R Y T H M E X® 150 mg

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TABLETS

Composition

Rythmex 150 mg
Each tablet contains:

Active Ingredient
Propafenone hydrochloride 150 mg

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Active Ingredient
Propafenone hydrochloride 300 mg

Other Ingredients
Microcrystalline cellulose, maize starch, carboxymethylcellulose (croscarmellose) sodium, methyl hydroxypropyl cellulose, polyethylene glycols (macrogol 400 and macrogol 6000), titanium dioxide E 171, magnesium stearate.

Sodium content: Rythmex 150 mg: 0.65-0.95 mg per tablet
Rythmex 300 mg: 1.3-1.9 mg per tablet.

Mechanism of Action

Pharmacotherapeutic group: Antiarrhythmics, class IC
ATC-Code: C01BC03

Propafenone is a class I c antiarrhythmic agent, with a membrane-stabilizing effect on the cardiac muscle cell.

The electrophysiological effect of propafenone manifests itself in a reduction of upstroke velocity (phase O) of the monophasic action potential.

Propafenone prolongs intra-atrial conduction while having little or no effect on sinus node function. AV nodal conduction time as well as His-Purkinje conduction time are prolonged following administration of propafenone.

In patients with Wolff-Parkinson-White (WPW) syndrome, propafenone reduces conduction and increases the effective refractory period of the accessory pathway in both directions.

Propafenone causes a decrease in single and multiple ventricular premature contractions (VPCs) and can suppress the recurrence of ventricular tachycardia.

Propafenone produces a mild negative inotropic effect on the myocardium. However, during treatment with oral propafenone in patients with depressed baseline function, well-tolerated decreases in left ventricular function have been reported.

Pharmacokinetic properties
Propafenone is a racemic mixture of S- and R-propafenone.

Absorption
Maximal plasma concentrations are reached between two to three hours following the administration of propafenone hydrochloride. Propafenone is known to undergo extensive and saturable presystemic biotransformation (CYP2D6 hepatic first pass effect) which results in a dose- and dosage formdependent absolute bioavailability. Although food increased the maximal plasma concentration and bioavailability in a single dose study, during multiple dose administration of propafenone to healthy subjects food did not change bioavailability significantly.

Distribution
Propafenone distributes rapidly. The steady-state volume of distribution is 1.9 to 3.0 L/kg. The degree of plasma protein binding of propafenone is concentration dependent and decreased from 97.3% at 0.25 ng/mL to 91.3% at 100 ng/mL.

Biotransformation and elimination
There are two genetically determined patterns of propafenone metabolism. In over 90% of patients, the drug is rapidly and extensively metabolized with an elimination half-life from two to ten hours (i.e., extensive metabolizers). These patients metabolize propafenone into two active metabolites: 5-hydroxypropafenone which is formed by CYP2D6 and N-depropylpropafenone (norpropafenone) which is formed by both CYP3A4 and CYP1A2. In less than 10% of patients, metabolism of propafenone is slower because the 5-hydroxy metabolite is not formed or is minimally formed (i.e., poor metabolizers). The estimated propafenone elimination half-life ranges from two to ten hours for extensive metabolizers and from ten to 32 hours for poor metabolizers. Clearance of propafenone is 0.67 to 0.81 L/h/kg.

Linearity/non-linearity
In extensive metabolizers, the saturable hydroxylation pathway (CYP2D6) results in nonlinear pharmacokinetics. In slow metabolizers, propafenone pharmacokinetics are linear.

Inter/intra subject variability
With propafenone hydrochloride, there is a considerable degree of individual variability in pharmacokinetics which is due in large part to the first pass hepatic effect and non-linear pharmacokinetics in extensive metabolizers. The large variability in blood levels requires that the dose be titrated carefully in patients, paying close attention to clinical and electrocardiographic evidence of toxicity.

Elderly population
Propafenone exposure in elderly subjects with normal renal function was highly variable, and not significantly different from healthy young subjects. Exposure to 5-hydroxypropafenone was similar, but exposure to propafenone glucuronides was doubled.

Renal impairment
In patients with renal impairment, exposure to propafenone and 5-hydroxypropafenone was similar to that in healthy controls, while accumulation of glucuronide metabolites was observed. Propafenone hydrochloride should be administered cautiously in patients with renal disease.

Liver impairment
Propafenone shows an increased oral bioavailability and half-life in patients with liver impairment. The dosage must be adjusted in patients with liver disease.

Following oral administration, propafenone is nearly completely absorbed, with peak plasma levels occurring approximately 3.5 hours after administration in most individuals. Steady-state conditions are achieved after 3 - 4 days of dosing in all patients.

