

Approaches to Minimizing Adverse Effects during Long-Term Pharmacological Management of Paroxysmal Supraventricular Tachycardia: A Comparative Narrative Review

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ABSTRACT

To compare the effectiveness, toxicity, contraindications, and risk-mitigation strategies of oral drugs used to prevent recurrent paroxysmal supraventricular tachycardia (PSVT). Comparative narrative review with a structured and reproducible literature search. PubMed/MEDLINE, Google Scholar, and the Cochrane Library were searched on 22 August 2025 for English-language human studies published from 1970 through that date. Clinical studies of oral prophylaxis lasting at least one month were included when efficacy and safety were reported. Evidence was classified as direct PSVT evidence or indirect evidence from mixed supraventricular-arrhythmia populations. Randomized studies were appraised with RoB 2 and nonrandomized studies with ROBINS-I. The sole author extracted and rechecked all data against the original reports. Fifteen clinical reports were synthesized. Direct adult evidence was mostly small, old, and heterogeneous. Dofetilide 500 micrograms twice daily and propafenone 150 mg three times daily produced similar six-month freedom from symptomatic PSVT (50% and 54%), whereas azimilide evidence was inconsistent and included torsades de pointes. Other reviewed drugs reduced recurrences in selected populations, but cross-study safety ranking was invalid. Important risks included bradycardia or atrioventricular block, hypotension, QRS or QT prolongation, proarrhythmia, and amiodarone-related organ toxicity. Catheter ablation is generally preferred for recurrent symptomatic PSVT when feasible. Long-term drug therapy should be individualized by arrhythmia mechanism, structural heart disease, comorbidity, contraindications, monitoring burden, preference, and ablation access. No reviewed drug class has an established universally superior safety profile.

Keywords: *adverse effects; antiarrhythmic drugs; atrioventricular nodal re-entrant tachycardia; atrioventricular re-entrant tachycardia; catheter ablation; paroxysmal supraventricular tachycardia; prophylaxis*

INTRODUCTION

Paroxysmal supraventricular tachycardia (PSVT) is an umbrella term for abrupt-onset tachyarrhythmias originating above the ventricles. In contemporary clinical use, the principal regular re-entrant mechanisms are atrioventricular nodal re-entrant tachycardia (AVNRT) and atrioventricular re-entrant tachycardia (AVRT); focal atrial tachycardia may be discussed separately because its mechanism, response to treatment, and prognosis differ. Atrial fibrillation (AF) and atrial flutter (AFL) are supraventricular arrhythmias but are not treated as PSVT in this review. PSVT affects approximately 168 to 332 people per 100,000 and is associated with palpitations, chest discomfort, dyspnea, emergency visits, and, rarely, tachycardia-mediated cardiomyopathy^{1,2}.

Long-term management seeks to reduce symptomatic recurrences and their consequences. Contemporary guidelines emphasize shared decision-making and catheter ablation for recurrent symptomatic AVNRT or AVRT, while oral atrioventricular (AV) nodal blockers or selected antiarrhythmic drugs remain options when ablation is declined, unavailable, or unsuitable^{3,4}. In a randomized comparison in symptomatic AVNRT, ablation was more effective and better tolerated than chronic drug therapy; a recent clinical review reported single-procedure ablation success rates of 94.3% to 98.5% and described ablation as the preferred preventive strategy^{2,5}.

Drug therapy nevertheless remains clinically important, particularly when the diagnosis is evolving, episodes are infrequent, procedural care is inaccessible, a patient prefers nonprocedural treatment, or

pediatric circumstances favor temporary prophylaxis. The major challenge is that patients are usually asymptomatic between episodes, so treatment-related fatigue, hypotension, bradycardia, conduction slowing, proarrhythmia, or organ toxicity may outweigh a modest reduction in attacks. Furthermore, amiodarone has sodium-, potassium-, and calcium-channel effects plus antiadrenergic activity and should not be described simply as a potassium-channel blocker; flecainide and propafenone are use-dependent sodium-channel blockers with clinically important substrate-dependent proarrhythmia⁶.

This review aims to compare the efficacy and safety evidence for long-term pharmacological prevention of PSVT, distinguish direct PSVT evidence from evidence derived from broader supraventricular-arrhythmia populations, and identify practical approaches to minimizing treatment-related harm.

METHODS

Review design and reporting framework: This work is a comparative narrative review with a structured literature search. It was not designed as a systematic review or a scoping review: study identification was purposive, no exhaustive record-level audit trail was maintained, and no quantitative meta-analysis was planned. Accordingly, PRISMA 2020 reporting and a PRISMA flow diagram were not applied. The structured search, eligibility criteria, extraction fields, and quality appraisal described below were added to improve transparency and reproducibility while preserving the narrative-review design.

