National Institute for Health and Care Excellence

Health Technology Evaluation

Aficamten for treating symptomatic obstructive hypertrophic cardiomyopathy [ID6575]

Response to stakeholder organisation comments on the draft remit and draft scope

Please note: 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.

Comment 1: the draft remit and proposed process

Section	Stakeholder	Comments [sic]	Action
Appropriateness of an evaluation and proposed evaluation route	Cytokinetics (company)	Cytokinetics agrees that it is appropriate for NICE to evaluate aficamten in obstructive hypertrophic cardiomyopathy (oHCM) and considers a cost-comparison evaluation versus mavacamten to be the most appropriate appraisal route, rather than a single technology appraisal as suggested in the draft scope. Cytokinetics intends to seek reimbursement for aficamten [redacted] Cytokinetics considers a cost-comparison evaluation (vs mavacamten) to be the most appropriate appraisal route for aficamten, which also aligns with	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator.

Section	Stakeholder	Comments [sic]	Action
		input from NICE Scientific Advice (February 2025) and feedback from UK clinical and payer experts consulted by Cytokinetics. NICE guidance indicates that technologies can be evaluated through the cost-comparison process if they are expected to provide similar or greater health benefits, at a similar or lower cost, compared with technologies that have been previously recommended in published NICE guidance for the same indication. Cytokinetics believes that a comparison of aficamten with previously recommended mavacamten satisfies these criteria (2). Detailed justification for this is provided in response to the consultation questions below and in summary consists of 3 key factors: • Aficamten has shown at least comparable efficacy versus mavacamten (recommended by NICE in TA913) based on pivotal Phase 3 studies and indirect treatment comparison (ITC) analyses • Experts consulted as part of an advisory board, including payers and clinicians from the UK, confirmed that clinical comparability was likely • [redacted]	
	Bristol Myers Squibb	1. Given the current clinical and guideline landscape, a **single technology appraisal (STA)** is the most appropriate evaluation route for aficamten in symptomatic obstructive hypertrophic cardiomyopathy. 2. Aficamten is a novel agent without UK marketing authorisation, and NICE TA913 for mavacamten clearly positions cardiac myosin inhibitors as second-line therapy—after inadequate response or intolerance to standard care (beta-blockers, calcium antagonists, disopyramide). The populations treated are discrete, and aficamten is not intended for first-line use.	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and

Section	Stakeholder	Comments [sic]	Action
		3. Current evidence for aficamten is limited to phase II data; there are no head-to-head studies with mavacamten or robust comparative outcome data versus standard therapies. There is insufficient evidence for equivalence in clinical effectiveness, safety, or resource use to justify cost-comparison or multiple technology appraisal at present. A highly specialised technology evaluation is not indicated, as the patient population is relatively common (not ultra-rare). 4. STA enables rigorous assessment of aficamten's efficacy, safety, and real-world applicability, ensuring robust patient population separation and alignment with UK clinical pathways before any reimbursement recommendations.	similarity of the NICE approved comparator.
	Cardiomyopathy UK	We agree on the appropriateness of evaluating this topic as a second in class drug and welcome the prospect of another medicine to treat symptomatic obstructive hypertrophic cardiomyopathy.	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator.
	Genetic Alliance UK	Genetic Alliance UK welcomes the opportunity to respond to the consultation on aficamten. We note that hypertrophic cardiomyopathy (HCM), including obstructive HCM, is lifelong, genetically inherited condition that may result in heart complications, including heart failure and in some cases, sudden	Thank you for your comment. NICE will continue this appraisal using the cost-