Protein binding is extensive in humans and has been reported to range between 77 and 89% in one study, and to exceed 95% in another.

In over 90% of patients, the drug is rapidly and extensively metabolized by the liver with an elimination half-life from 2 - 10 hours for extensive metabolizers and from 10 to 32 hours for poor metabolizers. While there are 11 metabolites accounting for 90% of the administered dose, the major one is 5-hydroxy- propafenone which is as active as the parent drug but present in the plasma in considerably lower concentrations than propafenone.

Excretion of propafenone metabolites is mainly via the feces (53% within 48 hours); however, a considerable percentage of the metabolites (18.5% - 38%) of the dose/48 hours are excreted in the urine.

Indications

Prophylaxis and treatment of ventricular arrhythmias.
Prophylaxis and treatment of atrial fibrillation and flutter.
Prophylaxis and treatment of paroxysmal supraventricular tachycardia (PSVT) associated with disabling symptoms.

Contraindications

Rythmex is contraindicated in the presence of uncontrolled congestive heart failure, cardiogenic shock (except for shock induced by arrhythmia), sinoatrial, atrioventricular and intraventricular disorders of impulse generation and/or conduction (e.g., sick sinus node syndrome, second degree or greater atrioventricular block, or bundle branch block or distal block) in the absence of an artificial pacemaker, severe symptomatic bradycardia, within three months after myocardial infarction, in patients with impaired cardiac output (left ventricular ejection fraction less than 35%) unless they have life-threatening ventricular arrhythmias, marked hypotension, severe obstructive pulmonary diseases, manifest electrolyte imbalance, myasthenia gravis, and known hypersensitivity to the drug or to any other ingredient of the preparation.

Known Brugada syndrome (see Warnings) .

Concomitant treatment with ritonavir and propafenone hydrochloride (see Drug Interactions)

Warnings

It is essential that each patient given propafenone hydrochloride be evaluated electrocardiographically and clinically prior to and during therapy to determine whether the response to propafenone hydrochloride supports continued treatment.

Notes:

1. Propafenone may alter both pacing and sensing thresholds of artificial pacemakers. Pacemakers should be monitored and programmed accordingly during therapy.
2. Propafenone should be administered with caution to patients with supraventricular tachycardia and structural heart disease with decrease of the left ventricular function.
3. Propafenone should be administered with caution to patients with atrial flutter who are not treated with drugs that decrease atrial-ventricular conduction.

4. There is the potential for conversion of paroxysmal atrial fibrillation to atrial flutter with accompanying 2:1 conduction block or 1:1 conduction (see Adverse Reactions).
5. As with other class 1c anti-arrhythmic agents, patients with significant structural heart disease may be predisposed to serious adverse events, therefore propafenone is contraindicated in these patients (see Contraindications).
6. Propafenone hydrochloride should be used with caution in patients with obstruction of the airways, e.g., asthma.

Brugada Syndrome

A Brugada syndrome may be unmasked or Brugada like electrocardiogram (ECG) changes may be provoked after exposure to propafenone in previously asymptomatic carriers of the syndrome. After initiating therapy with propafenone, an ECG should be performed to rule out changes suggestive of Brugada syndrome.

Acceleration of Ventricular Rate

Propafenone, like other antiarrhythmic agents, may cause new or worsened arrhythmias. Such proarrhythmic effects range from an increase in frequency of VPCs to the development of more severe ventricular tachycardia; e.g., tachycardia that is more sustained or more resistant to conversion to sinus rhythm with potentially fatal consequences.

Overall incidence reported in clinical trials with propafenone, where patients had new or worsened ventricular tachycardia is about 5.3 %. Their frequency appears to be related to the underlying cardiac disease.

It is therefore essential that each patient given propafenone be evaluated electrocardiographically and clinically prior to, and during therapy, to determine whether the response to propafenone supports continued treatment.

Patients with bronchospastic disease should, in general, not receive propafenone or other agents with β-adrenergic blocking activity.

Depressed Myocardial Function

Chronic propafenone therapy has been safely and successfully administered to patients with ejection fractions lower than 35%. However, since propafenone exerts a mild, dose-related negative inotropic effect on cardiac muscle, patients with congestive heart failure should be fully compensated before receiving Rythmex. If following propafenone therapy, congestive heart failure worsens, the drug should be discontinued, and, if indicated, restarted at a lower dosage only after adequate cardiac compensation has been established.

