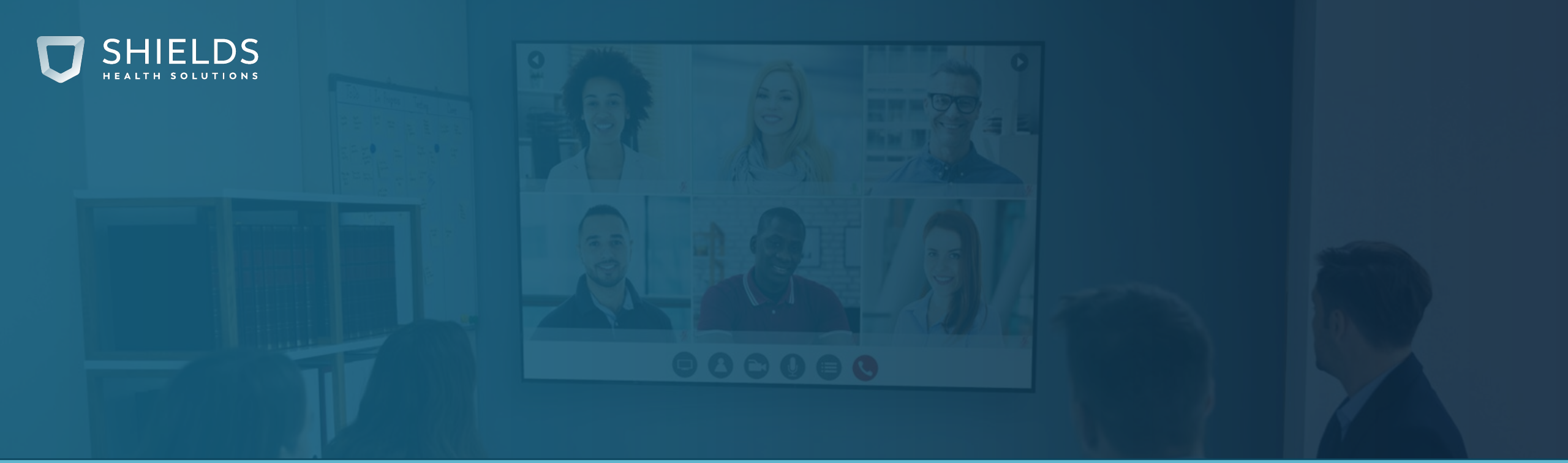

Hypertrophic Cardiomyopathy: A Focus on Treatment, Specialty Medication Access, and the Impact of Clinical Pharmacy Programs

SHIELDS WEBINARS

Meet Our Speakers

Carlee Montgomery, PharmD, CSP
Manager of Clinical Implementation

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Director, Rare Diseases and REMS Programs

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Learning Objectives

1. Understand the epidemiology and pathophysiology of HCM, emphasizing genetic factors, phenotypic diversity, and age-related progression.

2. Evaluate current and emerging therapies for HCM, including efficacy and safety data from pivotal clinical trials.

3. Discuss key considerations for the specialty pharmacy, including barriers to medication access and factors impacting adherence.

4. Review the FDA REMS requirements and evaluate the impact of pharmacist-led clinical management on safety, quality, and outcomes for patients on mavacamten.

Pathophysiology & Epidemiology

What is hypertrophic cardiomyopathy (HCM)?[1]

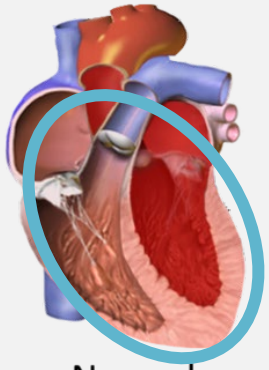
Hypertropic cardiomyopathy (HCM) is left ventricular cardiac hypertrophy caused by autosomal mutations increasing cross-bridges between cardiac muscle proteins.

Diagnosed by the presence of a mid systolic murmur, ECG findings, and ECHO findings.

2 Types of HCM
- Non-Obstructive HCM (nHCM)
- Obstructive HCM (oHCM)

Symptoms vary based on severity.

First line treatment is beta blockers or non-dhp calcium channel blockers.



Attribution: Npatchett at English Wikipedia

Fast Facts[1]

- Most common inherited cardiomyopathy
- Most common cause of sudden death in young people/athletes
- No increased risk between men/women or different ethnic groups
- USA estimated incidence of 1:200 to 1:500 (photo below)

1. Basit H, Alahmadi MH, Rout P, et al. Hypertrophic Cardiomyopathy. [Updated 2024 Jun 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2025 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK430788/

Mavacamten

FDA APPROVAL[1,2]

Approved in April 2022 for symptomatic obstructive HCM (oHCM) in NYHA II-III to improve functional capacity and symptoms.

