National Institute for Health and Care Excellence

Multiple Technology Appraisal (MTA)

Dual-chamber pacemakers for treating symptomatic bradycardia due to sick sinus syndrome without atrioventricular block, part review of Technology Appraisal 88

Response to consultee and commentator comments on the draft remit and draft scope (pre-referral)

Comment 1: the draft scope

Section	Consultees	Comments	Action
Background information	Heart Rhythm UK	The stated objective of this review is to appraise the clinical and cost effectiveness of dual-chamber pacemakers for treating symptomatic bradycardia in two groups: 1) ***people with sick sinus syndrome in whom there is no evidence of impaired atrioventricular conduction*** – this is an appropriate objective. 2) ***people with atrioventricular block and continuous atrial fibrillation*** – people in permanent (continuous) atrial fibrillation cannot benefit from dual chamber pacing as their atria are electrically and mechanically dysfunctional. The only appropriate pacing mode for symptomatic bradycardia and/or high degree atrioventricular heart block, is single chamber ventricular rate responsive pacing – VVIR or cardiac resynchronisation therapy (CRT). There are no data to support dual chamber pacing in permanent atrial fibrillation and this is not performed in clinical practice. There does not seem to be any advantage to include this group in the appraisal. Atrial fibrillation is classified as: • ***permanent*** when it is accepted and no attempt is made to regain sinus rhythm. • It is classified as ***persistent*** when it is continuous for more than 7 days and/or requires medical intervention (cardioversion) to terminate. • ***Paroxysmal*** atrial fibrillation is self-terminating, usually within 48-hours. • "***Continuous***" atrial fibrillation is not a recognised classification of the arrhythmia and should be avoided for clarity.	Comments noted. The scope will now only include those with sick sinus syndrome and no evidence of impaired atrioventricular conduction. The background section has also been updated.

Section	Consultees	Comments	Action
		The draft scope states that ***"A national survey conducted by the Network Devices Survey Group that analysed adherence to TA88 in England and Wales in 2008 reported a national average of 77% single chamber atrial-based pacing in sick sinus syndrome ..."*** The 2008 report shows that 77% of patients with sick sinus syndrome received atrial based pacing. However, this includes both atrial single chamber (AAI±R) and dual chamber (DDD±R) devices. In 2008 only 182 patients received single chamber atrial-based pacemakers in the UK, 0.54% of all implants. The most recent report from 2011 (available from https://nicor5.nicor.org.uk/__802571400070B77E.nsf?OpenDatabase) states that 69% of patients received atrial based pacing (atrial single chamber (AAI±R) and dual chamber (DDD±R) devices), while only 3 patients (0.009%) received single chamber atrial (AAI±R) pacemakers. The draft scope states that "***Pacemakers are indicated for use in the treatment of symptomatic bradycardia...***". Pacemakers are also indicated for high degree atrioventricular heart block regardless of symptoms because of significant prognostic benefit. The scope states that "***...pacing leads that are in contact with the inner wall of the right atrium and/or the right ventricle...***". Pacing leads may also be in contact with the outer wall of the heart, the epicardium, when placed surgically or via the coronary sinus. An alternative draft background is included here for clarity: Cardiac arrhythmias are abnormal heart rhythms which may be fast (tachycardia), slow (bradycardia), and/or irregular (most commonly atrial fibrillation). They are caused by abnormalities of impulse formation (e.g. sinus node disease) or electrical conduction (e.g. atrio-ventricular heart block) in the heart. For most people with bradycardia, no single cause is found, although the conditions become increasingly common with increasing age. The most commonly identified causes of abnormal heart rhythms are ischaemic heart disease, heart valve disorders and heart failure. If untreated, abnormal	

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		heart rhythms may lead to palpitations, light-headedness, syncope, heart failure and even sudden cardiac death. Pacemakers are used in the treatment of bradycardia to monitor the heart's intrinsic electrical activity and to prevent bradycardia by stimulating additional heart beats when required. In 2010 in England, more than 40,000 people underwent pacemaker implantation. Hospital Episode Statistics (HES) show that the total number of dual chamber cardiac pacemaker procedures performed in the NHS to treat bradycardia increased between 2006 and 2011 with a higher rate of uptake for the treatment of atrioventricular block compared with sick sinus syndrome. In 2010/11 there were 1,201 dual chamber pacemaker procedures for bradycardia due to sick sinus syndrome, and 5,273 due to atrioventricular block. A national survey conducted by the Network Devices Survey Group in 2011 reported a national average of 69% atrial-based pacing in sick sinus syndrome. The majority of devices were dual chamber with only 3 patients (0.009%) receiving single chamber atrial pacemakers (AAI or AAIR). The prevalence of sick sinus syndrome is thought to be about 0.03% of the whole population, and increases with age. Estimates of the prevalence of atrioventricular block (based on clinical studies) range from 0.015% to 0.1%, although it is common for people to have coexisting abnormalities of both the sinus node and the atrioventricular node.	
	Medtronic Limited	No comment	Comment noted. No action required.

