IOWA | Health and Human Services

New Drug Overview

Cardamyst (etripamil spray)

PDL Category: Calcium Channel Blockers

Introduction

Disease Background:

- Supraventricular tachycardias (SVTs) are described as tachyarrhythmias encompassing atrial, atrioventricular nodal tissue, or both for initiation and conduction (*DeSimone et al 2026*).
  - SVT is an umbrella name to designate tachycardias (atrial and/or ventricular rates greater than 100 beats per minute [bpm] at rest) (*Page et al 2015*) and should be suspected in patients that present with heart palpitations, though other symptoms such as dyspnea, fatigue, or dizziness may be present (*DeSimone et al 2026*).
- SVT types are categorized per location of the reentry circuit (*DeSimone et al 2026*).
  - One is atrioventricular nodal reentrant tachycardia (AVNRT).
    - Ventricular heart rate is generally 180-200 beats per minute (bpm); however, the range can be anywhere from 110 to >250 bpm and in unusual cases may be <100 bpm.
  - Another is atrioventricular reentrant tachycardia (AVRT), which is a tachycardia attributable to an extranodal accessory pathway.
    - AVRT also includes Wolff-Parkinson-White syndrome.
  - Atrial tachycardia (AT), where focal AT (FAT) heart rate is generally 100-250 beats/minute.
  - Other types of SVT, such as inappropriate sinus tachycardia (IST).
- Paroxysmal supraventricular tachycardia (PSVT) is a clinical condition described by having a regular and rapid tachycardia of sudden onset and termination. These qualities are typical of AVNRT or AVRT (*Page et al 2015*).
  - PSVT is a subset of SVT.
  - AVNRT is the most frequent form of PSVT (*DeSimone et al 2026*).
- PSVT impacts women more than men, as well as adults greater than 65 years of age (*DeSimone et al 2026*).
  - Between episodes of tachycardia, patients are generally asymptomatic. However, arrhythmia-related symptoms may include palpitations, fatigue, lightheadedness, dizziness, chest pain, dyspnea, anxiety, pounding in neck, presyncope, or rarely syncope.
- Cardamyst was FDA approved in 2025.

Pharmacology/Usage

- Cardamyst (etripamil) is a calcium channel blocker (CCB).
  - It is an L-type calcium influx inhibitor (slow channel blocker or calcium ion antagonist). Etripamil exerts its pharmacologic effect by modulating the influx of ionic calcium across the cell membrane of the AV nodal cells as well as arterial smooth muscles and contractile myocardial cells. By interrupting re-entry at the AV node, etripamil can restore sinus rhythm in patients with paroxysmal supraventricular tachycardia

Indications

Table 1. Food and Drug Administration Approved Indications

Indication	Cardamyst (etripamil)
• For the conversion of acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to sinus rhythm in adults.	✔

(Prescribing information: Cardamyst 2025)

- Information on indications, mechanism of action, pharmacokinetics, dosing, safety, and clinical efficacy summary has been obtained from the prescribing information for the individual products, except where noted otherwise.

Dosing and administration

Table 2. Dosing and Administration

Drug	Available Formulations	Route	Usual Recommended Frequency	Comments
Cardamyst (etripamil)	Solution in a nasal spray: 70mg of etripamil per device, with each device delivering two sprays for a total of 70mg.	Nasal	Administer one spray into each nostril for a total initial dose of 70mg. -If symptoms persist after 10 minutes, use the second nasal spray device to administer a second dose of one spray into each nostril (70mg total).	• Administer as soon as possible after PSVT symptom onset. • Patients and caregivers should call their healthcare provider or seek emergency medical help if symptoms do not improve within 20 minutes after a second dose. Do not exceed 140mg in a 24-hour period. • If a full initial dose is not administered due to device malfunction or misuse, the patient should wait at least 10 minutes before self-administering a second dose, if needed.

See the current prescribing information for full details.