Section	Stakeholder	Comments [sic]	Action
		cardiac death (SCD). Based on current estimates on the number of people affected by HCM and birth prevalence, we agree the proposed STA route is appropriate in line with current NICE guidelines.	comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator.
	NHSE Cardiology clinical reference group	Highly appropriate and correct appraisal method	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator.
Wording	Cytokinetics (company)	The wording of the remit indicates that the evaluation objective is to appraise the clinical and cost effectiveness of aficamten within its marketing authorisation for treating symptomatic obstructive hypertrophic cardiomyopathy. As indicated above, Cytokinetics intends to seek reimbursement for aficamten via a cost comparison process [redacted]	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including

Section	Stakeholder	Comments [sic]	Action
		[redacted] This aligns with the pivotal regulatory Phase 3 SEQUOIA-HCM study, which will provide the clinical and comparative data in this appraisal of aficamten	available evidence and similarity of the NICE approved comparator.
	NHSE Cardiology clinical reference group	Yes	Thank you for your comment. No action required
Timing Issues	Cytokinetics (company)	oHCM is a chronic and progressive cardiac condition with debilitating symptoms that affect all aspects of patients' lives. In addition, the disease is associated with a substantial burden to the healthcare system, with symptomatic oHCM costing the UK NHS £4,517 per patient-year (3). Prior to the introduction of mavacamten in 2023 (1), the only drug treatment option for symptomatic oHCM was SoC with BBs/CCBs/disopyramide, which lacked robust clinical evidence, may have suboptimal efficacy, and only offer symptom management without modifying the disease course (4, 5). If SoC did not achieve sufficient symptom relief, eligible patients could undergo invasive septal reduction therapy (SRT) which is costly for healthcare systems and associated with increased risks of complications, perioperative mortality, and need for retreatment (6-9). While mavacamten targets the underlying disease mechanism of oHCM, its use involves pre-treatment CYP testing, a complex titration process, slow accumulation to steady state, and frequent monitoring (10). There is also a lack of clinical evidence on the efficacy and safety of mavacamten with some SoC treatments used in UK clinical practice; as such, close monitoring is recommended when using mavacamten with disopyramide or combination BB + CCB (10).	Thank you for your comment. The appraisal will proceed using the timelines for a cost-comparison.

Section	Stakeholder	Comments [sic]	Action
		There is, therefore, a clear unmet need for an alternative treatment option for symptomatic oHCM that targets the underlying disease pathophysiology while also simplifying oHCM treatment to reduce the burden for patients and the NHS. Prompt completion of the NICE evaluation and a timely positive recommendation for aficamten could address these areas of unmet need and would represent an important development for both patients and the NHS	
	Cardiomyopathy UK	This evaluation is urgent for patients with obstructive HCM, as many are experiencing barriers accessing mavacamten. The findings of an unpublished survey by Cardiomyopathy UK, undertaken over a 6-week period from April to May 2025, showed that of the 116 eligible responses received, only a minority of respondents (23%) had been prescribed mavacamten. Given mavacamten's eligibility is determined by specific criteria, a significant portion of patients may not meet the requirements for it to be prescribed. However, this figure falls well below the expected 50% of 'real-world HOCM patients' that are likely to be eligible (*Bertero et al.,* 2024, https://doi.org/10.1002/ejhf.3120). Of those who said they are on mavacamten, several respondents reported frustration with how long this process took, while others described the difficulties they experienced trying to be transferred to their local hospital for the monitoring, resulting in a delay and time-consuming chasing. Although this wasn't an issue for all respondents, some also found the regular monitoring requirements challenging. Additionally, we are aware that some in the patient community have not been sure about whether to go onto mavacamten due to the monitoring requirements so any medication that gives them more choice, especially if there are likely to be fewer monitoring requirements, would be welcome.	Thank you for your comment. The appraisal will proceed using the timelines for a cost-comparison.