Conduction Disturbances

Propafenone slows atrioventricular conduction and may cause first degree AV block. PR interval prolongation and increases in QRS duration are closely correlated with dosage increases and concomitant increases in propafenone plasma concentrations.

Progression to second or third degree AV block requires a reduction in dosage or discontinuation of Rythmex. Bundle branch block and intraventricular conduction delay have been reported in patients receiving propafenone.

Hematologic Disturbances

Unexplained fever and/or decrease in white cell count, probably due to idiosyncratic reaction, particularly during the first three months of therapy, warrant consideration of possible hematologic reactions. Patients should be instructed to promptly report the development of any signs of infection such as fever, sore throat, or chills.

Use in Pregnancy

There are no adequate and well controlled studies in pregnant women.

Propafenone is known to pass the placental barrier in humans. The concentration of propafenone in the umbilical cord has been reported to be about 30% of that in the maternal blood.

Propafenone should be used during pregnancy only if the anticipated benefit justifies the potential risk to the fetus.

Use during Lactation

Excretion of propafenone in human breast milk has not been studied. Limited data suggest that propafenone may be excreted in human breast milk.

Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants, prescription of Rythmex should be given critical consideration in accordance with present views on the use of drugs. A decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pre-clinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential or toxicity to reproduction.

Adverse Reactions

Reactions from Clinical Trials or Postmarketing Surveillance

Summary of the safety profile

The most frequent and very common adverse reactions related to propafenone therapy are dizziness, cardiac conduction disorders and palpitations

The clinical adverse reactions that occurred in at least one of the 885 patients receiving propafenone hydrochloride SR *(sustained release formulation is not available in Israel)* in five phase II studies and two phase III studies are shown in the Table below. *It is expected that the adverse reactions and frequencies for regular release formulations would be similar*. This table also includes adverse reactions from post-marketing experience with propafenone. The reactions considered at least possibly related to propafenone are displayed by system organ class and frequency using the following convention: very common (≥1/10), common (≥ 1/100 to < 1/10), uncommon (≥ 1/1,000 to < 1/100) and not known (adverse reactions from post-marketing experience; cannot be estimated from the available data). Within each frequency grouping, adverse reactions are presented in order of decreasing seriousness when the seriousness could be assessed.

MedDRA System Organ Class	**Very common =1/10**	**Common = 1/100 to <1/10**	**Uncommon =1/1,000 to < 1/100**	**Not Known (cannot be estimated from the available data)**
Blood and lymphatic system disorders			Thrombocytopenia	Agranulocytosis Leukopenia Granulocytopenia
Immune system disorders				Hypersensitivity[1]
Metabolism and nutrition disorders			Decreased appetite	
Psychiatric disorders		Anxiety Sleep disorders	Nightmare	Conftsional state

MedDRA System Organ Class	Very common =1/10	Common = 1/100 to <1/10	Uncommon =1/1,000 to < 1/100	Not Known (cannot be estimated from the available data)
Nervous system disorders	Dizziness[2]	Headache Dysgeusia	Syncope Ataxia Paresthesia	Convulsion Extrapyramidal Symptoms Restlessness
Eye disorders		Vision blurred		
Ear and labyrinth disorders			Vertigo	
Cardiac disorders	Cardiac conduction disoders[3] Palpitations	Sinus bradycardia Bradycardia Tachycardia Atrial flutter	Ventricular tachycardia Arrhythmia[4]	Ventricular fibrillation Caridac failure[5] Heart rate reduced
Vascular disorders			Hypotension	Orthostatic hypotension
Respiratory, thoracic and mediastinal disorders		Dyspnea		
Gastrointestinal disorders		Abdominal pain Vomiting Nausea Diarrhoea Constipation	Abdominal distension Flatulence	Retching Gastrointestinal disturbance
Hepatobiliary disorders		Hepatic function abnormal[6]		Hepatocellular injury Cholestasis Hepatitis Jaundice
Skin and subcutaneous tissue disorders			Urticaria Pruritus Rash Erythema	
Musculoskeletal and connective tissue disorders				Lupus-like syndrome
Reproductive system and breast disorders			Erectile dysftnction	Sperm count decreased[7]
General disorders and administration site conditions		Chest pain Asthenia Fatigue Pyrexia		

[1] May be manifested by cholestasis, blood dyscrasias, and rash.

[2] Excluding vertigo.

[3] Including sinoatrial block, atrioventricular block and intraventricular block.

[4]Propafenone may be associated with proarrhythmic effects which manifest as an increase in heart rate (tachycardia) or ventricular fibrillation. Some of these arrhythmias can be life-threatening and may require resuscitation to prevent a potentially fatal outcome

[5] An aggravation of preexisting cardiac insufficiency may occur.