1 capsule of 5mg daily, with or without food to start

- Titrate to up to 15mg) based on week of therapy, repeat echo LVEF, and Valsalva LVOT gradient

MECHANISM OF ACTION[1]

First in class, selective, reversible cardiac myosin inhibitor

Directly targets the hypercontractile sarcomere, reducing actin-myosin cross-bridge formation

Decreasing LVOT gradients improves diastolic function

TRIAL HIGHLIGHTS[2]

Phase 3 EXPLORER-HCM trial

Primary composite endpoint achieved

Improvement of pVO2 by 1.5ml/kg/min or more, improvement in NYHA class by at least 1 or improvement of pVO2 by 3ml/kg/min or more and no worsening class- 37% vs 17% (p=0.0005)

Secondary endpoints (improved health status & symptoms)

↓LVOT Obstruction Gradient- mean difference -36 mmHg; p<0.0001

↓NYHA Class (by at least 1)- 65% vs 31%; p<0.0001

↑Peak 02 consumption (improved exercise capacity)- mean increase in pVO_2 +1.4 mL/kg/min; p=0.0006

↑KCCQ Score- mean difference +9.1 points; p<0.0001

Safety notes: LVEF dropping to <50% lead to dose interruptions. Atrial fibrillation, and heart failure also seen in trial.

1. Olivotto I, Oreziak A, Barriales-Villa R, et al. Mavacamten for treatment of symptomatic obstructive hypertrophic cardiomyopathy (EXPLORER-HCM): a randomised, double-blind, placebo-controlled, phase 3 trial. *Lancet*. 2020;396(10253):759-769. doi:10.1016/S0140-6736(20)31792-X
2. **Bristol Myers Squibb.** U.S. Food and Drug Administration Approves Camzyos™ (mavacamten) for the Treatment of Adults With Symptomatic New York Heart Association Class II–III Obstructive Hypertrophic Cardiomyopathy (HCM) to Improve Functional Capacity and Symptoms. *Bristol Myers Squibb Newsroom*. Published April 28, 2022. Accessed August 8, 2025. https://news.bms.com/news/details/2022/U.S.-Food-and-Drug-Administration-Approves-Camzyos-mavacamten-for-the-Treatment-of-Adults-With-Symptomatic-New-York-Heart-Association-Class-II-III-ObstructiveHypertrophic-Cardiomyopathy-HCM-to-Improve-Functional-Capacity-and-Symptoms/default.aspx

AFICAMTEN

- Next-in-class, selective, reversible cardiac myosin inhibitor for those with symptomatic HCM and LVOT obstruction[1]
- PDUFA target action date December 2025*[2]
- SEQUOIA-HCM phase 3 trial showed similar results to Mavacamten

Key Differences:[1,3]

Half Life	Population Studied	Adverse Effects
• Shorter half life vs Mavacamten (3.5d vs 6-23d) creating a shallower dose-response • Faster, finer titration and potentially wider therapeutic window • Dose adjustments can occur as early as every 2 weeks	• Included a more globally diverse population • Aficamten trial showed consistent benefits regardless of background beta blocker use.	• Lower rates of LVEF reduction and treatment interruption compared to Mavacamten, though follow-up with aficamten is shorter and data yields an indirect comparison.

Primary endpoint met: Improved peak oxygen uptake by a mean difference of 1.7ml/kg/min[1]

Clinically significant secondary endpoints met[1]

- International, randomized, double-blind, placebo controlled[1]
- 282 patients aged 18-85 years old[1]
- Followed for 24 weeks[1]

