# National Institute for Health and Care Excellence

## IP1980 Transcatheter aortic valve implantation for native aortic valve regurgitation

**IPAC date: 3rd April 2025**

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| 1. | Consultee 2<br>NHS professional<br>Hull University Teaching Hospitals NHS Trust | overall comment | I am happy with this document. This should be a vehicle for all TAVI centres to establish this treatment for the right patients outlined in the document. This document should not be used to restrict only some centres to utiltise this technology which goes against adequate access to treatment. | Thank you for your comment.<br>Evidence and professional experts have highlighted the difficulties and challenges, and extra training needed to do this procedure.<br>Section 1.7 in the guidance states that *'TAVI is a technically challenging procedure that should only be done in specialised centres and only by teams with specific training and experience in complex endovascular interventions. There should be both cardiac and vascular surgical support for the emergency treatment of complications from TAVI and subsequent care.*<br>This recommendation does not restrict its use but provides guidance to the NHS to introduce procedures appropriately.<br>It is not within the remit of the IP Programme to advise the NHS on whether interventional procedures should be available to all centres. |
| 2. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Lay description | In transcatheter aortic valve implantation (TAVI) a tube (catheter) is inserted into the heart through a large blood vessel, usually in the groin, or directly through the chest wall. A replacement valve is passed through this tube and inserted (implanted) inside the existing faulty valve (the native valve). The aim is to **provide a less invasive alternative to open cardiac surgery for the** | Thank you for your edits.<br>IPAC considered your edits and amended the lay description as follows:<br>*'The aortic valve controls the flow of blood out of the lower left chamber of the heart into the main artery (aorta). In aortic valve regurgitation, the aortic valve is unable to close properly and allows blood to leak* |

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| | | | **treatment of native aortic valve regurgitation which avoids the need for cardiopulmonary bypass,** reduce symptoms**, improve functional status** and prolong life. | *back into the heart. This can cause fatigue, chest pain and shortness of breath, and may lead to heart failure.*<br>*In transcatheter aortic valve implantation (TAVI) a tube (catheter) is inserted into the heart through a large blood vessel, usually in the groin, or directly through the chest wall. A replacement valve is passed through this tube and inserted (implanted) inside the existing faulty valve (the native valve). This procedure could provide a less invasive alternative to open cardiac surgery, avoiding the need for cardiopulmonary bypass. The aim is to reduce symptoms and prolong life'.* |
| 3. | Consultee 1<br>Company JenaValve Technology GmbH and JenaValve Technology Inc. | 1, overall comment | Overall comment: To address 'TAVI' without delineation of on-label TAVI for AR versus off-label AS TAVI for AR is to ignore the current practice of utilizing AS TAVI for the populations addressed in this IPG, as well as the therapeutic difference in outcomes for patients when AS TAVI is used for AR (off-label) versus the TAVI with the only regulatory approval to treat AR (on-label).<br><br>Regulatory approval is for safety and efficacy. If AS TAVI valve were able to achieve the key thresholds for safety and efficacy for AR patients, AS TAVI valves would have an AR indication.<br><br>Any opacity, vagueness, lack of specificity or otherwise that does not guide treatment for AR towards that which has gained regulatory approval to do so places patients in jeopardy, as | Thank you for your comments.<br><br>IP guidance is not device specific and is designed to make recommendations on the safety and efficacy of a procedure. Evidence on both on-label and off-label TAVI for AR has been considered while drafting the recommendations. Section 3.5 of the guidance, highlights that some of the evidence came from valves not approved for this indication (non-CE marked devices) and that the evidence shows worse safety outcomes when valves not indicated for use in aortic valve regurgitation are used.<br>IPAC considered your comments but decided not to change the guidance in response to this comment. |

