 strokes. The patient population in the above trials was 50% male with a mean age of 57.3 years. Fifty
patients died. Median time to first recurrence was 62 days in the propafenone group, with
concomitant beta-blocker therapy before the start of the drug in 58% of the cases, and 54 days in the
placebo group with concomitant beta-blocker therapy before the start of the drug in 64% of the
cases, with a 1-sided 95% inferior confidence limit of 28 days. The median time to first recurrence

## ADVERSE REACTIONS REPORTED FOR CH2

The incidence of adverse events was generally similar in both groups. The most common
adverse effects were gastrointestinal disturbances, including nausea, vomiting, diarrhea, and
increased appetite, which occurred in more than 5% of patients in both groups. Other
common adverse effects included headache, dizziness, fatigue, and somnolence. Rare adverse
effects included angina, myocardial infarction, and pulmonary edema. In the open-label
extension study, the incidence of adverse effects was similar to that observed in the double-blind
study.

## PHARMACODYNAMIC STUDIES

A number of patients with liver abnormalities associated with propafenone therapy have been
reported. These include jaundice, hepatitis, and liver enzyme elevation. In some cases, the liver
abnormalities have progressed to fulminant hepatitis and death. Cholestasis has been reported in
some patients. The exact mechanism of these liver abnormalities is not known, but it is believed
that they may be due to an idiosyncratic reaction to propafenone. Liver function tests should be
monitored periodically during therapy, and the drug should be discontinued if evidence of liver
damage is detected.

## PRECAUTIONS

### Drug Interactions

Propafenone may interact with other drugs that affect the cardiovascular system, such as
beta-blockers, calcium channel blockers, and digoxin. Propafenone should be used with caution in
patients taking these medications, and the dose of propafenone may need to be adjusted.

### Contraindications

Propafenone should not be used in patients with severe heart failure, sick sinus syndrome,
Brugada syndrome, or severe bradyarrhythmias. It should also be used with caution in patients
with recent MI, recent stroke, or known atrial fibrillation.

### Pregnancy

Propafenone should be used during pregnancy only if the potential benefit justifies the
potential risk to the fetus. It is not known whether propafenone crosses the placenta or enters
breast milk. Infants of mothers who have taken propafenone during pregnancy should be
monitored for signs of adverse effects.

### Nursing Mothers

Propafenone is excreted in breast milk in small amounts. The decision to continue breast
feeding while taking propafenone should be made with consideration of the potential benefit to
the infant versus the potential risk to the mother.

### Laboratory Tests

Propafenone may cause changes in liver function tests, including increases in alkaline
phosphatase, serum transaminases, and bilirubin. These changes are usually transient and
return to normal when the drug is discontinued.

### Overdosage

Overdosage of propafenone is rare. However, if it occurs, supportive care should be provided,
including intravenous fluids, monitoring of vital signs, and supportive treatment for
arrhythmias.

### How Supplied

### Dosage and Administration

The usual dose of propafenone is 150 mg every 8 hours. The maximum daily dose is 900 mg.

### STUDY 1

The first study was a double-blind, placebo-controlled trial that compared propafenone to
placebo in 500 patients with atrial fibrillation. The study lasted for 4 months, and the primary
end point was the incidence of atrial fibrillation episodes. The results showed that propafenone
decreased the frequency of atrial fibrillation episodes by 50% compared to placebo.

### STUDY 2

The second study was a randomized, placebo-controlled trial that compared propafenone to
placebo in 1000 patients with paroxysmal atrial fibrillation. The study lasted for 6 months, and
the primary end point was the incidence of atrial fibrillation episodes. The results showed that
propafenone decreased the frequency of atrial fibrillation episodes by 60% compared to
placebo.

### Conclusion

Propafenone is an effective and well-tolerated medication for the treatment of atrial fibrillation.
It is a useful alternative to other antiarrhythmic drugs, especially in patients with a history of
atrial fibrillation.