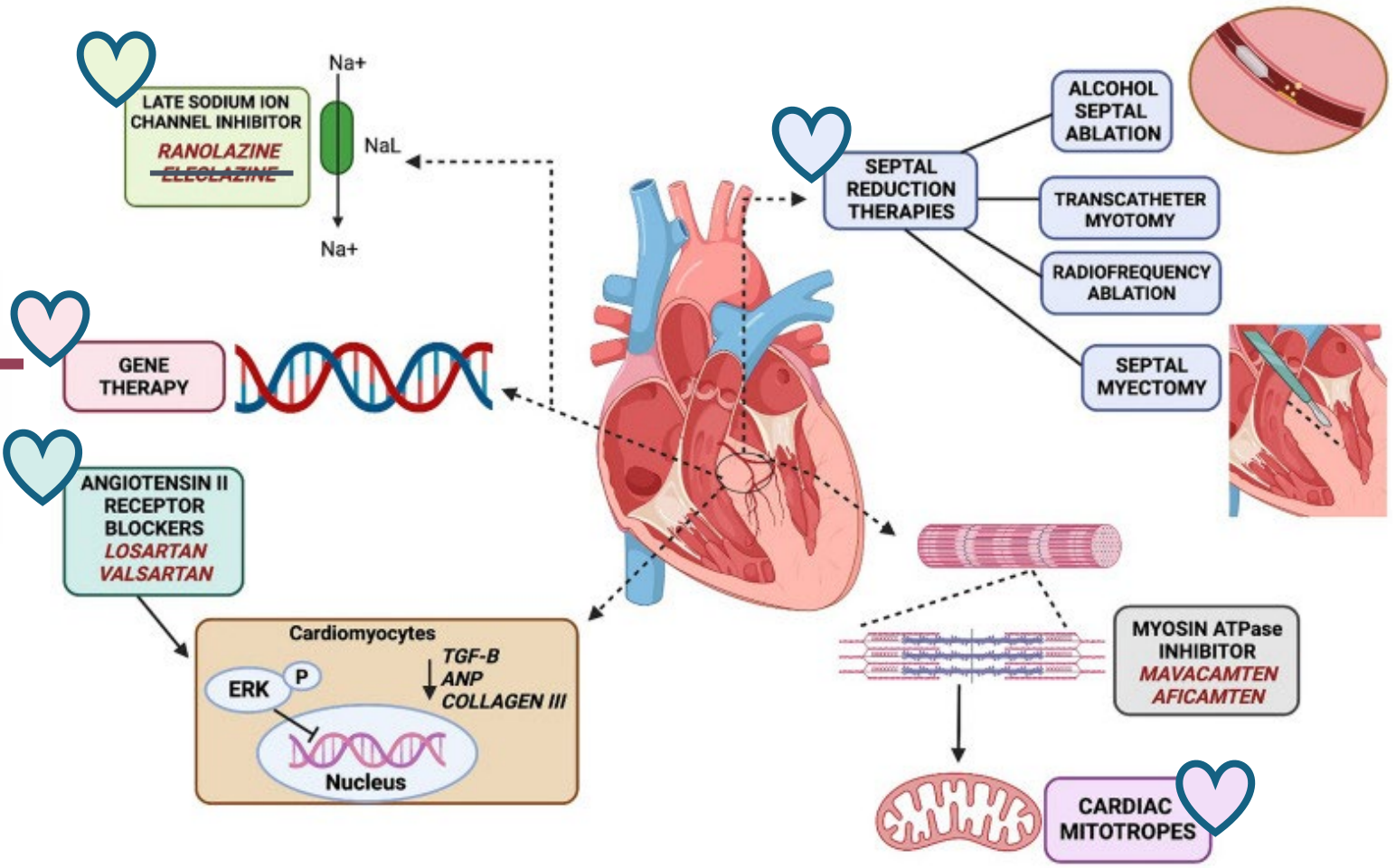
1. Maron MS, Masri A, Nassif ME, et al. Aficamten for Symptomatic Obstructive Hypertrophic Cardiomyopathy. N Engl J Med. 2024;390(20):1849-1861. doi:10.1056/NEJMoa2401424

2. Tenaya Therapeutics. Tenaya Therapeutics Announces Late Breaker and New Data Presentations at the American College of Cardiology's Annual Scientific Session. *Tenaya Therapeutics Investor Relations Website*. Published March 19, 2025. Accessed August 8, 2025. https://investors.tenayatherapeutics.com/news-releases/news-release-details/tenaya-therapeutics-announces-late-breaker-presentation-new-data

3. Davis BJ, Volk H, Nguyen O, et al. Safety and Efficacy of Mavacamten and Aficamten in Patients With Hypertrophic Cardiomyopathy. J Am Heart Assoc. 2025;14(6):e038758. doi:10.1161/JAHA.124.038758

Emerging Strategies

Gene therapy- TN-201 (Tenaya Therapeutics) is investigating an adeno-associated virus (AAV)-vector based gene therapy to deliver a functional copy of the MYBPC3 gene to heart muscle cells, aiming to restore normal protein levels and potentially reverse disease progression[1]



1. Packard E, de Feria A, Peshin S, Reza N, Owens AT. Contemporary Therapies and Future Directions in the Management of Hypertrophic Cardiomyopathy. Cardiol Ther. 2022;11(4):491-507. doi:10.1007/s40119-022-00283-5

HCM Therapies: Barriers to Access

Delayed Treatment

- Diagnosis of oHCM
- Evaluation of treatment options
- Patient REMS enrollment
- Order/schedule echocardiogram
- Determine start date