[6] This term covers abnormal liver function tests, such as aspartate aminotransferase increased, alanine aminotransferase increased, gamma-glutamyltransferase increased and blood alkaline phosphatase increased.

[7] Decreased sperm count is reversible upon discontinuation of propafenone.

Reporting of suspected adverse reactions is an important way to gather more information to continuously monitor the benefit/risk balance of the medicinal product. Any suspected adverse reaction should be reported.

Precautions

Use in Patients with Impaired Hepatic Function

Propafenone is highly metabolized by the liver and should therefore be administered cautiously to patients with impaired hepatic function. The dose of propafenone given to patients with impaired hepatic function should be the lowest recommended dosage for patients with normal hepatic function. Careful monitoring for excessive pharmacological effects should be carried out.

Use in Patients with Impaired Renal Function

Since a considerable percentage of propafenone metabolites are excreted in the urine, Rythmex should be administered cautiously to patients with impaired renal function.

Neuromuscular Dysfunction

Exacerbation of myasthenia gravis has been reported during propafenone therapy.

Effects on ability to drive and use machines

Propafenone may affect the patient's alertness and impair the individual's mental ability (blurred vision, dizziness, fatigue and postural hypotension). This should be taken into consideration when engaging in activities requiring mental alertness such as driving a car or operating machinery, especially when consumption of alcohol is also involved.

Drug Interactions

Propafenone/Drugs that Inhibit CYP2D6, CYP1A2, and CYP3A4 (e.g.: ketoconazole, cimetidine, erythromycin and grapefruit juice): Concomitant administration of these drugs might lead to increased levels of propafenone hydrochloride. When propafenone hydrochloride is administered with inhibitors of these enzymes, the patients should be closely monitored and the dose adjusted accordingly.

Propafenone/Drugs that are Metabolized by CYP2D6 (such as venlafaxine):
Coadministration of propafenone hydrochloride with drugs metabolized by CYP2D6 (such as venlafaxine) might lead to increased levels of these drugs. Increases in propranolol, metoprolol, desipramine, cyclosporine, theophylline and digoxin plasma levels or blood levels have been reported during propafenone hydrochloride therapy. Doses of these medicinal products should be reduced, as appropriate, if signs of overdose are observed.

Propafenone/Ritonavir: Due to the potential for increased plasma concentrations, co-administration of ritonavir and propafenone hydrochloride is contraindicated. (see Contraindications).

Propafenone/Amiodarone: Combination therapy of amiodarone and propafenone hydrochloride can affect conduction and repolarization and lead to abnormalities that have the potential to be proarrhythmic. Dose adjustments of both compounds based on therapeutic response may be required.

Propafenone/Lidocaine: No significant effects on the pharmacokinetics of propafenone or lidocaine have been seen following their concomitant use in patients. However, concomitant use of propafenone hydrochloride and lidocaine have been reported to increase the risks of central nervous system side effects of lidocaine.

Propafenone/Oral Anticoagulants: Close monitoring of the clotting status in patients receiving concomitant oral anticoagulants (e.g., phenprocoumon, warfarin) is recommended as propafenone hydrochloride may enhance the efficacy of these drugs resulting in an increased prothrombin time.

In healthy subjects receiving propafenone and warfarin concomitantly, mean steady-state warfarin plasma concentrations increased 39% with a corresponding increase in prothrombin times of approximately 25%. It is therefore recommended that prothrombin times be routinely monitored and the dose of warfarin be adjusted if necessary

Propafenone/Fluoxetine/Paroxetine: Elevated levels of plasma propafenone may occur when propafenone hydrochloride is used concomitantly with SSRIs, such as fluoxetine and paroxetine. Concomitant administration of propafenone hydrochloride and fluoxetine in extensive metabolizers increased the S propafenone Cmax and AUC by 39 and 50% and the R propafenone Cmax and AUC by 71 and 50%.. Lower doses of propafenone may be sufficient to achieve the desired therapeutic response.

Propafenone/Digitalis: Propafenone produces dose-related increases in serum digoxin levels ranging from about 35% at 450 mg/day to 85% at 900 mg/day propafenone without affecting digoxin renal clearance.

Patients on concomitant therapy should be monitored and reduction of digoxin dosage may be necessary.

Proarrhythmic events were reported in patients on therapy with propafenone and digoxin, receiving low-dose diuretic therapy including potassium-retaining diuretics. Although plasma concentrations of digoxin had been in the therapeutic range and those of potassium had been normal prior to propafenone treatment, the possibility of the existence of a more or less pronounced whole body potassium and magnesium depletion, should be borne in mind.

