National Institute for Health and Care Excellence

IP1822 Coronary sinus narrowing device implantation for refractory angina

IPAC date: 9 September 2021

Com. no.	Consultee name and organisation	Sec. no.	Comments	Response Please respond to all comments
1	Consultee 3 Neovasc Company	Title	"Comment from [redacted] For clinical reasons, it is important to distinguish the Reducer from a stent. A stent is implanted in an epicardial artery and is intended to keep the vessel patent. The Reducer has a very different purpose. It aims at operating a controlled closing of a vein to a specific value. For this reason, we recommend calling it “the Reducer” or a “Reduction device” and not a stent."	Thank you for your comment. The term ‘stent’ has been replaced with ‘narrowing device’.
2	Consultee 1 NHS Professional	1.1	Agree	Thank you for your comment. Consultee agrees with main recommendation.
3	Consultee 2 Royal College of Physicians and surgeons of Glasgow	1.1	"General Comment: Royal College of Physicians and Surgeons of Glasgow Our expert reviewer was concerned that there was only one randomised controlled study and six case studies. The RCT had only 52 patients in each group. Implantation of the stent failed in two patients so there were only 50 stented patients and follow up was for six months only. Two thirds of the treated group had an adverse event and 20% a serious adverse event. The case series did not randomise and is therefore open to bias by either the doctor or patient in those allocated to the treatment group. Two cases series had a mortality of 10%.	Thank you for your comment. Consultee agrees that there is a lack of evidence on efficacy.

			In the absence of more, larger and properly randomised studies with longer follow-up, it is difficult to be convinced of the true efficacy and benefit to the patient. Many of these patients may benefit from efforts to enhance lifestyle modification which are unlikely to have side effects and have more proven longer-term efficacy (not just in terms of CVS risk). The intervention comes with financial considerations which would be difficult to justify on the basis of current evidence"	
4	Consultee 7 NHS Professional	1.1	"Line 1 of the draft recommendations is about the complications of the procedure, not whether it helps with angina or not, which seems contrary to me. I would suggest the wording be revised to comment first on the procedure efficacy and then, comment on the complications, if that is felt to be a significant problem with this procedure"	Thank you for your comment. The committee considered this comment but decided not to change the guidance.
5	Consultee 9 NHS Professional	1.1	Specific comments 1.1 It is not clear to me which well-recognised complications are being referred to. All but one patient we treated went home the same day after 4 hours. There were no deaths, myocardial infarctions, conduction disturbance, or vascular complications. We have had two device embolisations. In one, the coronary sinus was too big (the maximum size of the device is 13 mm in diameter) and the device embolised to the pulmonary circulation without complication (overnight stay). The patient returned for a second device implanted higher successfully. In the second case, where we dislodged the stent from the deployment balloon, we pushed the device into the anterior interventricular vein and dilated it there without complication.	Thank you for your comment. Adverse events reported in the literature included myocardial infarction, device embolisation, migration or dislocation and coronary sinus dissection or perforation.
6	Consultee 1 NHS Professional	1.2	Agree	Thank you for your comment. Consultee agrees with section 1.2 of the draft guidance.

7	Consultee 2 Royal College of Physicians and surgeons of Glasgow	1.2	"It is our view that there is a real need for a more extensive RCT to justify further use of this procedure. There is also need to consider financial costs of the procedure compared to other measures. Whilst we accept the committee's recommendations we would go further and say this procedure should only be done in larger centres with expertise and RCT conditions."	Thank you for your comment. The IP programme does not consider cost-effectiveness. Section 1.5 of the draft guidance states: 'The procedure should only be done in specialist centres by interventional cardiologists with specific training in the technique.'
8	Consultee 4	1.2	"All patient leaflets should be written in plain English. Co produced with patients with a lived experience of Refractory Angina. This should include a patient describing how it felt to go through the procedure. A patient speaking about a positive result and also a patient speaking about no change in symptoms."	Thank you for your comment. The use of NICE's 'Information for the public' is recommended, but this is a lay description of the IP guidance recommendations and does not describe the procedure in detail. There are 2 lay members on the committee, who comment on the wording of this document. As part of the usual process, NICE's Public Involvement Programme sent questionnaires to clinicians for distribution to patients who had the procedure, but we did not receive any responses. Healthcare professionals should ensure that the patient understands the risks, benefits and possible consequences of different options through discussion and information sharing.
9	Consultee 4	1.4	"Pain is a complex condition. The Multidisciplinary team should include: A Cardiologist experienced in inserting the Coronary Sinus Reducer,	Thank you for your comment. Section 1.4 of the draft guidance states 'Patient selection should be done by a multidisciplinary team.'

