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Original Article

A Review On Overview Of Cardamyst Prescribing Information And Clinical Profile

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ABSTRACT

CARDAMYST (etripamil) nasal spray is an L-type calcium channel blocker indicated for the acute conversion of symptomatic paroxysmal supraventricular tachycardia (PSVT) episodes to sinus rhythm in adults. Formulated for patient self-administration at the onset of symptoms, it serves as a fast-acting, non-invasive alternative to emergency room intervention. The therapeutic administration consists of an initial dose delivered via a single-use, bi-dose device. If acute symptoms persist after a defined interval, a subsequent dose may be administered using a separate device. Prescribing constraints limit the maximum cumulative amount permitted within a specific timeframe. Clinical safety profiles necessitate administration in a sitting position to prevent injury from transient dizziness. Patients should refrain from nose-blowing immediately following administration to prevent drug loss and ensure optimal intranasal absorption.

Keywords: calcium channel blocker, CARDAMYST, Nasal spray, AV nodal cells, paroxysmal supraventricular tachycardia.

INTRODUCTION

CARDAMYST (etripamil) nasal spray is the first FDA-approved, self-administered calcium channel blocker designed to rapidly terminate acute symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) in adults. Approved on December 12, 2025, this novel treatment allows for on-demand control, shifting care away from emergency department visits. It works by rapidly acting on AV nodal cells to break re-entry circuits.

FULL PRESCRIBING INFORMATION

1. INDICATIONS AND USAGE

CARDAMYST is indicated for the rapid conversion of symptomatic episodes of paroxysmal supraventricular tachycardia (PSVT) to normal sinus rhythm in adult patients.

2. DOSAGE AND ADMINISTRATION

2.1 Recommended Administration

Treatment should begin as soon as symptoms of PSVT appear.

CARDAMYST is intended only for nasal administration.

Each disposable device provides two sprays containing a combined dose of 70 mg etripamil.

Recommended dosing:

- Use one spray in each nostril with a single device (total dose: 70 mg).
- If symptoms continue after 10 minutes, administer a second 70 mg dose using a new device.
- Patients or caregivers should seek medical attention if symptoms do not improve within 20 minutes after the second dose.
- Do not exceed 140 mg within a 24-hour period.

Follow the approved Instructions for Use for proper spray technique.

If the full first dose is not delivered due to misuse or malfunction, wait at least 10 minutes before giving another dose if needed.

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

3. DOSAGE FORMS AND STRENGTHS

Nasal Spray: clear to pale yellow solution containing 70 mg etripamil per device.

4. CONTRAINDICATIONS

CARDAMYST should not be used in patients with:

- Hypersensitivity to etripamil or any inactive ingredient
- NYHA Class II–IV heart failure
- Wolff-Parkinson-White syndrome, Lown-Ganong-Levine syndrome, or evidence of pre-excitation on ECG
- Sick sinus syndrome without a permanent pacemaker
- Second-degree Mobitz Type II AV block or higher-grade AV block

5. WARNINGS AND PRECAUTIONS

5.1 Syncope and Hemodynamic Effects

Because CARDAMYST affects blood pressure, heart rate, and cardiac conduction, some patients may experience dizziness or fainting.

Higher-risk patients include those with:

- A history of syncope
- Sinus node dysfunction
- High-grade AV block
- Previous syncope during PSVT episodes

Clinical studies showed a small number of patients developed clinically important hypotension during test dosing.

Patients prone to low blood pressure or cardiovascular instability should be monitored carefully during treatment initiation.

If fainting occurs, supportive measures and recumbent positioning are recommended.

Patients should administer CARDAMYST while seated and in a safe environment to reduce fall risk.

6. ADVERSE REACTIONS

The primary clinically significant adverse reaction associated with CARDAMYST is syncope related to cardiovascular effects.

6.1 Clinical Trial Experience

Safety data were pooled from randomized, placebo-controlled studies including NODE-1, NODE-301 Part 1, RAPID, and RAPID Extension.

A total of 321 patients received CARDAMYST in controlled trials.

Most treatment-related adverse events involved local nasal or throat irritation, including:

- Nasal discomfort
- Congestion
- Runny nose
- Throat irritation
- Nosebleeds
- Sneezing
- Eye watering

Most Common Adverse Reactions (≥5%)

Adverse Reaction	Placebo	CARDAMYST 70 mg	CARDAMYST 2×70 mg
Nasal discomfort	6%	28%	23%
Nasal congestion	1%	14%	12%
Rhinorrhea	2%	12%	10%
Throat irritation	1%	7%	6%
Epistaxis	1%	6%	7%

7. DRUG INTERACTIONS

Etripamil is metabolized mainly through CYP3A4 and CYP3A5 pathways and may interact with medications affecting these enzymes.