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	Syncope Trust And Reflex anoxic Seizures	It should be noted that the majority of people with an arrhythmia have a structurally normal heart and a pacemaker is implanted to maintain their normal heart rhythm. Why is dual-chamber pacing for the management of atrioventricular block in patients with continuous AF part of the appraisal when it is rare for this treatment to be considered for this condition?	Comments noted. The scope will now only include those with sick sinus syndrome and no evidence of impaired atrioventricular conduction. The background section has also been updated.
	Arrhythmia Alliance	The background is generally accurate. However the statement that 'The most common causes of abnormal heart rhythms are ischaemic heart disease, heart valve disorders and heart failure' is not correct as most people that have an arrhythmia actually have a structurally normal heart. In the next statement 'Pacemakers are used in the treatment of bradycardia to control or replace the heart's intrinsic electrical activity and restore a normal heart rate.' the word 'maintain' would be better than 'restore'. There will be very few if any specialists who would even consider let alone recommend 'dual-chamber pacing for the management of atrioventricular block in patients with continuous atrial fibrillation' and it is not clear why this is part of the appraisal. The DANPACE study seemed to favour dual chamber pacing in pure sinus node disease but there were some inconsistencies in the findings compared to other studies.	Comments noted. The scope will now only include those with sick sinus syndrome and no evidence of impaired atrioventricular conduction. The background section has also been updated. Scoping workshop attendees felt that the DANPACE study provided a robust source of evidence for this population.

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The technology/ intervention	Heart Rhythm UK	The scope defines the intervention as "***Permanent implantable dual-chamber pacemakers***". Since the defined population are those with sinus node disease, where impulse formation is deficient rather than just impulse conduction, a device which can modulate heart rate according to activity is required. The intervention should therefore be: Permanent implantable dual-chamber **rate responsive** pacemakers. As atrial fibrillation is commonly seen in patients with sinus node disease, the use of a mode-switch algorithm in dual chamber pacemakers is essential to prevent inappropriate fast pacing due to tracking of fast atrial rates.	Comments noted. The specific types of dual and single chamber pacemakers will be considered as part of the full appraisal.
	Medtronic Limited	No comment	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	The description is accurate	Comment noted. No action required.
	Arrhythmia Alliance	The description is accurate	Comment noted. No action required.
Population	Heart Rhythm UK	The first defined population "***People with symptomatic bradyarrythmias due to sick sinus syndrome without atrioventricular block***" is appropriate. The second population, "***atrioventricular block in people with continuous atrial fibrillation***" is not appropriate for dual chamber pacing as their atria are electrically and mechanically dysfunctional and there is no advantage to sensing or pacing in the atrium. The appropriate pacing mode for these people is a single chamber rate responsive ventricular pacemaker (VVIR).	Comments noted. The population section has been updated.
	BMJ-Technology Assessment Group (BMJ-TAG)	Based on expert clinical advice the ERG considers atrial pacing in people with atrioventricular block and continuous atrial fibrillation would be clinically inappropriate. The ERG therefore suggests that this population should not be considered in this MTA.	Comments noted. The population section has been updated.

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	Medtronic Limited	No comment	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	Dual chamber pacing is not usually recommended for AV block in patients with AF.	Comments noted. The population section has been updated.
	Arrhythmia Alliance	As in the background section it is not clear why patients with continuous AF are even being considered	Comments noted. The population section has been updated.
Comparators	Heart Rhythm UK	The appropriate comparator "***For people with sick sinus syndrome without atrioventricular block is single-chamber atrial pacemakers***". These should be rate responsive (AAIR, rather than AAI) as people with sick sinus syndrome have an abnormality of impulse formation and require a device which can modulate heart rate according to activity. Dual chamber pacing can provide no benefit in permanent atrial fibrillation for the reasons stated above***. "People with atrioventricular block and continuous atrial fibrillation***" should receive "***single-chamber ventricular pacemakers***" and these should include a rate response algorithm – VVIR.	Comments noted. The specific types of dual and single chamber pacemakers will be considered as part of the full appraisal.
	Medtronic Limited	No comment	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	The comparator is correct	Comment noted. No action required.
	Arrhythmia Alliance	The comparator is correct	Comment noted. No action required.