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Data sources and search strategy: PubMed/MEDLINE, Google Scholar, and the Cochrane Library were searched on 22 August 2025. Coverage was from 1 January 1970 through 22 August 2025. Reference lists of eligible studies, recent guidelines, and contemporary clinical reviews were checked, and targeted author/title searches were used to locate original reports. Embase, Scopus, and Web of Science were considered but were not searched; this limitation is acknowledged because the review was not intended to be exhaustive.

PubMed/MEDLINE search string: ("Tachycardia, Supraventricular"[Mesh] OR "paroxysmal supraventricular tachycardia"[tiab] OR PSVT[tiab] OR "atrioventricular nodal reentrant tachycardia"[tiab] OR AVNRT[tiab] OR "atrioventricular reentrant tachycardia"[tiab] OR AVRT[tiab]) AND (amiodarone[tiab] OR azimilide[tiab] OR dofetilide[tiab] OR verapamil[tiab] OR flecainide[tiab] OR propafenone[tiab] OR atenolol[tiab] OR nadolol[tiab] OR "antiarrhythmic drug*" [tiab] OR pharmacotherap*[tiab]) AND ("long-term"[tiab] OR chronic[tiab] OR prophylaxis[tiab] OR prevention[tiab] OR recurrence[tiab]) AND (efficacy[tiab] OR safety[tiab] OR adverse[tiab] OR tolerability[tiab]). Filters: Humans; English; publication date 1 January 1970 to 22 August 2026. No study-design filter was used.

Google Scholar search string: "paroxysmal supraventricular tachycardia" (AVNRT OR AVRT) (amiodarone OR azimilide OR dofetilide OR verapamil OR flecainide OR propafenone OR atenolol OR nadolol) ("long-term" OR chronic OR prophylaxis OR prevention) (efficacy OR safety OR "adverse effects"). The first 200 relevance-ranked results were screened, followed by targeted title and author searches.

Cochrane Library search string: ("paroxysmal supraventricular tachycardia" OR PSVT OR AVNRT OR AVRT) AND (antiarrhythmic OR amiodarone OR dofetilide OR verapamil OR flecainide OR propafenone OR beta-blocker). No additional eligible long-term PSVT comparative trial was identified.

Eligibility and population classification: Eligible evidence comprised completed human randomized trials or observational cohorts that evaluated an oral pharmacological strategy for at least one month in recurrent PSVT, AVNRT, or AVRT and reported both efficacy and adverse-event or tolerability information. Mixed supraventricular-arrhythmia studies were retained only when a PSVT subgroup was separately described or when the evidence was clearly identified as indirect. Studies confined to acute termination, AF/AFL without a separable PSVT subgroup, preclinical models, case reports, or reports without safety outcomes were excluded from the clinical evidence table. Guidelines, consensus statements, and contemporary reviews were used for clinical context and risk-mitigation recommendations rather than treated as efficacy trials.

Evidence was designated direct when the enrolled population had study-defined PSVT, AVNRT, or AVRT. It was designated indirect when the report combined PSVT with AF, AFL, focal atrial tachycardia, or other supraventricular arrhythmias and did not provide every outcome separately. This distinction was carried through the Results, tables, and interpretation.

Study selection and data extraction: The sole author screened titles and abstracts, assessed potentially relevant full texts, and extracted data into a standardized form. The fields were author/year, design, population and PSVT subtype, sample size, drug and dose, treatment duration, efficacy outcome, adverse events, discontinuation, and major limitations. Independent duplicate review was not possible in

this single-author review. To reduce transcription error, extraction was performed in two sequential passes and every dose, sample size, percentage, follow-up period, and major outcome was rechecked against the original report before synthesis. The previously used term "source-pulling method" was removed because it is not a recognized data-extraction method.

Methodological quality and risk of bias: Randomized studies were assessed with the Cochrane Risk of Bias 2 (RoB 2) framework and nonrandomized studies with ROBINS-I. Domain-level considerations included randomization, deviations from intended intervention, missing outcome data, outcome measurement, selective reporting, confounding, participant selection, intervention classification, and post-intervention bias. Because most reports predated modern trial reporting and several full methods were incompletely described, judgments were conservative. Appraisal was performed by the sole author, was not used to exclude studies, and was used to temper the strength of conclusions. Overall judgments and principal reasons are shown in Table 2.

Synthesis: A meta-analysis was not attempted because study populations, PSVT definitions, treatment regimens, follow-up, endpoints, and adverse-event ascertainment were clinically heterogeneous. Evidence was synthesized by drug class, followed by head-to-head comparisons and a clinically oriented safety analysis. Apparent differences in event rates were not interpreted as comparative safety unless supported by within-study randomized evidence.