Section	Stakeholder	Comments [sic]	Action
		A recent study published in the *Journal of the American Heart Association* on the safety and efficacy of mavacamten and aficamten (Davis *et al*., 2025) suggests that aficamten may offer significant benefits for patients, highlighting the importance of this evaluation. While the authors acknowledge the limitations of cross-trial comparisons, their review of 10 clinical trials indicates that patients enrolled in aficamten studies appeared to experience reduced incidence of atrial fibrillation, and lower rates of heart failure and treatment interruption than those in mavacamten trials. Aficamten was also associated with less side effects and an improved safety profile, which is important for the patient cohort. In addition, aficamten was faster to take effect, with reductions in resting and Valsalva LVOT gradients evident as early as two weeks, compared to four weeks for mavacamten. This means patients could see a change in their symptoms sooner. Aficamten may also be easier for patients to get on than mavacamten due to a shorter half-life which allows for more rapid up-titration	
	NHSE Cardiology clinical reference group	Given the current inequity of access to myosin inhibitors nationally, this should be relatively urgent	Thank you for your comment. The appraisal will proceed using the timelines for a cost-comparison.
Additional comments on the draft remit		No comments	

Comment 2: the draft scope

Section	Consultee/ Commentator	Comments [sic]	Action
Background information	Cytokinetics (company)	Cytokinetics generally considers the background information to be complete and appropriate. Cytokinetics suggests a change to the wording on current 1L treatments. The draft scope currently states "(European Society of Cardiology [ESC]) Guidelines… recommend that people with symptomatic disease, predominately with left ventricular outflow tract obstruction, receive beta-blockers to reduce symptoms ***and obstruction***." However, BBs are mainly used for symptom management in oHCM and there is limited evidence on their efficacy for treating obstruction (4, 5). Moreover, the ESC guideline recommendation makes no reference to BBs reducing obstruction, reading as follows: "Non-vasodilating BBs, titrated to the maximum tolerated dose, are recommended as first-line therapy to improve symptoms in patients with resting or provoked LVOTO" (4). Therefore, Cytokinetics suggests that the draft scope text is amended to: "…receive beta-blockers to improve symptoms ***~~and obstruction~~***." Cytokinetics also suggests a change to 'The technology' section. The draft scope states that "It [*aficamten*] has been studied in clinical trials alongside established care compared with metoprolol succinate and placebo in people with symptomatic obstructive hypertrophic cardiomyopathy." Cytokinetics is concerned that this does not accurately reflect the pivotal clinical trial (SEQUOIA-HCM) that supports the anticipated marketing authorisation for aficamten and that will underpin the reimbursement request to NICE. The comparison of aficamten versus metoprolol succinate refers to the MAPLE-HCM trial, in which aficamten was administered as monotherapy (i.e. 1L	Thank you for your comment. The background has been updated to remove reference to beta blockers improving obstruction The reference to the trials has been changed to "It has been studied in a clinical trial alongside established care compared with placebo plus standard care in people with

Section	Consultee/ Commentator	Comments [sic]	Action
		treatment). [redacted] for aficamten. Therefore, Cytokinetics requests that the wording is updated as follows: "It has been studied in ***the SEQUOIA-HCM Phase 3 randomised controlled trial*** alongside established care compared with ~~***metoprolol succinate and***~~ placebo plus established care in people with symptomatic obstructive hypertrophic cardiomyopathy."	symptomatic obstructive hypertrophic cardiomyopathy."
	Cardiomyopathy UK	We note that the draft scope states that 'people with HCM often need to make lifestyle changes, such as limiting their activity, to adjust for their disease'. We are concerned that this wording may not reflect current evidence or European Society of Cardiology (ESC) guideline recommendations regarding exercise in individuals with hypertrophic cardiomyopathy. The 2020 ESC guidelines on sports cardiology and exercise in patients with cardiovascular disease highlight 'there is limited evidence to indicate that all individuals with HCM are vulnerable to fatal arrhythmias during exercise and sport participation'. These guidelines go on to state that 'systematic restriction from competitive sports in all affected individuals is probably unjustified and a more liberal approach to sports participation is reasonable in some individuals after careful evaluation. This is particularly important for the majority of individuals with HCM who wish to participate in amateur sports or leisure-time exercise to maintain their physical and psychological wellbeing'.	Thank you for your comment. The section of the background has been changed to "People with HCM may need to make lifestyle changes, such as limiting their activity to adjust for their disease, if considered suitable by a specialist after individual evaluation"

