Drug Use Research & Management Program
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New Drug Evaluation: Cardamyst (etripamil), nasal spray

Date of Review: June 2026
Generic Name: Etripamil

End Date of Literature Search: 02/25/2026
Brand Name (Manufacturer): CARDAMYST (Milestone Pharmaceuticals)

Dossier Received: Yes

Plain Language Summary:

- This new drug evaluation looks at the evidence for the safety and effectiveness of CARDAMYST (etripamil), a nasal spray recently approved by the Food and Drug Administration (FDA) for management of an arrhythmia with an unusually fast heart rate known as paroxysmal supraventricular tachycardia (PSVT).
- People with PSVT can have very fast heartbeats which suddenly start and stop without warning. Symptoms of PSVT include dizziness, shortness of breath, feeling very tired, light-headedness, and chest pain.
- Etripamil is used to help restore normal heartbeat in adults with PSVT. The medicine is taken as one spray in each nostril for up to 2 doses. If symptoms do not improve after 2 doses, a medical provider should be contacted immediately, or the patient should get emergency help.
- In a clinical trial which compared self-administered etripamil nasal spray with placebo (fake medicine), people with PSVT were restored to a normal rate heart rate within 30 minutes more often than people who received placebo.
- Side effects reported with etripamil nasal spray include nose or throat irritation, runny or stuffy nose, and nosebleeds.
- The Drug Use Research and Management program recommends that a prescriber submit documentation why a person needs etripamil nasal spray. This process is called prior authorization.

Research Questions:

1. What is the evidence for the efficacy of etripamil nasal spray in converting PSVT to normal sinus rhythm in adults?
2. What is the safety of etripamil nasal spray in resolving PSVT?
3. Are there populations based on specific demographic characteristics (e.g., age, gender, race/ethnicity, socioeconomic status, etc.) for which etripamil is better tolerated or more effective than other available calcium channel blockers when used for managing tachycardia?

Conclusions:

- Etripamil nasal spray is FDA-approved for the conversion of PSVT episodes to normal sinus rhythm in adults, as a one-time dose, with a second dose if needed.[1]
- One double blind, placebo-controlled, phase 3 randomized controlled trial (RCT) which included adults (n=692) with a documented history of sustained PSVT episodes (typically lasting 20 minutes or longer) evaluated the safety and efficacy of etripamil 70 mg (**Table 2**).[2] All patients were required to successfully complete a test dose of etripamil to evaluate tolerability before they were randomized to active drug or placebo.[2] Of the randomized patients, 184 patients

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experienced a confirmed PSVT episode during the trial and self-administered either etripamil or placebo.[2] Approximately one third of enrolled patients were taking oral beta-blockers and 24% were taking an oral calcium channel blocker (verapamil or diltiazem).[2] Analysis of the prespecified primary efficacy population (184 patients who experienced a PSVT episode during the 24-month trial period) showed 64.3% and 31.2% in the etripamil and placebo arms converted to sinus rhythm within 30 minutes after taking the study drug, respectively (hazard ratio [HR] = 2.62; 95% confidence interval [CI], 1.66 to 4.15; p<0.001; moderate-quality evidence).[2] Sixty-six percent of patients who received etripamil required a second dose for persistent symptoms, compared with 79% of patients who received placebo.[2] In the placebo-treated group, 25% of patients required additional medical intervention after randomized treatment (adenosine) compared with 15% of etripamil-treated patients (p=0.103). Twenty-one percent of placebo-treated patients required an emergency department visit after randomized treatment compared with 14% etripamil-treated patients (p=0.209).[2]

- The most common adverse events reported with etripamil nasal spray in the clinical trials included nasal discomfort, nasal congestion, rhinorrhea, throat irritation, and epistaxis.[1] Rates of adverse events compared to placebo are summarized in **Table 1**.
- Etripamil has not been compared to oral calcium channel blockers or beta-blockers to assess efficacy in preventing PSVT. The safety and effectiveness of etripamil in pediatric patients has not been established.