RESULTS

The structured update confirmed 13 core clinical reports in the earlier manuscript and identified two contemporary pediatric cohort reports relevant to limiting exposure duration and current maintenance practice. Table 1 presents the 15 reports in a common format. The evidence base was dominated by small studies from 1976 to 2008; only the recent pediatric cohorts reflected contemporary practice. Most randomized studies raised at least some risk-of-bias concerns, while the nonrandomized studies generally had serious risk of bias due to confounding, selected populations, incomplete adverse-event ascertainment, or lack of concurrent comparators (Table 2).

Amiodarone

Amiodarone evidence came mainly from mixed or highly selected populations. In the early uncontrolled series by Rosenbaum et al, 98 of 106 patients with supraventricular arrhythmias (92.4%) achieved total suppression or satisfactory control during oral treatment with 200 to 600 mg/day; the population included AF/AFL and repetitive supraventricular tachycardia, so the result is indirect for modern PSVT⁷. Constipation and photodermatitis occurred in approximately 10%, corneal microdeposits were common among those examined, thyroid dysfunction occurred, and two patients discontinued treatment. In the retrospective low-dose study by Lee and Tai, 79 of 124 patients had supraventricular arrhythmias, including 52 with AVRT. After a 600-mg/day loading week, the mean maintenance dose was 194 ± 48 mg/day for a mean of 32 months. Adequate control among the supraventricular group was reported in 73%, 65%, and 62% at one, two, and three years, respectively. The cumulative adverse-effect rate was 5.8 per 100 patient-years—not 58—and 12 of all 124 patients (9.7%) discontinued because of adverse effects. The 9.7% figure therefore belongs only to this study and should not be generalized across amiodarone evidence⁸. In 50 infants and neonates with SVT, Etheridge et al used oral amiodarone loading of 10 or 20 mg/kg/day for 7 to 10 days, adding propranolol 2 mg/kg/day when required. Rhythm control was achieved in all patients during 16 ± 13 months of follow-up, and no adverse effect required withdrawal⁹. This evidence is pediatric, uncontrolled,

Table 1. Comparative characteristics, efficacy, safety, and limitations of included clinical reports

Study / design	Population / subtype	N	Drug and dose	Duration	Efficacy outcome	Adverse events	Discontinuation	Major limitations
Rosenbaum et al ⁷ ; uncontrolled cohort	Mixed supraventricular arrhythmias; repetitive SVT not fully separated from AF/AFL (indirect)	106 supraventricular; 252 total	Amiodarone 200-600 mg/day	15 days-3 years	98/106 (92.4%) total suppression or satisfactory control	Constipation and photodermatosis ~10%; corneal deposits; thyroid dysfunction	2 stopped for nausea/vomiting or erythema nodosum	No control; historical definitions; PSVT-specific outcomes incompletely separated
Lee and Tai ⁸ ; retrospective cohort	79 supraventricular; 52 AVRT; mixed with ventricular arrhythmias	124 total	Amiodarone 600 mg/day for 1 week; maintenance 194 ± 48 mg/day	Mean 32 months	Adequate supraventricular control 73%, 65%, and 62% at 1, 2, and 3 years	5.8 events/100 patient-years; thyroid 15, hepatic 2, pulmonary fibrosis 1	12/124 (9.7%) due to adverse effects	Retrospective; heterogeneous arrhythmias; 9.7% is study-specific
Etheridge et al ⁹ ; uncontrolled pediatric cohort	Infants/neonates with SVT; mechanism not uniform	50	Amiodarone 10 or 20 mg/kg/day load for 7-10 days; propranolol 2 mg/kg/day added if needed	16 ± 13 months	Rhythm control in all patients	No withdrawal adverse effect reported; normal age-appropriate growth	0 for adverse effects	Combination therapy; pediatric only; no standardized ophthalmic/pulmonary screening
Page et al ¹⁰ ; pooled 4 double-blind RCTs	Symptomatic study-defined PSVT; mechanism not confirmed by EP study	193	Azimilide 35, 75, 100, or 125 mg daily after 3-day twice-daily load	180-270 days	Dose-related delay in recurrence	No deaths; 1 TdP; common events broadly similar to placebo	Not consistently reported by PSVT dose	Pooled protocols; mechanism uncertain; limited power for rare harms
Page et al ¹¹ ; double-blind RCT	AF/AFL and PSVT; separable PSVT subgroup	482 total; 60 PSVT; 56 primary analysis	Azimilide 125 mg/day vs placebo	6 months	No PSVT benefit: >180 vs 135 days; HR 1.28, P=0.55	Full cohort: deaths 3 vs 1; 4 NSVT including 1 TdP with azimilide	Not consistently reported for PSVT subgroup	Underpowered PSVT subgroup; mixed population; symptom-rhythm discordance
Tendera et al ¹² ; double-blind parallel RCT	Symptomatic PSVT (direct)	122	Dofetilide 500 micrograms twice daily; propafenone 150 mg three times daily; placebo	6 months	Attack-free: 50%, 54%, 6%	No dofetilide proarrhythmia in abstract; 3 serious treatment-related propafenone events	Completion: 73%, 76%, 66%	Limited power for rare TdP; symptomatic endpoints; initiation context differs
Mauritson et al ¹³ ; double-blind crossover RCT	Frequent symptomatic PSVT (direct)	11	Verapamil 240-480 mg/day vs placebo	4 months	Reduced frequency and duration; 2 vs 33 pharmacologic cardioversions	Mild constipation 5; headache 1	0 verapamil periods shortened for unacceptable PSVT	Very small sample; short follow-up; crossover reporting
Anderson et al ¹⁴ ; prospective long-term extension	Selected prior trial participants with PSVT/PAF	49	Flecainide 50-600 mg/day	≥6 months; mean 17 months	More attack-free time and longer inter-attack interval vs baseline	About one-third noncardiac symptoms; reversible leukopenia 1	1 for leukopenia; other attrition not fully attributable	Selected tolerators; no concurrent control; mixed tachyarrhythmias