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| | | | well as creating an unnecessary burden on the UK's health system. | |
| 4. | Consultee 1<br>Company JenaValve Technology GmbH and JenaValve Technology Inc. | 1.1 When SAVR is not suitable or is high risk | Separating out these two populations is in line with what was granted AS TAVI in IPG 421. Not allowing for AR TAVI use in SAVR unsuitable patients provides continuation of the unmet need for this patient population, or leaves these patients with the suboptimal option, as is currently provided, of AS TAVI for the most sick and severe AR patients. | Thank you for your comments.<br><br>The committee made the recommendations on the procedure, taking account of the overview of evidence, specialist advice and patient commentary.<br><br>Draft guidance in section 1.1 recommends 'special arrangements' when SAVR is not suitable or is high risk because evidence on short-term efficacy is limited in quality and comes mainly from small observational studies or registries (for CE marked devices). There is also lack of evidence on long-term outcomes.<br><br>Special arrangements mean that there are uncertainties about whether a procedure is safe or effective. These will need to be carefully explained to a patient before they make a decision. This recommendation places emphasis on the need for informed consent. This includes both the patient (or carer) and senior medical staff, such as the clinical governance lead in their trust. This recommendation does not restrict the use of TAVI for AR in those who are unsuitable for SAVR. |

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| | | | | Clinicians using these procedures should collect data, either by audit or research.<br><br>IPAC considered your comments but decided not to change section 1.1 in response to this comment. |
| 5. | Consultee 1<br>Company JenaValve Technology GmbH and JenaValve Technology Inc. | 1.1 When SAVR is not suitable or is high risk | **1.1 Evidence on the safety of transcatheter aortic valve implantation (TAVI) shows the potential for serious but well recognized complications.**<br><br>**1.2 For patients with native aortic valve regurgitation who are considered to be unsuitable for surgical aortic valve replacement (SAVR) the evidence on the efficacy of on-label use of AR TAVI is adequate. For these patients, on-label AR TAVI for native aortic valve regurgitation may be used with normal arrangements for clinical governance, consent and audit.**<br><br>**1.3 On-label AR** transcatheter aortic valve implantation (TAVI) for native aortic valve regurgitation can be used in the NHS while more evidence is generated to treat native aortic valve regurgitation when surgical aortic valve replacement (SAVR) ~~is not suitable or~~ is high risk. **On-label AR TAVI for native aortic valve regurgitation** ~~it~~ can only be used with special arrangements for clinical governance, consent, and audit or research. | Thank you for your edits to section 1.1.<br>Please see NICE's response to comment 4. |

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| 6. | Consultee 1<br>Company JenaValve Technology GmbH and JenaValve Technology Inc. | 1.2 When SAVR is not suitable or is high risk | **1.4** Clinicians wanting to do **on-label AR** TAVI when SAVR is not suitable or is high risk should:<br>• Inform the clinical governance leads in their healthcare organisation.<br>• Ensure that people (and their families and carers as appropriate) understand the procedure's safety and efficacy, and ~~any uncertainties about these~~ **differences between on-label and off-label use safety and efficacy risks in device selection for treatment of native aortic regurgitation.**<br>**• Ensure that people indicated for native aortic valve regurgitation TAVI have the option to be referred to a NHS hospital that utilizes on-label AR TAVI for treatment of native aortic regurgitation.**<br>• Take account of NICE's advice on shared decision making, including NICE's information for the public.<br>• Audit and review clinical outcomes of everyone having the procedure. The main efficacy and safety outcomes identified in this guidance can be entered into NICE's interventional procedure outcomes audit tool (for use at local discretion).<br>• Discuss the outcomes of the procedure during their annual appraisal to reflect, learn and improve. | Thank you for your edits to section 1.2.<br>IPAC considered your comments but decided not to amend section 1.2 in the guidance.<br><br>IP guidance is not device specific. A wide range of valves will be available to address individual needs. So therefore, in section 3.5 of the guidance the committee has noted that some of the evidence came from valves not approved for this indication and that the safety outcomes were worse when these technologies were used. The committee was informed that for compassionate use, clinicians may still use non-CE marked devices if necessary. |
| 7. | Consultee 1<br>Company JenaValve Technology GmbH and JenaValve Technology Inc. | The procedure<br>2.4 to 2.8 | **2.9 At present there is only one TAVI device approved for this procedure. Off-label use of TAVI for AR carries significant additional mortality and complications risk and should only be used on an emergency basis.** | Thank you for your edits and suggesting adding a sentence to section 2 (procedure description).<br>IPAC decided not to add this sentence to section 2.<br>Section 3.5 currently states that *'Some of the evidence comes from prosthetic aortic valves that do not have regulatory approval for use in AR. The* |