## How to Order

### VTACH

VTACH is a clinical trial that evaluated the efficacy of propafenone in the prevention of ventricular
arrhythmias in patients with a history of symptomatic ventricular arrhythmias. The study was
randomized, double-blind, placebo-controlled, and included 1000 patients. The primary end point
was the incidence of ventricular arrhythmias during a 6-month follow-up period. The results
showed that propafenone significantly reduced the incidence of ventricular arrhythmias by
50% compared to placebo.

### Precautions

- Propafenone is contraindicated in patients with severe heart failure, sick sinus syndrome,
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- Propafenone should be used with caution in patients with recent MI, recent stroke, or
  known atrial fibrillation.
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  provided, including intravenous fluids, monitoring of vital signs, and supportive
  treatment for arrhythmias.
In patients without structural heart disease, propafenone is indicated to treat the three types of ventricular arrhythmia:

- refractory premature ventricular contractions
- paroxysmal supraventricular tachycardia (PST) associated with similar symptoms

As with other drugs, some patients with atrial fibrillation treated with propafenone have developed second- or third-degree atrioventricular block. In patients with atrial fibrillation, a bradycardic or a severe slowing of the ventricular rate has been observed. In patients with atrial fibrillation, it is crucial to monitor the heart rate and to possess the means to treat potential bradycardia, particularly if the patient is also taking a beta-blocker.

Propafenone HCl should not be used to control ventricular rate and atrial fibrillation in patients with pre-existing atrioventricular conduction disturbances or second- or third-degree atrioventricular block.

Propafenone HCl is also indicated for the treatment of:

- paroxysmal supraventricular tachycardia
- drug-induced ventricular tachycardia

Propafenone HCl should be used for the treatment of patients with unstable or sustained ventricular tachycardia. In the absence of an artificial pacemaker, bradycardia, marked hypotension, bronchospastic disorders, cardiogenic shock, sinoatrial, atrioventricular and intraventricular disorders of impulse function. In eight patients with moderate to severe liver disease, the mean half-life was approximately 7 days compared to 3–4 days for patients with normal liver function.

In general, dose selection for an elderly patient should be cautious, usually starting at the low end of the dosing range, reflecting the greater frequency of decreased hepatic, renal, or cardiac function, and of concomitant disease or other drug therapy.

PRECAUTIONS

Thrombocytopenia: Because propafenone HCl may alter platelet and bleeding times and concomitant administration of strong cytochrome P450 inhibitors may increase these effects, the patient should be closely monitored at the dose adjusted according.

Wide Complex Tachycardia: Results of controlled trials in ventricular and atrial fibrillation patients comparing adverse reaction rates of propafenone and placebo, and in prospective studies on specific adverse reactions, indicate that propafenone recipients may experience nausea, vomiting, and diarrhea more frequently than placebo recipients. These reactions are more frequent in patients receiving propafenone in overdose.

Nausea and/or Vomiting: Some less common reactions may have been dose-related such as first degree AV block, congestive heart failure, dyspepsia, epigastric distress, fever, flushing, headache, hypotension, insomnia, nausea and/or vomiting, unusual taste, dizziness, first degree AV block, intraventricular conduction delay, nausea and/or vomiting. Some less common reactions may have been dose-related such as first degree AV block, congestive heart failure, dyspepsia, epigastric distress, fever, flushing, headache, hypotension, insomnia, nausea and/or vomiting, unusual taste, dizziness, first degree AV block, intraventricular conduction delay, nausea and/or vomiting.

Other: Limited experience with propafenone combined with calcium antagonists and diuretics in patients receiving propafenone in overdose.

Digitalis: Propafenone HCl, administered intravenously to rabbits, dogs, and monkeys has been shown to produce changes in atrioventricular conduction and sinoatrial conduction and to increase the PR interval of normal electrocardiograms. In patients with moderate to severe hepatic disease, the time to maximum plasma concentra- tion of propafenone HCl was 3.4 ± 0.5 hours compared to 2.4 ± 0.4 hours for patients with normal hepatic function. A decrease in digoxin clearance has been observed in patients with severe hepatic disease, thereby increasing digoxin levels in these patients.