Restricted distribution

- LDD network
- Pharmacy participation agreement

Echocardiogram Requirements

- Once a month for first three months of therapy with LVEF and vLVOT gradient assessment
- Shift to every 3 months when stable
- Dose up-titrations require additional echocardiogram

Prior authorization

- Benefits investigation
- PA turnaround time
- PA denials/appeals

Financial burden

- Screen and apply for eligible programs
- Manufacturer copay cards (commercial plans)
- Foundation and charity grants (federally funded plans)
- Manufacturer patient assistance programs (PAP): uninsured or low-income households

FDA REMS

- Prescriber and pharmacy certification
- Patient enrollment
- Monthly REMS counsel

Care Coordination

- Echocardiogram results
- Patient status forms
- Warm transfer to pharmacist
- Pharmacy cutoff times for shipping

Shipping requirements

- Ship within 24 hours of logging a dispense
- Treatment for < 1 year: 35-day maximum per dispense
- Treatment for > 1 year: 90-day maximum per dispense
- One-time travel override for additional 35 days

Risk Evaluation and Mitigation Strategy (REMS)

REMS is a drug safety program required by the FDA for certain medications with serious safety concerns to ensure the benefits of the medication outweigh the risks

A REMS may include Elements to Assure Safe Use (ETASU), or evidence for safe use conditions:

- Monthly counsel
- Monthly laboratory test
- Communication plan
- Shipping restrictions
- Medication guide

Source: fda.gov/drugs/drug-safety-and-availability/risk-evaluation-and-mitigation-strategies-rems [Accessed August 11, 2025]

Mavacamten REMS Requirements

The purpose of the mavacamten REMS is to manage the risk of heart failure due to systolic dysfunction

Before Dispensing

- Counsel the patient on drug-drug interactions
- Assess the patient's prescription and non-prescription medications and supplements for drug-drug interactions
- Complete and submit the Drug Interaction & Counseling Checklist to the REMS
- Document the prescribed dose
- Report adverse events
- Obtain authorization to dispense to verify that:
  - Prescriber is certified and the patient is enrolled
  - Healthcare provider has authorized the patient to receive the drug, the patient was counseled and the pharmacist identified and resolved drug interactions

With Each Dispense

- Provide a patient brochure with each shipment
- Dispense no more than a 35-day supply to patients in their first year of treatment
- Dispense no more than a 90-day supply to patients beyond their first year of treatment
- Ship within 24 hours of logging a dispense
  - Ship for next business day or next calendar day delivery

Source: Camzyos. Prescribing Information. Bristol Myers Squibb, 2025. Accessed August 5, 2025

Mavacamten Drug Interactions

Boxed Warning:

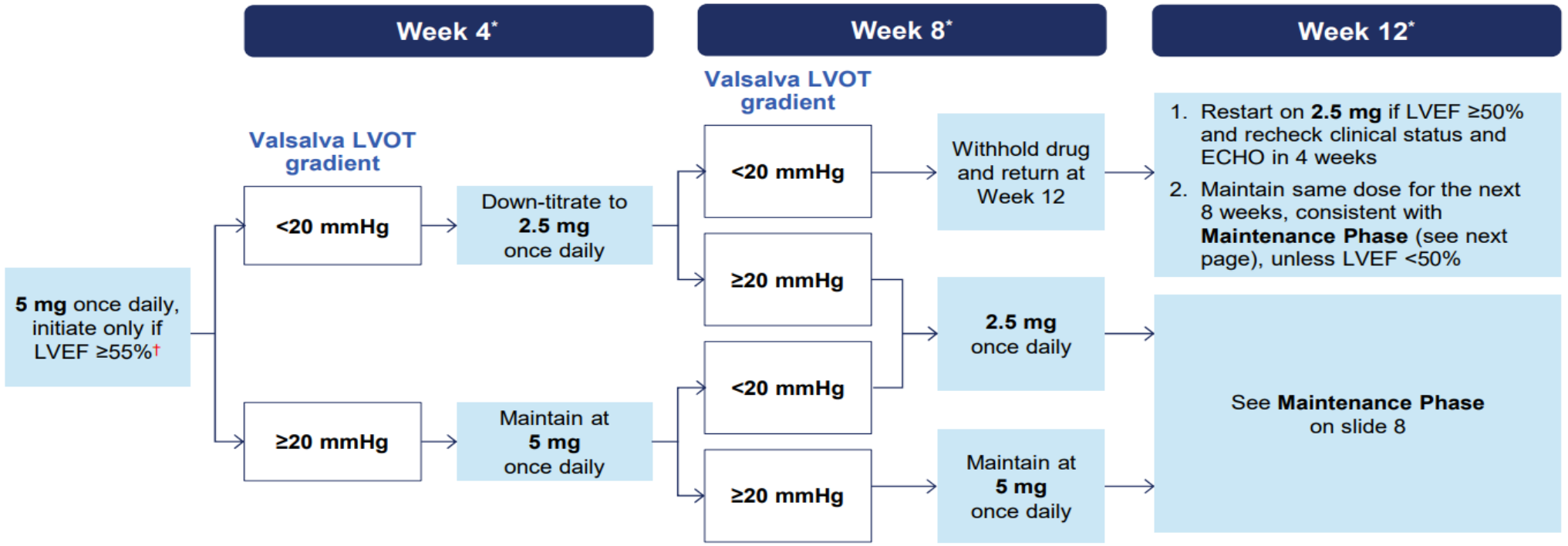
- Strong CYP2C19 inhibitors
  - ↑ mavacamten exposure; ↑ risk of heart failure due to systolic dysfunction
- Moderate to severe CYP2C19 inducers
  - ↓ mavacamten exposure; ↓ efficacy of mavacamten
- Moderate to severe CYP3A4 inducers
  - ↓ mavacamten exposure; ↓ efficacy of mavacamten

