MANAGEMENT IN CONFIDENCE

CLINICAL PRIORITIES ADVISORY GROUP
29 05 2019 and 30 05 2019

Agenda Item No	03.3
National Programme	Internal Medicine
Clinical Reference Group	Cardiac
URN	1714

Title
Percutaneous mitral valve leaflet repair for primary degenerative mitral regurgitation in adults.

Actions Requested	1. Support the proposition.
	2. Recommend the relative priority.

Proposition
NHS England currently has a 'not for routine commissioning' policy in place for percutaneous mitral valve leaflet repair for primary degenerative mitral regurgitation in adults (2013). A Commissioning through Evaluation (CtE) scheme was then established and designed to collect additional data on outcomes and safety and to consider later evidence. On behalf of NHS England, NICE produced an Evaluation report including clinical and cost effectiveness in March 2019. In parallel NHS England followed its agreed Methods to review the latest published evidence and to develop this revised policy proposition to routinely commission this intervention.

Clinical Panel recommendation
The Clinical Panel recommended that the policy progress as a routine commissioning policy.

The committee is asked to receive the following assurance:	
1.	The Head of Clinical Effectiveness confirms the proposal has completed the appropriate sequence of governance steps and includes an: Evidence Review; Clinical Panel Report.
2.	The Head of Acute Programme confirms the proposal is supported by an: Impact Assessment; Stakeholder Engagement Report; Consultation Report; Equality Impact and Assessment Report; Clinical Policy Proposition. The relevant National Programme of Care Board has approved these reports.
3.	The Director of Finance (Specialised Commissioning) confirms that the impact assessment has reasonably estimated a) the incremental cost and b) the

	budget impact of the proposal.
4.	The Clinical Programmes Director (Specialised Commissioning) confirms that the service and operational impacts have been completed.

The following documents are included (others available on request):	
1.	Clinical Policy Proposition
2.	Consultation Report
3.	Evidence Summary and CtE Evaluation Report
4.	Clinical Panel Report
5.	Equality Impact and Assessment Report

No	*Metric*	*Summary from evidence review*
1.	Survival	*Survival* Survival at one year for Mitraclip (85.8%) was similar to that after high risk surgery (HRS-85.2%). Both were superior to conservative medical management (CMM 67.7%). This was similar at two years (MC 75.5%, HRS 77.8%, CMM 52.5%) and 3 years (MC 62.3%, HRS 68.5%, CMM 45.8%). The survival outcomes for Mitraclip and surgery were not statistically significantly different (even though the Mitraclip group had a higher surgical risk as measured by the logistic Euroscore). However, Mitraclip was superior to CMM (Swaans et al.,2014). Caveats here are that the comparators were retrospective, and the patient population included FMR. *Mortality Rates* At one year after the Mitraclip procedure, mortality ranged between 16.3% to 24.7% (evidence review). CtE: The death rate during a 2 year follow up period was 15.1% in the England Commissioning through Evaluation Scheme (CtE), a procedural registry run by NHS England. It was 11% at one year. The in-hospital death rate was 5% and 6% at 30 days.
2.	Progression free survival	Not specified in the protocol. Not applicable. This is more related to cancer treatments.
3.	Mobility	Patient Experience and quality of life (QOL) (including points 3-7) was captured in the CtE by the EQ-5D-5L system, Utility Scores, Visual Analogue Scores and NYHA which is a measurement of dyspnoea and symptoms of heart failure. CtE analysis of each EQ-5D domain e.g. mobility, self-care, usual activities, pain/discomfort, anxiety/depression, showed a statistically significant improvement from base-line to 6 months and 12 months (except for self–care) but not at 24 months. This trend for significant QOL improvements over a year after MitraClip was additionally echoed by

		measurements of Utility Scores and VAS scores by the CtE. One study (Lim et al., 2014, n=122) reported HR-QOL using SF-36 methodology: MitraClip was associated with significant longitudinal improvements in all 12 domains and at all time points compared with baseline except for role emotional at 30 days. Statistically significant improvements in mobility associated with MitraClip were seen at 6 weeks, 6 months and 12 months.
4.	Self-care	Addressed within response to point 3 above. Statistically significant improvements in self-care associated with MitraClip treatment were seen at 6 weeks and 6 months but not at 12 months.
5.	Usual activities	Addressed within response to point 3. Statistically significant improvements in usual activities, associated with MitraClip were seen at 6 weeks, 6 months and 12 months.
6.	Pain	Addressed within response to point 3. Statistically significant improvements in pain/discomfort, associated with MitraClip were seen at 6 weeks, 6 months, 12 months and 24 months.
7.	Anxiety / Depression	Addressed within response to point 3. Statistically significant improvements in anxiety/depression associated with MitraClip were seen at 6 weeks, 6 months and 12 months.
8.	Replacement of more toxic treatment	Conventional medical management is associated with worse clinical outcomes. A study by Gianni (2016) showed that death rates at one and three years were 10.3% and 38.6% in patients receiving the MitraClip procedure, compared with 35.7% and 65.1% respectively for patients undergoing medical management. Another study by Velasquez (2015) reported a historically 10% higher mortality at one year with medical management compared with MitraClip.
9.	Dependency on care giver / supporting independence	*Discharge Destination* 72% discharged home (Access-EU, Maisano et al., 2013). 86% discharged home, 8% into extended care (TVT registry, Sorajja et al., 2017). A majority of patients with DMR receiving MitraClip treatment were discharged directly home.