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Outcomes	Heart Rhythm UK	We recommend that the outcomes should explicitly include atrial fibrillation and stroke: • mortality • morbidity (including incidence of heart failure, **atrial fibrillation and stroke**) • exercise **capacity** • cognitive function • adverse effects of treatment (including pacemaker syndrome, atrial fibrillation and device replacement) • health related quality of life.	Comment noted. The outcomes section has been updated.
	BMJ-Technology Assessment Group (BMJ-TAG)	Based on expert clinical advice the ERG suggests adding device upgrade as an outcome	Comment noted. The outcomes section has been updated.
	Medtronic Limited	No comment	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	The surgical procedure of upgrading to dual chamber pacemaker should be added to this list.	Comment noted. The outcomes section has been updated.
	Arrhythmia Alliance	The need for further surgery, specifically upgrade from single to dual chamber pacemaker should be included as an outcome	Comment noted. The outcomes section has been updated.
Economic analysis	Heart Rhythm UK	This is appropriate.	Comment noted. No action required.
	Medtronic Limited	No comment	Comment noted. No action required.

Section	Consultees	Comments	Action
	Syncope Trust And Reflex anoxic Seizures	Nothing further to add	Comment noted. No action required.
	Arrhythmia Alliance	No additional comment	Comment noted. No action required.
Equality and Diversity	Heart Rhythm UK	No comments.	Comment noted. No action required.
	Medtronic Limited	No comment	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	No issues	Comment noted. No action required.
	Arrhythmia Alliance	No issues	Comment noted. No action required.
Other considerations	Heart Rhythm UK	International guidance recommends a dual chamber rate responsive (DDDR) pacing mode for those with sinus node disease and a single chamber ventricular rate responsive (VVIR) mode in those with permanent partial fibrillation and atrioventricular heart block. We would welcome explicit recommendation for rate responsive devices in these situations to maximise the symptomatic improvement with pacing. Separate NICE guidance is available for implantable cardioverter defibrillators (ICD - http://guidance.nice.org.uk/TA95/Guidance/pdf/English) and/or cardiac resynchronisation therapy (CRT - http://guidance.nice.org.uk/TA120/Guidance/pdf/English). These are both under current review (http://guidance.nice.org.uk/TA/WaveR/111). Where a patient has an indication for one of these devices, this will supplant this guidance on pacing mode for bradycardia.	Comments noted. The specific types of dual and single chamber pacemakers will be considered as part of the full appraisal.
	Medtronic Limited	No comment	Comment noted. No action required.

Section	Consultees	Comments	Action
	Syncope Trust And Reflex anoxic Seizures	No further suggestions	Comment noted. No action required.
	Arrhythmia Alliance	Nothing to add	Comment noted. No action required.
Innovation	Heart Rhythm UK	The technology is innovative and makes a significant and substantial impact on health-related benefits. There is unlikely to be any step change in the management of the condition in the UK as single chamber atrial pacing has already almost entirely disappeared from UK practice since the publication of DANPACE in 2011.	Comment noted. No action required.
	Syncope Trust And Reflex anoxic Seizures	Nothing to add	Comment noted. No action required.
	Arrhythmia Alliance	No new innovation	Comment noted. No action required.

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Questions for consultation	Heart Rhythm UK	The most significant new data which have become available since the publication of the previous guidance on pacing mode, TAG 88, includes the DANPACE trial (Nielsen et al. A comparison of single-lead atrial pacing with dual-chamber pacing in sick sinus syndrome. Eur Heart J 2011;32:686–696) and 2013 ESC Guidelines on cardiac pacing and cardiac resynchronization therapy (available from http://eurheartj.oxfordjournals.org/content/34/29/2281.full.pdf+html). **Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?** The health-related benefits of pacing for bradycardia are satisfactorily covered by the QALY calculation. **Where do you consider single chamber pacing will fit into the existing NICE Chronic Heart Failure pathway?** Single chamber (ventricular) pacing is not a specific treatment for heart failure and would be appropriate only where heart failure symptoms are caused only by bradycardia in a patient with permanent atrial fibrillation and normal left ventricular systolic function. The NICE chronic heart failure pathway contains some inaccuracies including:  **Considering CRT – with or without pacing – and digoxin, or digoxin alone** For CRT to have any effect, a high prevalence of pacing is required. An alternative pathway for those people with heart failure due to left ventricular systolic dysfunction incorporating NICE guidance on ICD and CRT therapy is shown here:	Comments noted. Additional evidence will be considered as part of the full appraisal. Comment noted. The chronic heart failure pathway has now been removed from the scope as TA88 is not included in the pathway.