Recommendations:

- Maintain etripamil as nonpreferred on the Preferred Drug List (PDL).
- Implement PA criteria to ensure appropriate utilization of etripamil nasal spray (**Appendix 3**).

Background:

People with supraventricular arrhythmias are often symptomatic, requiring management with drugs and electrophysiological procedures.[3] The term supraventricular tachycardia (SVT) indicates an atrial rate greater than 100 beats per minute at rest.[3] Supraventricular tachycardias originate from or conduct through the atria or atrioventricular (AV) node.[4] SVT has been used to describe many types of tachycardias apart from ventricular tachycardias and atrial fibrilliation.[3] Prominent types of SVT include AV nodal reentrant tachycardia (AVNRT), AV reentrant tachycardia (AVRT) and atrial tachycardia.[4] Narrow QRS tachycardia indicates a QRS duration ≤120 milliseconds (ms).[3] A wide QRS tachycardia refers to a QRS duration >120 ms.[3] In clinical practice, SVT may present as narrow or wide QRS tachycardias, most of which present as regular rhythms.[3] The presence of SVT may result in palpitations, fatigue, light-headedness, chest discomfort, dyspnea, and altered consciousness.[3] In older patients, symptoms may be more extreme—with dizziness, presyncope, and syncope—due aging characteristics of the circulation; drops in blood pressure are usually immediate and tend to recover quickly.[3] Supraventricular tachycardias may be unrecognized at initial medical evaluation and the clinical characteristics can mimic panic disorder.[3]

Epidemiological studies on the SVT population are limited.[3] In the general population, the SVT prevalence is 2.25/1,000 persons and the incidence is 35/100,000 person-years.[3] Women have a risk of developing SVT that is 2-times greater than that of men, and persons aged 65 years or older have more than 5-times the risk of developing SVT than younger individuals.[3] Patients with lone paroxysmal SVT versus those with cardiovascular disease are younger, have a faster supraventricular tachycardia rate, have an earlier onset of symptoms, and are more likely to have their condition first documented in the emergency department.[3]

Patients with SVT are recurrent visitors to emergency departments, with an estimated 50,000 visits each year in the United States (US).[3] Emergency physicians may be the first to evaluate patients whose tachycardia mechanism is unknown and to diagnose the mechanism of arrhythmia.[5] It is important to record a 12-lead electrocardiogram (ECG) to differentiate tachycardia mechanisms according to whether the AV node is a component, because treatment that targets the AV node will not reliably terminate tachycardias that are not AV node-dependent.[5] Also, if the QRS duration is greater than 120 ms, it is crucial to distinguish

ventricular tachycardia from SVT with aberrant conduction, pre-existing bundle-branch block, or pre-excitation.[5] In particular, the administration of verapamil or diltiazem for treatment of either ventricular tachycardia or a pre-excited atrial fibrillation may lead to hemodynamic compromise or may accelerate the ventricular rate and lead to ventricular fibrillation.[5]

The initial approach to acute management of SVT tends to be non-drug-based (i.e., vagal maneuvers), with escalation to intravenous (IV) drugs or electrical cardioversion in the absence of early correction.[3] Adenosine, an endogenous purine nucleoside, is the drug-of-choice, as electrophysiological influences are mediated through cardiac adenosine receptors.[3] Calcium channel blockers (verapamil/diltiazem) and beta-blockers (e.g. esmolol/metoprolol) administered via the IV route are also recommended if the SVT is unresponsive to adenosine or vagal maneuvers, particularly in patients with frequent atrial or ventricular premature beats.[3] However, these drugs should be avoided in patients with hemodynamic instability, heart failure with reduced left ventricular ejection fraction (<40%), a suspicion of VT, or pre-excited atrial fibrillation.[3] Beta-blockers such as short-acting esmolol or metoprolol are more effective in reducing the tachycardia rate than in terminating it.[3] In rare instances, cardioversion is needed to terminate the arrythmia.[4] Most of the available drug therapies for acute events require IV administration and appropriate medical supervision in an emergency room or inpatient hospital stay.[4] Beta-blockers (metoprolol, atenolol, propranolol, nadolol) and calcium channel blockers (diltiazem, verapamil) may be prescribed to prevent future PSVT episodes.[4]