			A Clinical Psychologist experienced in working with patients living with chronic cardiac pain. Clinical Nurse Specialist experienced in caring for patients with refractory angina. Cardiac rehabilitation Specialist. The patient themselves should be involved in any multidisciplinary meetings"	The committee considered this comment but decided not to change the guidance.
10	Consultee 6 Specialist society BCS	1.4	- Patient selection is key and will always need to be within the governance structure of a multidisciplinary heart team as laid out in the recent BCS guidelines.	Thank you for your comment. Section 1.4 of the draft guidance states ‘Patient selection should be done by a multidisciplinary team.’
11	Consultee 4	1.5	This is very important and highlighted by Dr Jonathon Hill in his comments to the consultation.	Thank you for your comment. Consultee agrees with Section 1.5 of the draft guidance, which states ‘The procedure should only be done in specialist centres by interventional cardiologists with specific training in the technique’ and refers to the Professional Expert Questionnaire submitted by Jonathan Hill.
12	Consultee 1 NHS Professional	1.5	This can be any centre that offers a broad spectrum of treatments for angina including medical therapy, complex PCI including CTO PCI, exercise rehabilitation and other holistic approaches.	Thank you for your comment.
13	Consultee 5 Aquilant Ltd Company	1.5	"1. Local Company representative will present Clinical data, mode of action, patient assessment and suitability via a mixture of face to face meetings and using our marking material such as previous Clinical Webinars, Case videos, interactive PDF etc. 2. We then align the new Clinician with one of the Reducer proctors in different parts of the country depending	Thank you for your comment. Consultee has described the training that is provided by the device distributor in the UK.

			on geography. They will typically go and observe some cases at the proctor's hospital. 3. Once happy with the procedure the new clinician usually talks through prospective patients via a virtual MDT with the proctor and their local representative 4. A date is set where they can do a number of cases gathered (4-5) and the proctor attends as an honorary clinician to guide the new clinician in a series of cases on the same day to cement the techniques into the whole clinical team. 5. Just before this proctored Reducer day the local account manager will visit the hospital and train the clinical staff on the procedure, set up etc. 6. The local company representative will then be present at every Reducer case. If the new Clinician requires further proctoring, we facilitate this. Aquilant Ltd - Distributor for Neovasc in the UK."	
14	Consultee 3 Neovasc Company	1.7	From [redacted], We would like to highlight that Neovasc has been supporting the gathering of patient data to assess long term outcomes and safety data. The Reducer 1 will enroll 500 patients and follow them for 5 years. It is a multinational prospective study where the UK is to date the largest enroller. The interim results on the first 228 patients have been recently published, and show sustained benefit at 2 years, They also show that 42% of patients had an emergency department visit prior to Reducer implant. The number of visits per patient decreased 72% at 1 year (from 0.69 to 0 .19m p<0.0001))	Thank you for your comment. The Reducer 1 trial is included in the list of ongoing trials in the overview. The recent published study of interim results is included in the post consultation literature search and has been added to the key evidence in the overview (Verheye S et al. 2020).
15	Consultee 9 NHS Professional	1.7	1.7 All interventions in stable angina in the modern era are for symptom relief and quality of life. They do not impact on survival and thus mandating documentation of survival in future trials is not required. Furthermore, one would require a	Thank you for your comment.

			randomised trial in a very large number of patients to even attempt this highly likely negative trial (see 3.5).	The committee considered this comment but decided not to change the guidance. Survival was considered to be a relevant outcome to be reported in any future research, but the guidance does specifically state in section 3.6 that that the intention of the procedure is to improve symptoms and quality of life, rather than to improve survival.
16	Consultee 4	1.7	"There needs to be larger studies into the use of Coronary sinus reducers, including more women participants. Most of the present research focuses mainly on men with no long term follow up of outcomes. Are the improvements in the Quality of life sustained overtime? As women's hearts are physically smaller will this effect the efficiency of the device."	Thank you for your comment. Section 1.7 of the guidance states that further research should report details of patient selection and long-term patient outcomes.
17	Consultee 3 Neovasc Company	2.5	From [redacted], The vast majority of implants occur via the right jugular vein. There have been a few cases performed via the femoral vein for patients of smaller stature to accommodate the system length. Per the Reducer IFU, we would suggest the following wording: “The Reducer System is introduced to the coronary sinus by right heart catheterization through the right or left internal jugular vein.”	Thank you for your comment. Section 2.5 of the guidance has been changed.
18	Consultee 9 NHS Professional	2.5	2.5 The device is not inserted via the femoral vein. The left internal jugular vein (IJV) has been used occasionally if there is right IJV occlusion (post central line for example). Imaging is used to ensure that there is “hour-glass” device expansion, not to ensure that the coronary sinus is occluded. The device is a stent and thus venous blood flows through the stenosis in the centre as well as through the edges of the stent.	Thank you for your comment. Section 2.5 of the guidance has been changed.