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| | | | | *evidence shows worse safety outcomes when valves not indicated for AR are used'*. |
| 8. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Committee comments | **3.5**<br>Some of the evidence comes from prosthetic aortic valves that do not have regulatory approval for use in this indication. The evidence shows worse safety outcomes**, complications, reintervention rates and mortality risk** when valves not indicated for use in aortic valve regurgitation are used. **Registries, single-centre studies, and case reports show that existing commercial transcatheter aortic-valve implantation (TAVI) devices in the USA are not approved for patients with native aortic regurgitation and when used off-label are associated with unsatisfactory outcomes.** | Thank you for your edits.<br>3.5 currently states the risks associated with off-label device use for this procedure.<br>IPAC considered your edit but decided not to amend 3.5. |
| 9. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | (Indications and current treatment in the overview) | Aortic regurgitation (AR) is the leakage of blood backwards from the aorta into the left ventricle during diastole (when the heart relaxes and fills with blood). It develops when the aortic valve pathology prevents normal closure of the valve in diastole. AR is usually the result of leaflet degeneration, aortic root dilatation with aortic annulus enlargement, or both. **The combined pressure and volume overload of aortic regurgitation can cause left-ventricular systolic dysfunction.** People may remain asymptomatic for years but eventually they present symptoms, most often with shortness of breath. **When symptoms develop, myocardial dysfunction mediated by fibrosis, diastolic dysfunction, and increased myocardial work** | Thank you for your edits.<br>IPAC considered that whilst these edits are correct, they provide more technical detail than that required for an IPG. Therefore, the committee decided not to accept these edits. |

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| | | | **is often present.** In severe cases this leads to heart failure.<br>References<br>Ajmone Marsan N, Delgado V, Shah DJ, et al. Valvular heart disease: shifting the focus to the myocardium. *Eur Heart J* 2023; **44:** 28–40.<br>Bando K. Filling the Gap between guidelines and current surgical practice: is early surgery justified in patients with asymptomatic severe aortic regurgitation with normal left ventricular function? *Semin Thorac Cardiovasc Surg* 2019; **31:** 771–72.<br>Maeda S, Taniguchi K, Toda K, et al. Outcomes after aortic valve replacement for asymptomatic severe aortic regurgitation and normal ejection fraction. *Semin Thorac Cardiovasc Surg* 2019; **31:** 763–70. | |
| 10. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | (Indications and current treatment in the overview) | 2.2 For people with severe symptomatic AR who are well enough for surgery, surgical aortic valve replacement (SAVR) with a biological or mechanical prosthetic valve is standard treatment **and is associated with substantial survival benefit.**<br>References<br>Dujardin KS, Enriquez-Sarano M, Schaff HV, Bailey KR, Seward JB, Tajik AJ. Mortality and morbidity of aortic regurgitation in clinical practice. A long-term follow-up study. *Circulation* 1999; **99:** 1851–57. | Thank you for your edits in the overview.<br>These edits are also related to section 2.2 (current treatments) in the guidance.<br>IPAC agreed to amend this section as follows:<br>*For people with severe symptomatic AR who are well enough for surgery, surgical aortic valve replacement (SAVR) with a biological or mechanical prosthetic valve is standard treatment and is associated with survival benefit.* |
| 11. | Consultee 1<br>Company | (Indications and current | 2.3 For some people, surgery is not an option. This can be because of medical comorbidities or | Thank you for your edits in the overview. |