Catheter ablation is also used extensively for most varieties of SVT, and patient-reported outcome measures have shown that patients experience significant improvements in their quality-of-life following ablation.[3] Patient-reported outcome measures using various questionnaires are useful in the audit of ablation techniques.[3] Women are more often prescribed antiarrhythmic drugs before ablation for SVT than men, and recurrence rates following AVNRT ablation are higher in young women.[3] However, overall, no significant differences in health-related quality of life or access to healthcare resources between men and women have been reported.[3]

See **Appendix 1** for **Highlights of Prescribing Information** from the manufacturer, including Boxed Warnings and Risk Evaluation Mitigation Strategies (if applicable), indications, dosage and administration, formulations, contraindications, warnings and precautions, adverse reactions, drug interactions and use in specific populations. Pharmacology and Pharmacokinetic Properties are listed in **Appendix 2**.

Clinical Efficacy:
Etripamil is FDA-approved for the conversion of PSVT episodes to normal sinus rhythm in adults.[1] Etripamil is an analog of the non-dihydropyridine calcium channel blocker, verapamil, and is administered intranasally.[4] The pharmacologic action of etripamil is directed towards prolonging AV nodal refractoriness and slowing conduction through the AV node.[4] One phase 3, double blind, placebo-controlled RCT contributes to the efficacy data for this indication, which is described and evaluated in **Table 2**.

Etripamil was studied in a 3-part multi-center RCT (NODE-301).[2] Etripamil was self-administered by study participants at home. Each episode was documented by an ambulatory Cardiac Monitoring System (CMS) that was placed on the chest by the participants or caregiver when symptoms began and recorded at least 5 hours of continuous electrocardiogram (ECG).[2] Part 1 of the study included participants (n=198) that received the randomized study drug to treat an episode of PSVT until the 150th positively adjudicated PSVT episode.[4] Participants were randomized to etripamil 70 mg or placebo in a 2:1 ratio.[4] This was a phase 2 dose-ranging safety and efficacy analysis.[4]

Part 2 of the study was a phase 3 RCT (also referred as the RAPID study) which included adults (n=706) with a documented history of sustained PSVT episodes (typically lasting 20 minutes or longer) who did not receive the randomized study drug in Part 1.[2] Before randomization in the RAPID study, all participants

received a test dose of etripamil consisting of an initial dose of etripamil 70 mg followed by a second dose of etripamil 70 mg 10 minutes later to evaluate tolerability and to train participants on the study procedures.[2] All patients were required to successfully complete a test dose of etripamil to evaluate tolerability before they were randomized to active drug or placebo.[2] Nine patients did not tolerate the test dose, so 692 patients were randomized 1:1 to placebo or etripamil. Of the 692 randomized patients, 184 patients experienced a confirmed PSVT episode during the 24-month trial duration and self-administered either etripamil or placebo.[2] When experiencing a PSVT episode, participants were instructed to administer a first dose of randomized study drug (70 mg etripamil or placebo) followed 10 minutes later, if PSVT symptoms persisted, by a second dose of study drug (70 mg etripamil or placebo).[2] After having administered the randomized study drug for a perceived episode of PSVT, participants could enter Part 3 of the study, which was an open-label period during which they had the possibility to treat a second episode of PSVT with open-label etripamil (70 mg etripamil with optional second dose of 70 mg etripamil).[2]

An independent committee of 4 to 6 cardiac electrophysiologists, masked to study assignments, examined all data from the 5-hour ECG cardiac monitoring systems and adjudicated the following: whether ECG tracings were consistent with an atrioventricular-nodal-dependent PSVT; whether an event was terminated with vagal maneuver; whether the first dose of the drug was taken during an event (to exclude those that had already spontaneously terminated); whether PSVT, if converted to sinus rhythm, remained converted for at least 30 seconds; the time of any additional medical intervention; the time (in minutes and seconds) to conversion of atrioventricular-nodal-dependent PSVT to sinus rhythm; and safety surveillance for bradyarrhythmias and tachyarrhythmias.[2]