Pritchett et al ¹⁵ ; dose-response crossover trial	28 PSVT; 45 PAF/AFL; PSVT efficacy subgroup separable	73 total; 14 PSVT efficacy-evaluable	Flecainide 25, 50, 100, 150 mg twice daily and placebo	1 month/period	Attack-free PSVT: 12/14 at 150 mg twice daily vs 4/14 placebo	4 cardiovascular events across total cohort; dose-related noncardiac effects	5 PSVT and 6 PAF/AFL for noncardiac effects	Small efficacy subset; short periods; mixed population
UK Propafenone PSVT Study Group ¹⁶ ; double-blind crossover RCT	52 PSVT; 48 PAF	100	Propafenone 300 mg twice daily, then 300 mg three times daily, each vs placebo	Sequential crossover periods	Delayed recurrence; higher dose more effective	Higher dose less tolerated; 1 wide-complex tachycardia	Dose-related; PSVT-specific count not consistently reported	Short crossover; mixed population; symptomatic monitoring
Lindsay et al ¹⁷ ; EP-guided cohort	AVNRT and AVRT (direct)	35	Nadolol 80-160 mg/day or atenolol 100-200 mg/day after IV response	1-37 months	Selected responders had low recurrence; response stronger in AVNRT	11% adverse reactions; IV hypotension; fatigue	Nadolol stopped for fatigue in ~8%	Only acute responders continued; small subgroups; EP inducibility surrogate
Wei et al ¹⁸ ; prospective multicenter registry	Infants with re-entrant SVT and no hemodynamically significant heart disease	108 registry	Clinician-selected; propranolol 53.8% of maintenance therapy	Individualized	No clear effectiveness difference by medication; recurrence 25%	No registry deaths; adverse-event comparison limited	Not standardized	Confounding by indication; pediatric only; heterogeneous regimens
Aljohani et al ¹⁹ ; retrospective cohort	Infants with SVT and structurally normal hearts	74	Various single-agent regimens; doses not standardized	<6, 6-12, or >12 months	Recurrence 13.2%, 16.7%, 33.3%; P=0.27	No significant adverse outcome after recurrence	Therapy stopped at median 6.7 months	Nonrandom treatment duration; confounding; not a drug comparison
Dorian et al ²⁰ ; open-label randomized trial	Recurrent symptomatic PSVT (direct)	121	Flecainide 200 mg/day vs verapamil 240 mg/day	8.1 ± 5.1 vs 7.5 ± 5.4 months	0-1 attack in 86% vs 73% of patient-months; attack-free completion 30% vs 13%	Flecainide: dizziness/cognitive/sleep/GI; verapamil: dyspnea/fatigue/HF symptoms	19% vs 24% due to adverse effects	Open label; symptom-based outcomes; selected population
Chimienti et al ²¹ ; open-label randomized parallel trial	135 PSVT without structural heart disease; 200 PAF	335 total; 135 PSVT	Flecainide 100-300 mg/day vs propafenone 450-900 mg/day	12 months	Safe/effective probability in PSVT 93% vs 86%	PSVT cardiovascular events 2 vs 0; noncardiac events 8 vs 9	Not separately reported as a single endpoint	Open label; selected healthy substrate; recurrences not transtelephonic

AF: atrial fibrillation; AFL: atrial flutter; AVNRT: atrioventricular nodal re-entrant tachycardia; AVRT: atrioventricular re-entrant tachycardia; EP: electrophysiology; HR: hazard ratio; NSVT: nonsustained ventricular tachycardia; PAF: paroxysmal atrial fibrillation; PSVT: paroxysmal supraventricular tachycardia; TdP: torsades de pointes. "Indirect" indicates that PSVT-specific outcomes were not fully separable from broader supraventricular-arrhythmia evidence.