19	Consultee 9 NHS Professional	2.6	Over time, with endothelialisation, a functional stenosis occurs leading to an increase in the post-capillary venous pressure in the territory of the anterior interventricular and high lateral circumflex veins which drain the myocardial territory subtended by the left anterior descending artery and high obtuse marginal branches of the left circumflex artery. As the device is deployed in the great cardiac vein above the middle cardiac vein, it has no effect on coronary venous pressure in the territory of the right coronary artery.	Thank you for your comment. Section 2.6 has been changed to ‘’Over time, endothelialisation occurs which creates a functional stenosis. This leads to an increase in the post-capillary venous pressure and redistribution of blood from the less ischaemic epicardium to the ischaemic endocardium’.
20	Consultee 6 Specialist society BCS	3.1	- The data is undefined by one small placebo-controlled RCT (COSIRA, Verheye et al, NEJM 2015). The techniques used to blind patients and physicians in this trial had limitations and no data were provided on the integrity of blinding. - Data from the larger placebo-controlled COSIRA-II RCT is awaited.	Thank you for your comment. COSIRA-II is not currently listed on the ClinicalTrials.gov website.
21	Consultee 3 Neovasc Company	3.2	[redacted], A significant reduction in hospitalization and outpatient visits have also been documented. We would also suggest adding these as outcomes. In a published cost effectiveness study published by Gallone in the EHJ (ref doi:10.1093/ehjqcco/qcz027), Reducer therapy decreased hospital days per patient by 71% (from 3.4 to 1.0 total hospitalization days per patient year). Reducer therapy also reduced outpatient visits 67% (from 2.1 to 0.7 outpatient visits per patient year).	Thank you for your comment. The IP programme does not consider cost effectiveness. Section 3.2 notes the key efficacy outcomes and is not intended to be a comprehensive list of relevant outcomes.
22	Consultee 3 Neovasc Company	3.4	"[redacted], The mechanism of action is known. It is a process of redistribution of blood flow from the less ischemic sub epicardium to the more ischemic sub endocardium. The hourglass shaped Reducer creates a fixed focal narrowing in the lumen of the Coronary Sinus, leading to an increased backwards pressure that causes slight dilatation and a consequent reduction in the resistance to flow in the	Thank you for your comment. The committee considered this comment but decided not to change the guidance.

			arterioles of the ischemic subendocardial myocardium. This subsequently causes a redistribution of blood from the less ischemic sub-epicardium to the more ischemic sub-endocardium. This mechanism of action is supported by scientific reports showing reduction in myocardial ischemic burden, improvement in diastolic function and improvement in systolic function."	
23	Consultee 9 NHS Professional	3.4	3.4 The mechanism of action is the pressure-induced recruitment of additional arteriolar collateral vessels.	Thank you for your comment. The committee considered this comment but decided not to change the guidance.
24	Consultee 6 Specialist society BCS	3.4	- The mechanism of action is unclear and is the subject of an ongoing multi-centre clinical trial in the UK (https://clinicaltrials.gov/ct2/show/NCT04892537)	Thank you for your comment. The trial referred to is: Coronary Sinus Reducer Objective Impact on Symptoms, MRI Ischaemia and Microvascular Resistance (ORBITA-COSMIC), which is listed as 'not yet recruiting' with an estimated end date of January 2024. This will be added to the list of ongoing trials in the overview.
25	Consultee 4	3.4	"The issue that the exact mechanism of how the reducer works needs to be openly discussed with candour. Patients living with chronic pain are a very vulnerable group. There is a possible placebo effect that needs to be explained fully to patients. Also the issue that 20% of patients do not respond to treatment.	Thank you for your comment. Healthcare professionals should ensure that patients understand the risks, benefits and possible consequences of different options through discussion and information sharing.