CARDAMYST was administered safely in clinical studies alongside beta blockers and calcium channel blockers, although caution is advised because of possible additive cardiovascular effects.

Etripamil may inhibit:

- CYP2D6
- CYP3A4
- CYP2C9
- P-gp and MATE1 transporters

Healthcare providers should evaluate possible drug interactions before prescribing CARDAMYST.

8. USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

There are no adequate human data regarding use during pregnancy.

Animal studies did not demonstrate fetal malformations at clinically relevant exposure levels, although maternal toxicity occurred at higher doses.

8.2 Lactation

Data regarding excretion into human milk are unavailable.

Because related calcium channel blockers are known to appear in breast milk and may potentially affect nursing infants, breastfeeding should be interrupted for 12 hours after treatment.

8.4 Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

Related medications in the same class have been associated with severe cardiovascular complications in infants younger than one year.

8.5 Geriatric Use

No significant differences in safety or efficacy were observed between elderly and younger adult patients in clinical studies.

9. DRUG ABUSE AND DEPENDENCE

There is no evidence suggesting that CARDAMYST causes physical dependence, abuse, or withdrawal symptoms.

No controlled substance scheduling has been proposed for etripamil.

10. OVERDOSAGE

Excessive exposure to CARDAMYST may result in:

- Marked hypotension
- Reflex tachycardia
- AV conduction disturbances
- Cardiac pauses or asystole

Management should be supportive and symptom-directed.

Potential interventions include:

- Intravenous fluids
- Vasopressor therapy
- Cardiac pacing for severe AV block
- Standard cardiopulmonary resuscitation if necessary

Calcium administration or beta-adrenergic stimulation may help counteract calcium channel blockade effects.

The extent to which etripamil can be removed by dialysis is unknown.

11. DESCRIPTION

Etripamil, the active ingredient in CARDAMYST, is a calcium channel blocker.

Chemical name: Benzoic acid, 3-[2-[[(4S)-4-cyano-4-(3,4-

dimethoxyphenyl)-5-methylhexyl]methylamino]ethyl]-, methyl ester.

- Molecular formula: C27H36N2O4
- Molecular weight: 452.59

Etripamil is a colorless to slightly yellow oily substance.

Each CARDAMYST device contains 70 mg etripamil delivered in two sprays.

Inactive ingredients include:

- Acetic acid
- Edetate disodium
- Sulfuric acid
- Water for injection

12. CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Etripamil blocks L-type calcium channels, slowing calcium entry into AV nodal tissue and cardiac muscle.

By interrupting AV nodal reentry pathways, CARDAMYST can restore normal sinus rhythm in patients experiencing PSVT.

12.2 Pharmacodynamics

Cardiac Electrophysiology
A 70 mg intranasal dose causes temporary PR interval prolongation beginning within approximately 5 minutes.

No clinically relevant QTc prolongation has been observed at therapeutic doses.

Hemodynamics
Dose-dependent reductions in systolic blood pressure were observed during electrophysiology studies, with larger decreases occurring at higher doses.

12.3 Pharmacokinetics

Absorption
Peak plasma levels generally occur:

- About 7 minutes after a single dose
- About 13 minutes after repeat dosing

Distribution
Protein binding is approximately 50%.

Metabolism
Etripamil is metabolized by blood esterases and hepatic CYP3A enzymes.

Excretion
Approximately:

- 29% recovered in urine
- 26% recovered in feces

Most administered drug is recovered within 7–10 days.

13. NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

- Long-term carcinogenicity studies have not been completed.
- Etripamil demonstrated no genotoxic effects in standard testing.
- Fertility studies in rats showed no adverse effects on reproductive function.

14. CLINICAL STUDIES

The RAPID trial (NCT #03464019) was a multicenter, randomized, double-blind, placebo-controlled Phase 3 study designed to evaluate the safety and effectiveness of CARDAMYST in adults with symptomatic PSVT.

A total of 692 patients were randomized in a 1:1 ratio to receive either CARDAMYST 70 mg or placebo. Patients self-administered the medication intranasally during a perceived PSVT episode outside of a supervised medical setting. If symptoms continued after 10 minutes, a second dose could be administered.

Electrocardiographic recordings collected during the episodes were independently reviewed to confirm PSVT events.

Primary Efficacy Endpoint

The primary endpoint evaluated the time required for conversion from confirmed PSVT to sinus rhythm lasting at least 30 seconds within 30 minutes following the first dose.