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		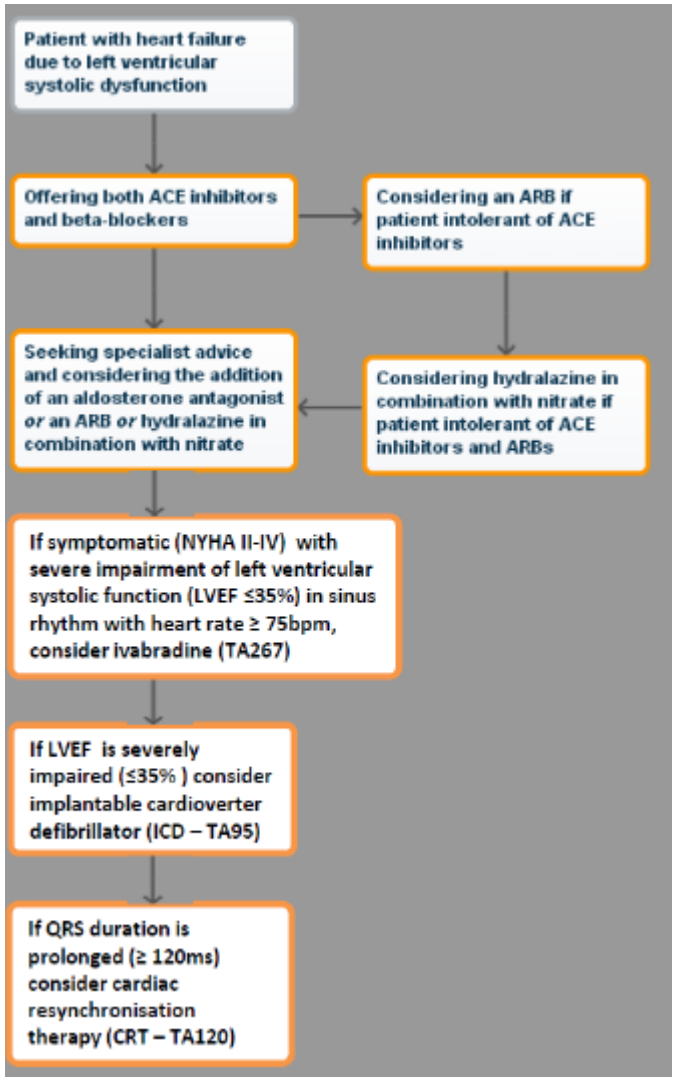	

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	Medtronic Limited	UK clinical practice has progressed since the publication of TA88 in 2005 in patients with sick sinus syndrome and no atrioventricular block and the majority of these patients now receiving dual chamber pacemakers. Medtronic would be supportive of an update in Guidance in line with European Society of Cardiology Guidelines, without a part review of this appraisal, if this is the consensus of the clinical community and industry.	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.
	Syncope Trust And Reflex anoxic Seizures	Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? Not really as dual pacing for atrial fibrillation and AV block is hardly used. Dual pacing is used for the progression of sinus node dysfunction without AV block to with AVB and data suggests this is high. Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Cost of upgrade to dual pacing needs to be considered. Where do you consider single chamber pacing will fit into the existing NICE Chronic Heart Failure pathway? For patients with atrial fibrillation and AVB/bradycardia with normal LV function, but still experiencing heart failure symptoms then you might consider a VVI pacemaker. If impaired LV then a cardiac resynchronisation therapy (CRT) device should be considered.	Comments noted. No action required. Comments noted. Cost of upgrade will be considered as part of the full appraisal.

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	Arrhythmia Alliance	Do you consider the technology to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)? No. No one uses DDD PPM for AF and AVB regularly so irrelevant. Data suggest progression of SND without AVB to with AVB is high so often DDD implanted. Unlikely to significantly change practice given findings in DANPACE, even with its limitations. Do you consider that the use of the technology can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation? Only if you can persuade everyone to implant only AAI PPMs then you may save some cost but cost of upgrade to DDD in some patients may negate this Where do you consider single chamber pacing will fit into the existing NICE Chronic Heart Failure pathway? For patients with AF and AVB/bradycardia with normal left ventricular (LV) function, but still has heart failure symptoms then you might consider a VVI pacemaker. If impaired LV at all then would get a cardiac resynchronisation therapy (CRT) device.	Comments noted. No action required. Comments noted. Patients with atrioventricular block and atrial fibrillation are no longer part of this appraisal.
Additional comments on the draft scope.	Heart Rhythm UK	The title of the MTA is "***Dual-chamber pacemakers for treating symptomatic bradycardia due to sick sinus syndrome or atrioventricular block, part review of Technology Appraisal 88 [ID697]***" and is an appraisal of pacing mode in patients with an established pacemaker indication. It is not an appraisal of the indications for pacing which are extensively reviewed elsewhere (for example, the European Society of Cardiology - http://eurheartj.oxfordjournals.org/content/34/29/2281.full.pdf+html). A statement to this effect would improve the clarity of the evaluation.	Comments noted. The scope will now only include those with sick sinus syndrome and no evidence of impaired atrioventricular conduction.