The primary efficacy endpoint in Part 2 of the study was percent of patients with adjudicated conversion of confirmed atrioventricular-nodal-dependent PSVT to sinus rhythm for at least 30 seconds within 30 minutes of drug administration.[2] This endpoint was centrally and independently assessed.[2] Secondary efficacy endpoints were time to conversion at time points before and after 30 minutes; the percentage of patients requiring additional medical intervention in emergency departments to terminate an episode of PSVT; rating from the Treatment Satisfaction Questionnaire for Medication (TSQM-9); changes in predefined symptoms of PSVT from a questionnaire based on the Patient Symptom Global Impressions of Improvement (PGI-I); and sensitivity analyses to assess the robustness of the primary endpoint results. Secondary analyses were hierarchically prespecified.[2]

The efficacy population comprised all randomly assigned participants who self-administered study drug at the time of a confirmed episode of atrioventricular-nodal-dependent PSVT (n=184); only one episode could be included for each participant.[2] The efficacy population excluded participants who took study drug after PSVT conversion, those who had an episode that was adjudicated as non-atrioventricular-nodal-dependent paroxysmal supraventricular tachycardia (e.g., atrial flutter or sinus tachycardia), and those for whom substantial loss of ECG signal occurred.[2]

Of the 184 subjects with confirmed PSVT, 31.2% and 64.3% converted to sinus rhythm within 30 minutes in the placebo and etripamil arms, respectively (hazard ratio [HR] = 2.62; 95% confidence interval [CI], 1.66 to 4.15; $p<0.001$).[2] In the modified intent-to-treat (mITT) population (n=255) with perceived PSVT episodes, 22.7% and 49.6% converted to sinus rhythm within 30 minutes in the placebo and etripamil arms, respectively (HR 2.59; 95% CI 1.64 to 4.09; $p<0.001$).[4] The percentage of subjects converted to sinus rhythm within 30 minutes by treatment arm is lower in the mITT population than the estimate based on efficacy population.[4] This is due to the 27.8% of subjects in the mITT population who took study drug for a perceived episode of PSVT but were not confirmed PSVT.[4] These episodes cannot be converted by the treatment but nevertheless these subjects took the study drug because they thought they had an episode of PSVT based on the symptoms they experienced.[4]

The first key secondary endpoint was time to confirmed conversion within 10 minutes, which was 14.76% for the placebo arm and 24.41% for the etripamil arm ($p=0.052$).[4] Since the endpoint was not statistically significant, the remaining secondary endpoints were not formally tested due to the prespecified hierarchical design.[4] Sixty-six percent of patients who received etripamil required a second dose for persistent symptoms compared with 79% of patients who received

placebo.[2] In the placebo-treated group, 25% of patients required additional medical intervention after randomized treatment (adenosine) compared with 15% of etripamil-treated patients (p=0.103). Twenty-one percent of placebo-treated patients required an emergency department visit after randomized treatment compared with 14% etripamil-treated patients (p=0.209).[2]

Trial Limitations

The FDA commented that it is unclear if the success of the primary endpoint was evaluated in the appropriate intent-to-treat (ITT) population. The manufacturer prespecified the efficacy population as the primary analysis population. The FDA considered the modified intent-to-treat (mITT) population as a more appropriate analysis population for conducting efficacy analyses.[4] The objective of the RAPID study was to demonstrate the safety and effectiveness of etripamil in the treatment of spontaneous episodes of PSVT when self-administered by subjects, prompted by their symptoms of PSVT, in a medically unsupervised setting.[4] As the medicine was developed for self-administration at a home setting (to reduce the hospital burden), patients need to decide whether and when to take the medicine based on their symptoms, after some training.[4] The reported accuracy of patients' perception of PSVT symptoms was 75.4%. That is, only 75.4% of subjects who thought they had an episode of PSVT were verified by adjudicators to have had PSVT.[4] In the manufacturer's report, the median conversion time of 17 minutes for the etripamil arm was reported.[4] This information can be misleading, as only subjects with confirmed PSVT were counted.[4] As subjects self-administered the treatment in a home setting, the actual probability of conversion among subjects who took medication is lower than the estimate based on the efficacy population.[4] About one quarter of subjects are considered not treatable by the study drug and not counted in the efficacy population.[4] The estimate of treatment effect based on the mITT population resembles the clinical practice and provides a more realistic estimate of the treatment effect.[4]