			This needs to be further investigated by invasively testing for microvascular dysfunction and coronary vasospasms with acetylcholine. Non obstructive causes of coronary heart disease are more common in women. Vasomotion motion disorders can also occur with obstructive CAD. Some patients can develop on going angina following an insertion of stent. Because the mechanism of the coronary sinus reducer is not known patients with confirmed ischaemia and non obstructive coronary arteries INOCA, should not be offered Coronary sinus reducers until there is more evidence to prove their safety and efficiency."	The fact that non-obstructive coronary artery disease is more common in women will be noted in the equality impact assessment, which is published on the NICE website when the guidance is published. Section 1.4 of the guidance states that 'Patient selection should be done by a multidisciplinary team.'. Section 1.7 of the guidance notes that further research should include details of patient selection.
26	Consultee 4	3.5	"Patients should be offered alternative pain management strategies to manage their angina pain prior to the recommendation of a sinus coronary reducer. A pain Management programme run by a Clinical Psychologist, Clinical Nurse Specialist, Cardiac rehabilitation with input from patient support groups with a lived experience of pain and angina. Non pharmacological approaches can include, Cognitive behavioural Therapy, Breathing and relaxation exercises, Self hypnosis, Tai Chi, Yoga and exercise including pacing techniques. Peer to peer support groups.	Thank you for your comment. Section 3.6 of the guidance states that the procedure is indicated for angina that is refractory to medication or further coronary artery intervention. The IP programme does not assess the efficacy and safety of comparator interventions.

			At present there has been little research into these methods of patients managing their angina and would benefit from further research. The Angina Plan should be offered to patients. The Angina plan is currently being revised by Prof Patrick Doherty https://www.york.ac.uk/healthsciences/our-staff/patrick-doherty/#profile-content https://www.touchcardio.com/interventional-cardiology/journal-articles/the-coronary-sinus-reducer-clinical-evidence-and-new-perspectives-on-an-emerging-tool-in-the-treatment-of-refractory-angina/"	
27	Consultee 6 Specialist society BCS	3.5	- The coronary sinus reducer (stent) is certainly a device that should only be considered for improvement of quality of life and angina. The procedure will not improve prognosis.	Thank you for your comment. Section 3.5 of the guidance states that 'The committee noted that the intention of the procedure is to improve symptoms and quality of life, rather than to improve survival.'
28	Consultee 6 Specialist society BCS	3.6	- It should only be considered in patients with refractory symptoms despite optimum medical therapy and in the absence of revascularization options. These criteria will need to be reviewed by the heart team with clear documentation of the discussion.	Thank you for your comment. Section 3.6 of the guidance states 'The committee noted that the procedure is indicated for angina that is refractory to medication or further coronary artery intervention.'
29	Consultee 6 Specialist society BCS	3.6	I think the key to this is that patients who have other options should not be offered the therapy. It is expensive and the data is patchy. If patients can have revascularization or indeed more medical therapy I believe the evidence base would favour this approach. The last thing we would want is patients who could have their CTO opened by an	Thank you for your comment. Section 3.6 of the guidance states 'The committee noted that the procedure is indicated for angina that is refractory to medication or further coronary artery intervention.'

			experienced operator just having a CSR implanted because it is the easier procedure!	
30	Consultee 8 Specialist society RCP	General	The RCP is grateful for the opportunity to respond to the above consultation. We would like to endorse the response submitted by the British Cardiovascular Society (BCS).	Thank you for your comment.
31	Consultee 9 NHS Professional	General	In Edinburgh, we have the largest experience of Reducer implantation in the UK having contributed to the COSIRA trial and subsequently in regular clinical practice. In total, we have implanted 65 such devices from 2012 to date. We have selected patients with refractory angina on maximally tolerated medical therapy who have mostly undergone previously revascularisation (usually CABG) and who do not have a percutaneous interventional option. In our experience, these patients who have nowhere further to go therapeutically, undergo a very safe procedure via the internal jugular vein with an average skin-to-skin procedure time of 30 minutes. Overall, I would say that ¾ of patients treated notice a benefit in terms of angina frequency/severity and improved exercise capacity. Around ¼ notice very little difference. My opinion is similar to that of Dr Jonathan Hill in his Professional Expert Questionnaire.	Thank you for your comment.