Section	Consultees	Comments	Action
	Medtronic Limited	In addition Medtronic are in full agreement with the response submitted by the ABHI and so these comments should be taken as our own submission. “The ABHI believe as indicated in previous communications that it is not necessary to perform an appraisal of this technology at this time as it would not be the best use of NHS resources. If however, this is to proceed we do not have any additional comment on this scope”	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.
	Syncope Trust And Reflex anoxic Seizures	It is not clear this subject is being reviewed, particularly the use of a dual chamber pacemaker in continuous AF. This is not done in clinical practice.	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.
	Arrhythmia Alliance	It is not clear this subject is being reviewed, particularly the use of a dual chamber pacemaker in continuous AF. This is not done in clinical practice.	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.
	Association of British Healthcare Industries (ABHI)	The ABHI believe as indicated in previous communications that it is not necessary to preform an appraisal of this technology at this time as it would not be the best use of NHS resources. If however, this is to proceed we do not have any additional comment on this scope.	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.

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	St Jude Medical	St Jude Medical support the comments made by the Association of British Healthcare Industries and have nothing further to add to this	Comments noted. It is not possible to place this guidance on the static list as the recommendation is out of date. A part review of this guidance is therefore necessary.

The following consultees/commentators indicated that they had no comments on the draft remit and/or the draft scope

British Cardiovascular Intervention Society

Department of Health

Association of British Healthcare Industries (The ABHI believe as indicated in previous communications that it is not necessary to preform an appraisal of this technology at this time as it would not be the best use of NHS resources. If however, this is to proceed we do not have any additional comment on this scope.)

St Jude Medical (St Jude Medical support the comments made by the Association of British Healthcare Industries and have nothing further to add to this).

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Multiple Technology Appraisal (MTA)

Dual-chamber pacemakers for treating symptomatic bradycardia due to sick sinus syndrome or atrioventricular block, part review of Technology Appraisal 88

Response to consultee and commentator comments on the provisional matrix of consultees and commentators (pre-referral)

Version of matrix of consultees and commentators reviewed: Provisional matrix of consultees and commentators sent for consultation					
Summary of comments, action taken, and justification of action:					
	Proposal:	Proposal made by:		Action taken: Removed/Added/Not included/Noted	Justification:
	Remove Independent Age	Independent Age		Removed	Independent Age requested removal as a stakeholder for all technology appraisals.

	Heart Rhythm UK is a major omission on the list There are a large number of groups on the list that seem to have no relationship to the topic e.g. all of the religious groups and this list needs to be reviewed completely. Why is only one specific hospital research unit included, and only a small number of CCGs? .	Arrythmia Alliance		Added and noted	Heart Rhythm UK meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a professional consultee. The groups referred to with no relationship to the topic are equality organisations that are included on all technology appraisals, without specific names of organisations we are unable to verify the full reasoning for inclusion. Research organisations must meet the inclusion criteria to be listed on the matrix of stakeholders, we offer this opportunity at consultation to identify any extra groups that consultees and commentators consider may have an interest and to consider them at this point in the process. For each technology appraisal 2 Clinical Commissioning Groups or Local Health Boards are chosen at random as part of the appraisal process noted in the Multiple Technology Appraisals Process Guide.
	Add Heart Rhythm UK	Medtronic		Noted	Heart Rhythm added as a professional consultee as noted above.

	Add STARS UK	STARS UK		Added	STARS UK meets the inclusion criteria and has a close interest in this appraisal topic therefore this organisation has been added to the matrix as a patient consultee.
	Remove National Heart Research Fund	NICE Secretariat		Removed	National Heart Research Fund rebranded to become Heart Research UK. The organisation requested removal from all appraisal topics as a research commentator.
	Remove British Association for Services to the Elderly	NICE Secretariat		Removed	The British Association for Services to the Elderly disbanded in 2012 therefore they have been removed as a professional consultee.