Clinical Safety:

The most common adverse events reported with etripamil nasal spray in the etripamil clinical trials (Phase 2 , Phase 3 and the open-label phase of the NODE trial) included nasal discomfort, nasal congestion, rhinorrhea, throat irritation, and epistaxis.[1] Rates of adverse events compared to placebo are summarized in **Table 1**, as reported by the manufacturer. Because of effects on blood pressure, heart rate, and cardiac conduction, etripamil may cause dizziness or syncope, especially in patients with a history of syncope and high-grade AV block or sinus node dysfunction, or those with a history of syncope during an episode of PSVT.[1] In the phase 3 RAPID RCT, 9 patients (0.4%) experienced clinically significant hypotension during test dosing prior to randomization, which precluded further participation in the study.[1] Patients with a history of hypotensive episodes or those at increased risk for hemodynamic instability should be monitored appropriately when initiating etripamil.[1] Contraindications to etripamil include New York Heart Association (NYHA) Class II to IV heart failure, Wolff-Parkinson-White, Lown-Ganong-Levine syndromes, sick sinus syndrome without a permanent pacemaker, and second degree or higher degree of AV block.[1] No clinical drug interaction studies have been conducted with etripamil.

Table 1. Most Frequent Adverse Events Observed in Etripamil Clinical Studies[1]

Adverse Event	Placebo N=223	Etripamil 70 mg x 1 dose N=235	Etripamil 70 mg x 2 doses N=86
Nasal Discomfort	6%	28%	23%
Nasal Congestion	1%	14%	12%
Rhinorrhea	2%	12%	10%
Throat Irritation	1%	7%	6%
Epistaxis	1%	6%	7%

Look-alike / Sound-alike Error Risk Potential: No results reported in Micromedex

Comparative Endpoints:

Clinically Meaningful Endpoints:

1) Time to convert PSVT to normal rhythm
2) Need for additional medical intervention to terminate PSVT (e.g., emergency department visit or hospitalization)
3) Serious adverse events
4) Study withdrawal due to an adverse event

Primary Study Endpoint:

1) Time to conversion of confirmed PSVT to sinus rhythm for at least 30 seconds within 30 minutes of drug administration

Table 2. Comparative Evidence Table.