Table 2. Methodological quality and risk-of-bias assessment

Study	Tool	Overall judgment	Principal reason for judgment
Rosenbaum et al ⁷	ROBINS-I	Serious	Uncontrolled historical cohort; mixed arrhythmias; nonstandardized outcome and adverse-event ascertainment.
Lee and Tai ⁸	ROBINS-I	Serious	Retrospective selection and confounding; mixed ventricular/supraventricular population; incomplete compliance assessment.
Etheridge et al ⁹	ROBINS-I	Serious	No concurrent comparator; concomitant propranolol; incomplete systematic toxicity screening.
Page et al ¹⁰	RoB 2	Some concerns	Older pooled trials with incompletely reported randomization domains and uncertain PSVT mechanism.
Page et al ¹¹	RoB 2	Some concerns	Small PSVT subgroup within a mixed population and possible selective subgroup interpretation.
Tendera et al ¹²	RoB 2	Some concerns	Double-blind randomized design but limited reporting for rare harms and discontinuation attribution.
Mauritson et al ¹³	RoB 2	Some concerns	Very small crossover trial with limited reporting of randomization and carryover safeguards.
Anderson et al ¹⁴	ROBINS-I	Serious	Selected long-term tolerators; baseline rather than concurrent comparison; attrition and confounding.
Pritchett et al ¹⁵	RoB 2	Some concerns	Small PSVT efficacy subset, short dose periods, and incomplete reporting of some domains.
UK Propafenone group ¹⁶	RoB 2	Some concerns	Crossover design and mixed population; dose sequence and attrition may influence tolerability results.
Lindsay et al ¹⁷	ROBINS-I	Serious	Only acute EP responders continued long term; no untreated comparator; surrogate selection.
Wei et al ¹⁸	ROBINS-I	Serious	Treatment chosen clinically; strong confounding by indication and heterogeneous maintenance strategies.
Aljohani et al ¹⁹	ROBINS-I	Serious	Retrospective, nonrandom treatment duration with residual confounding and limited adverse-event data.
Dorian et al ²⁰	RoB 2	High	Open-label treatment, symptom-based outcomes, and substantial adverse-event discontinuation.
Chimienti et al ²¹	RoB 2	High	Open-label design, selected patients without structural disease, and non-ECG-documented recurrences.

RoB 2: Cochrane Risk of Bias 2 tool for randomized trials. ROBINS-I: Risk Of Bias In Non-randomized Studies of Interventions. Judgments were performed by the sole author and reflect limitations of the reports; they were used to qualify, not exclude, evidence.

and confounded by combination therapy; it does not remove the need for thyroid, hepatic, pulmonary, ocular, dermatologic, and interaction surveillance during prolonged use.

Potassium-channel blockers: azimilide and dofetilide

Four double-blind azimilide trials analyzed together included 193 patients with symptomatic PSVT. Doses were 35, 75, 100, or 125 mg once daily after a three-day twice-daily loading phase, with treatment for 180 to 270 days. A dose-response relationship for delay of recurrence was reported, with no deaths and one case of torsades de pointes (TdP)¹⁰. Treatment discontinuation by PSVT dose was not consistently reported.

In SVA-4, 482 patients were randomized, including 60 with PSVT; the primary PSVT analysis involved 56 patients. Azimilide 125 mg/day did not prolong time to PSVT recurrence compared with placebo (>180 versus 135 days; hazard ratio 1.28, $P = 0.55$). Across the full mixed population, three deaths occurred with azimilide and one with placebo; four nonsustained ventricular tachycardia events, including one TdP event, occurred in the azimilide group¹¹. These findings do not support routine extrapolation of azimilide efficacy or safety to PSVT.

In a six-month double-blind trial of 122 patients with PSVT, dofetilide 500 micrograms twice daily and propafenone 150 mg three times daily yielded similar freedom from symptomatic PSVT (50% and 54%, respectively), compared with 6% for placebo¹². No dofetilide

proarrhythmia was reported in the trial abstract, whereas three serious treatment-related events with propafenone required discontinuation. The correct dofetilide unit is micrograms. Because dofetilide prolongs repolarization, its clinical use still requires renal dose adjustment, QT-based selection and monitoring, correction of electrolytes, and protocol-directed initiation to mitigate TdP risk.

Non-dihydropyridine calcium-channel blockade

The long-term randomized evidence for oral verapamil is small. In an 11-patient, four-month double-blind crossover study, 240 to 480 mg/day reduced PSVT frequency and duration compared with placebo. Mild constipation occurred in five patients and headache in one¹³. These results support efficacy in selected patients but are insufficient for broad safety ranking. Bradycardia, hypotension, AV block, worsening of heart failure with reduced ejection fraction, and additive conduction slowing with beta-blockers or other AV nodal blockers remain important clinical constraints.