Advise patient of the potential for drug interactions, including OTC medications such as omeprazole and esomeprazole, prior to and during treatment with mavacamten

Source: Camzyos. Prescribing Information. Bristol Myers Squibb, 2025. Accessed August 5, 2025

Mavacamten Dosing: Treatment Initiation

Dosing and Administration: Initiation Phase

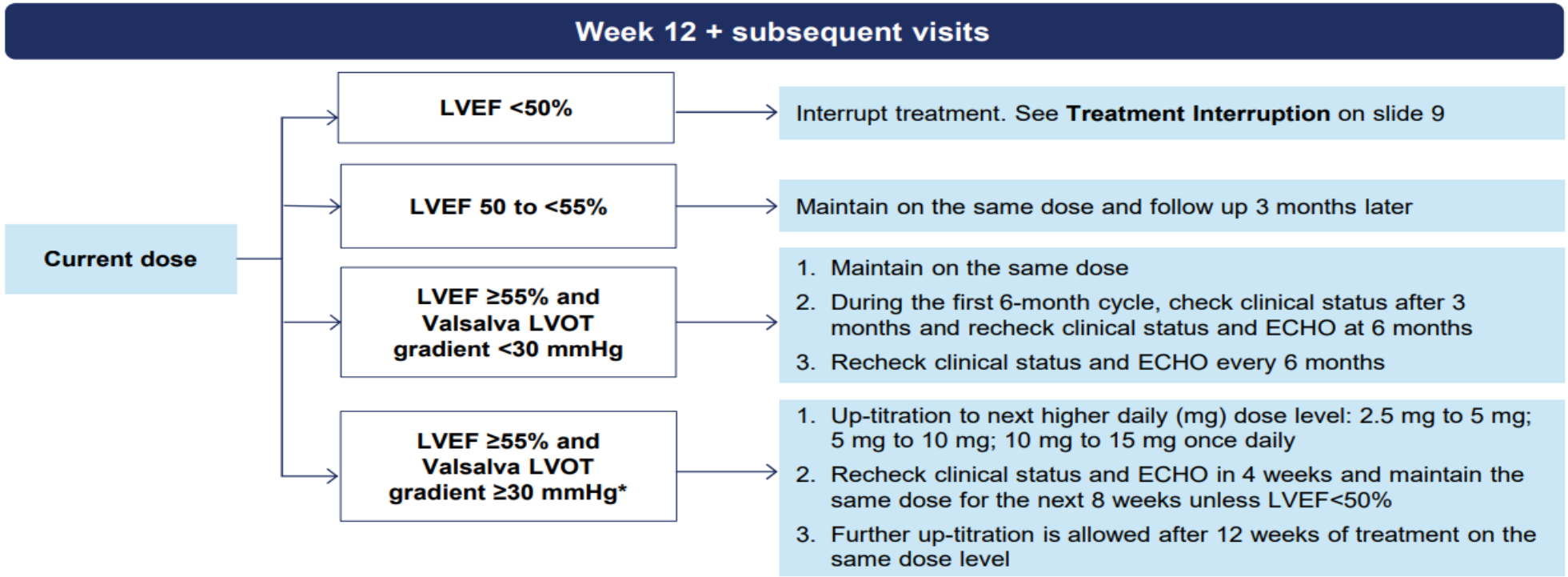


*Interrupt treatment if LVEF <50% at any clinic visit; restart treatment after 4 weeks if LVEF ≥50%. See **Treatment Interruption** (slide 9).
†For patients initiating CAMZYOS on stable therapy with a moderate CYP2C19 inhibitor or a strong CYP3A4 inhibitor, see slide 12 for dosing instructions.
CYP=cytochrome P450; ECHO=echocardiogram; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract.