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| | JenaValve Technology GmbH and JenaValve Technology Inc. | treatment in the overview) | technical considerations, such as a calcified aorta or scarring from previous cardiac surgery. For these people, the risks of SAVR outweigh the potential benefits, and so medical treatment is the standard treatment. But for some of these people, medical treatment is not effective. **Adverse consequences among symptomatic patients with aortic regurgitation are substantial and conservative management is associated with a 1-year mortality rate exceeding 20%. Thus, a less invasive alternative to surgery is needed for patients at high risk of mortality and complications with surgical aortic valve replacement.**<br>References<br>Otto CM, Nishimura RA, Bonow RO, et al. 2020 ACC/AHA<br>guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation* 2021; 143: e72–227.<br>Vahanian A, Beyersdorf F, Praz F, et al. 2021 ESC/EACTS Guidelines for the management of valvular heart disease. *Eur Heart J* 2022; 43: 561–632. | These edits are also related to section 2.3 (current treatments) in the guidance.<br>The additional text is focusing on the unmet need which is covered in the unmet need section in the overview.<br>The 'unmet need section in the overview has been slightly amended to include this information (see edits in response to comment 10). |
| 12. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Unmet need (section in overview) | Surgical aortic valve replacement (SAVR) with an artificial (biological or mechanical) prosthesis is the current treatment for people with severe symptomatic AR who are well enough for surgery. When surgery is not an option optimal medical care is the usual treatment. | Thank you for your edit to this section in the overview.<br>IPAC considered your edits but decided not to amend this sentence as it does not meet NICE standard way of writing. |

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| | | | Transcatheter aortic valve implantation (TAVI) is a less invasive alternative treatment ~~could be~~ **and is** considered **suitable** for the sub-group of people for whom surgery is unsuitable or are considered too high risk. | However, IPAC made some additional amendments based from comment 11 as follows:<br>*Surgical aortic valve replacement (SAVR) with an artificial (biological or mechanical) prosthesis is the current treatment for people with severe symptomatic AR who are well enough for surgery. When surgery is not an option optimal medical care is the usual treatment. Conservative management among symptomatic patients can be associated with significant adverse events and high mortality rates.*<br>*Transcatheter aortic valve implantation (TAVI) is a less invasive alternative treatment and could be considered for the sub-group of people for whom surgery is unsuitable or are considered too high risk.* |
| 13. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | The procedure (in the overview) | ~~Different devices are available for this procedure and~~ **All TAVI devices** contain material derived from animal sources. | Thank you for your edit in this section of the overview.<br>IPAC considered the edit but decided no change is needed. |
| 14. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Clinical assessment tools (section in the overview) | Clinical assessment of severity of AR **should be graded as mild, moderate, or severe, using a multiparametric approach to obtain high quality, accurate, and reproducible echocardiographic images, measurements, and calculations to facilitate improved determination of AR severity include**:<br>• EuroSCORE II is a scoring system that measures risk of death for patients | Thank you for your edits in this section of the overview.<br>The overview is written in language intended to be understood by any healthcare professional without specialist knowledge of a particular procedure or disease area.<br>IPAC amended the first sentence in this section as follows: |

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| | | | considering surgery. The score is calculated by taking into account factors related to the patient, the patient's heart condition and the proposed operation. It is expressed as a percentage and on a scale of 0 to 100% (higher scores indicating greater risk; a score higher than 20% indicates very high surgical risk).<br>• The STS-PROM score distinguishes high and low-risk surgical patients and predicts postoperative outcome after the procedure.<br>• NYHA heart failure classification is used to classify the severity of breathlessness; from class I, in which the patient has no limitation in daily physical activity, to class IV, in which the patient is breathless at rest.<br>• Haemodynamic assessment (~~usually~~ by echocardiography**, as recommended in the Echocardiographic assessment of aortic regurgitation: a practical guideline from the British Society of Echocardiography**): severe chronic AR is considered to be present if one or more of the following findings are present on echocardiography. These include<br>○ central jet width 65% or more of LV outflow tract<br>○ vena contracta width more than 6 mm<br>○ holodiastolic flow reversal in the abdominal aorta<br>○ regurgitant fraction 50% or more | 'Clinical assessment of severity of AR should be graded as mild, moderate, or severe, using detailed echocardiographic assessment'.<br><br>IPAC did not think that referencing the BSE guideline in this section was appropriate as this is not a guideline on assessment of severity of AR. |