Among patients with confirmed PSVT episodes:

- **64%** of patients receiving CARDAMYST converted to sinus rhythm within 30 minutes
- **31%** of placebo-treated patients converted within the same timeframe

The estimated hazard ratio for conversion was **2.6** (95% CI: 1.7–4.2; p <0.001).

Median time to conversion:

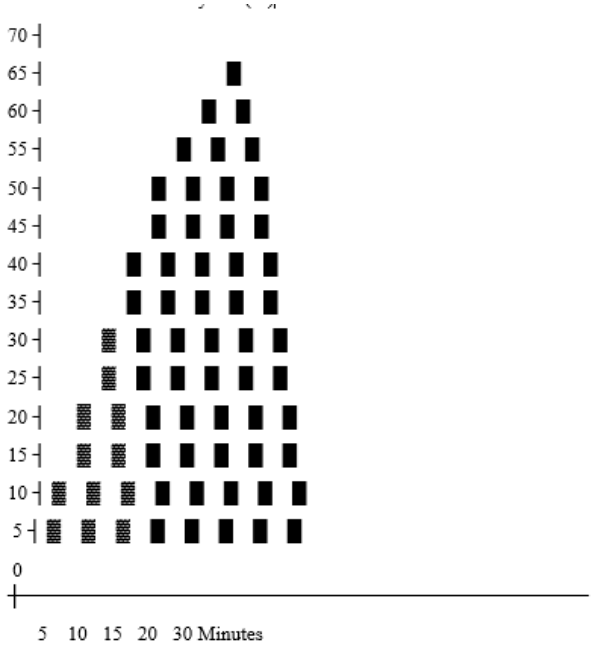
- **CARDAMYST:** 17.2 minutes
- **Placebo:** 53.5 minutes

Time After Dose (Minutes)	CARDAMYST (%)	Placebo (%)
5 min	18	8
10 min	38	15
15 min	52	23
20 min	59	27
30 min	64	31

Figure 1. Estimated Conversion to Sinus Rhythm Within 30 Minutes

Graphical Representation

Conversion to Sinus Rhythm (%)



Additional Findings

Among the 255 patients who self-administered treatment for perceived PSVT:

- 28% did not have ECG-confirmed PSVT due to missing ECG recordings, spontaneous resolution before dosing, or alternative rhythm diagnoses.

When these patients were included as non-converters:

- Conversion rates within 30 minutes were estimated at **50%** for CARDAMYST and **23%** for placebo.

The treatment effect remained statistically favorable for CARDAMYST with a hazard ratio of **2.6** (95% CI: 1.6–4.1).

Subgroup	Hazard Ratio Favoring CARDAMYST
Overall Population	2.6
Age <65 Years	2.5
Age ≥65 Years	2.4
Female Patients	2.7

Subgroup	Hazard Ratio Favoring CARDAMYST
Male Patients	2.5
Beta Blocker Use	2.3
Calcium Channel Blocker Use	2.2

Figure 2. Subgroup Analysis — Hazard Ratios for Conversion to Sinus Rhythm

Simplified Forest Plot

Less Effective ←——————————→ More Effective

Overall Population ——●—— 2.6

Age <65 Years ——●—— 2.5

Age ≥65 Years ——●—— 2.4

Female Patients ——●—— 2.7

Male Patients ——●—— 2.5

Beta Blocker Use ——●—— 2.3

CCB Use ——●—— 2.2

The efficacy outcomes were generally consistent across patient subgroups, including age, sex, geographic region, and use of concomitant cardiovascular medications.

15. HOW SUPPLIED/STORAGE AND HANDLING

15.1 Supply Information

CARDAMYST is available in cartons containing:

- Two disposable nasal spray devices
- A plastic carrying case

NDC: 83468-070-03

15.2 Storage and Handling

Store at:

- 20°C to 25°C (68°F to 77°F)
- Permitted excursions between 15°C and 30°C

Do not prime or test the spray before use.

Dispose of the device after administration.

17. PATIENT COUNSELING INFORMATION

Patients and caregivers should review the FDA-approved Patient Information and Instructions for Use before administering CARDAMYST.

Counsel patients regarding:

- Recognition of PSVT symptoms
- Proper administration timing
- Correct spray technique
- Monitoring after dosing
- When emergency medical care is necessary

Patients should contact a healthcare provider or seek emergency assistance if symptoms remain unresolved 20 minutes after the second dose.

CONCLUSION

CARDAMYST (etripamil) is a fast-acting, self-administered nasal spray for the acute treatment of paroxysmal supraventricular tachycardia (PSVT) in adults. The protocol involves sitting before administration and using a single-use device to deliver one spray into each nostril, with a potential second dose if symptoms persist.

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