Ref./ Study Design	Drug Regimens/ Duration	Patient Population	N	Efficacy Endpoints	ARR/NNT	Safety Outcomes	ARR/NNH	Risk of Bias/ Applicability
1. Stambler, BS et al.[2,4] Part 2 RAPID study NCT03464019 DB, MC, PC, RCT	1. Etripamil 70 mg in each nostril once. If symptoms persisted, a second 70 mg dose could be administered 10 minutes later, PRN. Vs. 2. Placebo	Demographics: -Mean age: Placebo: 56.7y Etripamil: 50.8 y -Female Placebo: 73% Etripamil: 70% -Race White: 93% Black: 2.5% Asian: 1% Other: 3% -Mean number of PSVT episodes in past year Placebo: 9.2 Etripamil: 6.4 -Mean number of lifetime ED visits for PSVT Placebo: 4.6 Etripamil: 5.2 -Percent of enrolled patients taking a beta blocker Placebo: 32% Etripamil: 33% -Percent of enrolled patients take a calcium channel blocker Placebo: 21%	ITT: 1. 135 2. 120 PP: 1. 99 2. 85 Attrition: 1. 13 (9.6%) 2. 17 (14.2%)	Primary Endpoint: Percent of patients with adjudicated termination of a confirmed episode of PSVT and conversion to SR for at least 30 seconds within 30 minutes of drug dosing (PP population) 1. n = 63/99 (64.3%) 2. n = 26/85 (31.2%) HR 2.62 95% CI 1.66 to 4.15 P<0.001 Secondary Endpoint: Conversion of PSVT within 10 minutes of drug administration 1. 14.76% 2. 24.41% HR 1.74 95% CI 0.96 to 3.14 P=0.52 Patients obtaining additional medical treatment after randomized treatment 1. n=21 (25%) 2. n=15 (15%)	NA	Any TEAE 1. n=68 (50%) 2. n=12 (11%) Any Serious TEAE 1. n=19 (14.1%) 2. n=1 (0.8%) TEAE leading to drug discontinuation 1. 3 (2.2%) 2. 0 Nasal Discomfort 1. n=31 (23%) 2. n=6 (5%) Epistaxis 1. n=8 (6%) 2. n=2 (2%)	NA	**Risk of Bias (low/high/unclear)**: Selection Bias: Low. Randomized 1:1 via IRT if subject tolerated 2 tests doses of active drug during sinus rhythm. Baseline demographics balanced between the 2 groups. Performance Bias: Unclear. Investigators and patients blinded. Blinding potentially broken for participants due to differences observed with adverse events between study arms. Detection Bias: Unclear. No details about blinding of outcome assessors. FDA had concerns there was potential detection bias from which populations were selected for the primary endpoint (PP vs. mITT). Attrition Bias: Low. Low attrition rates in both arms. Tolerance to active drug assessed prior to randomization. Reporting Bias: Low. Study protocol is available online. All results reported as prespecified. Other Bias: High. Funded by manufacturer. Several authors are consultants for the manufacturer. **Applicability**: Patient: Enrolled patients were mostly female, which reflects prevalence of PSVT. Enrollment was primarily White, which limits applicability to other racial and ethnic groups. Population studied already demonstrated

		Etripamil: 24% Key Inclusion Criteria: -Age ≥18 y with electrographically documented PSVT and history of sustained episodes of PSVT (≥ 20 minutes). Key Exclusion Criteria: -SBP < 90 mm Hg at screening -History of severe hypotension symptoms, especially syncope during PSVT episodes -History of atrial arrythmia that did not involve the AV node (e.g., atrial fibrillation, atrial flutter, intra-atrial tachycardia) -On digoxin, amiodarone, Class I or II antiarrhythmic drug -Second- or third-degree AV-block -History of ventricular arrythmia -NYHA Class II to IV HF -History of stroke		p=0.103 ED visits after treatment 1. n=18 (21%) 2. n=14 (14%) P=0.209				tolerability of drug, which would not apply to new patients in real world setting. Intervention: Dosing assessed in phase 2 RCT. Comparator: Placebo used as a comparator. No other oral medicines are approved to convert PSVT in an outpatient setting. Outcomes: Termination of PSVT was assessed by trained cardiologists. Additional medical treatment and ED outcomes were included as secondary outcomes. Setting: 160 centers, 8 countries in North America and Europe
Abbreviations: ARR = absolute risk reduction; AV = atrioventricular; SBP = systolic blood pressure; CI = confidence interval; DB = double blind; ED = emergency department; HF = heart failure; Hg = mercury; HR = hazard ratio; IRT = interactive response technology; ITT = intention to treat; MC = multi-center; mITT = modified intention to treat; mm = millimeters; N = number of subjects; NA = not applicable; NNH = number needed to harm; NNT = number needed to treat; NYHA = New York Heart Association; PC = placebo controlled; PP = per protocol; PRN = if needed; PSVT = paroxysmal supraventricular tachycardia; RCT = randomized clinical trial; TEAE = treatment-emergent adverse event; y = years.								

References:

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Appendix 1: Prescribing Information Highlights

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use CARDAMYST™ safely and effectively. See full prescribing information for CARDAMYST™.

CARDAMYST™ (etripamil) nasal spray
Initial U.S. Approval: 2025

----------INDICATIONS AND USAGE----------

CARDAMYST is a calcium channel blocker indicated for the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults (1).