10.	Safety	The typical spectrum of complications with MitraClip, as observed with other cardiac interventional procedures can be related to pre-existing patient co-morbidities and/or the procedure/device. The nature of complications listed included stroke, transient ischaemic attack (TIA), myocardial infarction (MI), cardiac tamponade, cardiac arrhythmias, cardiogenic shock, severe bleeding/transfusion, vascular, major bleeds additional/re-interventions (retrieval of device, partial detachment), conversion to surgery, renal failure, cardiac / trans-septal perforation, chordal rupture, oesophageal damage, sepsis and death. In the large (1867 patients) TVT Registry which comprised mainly patients with Degenerative Mitral Valve Disease (representative of the population for this policy), the following table sets out complications seen at 30 days and at one year following the procedure: **Complications** — **30 days (%)** — **1 year (%)** Deaths — 5.2 — 25.8 MI — 0.2 — 2.5 Stroke — 1.0 — 2.7 Heart Failure — 4.7 — 20.2 Mitral Valve Surgery — 0.4 — 2.1 Repeat MitraClip — 1.3 — 6.2 **CtE** The major complication rate including deaths was 8.2% in-hospital and after discharge was 14.7%. Whilst comparability may be affected by differing definitions and follow up durations, these are lower than reported in the literature. **Updated report on outcomes from linked datasets.** Using linked data from HES / ONS / CtE a mortality rate of 12.7% (95% CI 7.5 to 15.9%) was reported at 1 year and at 2 years a rate of 22.7% (95% CI 15.3 to 29.4) was reported. Although in the ONS data the number of deaths was higher the improved coverage meant that the annualised mortality rate was lower at 13.6% (95% CI 9.8 to 18.8) per 100 PY than in the CtE alone. These data were consistent with published studies. For the elective sub group this was 11.5 % (95% CI 7.7 to 16.6) per 100 PY and for the urgent / emergency sub group 31.3% (95% CI 14.3 to 59.5) per 100 PY. Linked data also reported readmission rates; with 67% of patients having at least one admission in the first year resulting in a rate of 176.4 per 100 PY which was higher than reported in the literature.
11.	Delivery of intervention	*Procedural and technical success rate* Definitions of success varied. Overall success rates ranged between 88%- 97% across the studies within the evidence

		review. The lower figures were associated with overall technical/procedural and clinical success i.e. reduction in grade of mitral valve regurgitation/incompetence +/- no mortality and no cardiac surgery. The higher figures tended to relate to technical success. The success rate of the MitraClip procedure, from the evidence review in patients with DMR at high risk of surgery was about 93%. In the CtE evaluation, the success rate defined as successful device deployment with no major complications was 86%. Re-Intervention Rate There is evidence of re-interventions occurring and the rate can be between 2.4 - 8% in the first year (Lim et al., 2014; Rudolph et al., 2013). Re-interventions can be mitral valve surgery (repair/replacement) or more frequently additional MitraClips. There is limited evidence from two observational studies (Braun et al., 2016; Rudolph et al., 2013) that MitraClip procedures may be repeated in about 5% of DMR patients.

Other health outcome measures determined by the evidence review		
No	Metric	Summary from evidence review
1	Reduction in severe and symptomatic mitral valve regurgitation (MR) or incompetence as measured by MR Grade	This is a key echocardiographic outcome and measure of clinical efficacy. All studies in the evidence review reported similar MR outcomes to the CtE registry: that is an immediate and dramatic, clinically and statistically significant reduction in MR grade at discharge (typically more than 90% of patients achieved mild or absent MR). Few patients, if any, had severe MR following treatment with MitraClip. This reduced by 20% at 12 months follow up, suggesting that 70% of patients with moderate or severe MR had sustained mitral valve functional integrity. **CtE** Evidence reported from the CtE registry shows that the MitraClip procedure resulted in immediate and dramatic improvements in MR grade with the proportion of patients with moderate/severe or severe MR (≥3+) reduced from 99.5% before the procedure to 6.7% after the procedure. However, after 6 weeks there was evidence that there was some deterioration in mitral valve function, with 24% of patients reporting moderate-severe or severe MR. This is fully consistent with the published literature.

		There is unequivocal evidence that treatment with MitraClip is associated with a statistically and clinically significant reduction in MR Grade at discharge and follow up to one year.
2	Improvement in symptoms as measured by the New York Heart Association (NYHA) scores NYHA Class I represents no limitation of physical activity and Class IV represents inability to conduct any activity without physical discomfort.	*Improvement in symptoms/NYHA Class* The NYHA classification system is a measure of the level of dyspnoea which is the principal symptom associated with MR. 1. At 12 months, most studies in the evidence review reported statistically and clinically significant improvements from more than 90% with NYHA Class III/IV pre-procedure, to more than 80% - 90% in NYHA Class I/II post procedure. Results showed a dramatic improvement from Classes III and IV to I and II. **CtE** The CtE results for improvements in NYHA class are consistent with those seen in the evidence review.
3	Cost Effectiveness	Updated economic analysis The CtE / HES / ONS linked data looked at 1 year pre and post the intervention and reported overall post procedural reductions in hospital readmission rates, total hospitalisation rates and mean per patient hospitalisation rates. However, these savings were unlikely to be offset by the device and procedural costs within the NHS.

Considerations from review by Rare Disease Advisory Group
Not applicable.

Pharmaceutical considerations
Not applicable.

Considerations from review by National Programme of Care
1) The proposal received the full support of the Internal Medicine National Programme of Care Business Meeting on 10th April 2019 and reported to the full Board on 25th April 2019.