Section	Consultee/ Commentator	Comments [sic]	Action
		Similarly, the 2023 ESC Guidelines for the management of cardiomyopathies indicate that 'recent pre-clinical and clinical data suggest that moderate exercise may be beneficial and safe in patients with HCM'. In light of these recommendations, we would suggest that the background section of the scope be revised to reflect ESC guidance, emphasising the importance of individual evaluation and the potential benefits of suitable exercise for many people with HCM. We also note the emphasis in the draft scope on how most people with HCM have few, if any, symptoms. However, this does not fully reflect the wide variability in symptom severity in patients with HCM. For example, a substantial proportion of patients with HCM report limiting symptoms of exertional dyspnoea (Maron et al., 2018 doi.org/10.1016/j.jchf.2017.09.011). As Prondzynski, Mearini and Carrier (2018) highlight 'clinical manifestations of HCM are variable in terms of disease development, age of onset, and severity of symptoms', with some individuals experiencing chest pain, vertigo, syncope, and dyspnoea, while others may require early heart transplantation, or die of sudden cardiac death. We feel this variability should be more clearly reflected in the background information	The section of the background has been changed to "Most people with HCM have no symptoms or feel stable throughout their life" to better reflect the reference material. The potential symptoms of people with HCM are included in the first paragraph of the background
	Genetic Alliance UK	To our understanding, the background information appears accurate and complete. However, we defer to our member organisation, Cardiomyopathy UK, and clinicians with expertise in this condition to gauge accuracy and completeness. For example, Cardiomyopathy UK published a factsheet on the condition in 2022, as well as other supporting information to guide	Thank you for your comment. All relevant evidence will be

Section	Consultee/ Commentator	Comments [sic]	Action
		development of the scope for this evaluation, such as guidelines on risk associated with SCD. Of note, is the anticipated findings from the 2025 My-Insight national survey of people living with Cardiomyopathy UK. Findings of the 2022 edition of this data were submitted as evidence to support a decision for mavacamten and tafamadis, and so will be also important addition to the evidence supporting the consultation process for aficamten. A copy of the survey questions has been published: Cardiomyopathy UK MyInsight survey 2024_FINAL.pdf https://www.cardiomyopathy.org/my-insight Hypertrophic cardiomyopathy factsheet January 2022.pdf https://www.cardiomyopathy.org/about-cardiomyopathy/types-cardiomyopathy/hypertrophic-cardiomyopathy	considered during the appraisal process
	NHSE Cardiology clinical reference group	Accurate, might be worth adding a small section on echocardiographic monitoring as this is a key clinical and financial factor	Thank you for your comment. “People with HCM may also have their condition monitored using echocardiographs” has been added to the background.
Population	Cytokinetics (company)	[redacted] Cytokinetics suggests that the population wording is updated as follows:	Thank you for your comment. The population in the scope can not be confidential.

Section	Consultee/ Commentator	Comments [sic]	Action
		[redacted]	The population has been updated to reflect the key inclusion criteria in clinical trial.
	Cardiomyopathy UK	Yes, as far as we are aware	Thank you for your comment. The population has been updated to reflect the key inclusion criteria in clinical trial.
	NHSE Cardiology clinical reference group	Yes	Thank you for your comment. The population has been updated to reflect the key inclusion criteria in clinical trial.
Subgroups	Cytokinetics (company)	No subgroups are specified in the draft scope.	Thank you for your comment. The population has been updated to reflect the key inclusion criteria in clinical trial.
	NHSE Cardiology clinical reference group	There should be clear differentiation between using it as first line therapy vs second line in symptomatic patients	Thank you for your comment. The population has been updated to reflect the