Clinical Efficacy Summary

- The RAPID study was a randomized, double-blind, placebo-controlled, multicenter, event-driven, phase 3 study designed to assess the safety and efficacy of Cardamyst in patients with a history of symptomatic PSVT.
  - Patients (N=692) were randomized to Cardamyst or placebo.
    - Patients with an episode of perceived PSVT were to self-administer the study drug intranasally in a medically unsupervised setting and self-administer a second dose of the study drug if symptoms persisted at 10 minutes after the first dose.
    - Continuously obtained electrocardiographic data during the episode of PSVT were blindly adjudicated.
  - Of the randomized patients (N=692), 255 patients perceived an episode of PSVT and self-administered the study drug; 184 episodes (72%) were confirmed by blinded adjudication to be PSVT.
    - Patients had a median age of 54 years (range 19 to 78), while 71% were female and 93% were Caucasian.
    - In addition, 63% with confirmed PSVT episode were taking concomitant beta-blocker or calcium channel blocker.
  - The primary endpoint was time-to-conversion of confirmed PSVT to sinus rhythm for at least 30 seconds within 30 minutes of the first dose.

- In the study's primary analysis, patients with confirmed episodes of PSVT, Kaplan-Meier Estimates of those who converted to sinus rhythm within 30 minutes were 64% and 31% for Cardamyst and placebo, respectively, with a HR of 2.6 ($p<0.001$).
- Median time-to-conversion was 17.2 minutes with Cardamyst versus 53.5 minutes with placebo.
- Kaplan-Meier estimates of conversion remained in favor of Cardamyst at 300 minutes (HR 1.7).
  - 71/255 (28%) patients who self-administered Cardamyst for a perceived episode of PSVT did not have confirmed PSVT and are excluded.
  - 71 of 255 patients (28%) who self-administered Cardamyst for a perceived episode of PSVT did not have PSVT confirmed due to missing ECG data (4%), resolution of PSVT prior to dosing (5%), or other rhythm diagnoses (19%).
  - In an analysis assuming all 71 of these patients did not convert, the Kaplan-Meier estimates for conversion to sinus rhythm within 30 minutes were 50% and 23% for the Cardamyst and placebo groups, respectively, with a HR of 2.6.

Clinical guidelines

- There are currently no published guidelines found addressing the use of Cardamyst.
- **2015 ACC/AHA/HRS Guideline for the management of adult patients with supraventricular tachycardia: A Report of the American College of Cardiology (ACC)/American Heart Association (AHA) Task Force on Clinical Practice Guidelines and the Heart Rhythm Society (HRS)** (*Page et al 2015*).
  - Vagal maneuvers and adenosine are recommended for acute treatment of regular SVT (SVT of unknown mechanism).
    - For ongoing management of SVT (of unknown mechanism), oral beta-blockers, diltiazem, or verapamil may be useful for symptomatic SVT in patients who do not have ventricular pre-excitation during sinus rhythm.
  - Vagal maneuvers should be first-line intervention to terminate SVT for acute treatment in patients with atrioventricular nodal reentrant tachycardia (AVNRT). Adenosine is also recommended. In addition, IV beta-blockers, diltiazem, or verapamil are appropriate for acute treatment in hemodynamically stable patients with AVNRT. Oral beta blockers, diltiazem or verapamil may be reasonable for use.
    - Oral verapamil or diltiazem is recommended for ongoing management of AVNRT if patients are not candidates for or prefer to not undergo catheter ablation. Oral beta-blockers are also recommended.

Safety summary

- **Contraindications:**
  - In patients with:
    - Hypersensitivity to Cardamyst or any of its components.
    - Heart failure- New York Heart Association (NYHA) Class II to IV.
    - Wolff-Parkinson-White (WPW), Lown-Ganong-Levine (LGL) syndromes, or manifest pre-excitation (delta wave) on a 12-lead electrocardiogram (ECG).
    - Sick sinus syndrome without a permanent pacemaker.
    - Second degree atrioventricular (AV) Mobitz 2 block or higher degree of AV block.