Source: Camzyos. Prescribing Information. Bristol Myers Squibb, 2025. Accessed August 5, 2025

Mavacamten Dosing: Treatment Maintenance

Dosing and Administration: Maintenance Phase



*For patients with normal or near-normal Valsalva LVOT gradient (approximately 30 mmHg) prior to initiating treatment with CAMZYOS, if LVEF is ≥55% and post-exercise LVOT gradient is ≥30 mmHg, the dose may be increased to the next higher daily (mg) dose level if symptoms persist.

ECHO=echocardiogram; LVEF=left ventricular ejection fraction; LVOT=left ventricular outflow tract.

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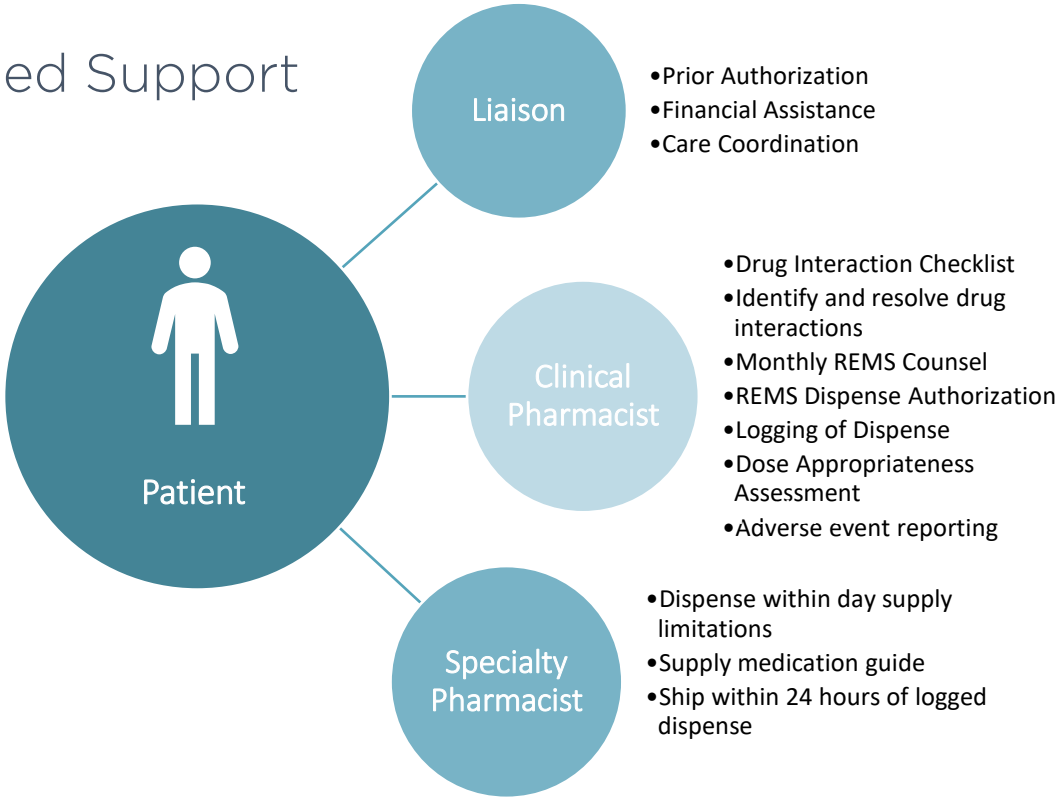
Source: Camzyos. Prescribing Information. Bristol Myers Squibb, 2025. Accessed August 5, 2025

Specialty Pharmacy Considerations

Dedicated Support Team



- Prior Authorization
- Financial Assistance
- Care Coordination

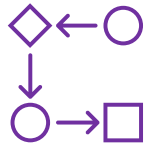
- Drug Interaction Checklist
- Identify and resolve drug interactions
- Monthly REMS Counsel
- REMS Dispense Authorization
- Logging of Dispense
- Dose Appropriateness Assessment
- Adverse event reporting

- Dispense within day supply limitations
- Supply medication guide
- Ship within 24 hours of logged dispense

Additional Considerations:

Policies & Procedures

Documented Training



Workflow Revision

Post-Dispense Audit Support

Patient Education Highlights

GOALS OF THERAPY

DISEASE STATE EDUCATION

COMMON DRUG INTERACTIONS

SIDE EFFECT MANAGEMENT

MISSED DOSE MANAGEMENT

ADHERENCE

REMS COMPLIANCE

LIFESTYLE EDUCATION AND SUPPORT

PATIENT RESOURCES

Shields Clinical Pharmacist Journey

- Shields incorporates the mavacamten REMS requirements into the clinical services model via monthly patient assessments for heart failure symptoms and drug interactions.
- Includes clinical pharmacist prescreening prior to the dispense of medication and REMS Refill Screening prior to each subsequent dispense of mavacamten.