Section	Consultee/ Commentator	Comments [sic]	Action
			key inclusion criteria in clinical trial. We will ensure this distinction is considered in the evaluation.
Comparators	Cytokinetics (company)	The only appropriate comparator for this appraisal is mavacamten + SoC as it is the only NICE-approved second-line (2L) treatment for symptomatic oHCM. Cytokinetics will seek reimbursement for aficamten [redacted]). The first-line (1L) treatment of symptomatic oHCM would still be SoC, with patients only eligible for 2L treatment with either aficamten or mavacamten if they remained symptomatic on 1L treatment. Patients would continue their SoC treatment during aficamten (or mavacamten) treatment. This proposed approach reflects the SEQUOIA-HCM trial, in which either aficamten or placebo was administered in addition to SoC in the majority (>85%) of the population (11). The ESC guidelines for cardiomyopathy also recommend that a cardiac myosin inhibitor is administered 2L in addition to a BB or CCB to improve symptoms in patients with symptomatic oHCM (4). Individually optimised SoC without aficamten or mavacamten is not an appropriate comparator; [redacted] Cytokinetics requests that the scope is updated to reflect the fact that mavacamten + SoC is the only appropriate comparator for this appraisal, as follows:	Thank you for your comment. Individually optimised standard care without aficamten or mavacamten has been removed from the comparator section.

Section	Consultee/ Commentator	Comments [sic]	Action
		• ~~***Individually optimised standard care without aficamten or mavacamten***~~ • Mavacamten in combination with standard care	
	Cardiomyopathy UK	Our understanding is that as aficamten belongs to a new classification of medicine to treat obstructive HCM, it could only be compared to mavacamten.	Thank you for your comment. The comparators in the scope are intended to be as inclusive as possible. If a comparator is considered inappropriate, its exclusion can be justified in the company submission.
	NHSE Cardiology clinical reference group	Yes, Mavacamten is the only comparator	Thank you for your comment. The comparators in the scope are intended to be as inclusive as possible. If a comparator is considered inappropriate, its exclusion can be justified in the company submission.

Section	Consultee/ Commentator	Comments [sic]	Action
Outcomes	Cytokinetics (company)	Cytokinetics considers the outcomes listed to be largely appropriate. It is important to note that as HCM-related deaths are infrequent (11), endpoints based on functional capacity and symptom relief form the basis of the aficamten regulatory submissions and will provide the main evidence for the NICE appraisal	Thank you for your comment. No action required.
	NHSE Cardiology clinical reference group	Yes	Thank you for your comment. No action required.
Equality	Cytokinetics (company)	While Cytokinetics does not believe there is a need to amend the Equality section of the draft remit and scope, it is important to note that there may be some equality issues related to oHCM and its management within the UK NHS. Epidemiological data suggest that oHCM is more prevalent in men than in women (12, 13) although it is thought that the difference may be due to underdiagnosis in women (14). Moreover, women with oHCM have a poorer prognosis than men, including increased risk of HCM-related events including major adverse cardiovascular events and mortality (15), as well as higher healthcare resource use, including more hospitalisations with longer length of stay and more outpatient visits (16). The underlying reasons for these sex-based differences in diagnosis and outcomes is unclear. Evidence from clinical trials suggests that aficamten has comparable efficacy in women and men (17), offering a treatment option that is not affected by the sex-based differences in the natural history of oHCM. Aficamten has the potential to improve some of the equality issues faced by patients with symptomatic oHCM, including those associated with mavacamten treatment. Patients must be able to frequently access tertiary	Thank you for your comment. These issues have been added to the equality impact assessment (EIA) form