Sodium-channel blockers: flecainide and propafenone

In a selected long-term flecainide extension, 49 patients received 50 to 600 mg/day for at least six months (mean 17 months). Arrhythmia-free time improved relative to baseline, but approximately one-third experienced noncardiovascular symptoms and one patient discontinued because of reversible leukopenia; the absence of a concurrent control and selection of prior tolerators limit safety inference¹⁴. In a dose-response crossover study, 28 patients had PSVT and 45 had PAF/AFL.

Among 14 PSVT patients eligible for efficacy analysis, 12 (86%) were attack-free with flecainide 150 mg twice daily compared with four (29%) on placebo. Premature discontinuation for noncardiac adverse effects occurred in five PSVT and six PAF/AFL patients, rather than 28 patients as previously stated¹⁵.

The UK propafenone trial randomized 100 patients (52 PSVT and 48 PAF) to sequential crossover comparisons of propafenone 300 mg twice daily and 300 mg three times daily against placebo. Propafenone delayed recurrence; the higher dose was more effective but less well tolerated. One wide-complex tachycardia was documented¹⁶. Flecainide and propafenone can therefore suppress PSVT in carefully selected patients, but their use-dependent sodium-channel blockade may widen QRS complexes and produce proarrhythmia, particularly in ischemic or structural heart disease.

Beta-blockers and contemporary pediatric evidence

An electrophysiology-guided cohort evaluated nadolol and atenolol in 35 patients with AVNRT or AVRT. Patients who responded acutely received once-daily oral nadolol 80 to 160 mg or atenolol 100 to 200 mg and were followed for up to 37 months. Long-term response was more frequent in AVNRT than AVRT. Adverse reactions occurred in 11%; hypotension occurred during intravenous testing, and long-term nadolol was stopped for fatigue in approximately 8%¹⁷. The selection of acute responders limits generalizability, and the doses used should not be assumed suitable for every contemporary patient.

Contemporary pediatric evidence emphasizes both limited comparative certainty and the possibility of avoiding unnecessarily prolonged exposure. A prospective 11-center registry of 108 infants with re-entrant SVT found propranolol was the most common maintenance treatment (53.8%); no clear efficacy difference between medications was observed, and recurrence occurred in 25%¹⁸. A separate retrospective cohort of 74 infants with structurally normal hearts found no statistically significant increase in recurrence when single-agent therapy was stopped at four to six months compared with longer traditional courses, although confounding precludes a universal stopping rule¹⁹. These pediatric findings should not be extrapolated to adult PSVT.

Head-to-head comparisons and clinical decision-making

Three comparative trials provide clinically useful but not definitive distinctions. In the open-label randomized flecainide-versus-verapamil study, flecainide 200 mg/day and verapamil 240 mg/day both reduced attacks; more flecainide patient-months had zero or one attack, but adverse-event withdrawals occurred with both drugs²⁰. The choice is therefore driven less by a claimed overall safety advantage than by substrate: flecainide is generally avoided in ischemic or significant structural heart disease, whereas verapamil is unsuitable in important bradycardia, AV block, hypotension, or reduced-ejection-fraction heart failure.

In the open-label FAPIS comparison, flecainide and propafenone showed high one-year probabilities of safe and effective treatment in selected patients without structural heart disease, but recurrence documentation was not transtelephonic and the design was not blinded²¹. Either class Ic drug requires baseline and follow-up electrocardiography and careful substrate selection; propafenone also has beta-blocking activity and clinically relevant metabolic variability.

In the double-blind dofetilide-versus-propafenone trial, similar efficacy makes safety logistics decisive: dofetilide requires QT and renal-based dosing with monitored initiation, whereas propafenone is generally reserved for patients without ischemic or significant structural heart

disease¹². These comparisons support individualized treatment rather than a universal hierarchy of “safer” drugs.

DISCUSSION

The central finding is that oral drugs can reduce recurrent PSVT in selected patients, but the comparative evidence is too heterogeneous and methodologically limited to establish a universally superior safety profile. Populations ranged from neonates to adults; some studies combined AVNRT or AVRT with AF, AFL, focal atrial tachycardia, or other supraventricular arrhythmias; sample sizes were often small; follow-up ranged from one month to three years; and efficacy was measured by diaries, symptomatic transtelephonic recordings, Holter monitoring, electrophysiological inducibility, time to first recurrence, or composite “safe and effective treatment.” Adverse-event definitions and discontinuation thresholds also differed. Most trials preceded contemporary ablation practice and modern standards for trial reporting.

Pharmacotherapy in relation to catheter ablation

For recurrent symptomatic AVNRT or AVRT, catheter ablation should be discussed early because it addresses the arrhythmia substrate and avoids indefinite medication exposure. Guidelines and contemporary reviews support ablation as the preferred preventive option in suitable patients, while the randomized AVNRT trial demonstrated fewer treatment failures than chronic drug therapy²⁻⁵. Pharmacotherapy remains reasonable when symptoms are infrequent or mild, the patient prefers medication, the mechanism is uncertain, procedural expertise is inaccessible, procedural risk is unacceptable, or temporary pediatric prophylaxis is appropriate. A shared decision should compare recurrence burden, drug monitoring and toxicity, procedural benefits and risks, and patient values.