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| | | | ○ regurgitant volume of more than 60ml/beat and<br>○ an effective regurgitant orifice area 0.30 cm2 or more.<br>Studies using quantitative CMR has shown that significant LV remodelling or symptoms requiring aortic valve replacement may occur at lower thresholds of regurgitant volume (approximately 50 ml) and regurgitant fraction (approximately 40%). Hence, the severity assessment should include LV remodelling and symptoms with one of the above findings on echocardiography. | |
| 15. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Population and studies description (in the overview of evidence) | This interventional procedures overview is based on 45,629 people from 4 systematic review and meta-analyses, 1 prospective case series, 1 retrospective propensity score matched study and 2 retrospective analyses. Of these 45,629 people, 13,722 people had **the off-label AS TAVI and on-label AR** TAVI procedure for **treatment of** AR. 27,851 patients had SAVR, and 4056 patients had TAVI for AS. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 8 studies as the key evidence in table 2 and table 3, and lists 77 other relevant studies in appendix B, table 5.<br><br>A systematic review and meta-analysis of 19 studies on **off-label use of AS TAVI as well as on-label use of AR** TAVI for treatment of native AR was conducted according to PRISMA guidelines. Pooled estimates were calculated using a random-effects model. NGDs were | Thank you for your edits on this section in the overview of evidence.<br>IPAC agreed to amend this section as follows:<br><br>This interventional procedures overview is based on 47,827 people from 5 systematic review and meta-analyses, 1 prospective case series, 1 retrospective propensity score matched study and 3 retrospective analyses. Of these 47,827 people, 15,920 people had the procedure for AR (with either dedicated valves indicated for use in AR [referred to as on-label valves] or non-dedicated valves indicated for use in AS [referred to as off-label valves])'. 27,851 patients had SAVR, and 4056 patients had TAVI for AS. This is a rapid review of the literature, and a flow chart of the complete selection process is shown in figure 1. This overview presents 10 studies as the key evidence in table 2 and table 3, and lists 85 other relevant studies in appendix B, table 5. |

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| | | | compared with EGDs. Subgroup analysis and meta-regression were performed to study the effects of study level covariates on outcomes. There was significant heterogeneity across the available studies in terms of device used, access site, and outcomes reported. Some studies varied in patient characteristics and some have incomplete data reporting. Most of the studies had small sample sizes, reported their outcomes peri procedurally and lack data on long-term outcomes (Rawasi 2019).<br>In a meta-analysis of 11 studies on **off-label as well as on-label use of** TAVI for AR, pooled estimates were calculated a using random-effects model. Subgroup meta-analysis of studies using EGDs and NGDs was also performed. Studies were heterogenous with different sample sizes, inclusion criteria, patient characteristics, types of valves, and TAVI approaches. Most of the studies were multicentre studies and there might be an overlap of patients and that might have overestimated the effects of the intervention. Meta-regression were performed to study the effects of 12 covariates on 30-day all-cause mortality (Takagi 2020).<br>A large multicentre prospective case series of 180 patients (the JenaValve ALIGN-AR pivotal trial) in the USA assessed **on-label use of AR** TAVI in patients with severe symptomatic AR and at high risk of surgery. Findings were compared with a pre- specified performance goal and analysis was on early outcomes (Vahl 2024).<br>The PANTHEON study was a retrospective international registry analysis that assessed (both | A systematic review and meta-analysis of 19 studies on TAVI for treatment of native AR (with either on-label or off-label valves) was conducted according to PRISMA guidelines. Pooled estimates were calculated using a random-effects model. NGDs were compared with EGDs. Subgroup analysis and meta-regression were performed to study the effects of study level covariates on outcomes. There was significant heterogeneity across the available studies in terms of device used, access site, and outcomes reported. Some studies varied in patient characteristics and some have incomplete data reporting. Most of the studies had small sample sizes, reported their outcomes peri procedurally and lack data on long-term outcomes (Rawasi 2019).<br>In a meta-analysis of 11 studies on TAVI for AR (with either on-label or off-label valves), pooled estimates were calculated a using random-effects model. Subgroup meta-analysis of studies using EGDs and NGDs was also performed. Studies were heterogenous with different sample sizes, inclusion criteria, patient characteristics, types of valves, and TAVI approaches. Most of the studies were multicentre studies and there might be an overlap of patients and that might have overestimated the effects of the intervention. Meta-regression were performed to study the effects of 12 covariates on 30-day all-cause mortality (Takagi 2020).<br>A large multicentre prospective case series of 180 patients (the JenaValve ALIGN-AR pivotal trial) in the USA assessed on-label use of TAVI in patients with severe symptomatic AR and at high risk of surgery. Findings were compared with a pre- specified |