Section	Consultee/ Commentator	Comments [sic]	Action
		specialist centres for monitoring during mavacamten treatment, which can lead to geographic inequalities in access depending on where patients live (i.e. access may be more difficult for those who live in rural areas and/or far from major treatment centres). Compared with mavacamten, it is expected that aficamten use will allow for simpler disease management, including a more straightforward dose titration process and potential for fewer hospital visits for echocardiograms and follow up appointments, thereby reducing the patient burden of frequent hospital visits	
	Genetic Alliance UK	As is the situation with other rare conditions, not all people living with HCM may be under regular specialist follow-up. For example, some may be undiagnosed or have limited access to genetic testing or specialist centres. A therapy like aficamten must therefore be considered in the context of these inequalities, and any guidance should ensure access does not become inequitable. To better situate this consultation process in the experience of people living with HCM and similar cardiac conditions, we encourage reviewers to consider the report that Cardiomyopathy UK published on the state of cardiomyopathy care in the UK in 2023, which was based on its 2022 My-Insight survey findings. This provides a succinct but clear overview of some of the challenges already facing the patient community: State of cardiomyopathy care 2022 survey report.pdf	Thank you for your comment. This issue has been added to the equality impact assessment (EIA) form
	NHSE Cardiology clinical reference group	Restricting prescribing to commissioned centres only can lead to inequities in prescribing, particularly affecting those with more comorbidities who struggle to travel long distances for monitoring. A hub and spoke prescribing model should be adopted within the governance structures of commissioned centres and their networks, to reduce inequities of access.	Thank you for your comment. This issue has been added to the equality impact assessment (EIA) form

Section	Consultee/ Commentator	Comments [sic]	Action
Other considerations	NHSE Cardiology clinical reference group	A major financial and clinical consideration is the echocardiographic monitoring and its comparison with mavacamtem. This merits a detailed evaluation.	Thank you for your comment. All relevant costs will be considered during the appraisal.
Questions for consultation	Cytokinetics (company)	**Will aficamten be used in the same position in the treatment pathway as mavacamten?** Yes, aficamten will be used in the same position in the treatment pathway as mavacamten. **Will aficamten have the same restrictions on use (i.e. NYHA class) as mavacamten?** Yes, aficamten will be subject to the same restrictions on use by NYHA class as mavacamten. **Will aficamten be used in combination with standard care?** Yes, aficamten will be used as an add-on treatment alongside SoC. **Where do you consider aficamten will fit into the existing care pathway for symptomatic obstructive hypertrophic cardiomyopathy?** Cytokinetics considers that aficamten will fit into the existing care pathway in the same position as mavacamten (i.e. 2L) and would therefore represent an additional treatment option in that position. **Please select from the following, will aficamten be:** D. Other - prescribed in specialist tertiary care centres that provide services for inherited cardiac conditions (ICC) with routine follow-up in those same specialist tertiary care centres.	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator

Section	Consultee/ Commentator	Comments [sic]	Action
		For comparators and subsequent treatments, please detail if the setting for prescribing and routine follow-up differs from the intervention. There is no difference in the settings for prescribing and routine follow-up between aficamten and mavacamten. **Would aficamten be a candidate for managed access?** No, aficamten is not expected to be a candidate for managed access. **Do you consider that the use of aficamten can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation? Please identify the nature of the data which you understand to be available to enable the committee to take account of these benefits.** As the proposed approach for this appraisal is cost-comparison, a QALY calculation will not be presented. The benefits of aficamten, including its comparable efficacy with mavacamten, manageable safety profile and simpler disease management process, are described in earlier responses and will be reflected in the cost-comparison model that Cytokinetics intends to submit. ***The following questions and responses relate to the suitability of a cost-comparison appraisal for aficamten:*** **Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators? Clinical effectiveness:** Aficamten is likely to have at least comparable clinical efficacy to mavacamten, based on the available trial data and clinical expert opinion. Aficamten and mavacamten belong to the same treatment class of cardiac myosin inhibitors which target the underlying pathophysiology and disease course of oHCM.	