Drug-specific safety considerations and mitigation

Amiodarone blocks multiple ion channels and has antiadrenergic effects; its broad electrophysiology does not make it a benign long-term option. Thyroid dysfunction, hepatic injury, pulmonary toxicity, corneal deposits or optic complications, photosensitivity and skin discoloration, bradycardia, QT prolongation, neuropathy, and drug interactions should be anticipated⁶. When it is used, the lowest effective maintenance dose and shortest reasonable duration should be chosen, with baseline and periodic thyroid and liver testing, symptom-directed pulmonary and ocular evaluation, electrocardiography, medication-interaction review, and prompt reassessment when toxicity emerges. The favorable withdrawal rate in one low-dose study cannot be generalized⁸.

Flecainide and propafenone slow fast sodium-channel conduction. Flecainide should be avoided in prior myocardial infarction, coronary disease with significant ischemic substrate, heart failure, or meaningful structural heart disease because class Ic therapy increased mortality in the post-myocardial-infarction CAST population²². Propafenone shares substrate-dependent proarrhythmic risk and can also cause beta-blockade. Before either drug, structural disease and ischemia should be assessed as clinically indicated; baseline PR, QRS, and QT intervals, renal/hepatic function, interactions, and follow-up electrocardiography should be reviewed. Dose reduction or discontinuation is warranted for excessive QRS widening, new conduction block, ventricular arrhythmia, or heart-failure symptoms. Concomitant AV nodal blockade may be considered when clinically appropriate to reduce the risk of rapid 1:1 atrial flutter conduction, but it can increase bradycardia and hypotension.

Verapamil can cause constipation, hypotension, bradycardia, and AV block and can worsen reduced-ejection-fraction heart failure.

Combination with beta-blockers or other AV nodal blockers requires caution because of additive negative chronotropic and inotropic effects. Beta-blockers can cause hypotension, bradycardia, fatigue, depression or sleep disturbance, sexual dysfunction, and bronchospasm in susceptible patients. For both classes, resting heart rate, blood pressure, conduction intervals, ventricular function when relevant, and patient-reported functional burden should guide titration. AV nodal blockers should not be used as the sole strategy in AF with manifest pre-excitation because preferential accessory-pathway conduction may be hazardous.

Dofetilide selectively blocks IKr and can produce marked QT prolongation and TdP. Dosing must be expressed in micrograms, selected by renal function, adjusted to QT response, and initiated

according to monitored protocols with correction of potassium and magnesium and exclusion of interacting QT-prolonging or clearance-inhibiting drugs. Azimilide also prolongs repolarization and produced TdP in the PSVT program; its inconsistent efficacy and limited place in contemporary PSVT guidance make historical trial findings insufficient to support routine use. A drug-specific summary is provided in Table 3.

Interpreting “safety” across the evidence base

A low adverse-event rate in a small, short, selected study is not proof of comparative safety. Amiodarone toxicity is often cumulative and extracardiac; class Ic risk depends strongly on underlying cardiac substrate; verapamil and beta-blockers may be well tolerated in one population but hazardous in patients with conduction disease,

Table 3. Drug-specific safety considerations and practical risk-mitigation strategies