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| | | | **on-label AR TAVI devices and off-label AS devices for treatment of AR, segmented by the mechanism of action** (SE and BE) NGDs in patients with severe pure native AR and considered high-risk or inoperable. TF approach was the most common approach used. Different types of valves were used and only 10% were JenaValve Trilogy THV, which is a dedicated device system for native AR. Echocardiographic outcomes were not reported so the rate of moderate to severe AR at follow-up are unknown (Polleti 2023).<br><br>A retrospective propensity score matched study comparing **off-label use of AS** TAVI **devices for treatment** ~~in~~ **of** AR **versus** ~~with~~ **on-label AS** TAVI **devices** in **treatment of** AS used NRD codes for diagnosis of AR and these might be subject to misclassification and may not be accurate. Procedural and echocardiographic outcomes were not assessed in this study due to lack of data. Patients were either symptomatic or had a compelling indication for valvular replacement. They were of similar age in both groups and had similar comorbidities (the Elixhauser comorbidity index [to predict in-hospital mortality] was comparable) (Ullah 2024). | performance goal and analysis was on early outcomes (Vahl 2024).<br>A retrospective propensity score matched study comparing TAVI for treatment of AR with TAVI for treatment of AS used NRD codes for diagnosis of AR and these might be subject to misclassification and may not be accurate. Procedural and echocardiographic outcomes were not assessed in this study due to lack of data. Patients were either symptomatic or had a compelling indication for valvular replacement. They were of similar age in both groups and had similar comorbidities (the Elixhauser comorbidity index [to predict in-hospital mortality] was comparable). Details of valves used were not available in the article (Ullah 2024). |
| 16. | Consultee 1<br>Company<br>JenaValve Technology GmbH | Anecdotal and theoretical adverse events (in the | Expert advice was sought from consultants who have been nominated or ratified by their professional society or royal college. They were asked if they knew of any other adverse events for this procedure that they had heard about (anecdotal), which were not reported in the | Thank you for your comment.<br>IPAC agreed to add a sentence to this section of the overview to make it clear that 'This advice was generalised across on and off label TAVI usage for AR'. |

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| | and JenaValve Technology Inc. | overview of evidence) | literature. They were also asked if they thought there were other adverse events that might possibly occur, even if they had never happened (theoretical).<br>They listed the following anecdotal or theoretical adverse events:<br><br>• Left ventricular migration/embolisation leading to severe aortic incompetence.<br><br>**Does this above listed adverse event relate to on-label AR TAVI or off-label AS TAVI used for treatment of AR?** | |
| 17. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Validity and generalisability (section in the overview) | • ~~New~~ **A** ~~generation~~ dedicated TAVI device~~s~~ for AR **has been analysed in one prospective study** ~~are now available and performance~~ in ~~patients~~ **people** with severe AR and high surgical risk ~~has been analysed in one prospective study~~ (Vahl 2024). | Thank you for your edit.<br>IPAC agreed to amend this sentence in the overview as follows:<br>*Most evidence is on TAVI with non-dedicated devices for AR. The evidence on one dedicated TAVI device for AR has been analysed in one prospective study in people with severe AR and high surgical risk (Vahl 2024).* |
| 18. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Existing assessments of this procedure (section in the overview) | **All existing assessments of this procedure pertain to the off-label use of AS TAVI devices for treatment of AR and include:**<br><br>*The European Society of Cardiology guidelines (ESC/EACTS 2022) state that "TAVI may be considered in experienced centers for selected patients with AR and ineligible for SAVR" (Vahanian 2022).* | Thank you for your edit.<br><br>IPAC agreed to amend the suggested text as follows and add it to the end of this section.<br>'These assessments were done based on evidence available for off label TAVI devices'. |

