the other.	Thank you for your comment. A committee comment has been added, stating that in common with valve-sparing aortic root replacement, patients may need further surgery on the aortic valve at a later date.
2	Consultee 2	**General**	Since the first Aortic PEARS operation in 2004 we have become sufficiently confident in the safety of the operation after 500 patients to extend its application as an adjunct to the Ross pulmonary autograft procedure for aortic valve disease. Over the last 6 years 60 Ross-PEARS procedures have been carried out with one mortality. The objective is to use the PEARS sleeve to prevent dilatation of the pulmonary autograft, placed in the systemic circulation, which occurs in one third of patients, and thus make the procedure more durable. A single surgeon series of 35 patients was presented by Redondo A and Austin C in November 2021 to the Aortic Forum at the European Association of Cardiothoracic Surgeons and a manuscript is about to be submitted.	Thank you for your comment. A committee comment has been added, stating that the procedure may be used in conjunction with other procedures.

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3	Consultee 3 Company	**1.1**	We question the validity of the draft recommendation that reads “Evidence is limited on long-term outcomes in quantity and quality” and believe in reaching this conclusion that the Committee may not have referred to all the data provided by Exstent Limited, especially as this relates to all the data collected from each case in accordance with the recommendation made by NICE in their original guidance in May 2011.	Thank you for your comment. The committee considered this comment but decided not to change the guidance.
4	Consultee 3 Company	**1.1**	The consultation document does not define what is meant by “long-term”. The published literature on the PEARS procedure considered by the Committee includes patients followed up for a median 21 months and a maximum 15 years. In data provided to the Committee by Exstent Limited in August 2021, the post-operative experience was advised as exceeding 1,430 patient years, with 25 patients at more than 10 years and 76 patients at more than 5 years post-op. (The current figures are 1,607 post-operative patient years on 561 patients, with 29 patients at more than 10 years and 84 patients at more than 5 years post-op). We note that in the related guidance quoted in the Overview document on the E-vita device for treating complex aneurysms and dissections of the thoracic aorta the data considered reported on 5-year follow-up, and yet no reference is made to there being insufficient long-term data on outcomes.	Thank you for your comment. The committee considered this comment but decided not to change the guidance. Although there is some long-term evidence, the committee felt that there is still some uncertainty about potential long-term safety events and long-term efficacy in the context of a pre-emptive procedure being used to treat a condition with an unpredictable natural history. In particular, the committee wanted to see more evidence on the progress and extent of aortic dilatation and the occurrence of aortic dissection.

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5	Consultee 3 Company	**1.1**	In terms of the quantity of evidence, the published data considered by the Committee included a study that reported on all the first 200 patients to receive the PEARS procedure, and in its submission to the Committee, Exstent Ltd reported on having data on the 519 patients that had been treated up to August 2021. We note that in the related guidance quoted in the Overview document on the E-vita device for treating complex aneurysms and dissections of the thoracic aorta reference is made to a study on 274 patients and yet there is no reference to a shortcoming in the quantity of data provided.	Thank you for your comment. Section 1.1 of the draft guidance states that evidence on short-term outcomes is adequate, but evidence on long-term outcomes is limited in quantity and quality. Efficacy data that are unpublished or not peer reviewed are not normally selected for presentation to the Committee.
6	Consultee 3 Company	**1.1**	As to the quality of the evidence, both the published data considered by the Committee and the information provided to the Committee by Exstent Limited is based upon clinical data obtained from a data collection form completed for all patients that includes all the items recommended by NICE in the original guidance in May 2011. We fail to see that this can be accurately described as limited.	Thank you for your comment. Section 1.1 of the draft guidance states that evidence on short-term outcomes is adequate, but evidence on long-term outcomes is limited in quantity and quality. Efficacy data that are unpublished or not peer reviewed are not normally selected for presentation to the Committee.

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7	Consultee 3 Company	**1.1**	We believe that in justifying its qualification on evidence of long-term outcome it is relevant for the Committee to fully consider the data on the success of the PEARS procedure and the unlikely theoretical risks that might be seen in the longer term. In terms of success, it should be noted that in 100% of the cases in which the ExoVasc PEARS implant has been correctly implanted there has been no further dilatation of the ascending aorta and no incidence of dissection. The evidence cited in the submission to the Committee by Exstent Limited includes a histological study confirming that within a period of 4.5 years the ExoVasc PEARS implant is fully incorporated in the tissue of the aortic wall and that this allows the generation of a normal media layer within the vessel. Further evidence from animal experiments suggests that this incorporation occurs within a matter of months after implantation. It is thus doubtful that any material adverse events associated with the PEARS implant are likely to occur over the longer-term period. It should also be noted that in the clinical studies considered by the Committee reference is made to the fact that in the unlikely event that a further procedure was required in the longer-term all the conventional surgical approaches remain open.	Thank you for your comment. The cited histological study is included in the key evidence in the overview (study 6). In accordance with the IP programme manual, animal studies are not included in the overview and not considered by the committee.

"Comments received in the course of consultations carried out by NICE are published in the interests of openness and transparency, and to promote understanding of how recommendations are developed. The comments are published as a record of the submissions that NICE has received, and are not endorsed by NICE, its officers or advisory committees."

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