Real World Experience: Clinical Outcomes Data

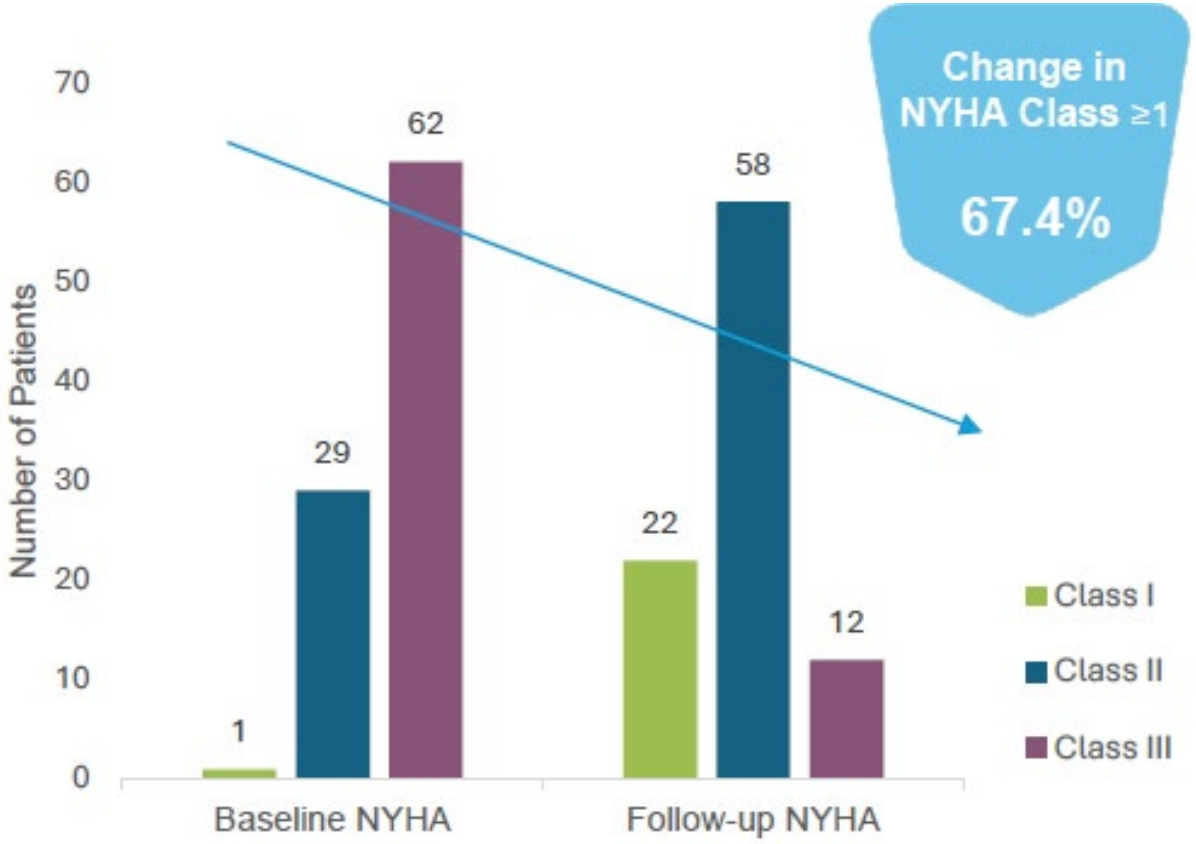
Clinical, Safety, and Quality Outcomes of a Hypertrophic Cardiomyopathy Clinical Pharmacy Management Program

- Retrospective study including ninety-two HCM patients new to mavacamten therapy and enrolled in the patient management program for a minimum of 6 months (5/2022 – 12/2024).
- Primary outcome: percentage of patients with an improvement in NYHA class by ≥ 1 class
- Secondary outcomes: ER visits, hospitalizations, serious adverse events, adherence measured by PDC, number and type of pharmacist interventions, and REMS audit results

Characteristic	N=92
Mean age (years)	71
Sex (n, %)	
M	31 (34)
F	61 (66)
Mavacamten Dose (mg) (n, %)	
2.5	24 (26)
5	33 (36)
10	29 (32)
15	6 (6)
Initial NYHA Class (n, %)	
I	1 (1)
II	29 (32)
III	62 (67)
Insurance Type (n, %)	
Medicare	60 (65)
Commercial	29 (32)
Medicaid	3 (3)