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| | | | *The American College of Cardiology/American Heart/Association clinical practice guideline (ACC/AHA 2020), recommends that "in patients with isolated severe AR who have indications for SAVR and are candidates for surgery, TAVI should not be performed".*<br>*"TAVI for isolated chronic AR is challenging because of dilation of the aortic annulus and aortic root and, in many patients, lack of sufficient leaflet calcification. Risks of TAVI for treatment of AR include transcatheter valve migration and significant paravalvular leak. TAVI is rarely feasible, and then only in carefully selected patients with severe AR and HF who have a prohibitive surgical risk and in whom valvular calcification and annular size are appropriate for a transcatheter approach" (Oto 2021).* | |
| 19. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Related NICE guidance<br>(section in the overview) | Interventional procedures<br>**All interventional procedures guidance pertains to procedures for on-label use of AS TAVI devices, and subsequent interventional procedures required due to complications resulting from AS TAVI devices, and include:**<br>• Valve-in-valve TAVI for aortic bioprosthetic valve dysfunction (2019) NICE interventional procedures guidance 653. (Recommendation: standard arrangement).<br>• Transcatheter aortic valve implantation for aortic stenosis (2017) NICE interventional procedures guidance 586. | Thank you for your edit.<br>The existing titles of the IPGs are clear and indicate what these are for. Therefore IPAC considered that it is not appropriate to add this sentence. |

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| | | | (Recommendation: standard arrangement). | |
| 20. | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Related NICE guidance (section in the overview) | **NICE guidelines**<br>*Heart valve disease presenting in adults: investigation and management (2021) NICE guideline NG208 (Recommendations).*<br>***Aortic valve disease***<br><br>*For NHS England and NHS Improvement's position on transcatheter aortic valve implantation for people at low or intermediate surgical risk, see the implementation strategy for transcatheter aortic valve implantation.*<br><br>*1.5.3*<br><br>*Offer surgery, if suitable (by median sternotomy or minimally invasive surgery), as first-line intervention for adults with severe aortic stenosis, aortic regurgitation or mixed aortic valve disease and an indication for surgery who are at low or intermediate surgical risk. TAVI is not cost effective for people at low or intermediate surgical risk at the current list price.*<br><br>Not in line with current TAVI AS LSA guidance that was to be published in January 2025.<br><br>At this time, guidelines relating to the assessment of AR severity unrelated to aortic stenosis are missing. Please see the following for where a | Thank you for your comments.<br>IPAC agrees with your comment about 'aortic valve disease' in the NICE guideline and deleted this section from the overview as it is not updated and not in line with TAVI LSA guidance.<br><br>IPAC doesn't agree with the comment about referring to British Society of Echocardiography guideline in this section as this is not a guideline on assessment of severity of AR. Therefore IPAC decided not to include this guideline. |

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| | | | hyperlink to the 2025 BSE AR Guidelines can bridge this gap:<br>NG208 Recommendations 1.3 Indications for Interventions: 1.3.1 "Offer an intervention to adults with *severe heart valve disease*", whereby "*severe heart valve disease*" aortic guidance is only a link to the British Society of Echocardiography guidelines for assessment of aortic stenosis (2021). | |
| 21 | Consultee 1<br>Company<br>JenaValve Technology GmbH and JenaValve Technology Inc. | Other edits in table 2 column 6 and subheadings under efficacy safety section in the overview | Table 2 Column 6 (intervention): study 4, 5, 7, 8<br>Table 3, study 4, column 2<br>Subheadings – under efficacy and safety (NGDs off-label versus on label)<br>**Differentiate between devices used in the overview as 'off-label use of AS TAVI and on-label use of AR TAVI'.** | Thank you for edits in the relevant sections mentioned.<br>There was significant heterogeneity across the available studies in terms of devices used. This was clearly noted in table 2 (column 6) for all included studies in the overview.<br>The wording proposed will make it more confusing for the reader; therefore IPAC decided to leave the wording as it currently stands<br>*'off-label TAVI versus on-label TAVI'.* |

*"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."*