Section	Consultee/ Commentator	Comments [sic]	Action
		Results from key Phase 3 RCTs (SEQUOIA-HCM for aficamten and EXPLORER-HCM for mavacamten) show similar efficacy results for each treatment versus placebo, including peak oxygen uptake (a measure of exercise capacity), Kansas City Cardiomyopathy Questionnaire (health status), and NYHA class (symptom burden). Results of an ITC also show comparable efficacy between aficamten and mavacamten, with consistent findings across analysis methods. When presented with aficamten clinical evidence at an advisory board, clinician and payer experts (including from the UK) confirmed they viewed the treatments as clinically comparable. **Resource use:** Aficamten may require fewer healthcare resources than mavacamten due to not requiring genetic testing prior to use, and having simpler and more rapid dose titration potential and therefore potential for reduced resource use during the titration phase: • Prior to initiating mavacamten, patients require genetic testing for CYP2C19 to determine the appropriate dose as poor CYP2C19 metabolisers are at increased risk of systolic dysfunction with mavacamten (10). Aficamten is metabolised by CYP enzymes other than CYP2C19 and therefore CYP genetic testing is not required • Patients receiving both mavacamten and aficamten require echocardiographic monitoring during their drug initiation and dose titration period due to the risk of heart failure from systolic dysfunction (left ventricular ejection fraction [LVEF] <50%). Mavacamten use requires more echocardiograms during the first year of treatment than aficamten; depending on the effective dose required, patients need a minimum of 6 and up to 11 echocardiograms in their first year on	

Section	Consultee/ Commentator	Comments [sic]	Action
		mavacamten (10) [redacted] • Aficamten is expected to have a more manageable safety profile with lower rates of LVEF <50% than observed with mavacamten treatment. As patients experiencing LVEF <50% require closer echocardiogram monitoring, the lower rates observed with aficamten are also expected to reduce the overall echocardiogram monitoring burden relative to mavacamten for patients and hospitals • Aficamten is expected to offer improved ease of use versus mavacamten due to its shorter half-life, faster time to reach steady state, and wider therapeutic window. These factors mean patients should achieve their optimal dose more quickly and is expected to contribute to an overall reduction in resource use due to fewer echocardiograms and associated outpatient visits **Will the intervention be used in the same place in the treatment pathway as the comparator(s)? Have there been any major changes to the treatment pathway recently? If so, please describe.** Yes, aficamten is expected to be used as an add-on to individually optimised SoC and in the same therapy line as mavacamten (2L) (1). Since the introduction of mavacamten to the NHS in 2023, no major changes to the treatment pathway have occurred. **Will the intervention be used to treat the same population as the comparator(s)?** Yes. Aficamten will be used in the same population as recommended for mavacamten in TA913 (1).	

Section	Consultee/ Commentator	Comments [sic]	Action
		Overall is the technology likely to offer similar or improved health benefits compared with the comparators? Yes, please refer to responses above (*Is the technology likely to be similar in its clinical effectiveness and resource use to any of the comparators? Or in what way is it different to the comparators?)*. **Would it be appropriate to use the cost-comparison methodology for this topic?** Yes. Cytokinetics is convinced a cost-comparison route is the appropriate methodology for this topic for the reasons outlined above and believes all NICE criteria for this approach have been met.	
	Bristol Myers Squibb	1. **Will aficamten be used in the same position in the treatment pathway as mavacamten?** Based on ESG Guidelines and NICE TA913, aficamten should not be positioned identically to mavacamten. Current European consensus and NICE advice restrict myosin inhibitors (including mavacamten) to second-line—after failure or intolerance of standard care (beta-blockers, calcium channel blockers, disopyramide). First-line and second-line populations are clinically distinct: patients eligible for second-line therapy have already failed to achieve adequate control or have contraindications to existing first-line agents.	Thank you for your comment. NICE will continue this appraisal using the cost-comparison methodology. The appropriateness of a cost-comparison will be considered, including available evidence and similarity of the NICE approved comparator