----------DOSAGE AND ADMINISTRATION----------

- For intranasal use only (2.1).
- Initial dosage: A dose of 70 mg is administered as two nasal sprays, one spray into each nostril. Each nasal spray device delivers two sprays. The two sprays together contain a total of 70 mg etripamil (2.1).
- Repeat dosage (if needed): Should symptoms persist for 10 minutes after administration of CARDAMYST, take a second dose of 70 mg administered as two nasal sprays, one spray into each nostril. Do not exceed 140 mg in a 24-hour period (2.1).

----------DOSAGE FORMS AND STRENGTHS----------

Nasal spray: 70 mg etripamil per device (3).

----------CONTRAINDICATIONS----------

- Hypersensitivity to CARDAMYST or any of its components (4).
- Heart failure - New York Heart Association (NYHA) Class II to IV (4).
- Wolff-Parkinson-White (WPW), Lown-Ganong-Levine (LGL) syndromes, or manifest pre-excitation (delta wave) on a 12-lead ECG (4).
- Sick sinus syndrome (except in patients with a permanent pacemaker) (4)
- Second degree atrioventricular (AV) Mobitz 2 block or higher degree of AV block (4)

----------WARNINGS AND PRECAUTIONS----------

- Syncope: May cause dizziness and/or syncope, especially in patients with a history of syncope. Administer in a sitting position (5.1).

----------ADVERSE REACTIONS----------

Most common adverse reactions (incidence > 5%) are nasal discomfort, nasal congestion, rhinorrhea, throat irritation, and epistaxis (6.1).

To report SUSPECTED ADVERSE REACTIONS, contact Milestone Pharmaceuticals USA, INC. at toll-free phone 1-877-207-4764 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

----------USE IN SPECIFIC POPULATIONS----------

- Lactation: A lactating woman should pump and discard breastmilk for 12 hours after CARDAMYST administration (8.2).

See 17 for PATIENT COUNSELING INFORMATION and FDA-approved patient labeling.

Revised: 12/2025

Appendix 2. Pharmacology and Pharmacokinetic Properties.

Parameter	
Mechanism of Action	Calcium Channel Blocker
Oral Bioavailability	Not Applicable
Distribution and Protein Binding	Volume of Distribution; 2,200 to 3,500 Liters 50% Protein Binding
Elimination	29% via urine and 25% via feces
Half-Life	2.5 hours
Metabolism	Hepatic primarily via blood esterases and CYP3A4 and CYP3A5

Abbreviations:

Appendix 3: Proposed Prior Authorization Criteria

Etripamil (Cardamyst™) Nasal Spray

Goal(s):

- To ensure appropriate use of etripamil nasal spray that is consistent with medical evidence.

Length of Authorization:

- Up to 12 months

Requires PA:

- Etripamil nasal spray (pharmacy claims)

Covered Alternatives:

- Current PMPDP preferred drug list per OAR 410-121-0030 at www.orpdl.org
- Searchable site for Oregon FFS Drug Class listed at www.orpdl.org/drugs/

Approval Criteria		
1. What diagnosis is being treated?	Record ICD10 code.	
2. Is this an FDA-approved indication?	**Yes**: Go to #3	**No:** Pass to RPh. Deny; medical appropriateness

Approval Criteria		
3. Is there a positive history of premature supraventricular tachycardia (PSVT) documented by ECG requiring emergency care in the last 12 months?	**Yes:** Go to #4	**No:** Pass to RPh. Deny; medical appropriateness
4. Is the medication prescribed by or in consultation with a cardiologist?	**Yes:** Go to #5	**No:** Pass to RPh. Deny; medical appropriateness
5. Does the patient have any of the following conditions: • New York Heart Association (NYHA) Class II to IV heart failure or • Wolff-Parkinson-White syndrome or • Lown-Ganong-Levine syndrome or • Sick sinus syndrome without a permanent pacemaker or • Second degree or higher degree of AV block?	**Yes:** Pass to RPh. Deny; medical appropriateness	**No:** Go to #6
6. Does the provider attest that catheter ablation is not suitable or has been considered but is not appropriate at this time?	**Yes:** Approve requested number of nasal sprays for up to 12 months	**No:** Pass to RPh. Deny; medical appropriateness

P&T/DUR Review: 6/2026 (DM)
Implementation: TBD