- **Box Warning:** None.

- **Warnings and precautions:**

- Because of effects on blood pressure, heart rate, and cardiac conduction, Cardamyst may cause dizziness and/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.
  - Patients with a history of hypotensive episodes or those at increased risk for hemodynamic instability should be monitored appropriately when starting Cardamyst.
  - If syncope occurs, patients should be placed in the recumbent position and treated supportively.
  - Patients should be cautioned about these possible adverse effects and advised to administer Cardamyst in a sitting position, and in a location where the risk of fall is minimal.

- **Common adverse drug reactions**:
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Cardamyst 70mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included nasal discomfort (22%), nasal congestion (13%), rhinorrhea (10%), throat irritation (6%), and epistaxis (5%).
  - Listed % incidence for adverse drug reactions= reported % incidence for drug (Cardamyst 2X 70mg) minus reported % incidence for placebo. Please note that an incidence of 0% means the incidence was the same as or less than placebo.
    - The most frequently reported adverse events included nasal discomfort (17%), nasal congestion (11%), rhinorrhea (8%), throat irritation (5%), and epistaxis (6%).

- **Drug interactions:** None.

- **Special populations:**
  - There is no pregnancy category for this medication; however, the risk summary indicates that there are no available data on use during pregnancy to inform a drug-associated risk of major birth defects, miscarriage, or adverse maternal or fetal outcomes.
  - The safety and efficacy of use in the pediatric population have not been established.

Conclusion

- Paroxysmal supraventricular tachycardia (PSVT) is a clinical condition described by having a regular and rapid tachycardia of sudden onset and termination (*Page et al 2015*).
- Cardamyst is an intranasal CCB indicated for the conversion of acute symptomatic episodes of PSVT to sinus rhythm in adults.
- Contraindications to use should be reviewed, including heart failure; WPW, LGL syndromes, or manifest pre-excitation (delta-wave) on a 12-lead ECG; sick sinus syndrome without a permanent pacemaker; 2nd degree AV Mobitz 2 block or higher degree of AV block; or hypersensitivity to Cardamyst or any of the components of the product.
- Its efficacy was assessed in a randomized, double-blind, placebo-controlled, event-driven phase 3 study.
  - Patients with an episode of perceived PSVT were to self-administer the study drug intranasally in a medically unsupervised setting and self-administer a second dose of the study drug if symptoms persisted at 10 minutes after the first dose.
  - In the study's primary analysis, patients with confirmed episodes of PSVT, Kaplan-Meier estimates of those who converted to sinus rhythm within 30 minutes were 64% and 31% for Cardamyst and placebo, respectively, with a HR of 2.6 ($p<0.001$).
  - Median time-to-conversion was 17.2 minutes with Cardamyst as compared with 53.5 minutes with placebo.
  - Kaplan-Meier estimates of conversion remained in favor of Cardamyst at 300 minutes (HR 1.7).

- Guidelines do not currently include Cardamyst as they were published prior to FDA approval of Cardamyst, but comparators with Cardamyst may include oral CCBs or oral beta blockers.

- There is no evidence to suggest that Cardamyst is safer or more effective than other currently preferred, more cost-effective medications. It is therefore recommended that Cardamyst remain non-preferred and require prior authorization and be available to those who are unable to tolerate or who have failed on preferred medications.

- **PDL Placement:**
  - ☐ Preferred
  - ☒ Non-Preferred

References

- Cardamyst. Package insert. Milestone Pharmaceuticals USA, Inc; December 2025.
- DeSimone CV, Chrispin J, Oettgen P, et al. Supraventricular Tachycardia (SVT). Dynamed website. Updated March 31, 2026. Accessed April 24, 2026. https://www.dynamed.com.
- Page RL, Joglar JA, Caldwell MA, et al. 2015 ACC/AHA/HRS Guideline for the Management of Adult Patients With Supraventricular Tachycardia: A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *Circulation*. 2016; 133(14):e506-e574.

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