Section	Consultee/ Commentator	Comments [sic]	Action
		2. **Will aficamten have the same restrictions on use (i.e. NYHA class) as mavacamten?** Aficamten, if approved, should be restricted to the same NYHA populations as mavacamten—namely symptomatic obstructive HCM patients (NYHA Class II–III) who remain insufficiently controlled despite standard care. This ensures alignment with both current guideline recommendations and the labelled population supported by pivotal mavacamten studies (EXPLORER-HCM, VALOR-HCM). 3. **Will aficamten be used in combination with standard care?** Yes; per guideline and emerging evidence, myosin inhibitors are add-on agents in patients not adequately managed by optimised standard care—meaning aficamten's role, if approved, would be as an adjunct or alternative when beta-blockers, calcium antagonists, and/or disopyramide are ineffective, contraindicated, or poorly tolerated, mirroring the use of mavacamten. Combination with disopyramide should not be routinely recommended due to potential overlapping safety concerns. 4. **Where do you consider aficamten will fit into the existing care pathway for symptomatic obstructive hypertrophic cardiomyopathy?** Aficamten would be considered a second-line therapeutic option, reserved for those who do not achieve adequate symptom control or remain intolerant to standard care (beta-blockers, verapamil/diltiazem, disopyramide). It should not be administered first-line and must maintain clear population separation from those suitable for first-line therapy. Patients in this group form a distinct subpopulation, typically with NYHA II–III symptoms and persistent LVOTO despite optimal first-line treatment. This scope ensures clarity for clinical practice and appropriate health technology evaluation.	

Section	Consultee/ Commentator	Comments [sic]	Action
		5. **Prescribing and follow-up setting:** Prescribed in secondary care with routine follow-up in secondary care. Myosin inhibitors require regular echocardiographic monitoring and expertise in heart failure/cardiomyopathy management, reflecting the value of centralised care as recommended for mavacamten and supported by the current evidence base. 6. **For comparators and subsequent treatments, does the setting differ from the intervention?** No; both mavacamten and aficamten (if licensed) should be prescribed and monitored in secondary/tertiary care, consistent with the need for multidisciplinary management and cardiac imaging. 7. **Would aficamten be a candidate for managed access?** Potentially, but only if there is significant uncertainty about long-term effectiveness or safety in UK clinical practice that warrants collection of additional real-world data. This would mirror precedent from other medicines with novel mechanisms for rare diseases. 8. **Do you consider the use of aficamten can result in any potential substantial health-related benefits that are unlikely to be included in the QALY calculation?** Any benefits must be proven in robust clinical trials. Health-related benefits outside QALY (e.g., carer burden, patient empowerment, reduction of hospital procedures) are conceivable but not currently substantiated by published aficamten evidence. These should only be considered if supported by specific UK patient-reported outcomes data, consistent with NICE methods.	
		9. **Cost comparison:** Given the clear separation of populations—first-line (standard care)	

Section	Consultee/ Commentator	Comments [sic]	Action
		versus second-line (mavacamten, aficamten)—and differences in clinical trial maturity and guideline endorsement, cost-comparison is inappropriate. Aficamten does not currently have the requisite comparative evidence, nor established equivalence in long-term safety or real-world effectiveness versus mavacamten. A single technology appraisal (STA) permits a full review of aficamten's evidence base and ensures robust, independent scrutiny, avoiding premature adoption based merely on class similarities.	
	Cardiomyopathy UK	1) *Will aficamten be used in the same position in the treatment pathway as mavacamten?* Yes, as far as we are aware 3) *Will aficamten be used in combination with standard care?* Yes, as far as we are aware. *4) Where do you consider aficamten will fit into the existing care pathway for symptomatic obstructive hypertrophic cardiomyopathy?* D, Other. We expect it would be used in a specialised service within tertiary healthcare.	Thank you for your comment. No action required.
Additional comments on the draft scope		No comments	