Results

Primary Outcome: Change in NYHA Class



Primary Outcome

- 62 (67.4%) patients with NYHA class improved ≥1
- Number with NYHA Class III reduced from 62 patients down to 12 patients at study conclusion
- Consistent with VALOR-HCM trial results in which 63% of patients had NYHA Class improved ≥ 1

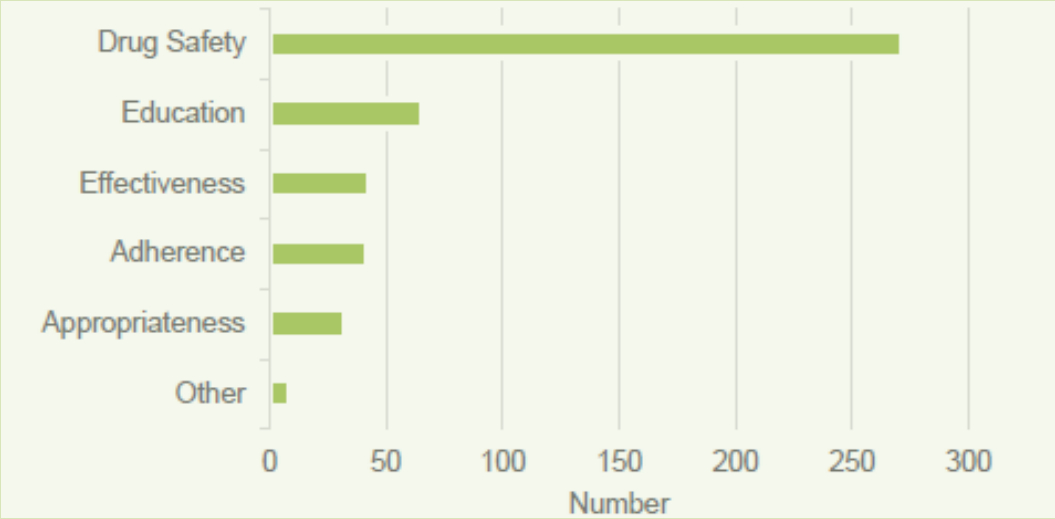
Source: Desai MY, Owens A, Wolski, K, et al. Mavacamten in Patients with Hypertrophic Cardiomyopathy Referred for Septal Reduction Week 56 Results from the VALOR-HCM Randomized Clinical Trial. JAMA Cardiol. 2023;8(10):968-977. doi:10.1001/jamacardio.2023.3342

Results

Secondary Outcomes	
ER visits (n)	5
Hospitalizations (n)	8
Serious adverse events (n)*	12
PDC (%)	96
Successful REMS audits	4

- * Serious adverse events were defined as hospitalization, disability or permanent damage, congenital anomaly/birth defect, required intervention to prevent permanent impairment or damage, other serious medical event, life-threatening, or death.

Clinical interventions (N= 465)



Evaluation Conclusions

- Supports the results from the VALOR-HCM trial
- Demonstrates real-world clinical outcomes associated with a pharmacist-led patient management program for patients with HCM

Promotion of Clinical Outcomes

Improved Medication Safety

Higher Quality Patient Care

Summary

- HCM is the most common cardiomyopathy, is underdiagnosed, and progresses to cause significant impact on a patient's overall health.
- Mavacamten serves as the only approved treatment for those with identified gene mutations causing oHCM. Emerging treatments like aficamten and gene therapy show promise.
- Barriers to accessing HCM therapies include LDD networks, intensive echocardiogram schedules and FDA REMS requirements.
- Specialty pharmacists play a role in identifying and resolving clinically significant drug interactions, assessing for dose appropriateness and enforcing medication safety.
- The real-world evaluation of a HSSP model for managing HCM patients demonstrated positive clinical outcomes and a reduction in NYHA Class consistent with clinical trial results.
- The implementation of a pharmacist-led patient management program promoted improved clinical and safety outcomes for patients prescribed mavacamten.

THANK YOU

FOR YOUR VALUABLE TIME

Additional Resources

Resource	Website
Coylewright M et al. 2024 Hypertrophic cardiomyopathy guideline-at-a-glance. JACC 2024;83(23):2406-2410.	2024 Hypertrophic Cardiomyopathy Guideline-at-a-Glance | JACC
American Heart Association: Hypertrophic Cardiomyopathy Resources for Professionals	https://professional.heart.org/en/education/hypertrophic-cardiomyopathy-for-professionals
Hypertrophic Cardiomyopathy Association	https://4hcm.org/