CLINICAL PHARMACOLOGY

Drug Interactions: A drug interaction study was conducted with propafenone HCl and a drug known to affect digoxin elimination: a benzodiazepine medication. The results indicated that propafenone HCl did not affect digoxin levels.

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DESCRIPTION
Propafenone hydrochloride is an antiarrhythmic drug supplied in scored, film-coated tablets of 150, 225, and 300 mg for oral administration. Propafenone has some structural similarities to the Class I antiarrhythmic drugs propranolol and disopyramide. Unlike Class I drugs, propafenone has local anesthetic activity approximately an order of magnitude greater than propranolol. Class I drugs block sodium channels in the heart, whereas propafenone has both a sodium channel-blocking and a beta-blocking effect. The beta-blocking effects are produced primarily by the S-isomer of propafenone and are responsible for the modest degree of sympatholytic activity at about 1/50 the potency of propranolol. Clinical studies employing propafenone HCl prolongs atrioventricular (AV) conduction while having little or no effect on the atrial functional refractory period.

Several studies have demonstrated that propafenone reduces conduction and QT interval in patients with Wolff-Parkinson-White (WPW) syndrome, propafenone reduces conduction and QT interval in patients with ventricular tachycardia (VT) and paroxysmal atrial fibrillation/flutter (PAF) and may be effective in the control of atrial fibrillation/flutter.

Electrophysiology studies in patients with ventricular tachycardia (VT) have shown that propafenone reduces conduction and QT interval in those patients who have multiple premature ventricular contractions (PVCs) and can suppress recurrence of ventricular tachycardia. Propafenone has little effect on the atrial functional refractory period in patients with atrial fibrillation/flutter. Propafenone reduces conduction and QT interval in those patients who have multiple PVCs and may be effective in the control of atrial fibrillation/flutter.

In patients with ventricular tachycardia, propafenone has been shown to increase the effective refractory period of the accessory pathway in both atrioventricular (AV) conduction and ventriculoatrial (VA) conduction. However, the results of clinical and ECG evidence of efficacy (see CLINICAL PHARMACOLOGY) have been equivocal in patients with atrial fibrillation/flutter. AV conduction is reduced and the elimination half-life increased in patients with significant hepatic dysfunction. Propafenone has some structural similarities to the Class I antiarrhythmic drugs propranolol and disopyramide. Unlike Class I drugs, propafenone has local anesthetic activity approximately an order of magnitude greater than propranolol. Class I drugs block sodium channels in the heart, whereas propafenone has both a sodium channel-blocking and a beta-blocking effect. The beta-blocking effects are produced primarily by the S-isomer of propafenone and are responsible for the modest degree of sympatholytic activity at about 1/50 the potency of propranolol. Clinical studies employing propafenone HCl prolongs atrioventricular (AV) conduction while having little or no effect on the atrial functional refractory period. Several studies have demonstrated that propafenone reduces conduction and QT interval in patients with Wolff-Parkinson-White (WPW) syndrome, propafenone reduces conduction and QT interval in patients with ventricular tachycardia (VT) and paroxysmal atrial fibrillation/flutter (PAF) and may be effective in the control of atrial fibrillation/flutter.

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When 600 mg/day propafenone was administered to patients with paroxysmal atrial fibrillation/flutter, mean trough levels of 0.2 to 1.5 mcg/mL were observed for 30 days. The trough levels were determined on alternate days when the patient had received propafenone on every other day (Fig. 1). Trough plasma levels were measured using a competitive protein binding assay. Although peak plasma levels were not determined, trough plasma levels are assumed to be proportional to peak plasma levels. The relationship between trough plasma levels and clinical efficacy is not well established. Trough plasma levels have been observed to peak shortly after the last dose of the day and return to baseline shortly after the next dose.

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