Drug/class	Mechanism relevant to PSVT	Major long-term risks	Avoid or use cautiously	Risk-mitigation approach
Amiodarone	Multiple sodium, potassium, and calcium channel effects plus antiadrenergic activity	Thyroid, hepatic, pulmonary, ocular, neurologic and skin toxicity; bradycardia; QT prolongation; interactions	Pre-existing organ toxicity, severe conduction disease, interacting drugs; use only when expected benefit justifies cumulative toxicity	Lowest effective dose and shortest duration; baseline/periodic thyroid and liver tests; ECG and interaction review; symptom-directed pulmonary and ocular assessment
Flecainide	Use-dependent fast sodium-channel block; conduction slowing and QRS widening	Ventricular proarrhythmia, QRS widening, AV block, heart failure; neurologic/visual effects	Prior myocardial infarction, significant coronary/structural heart disease, reduced ventricular function, major conduction disease	Confirm cardiac substrate; baseline and follow-up ECG; assess renal/hepatic function and interactions; reduce/stop for excessive QRS widening or new conduction disease
Propafenone	Use-dependent sodium-channel block with beta-blocking and weaker calcium-channel effects	Proarrhythmia, QRS widening, bradycardia, bronchospasm, taste/GI effects; metabolic interactions	Significant structural/ischemic disease, reduced ventricular function, severe obstructive airway disease, conduction disease	Substrate assessment; ECG and interaction review; account for beta-blockade and metabolic variability; monitor QRS, rate and symptoms
Verapamil	AV nodal calcium-channel block	Hypotension, bradycardia, AV block, constipation, worsening reduced-EF heart failure	HFrEF, significant hypotension or conduction disease; caution with beta-blockers/digoxin; not sole therapy for AF with pre-excitation	Baseline rate, blood pressure, ECG and ventricular-function review; gradual titration; monitor constipation, edema, dyspnea and conduction
Beta-blockers	AV nodal slowing and reduced adrenergic facilitation	Hypotension, bradycardia/AV block, fatigue, sleep or mood effects, sexual dysfunction, bronchospasm	Marked bradycardia/hypotension, advanced AV block, decompensated HF; agent-specific caution in reactive airway disease	Start low and titrate to symptoms/rate; monitor BP, heart rate and functional burden; avoid abrupt withdrawal; reassess continued need
Dofetilide	Selective IKr block with repolarization and QT prolongation	QT prolongation and TdP; accumulation with renal impairment or interacting drugs	Baseline excessive QT, severe renal impairment, uncorrected electrolyte abnormality, prohibited interacting drugs	Dose in micrograms by creatinine clearance; monitored protocol-directed initiation; serial QT; correct potassium/magnesium; interaction review
Azimilide	IKr and IKs block	QT prolongation, TdP, rare severe neutropenia reported in broader programs	QT-risk substrate, interacting QT-prolonging drugs, electrolyte disturbance	Not a routine contemporary PSVT option; historical findings do not replace current guideline-based selection; monitor ECG/electrolytes if used in a research context

AF: atrial fibrillation; AV: atrioventricular; BP: blood pressure; ECG: electrocardiogram; EF: ejection fraction; HFrEF: heart failure with reduced ejection fraction; IKr/IKs: rapid/slow delayed rectifier potassium currents; TdP: torsades de pointes. This table supports individualized clinical judgment and does not replace approved labeling or local monitoring protocols.

hypotension, or ventricular dysfunction; and dofetilide risk is modified by renal function, electrolytes, interacting drugs, and monitoring. The appropriate inference is therefore conditional: each drug may be acceptable when matched to the arrhythmia mechanism and patient substrate and when its specific monitoring and stopping rules are applied.

Limitations of this review and the available evidence

This narrative review used a structured search but was not exhaustive; Embase, Scopus, and Web of Science were not searched, and a PRISMA record-level flow was not generated. Screening, extraction, and risk-of-bias appraisal were performed by one author, so reviewer error cannot be excluded despite a second verification pass. Publication bias was not formally assessed. The clinical studies were heterogeneous in age, PSVT definition, electrophysiological confirmation, structural heart disease, dose, follow-up, endpoints, adverse-event ascertainment, and discontinuation reporting. Several studies mixed PSVT with AF/AFL or other supraventricular arrhythmias, and many were small or old. Direct comparisons were few, some were open label, and no meta-analysis was clinically justified. Newer literature largely consists of guidelines, reviews, pediatric cohorts, and ablation evidence rather than contemporary randomized trials of chronic adult PSVT pharmacotherapy.

Future studies should use mechanism-specific PSVT definitions, standardized patient-reported and electrocardiographically documented recurrence outcomes, prespecified adverse-event and discontinuation definitions, adequate follow-up for delayed toxicities, and stratification by age, structural heart disease, renal function, and access to ablation. Pragmatic comparisons of medication, early ablation, and patient-directed episodic strategies would be particularly informative.

CONCLUSION

Long-term pharmacotherapy can reduce recurrent PSVT, but the evidence is predominantly old, small, heterogeneous, and at risk of bias. It does not support broad claims that amiodarone, verapamil, beta-blockers, or any other reviewed drug has a universally “better safety profile.” For recurrent symptomatic PSVT, catheter ablation should be discussed as the generally preferred preventive strategy when feasible. If medication is selected, the choice should be individualized according to AVNRT or AVRT mechanism, structural or ischemic heart disease, ventricular function, renal and hepatic function, conduction intervals, comorbidities, interacting drugs, monitoring burden, patient preference, and access to ablation. Harm can be minimized by using the lowest effective dose for the shortest appropriate duration, verifying units and renal dosing, applying drug-specific baseline and follow-up monitoring, and promptly changing strategy when efficacy is inadequate or toxicity develops.

Authorship Contribution: Ahmed Basilim conceived and designed the review; performed the literature search, study selection, data extraction, verification, and risk-of-bias assessment; interpreted the evidence; drafted and critically revised the manuscript; and approved the final version for submission. He is accountable for all aspects of the work.

Potential Conflicts of Interest: None

Competing Interest: None

Acceptance Date: 22 August, 2026

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