Propafenone/Local Anesthetics: Concomitant use of local anesthetics (i.e., during pacemaker implantations, surgery, or dental use) may increase the risks of central nervous system side effects.

Propafenone/Beta-Blockers: Experience with combined use of propafenone and beta blockers is limited; however, concomitant use of propafenone and propranolol resulted in an increase of propranolol plasma levels. Propafenone has also been reported to increase metoprolol serum levels upon concomitant administration of both drugs. Cardiac function should therefore be monitored and the dose of the β-blocker adjusted as needed.

Propafenone/Calcium Antagonists/Diuretics: Limited experience with propafenone combined with calcium antagonists and with diuretics has been reported without evidence of clinically significant adverse reactions.

Propafenone/Tricyclic Antidepressants (Imipramine, Desipramine): Concomitant administration may lead to an increase in the pharmacologic and toxic effects of the tricyclic antidepressants. The mechanism of this interaction is unknown, but it may possibly involve inhibition of metabolism of the tricyclic antidepressants. Therefore, serum tricyclic antidepressants should be monitored and their dosage adjusted accordingly.

Propafenone/Cyclosporine: Concomitant administration may lead to increased cyclosporine plasma levels. The mechanism may involve propafenone interference with cyclosporine metabolism or increased cyclosporine absorption. Decreased renal function may also occur. Therefore, cyclosporine plasma levels, as well as renal function, should be monitored upon concomitant administration of this combination.

Propafenone/Theophylline: Concomitant administration has been reported to double the theophylline plasma levels. The mechanism may involve inhibition of theophylline metabolism caused by propafenone. Therefore, serum theophylline levels should be monitored and the theophylline dosage adjusted as needed.

Propafenone/Quinidine: Plasma propafenone levels have been reported to increase upon concomitant administration of this combination. The mechanism involves inhibition of the enzyme cytochrome P450 II D6 by quinidine; since propafenone is metabolized by this enzyme, the hepatic hydroxylation metabolic pathway of propafenone is thus inhibited by quinidine. Therefore, cardiac function should be monitored and the dose of propafenone or its frequency may need to be reduced.

Propafenone/Cimetidine: Plasma propafenone levels have been reported to increase upon concomitant administration of this combination. The mechanism may involve inhibition of propafenone metabolism by cimetidine. No special precautions other than usual monitoring of cardiac function are needed.
Propafenone/Rifampin: Decreased plasma concentrations of propafenone (possibly to subtherapeutic levels) have been reported upon concomitant administration of this combination. Rifampin may induce hepatic microsomal enzymes responsible for metabolizing propafenone, leading to increased propafenone clearance. Monitoring of propafenone plasma levels or an alternate anti-infective agent may be considered.
Propafenone/Phenobarbital (a Known Inducer of CYP3A4): Propafenone plasma levels have been reported to decrease possibly to subtherapeutic levels. Response to propafenone hydrochloride therapy should be monitored during concomitant chronic phenobarbital use. This should be taken into consideration when administering this combination.

Diagnostic Interference

Transient positive Antinuclear Antibody (ANA) titers have been reported and may disappear even in the face of continued propafenone treatment.

Patients in whom an abnormal ANA test has occurred should be carefully evaluated and, if persistent or worsening elevation of ANA titers is detected, consideration should be given to discontinuing therapy.

Dosage and Administration

Note:

Patients with ventricular arrhythmias require careful cardiological surveillance at the beginning of propafenone treatment. These patients should only be started on the drug if emergency cardiological equipment is available and if the possibility of monitoring is assured.

The individual maintenance dose should be determined under cardiological surveillance including ECG monitoring and repeated blood pressure control (adjustment phase). A decision should be made as to whether to continue treatment if there are ECG changes such as QRS or QT prolongation greater than 25% or PR prolongation greater than 50% or QT prolongation to more than 500 ms, or an increase in the incidence or severity of cardiac arrhythmias.

Elderly patients: *No overall differences in safety or effectiveness were observed in this patient population, but greater sensitivity of some older individuals cannot be ruled out, therefore, these patients should be carefully monitored. The same applies to maintenance therapy. In such patients it is recommended to postpone therapeutically necessary dose increases until steady state plasma concentrations have been reached, usually after around 5 to 8 days. This precaution reduces the risk of inducing proarrhythmic effects in these patients during the initial phase of treatment.*

In those patients in whom significant widening of the QRS complex or second or third degree AV block occurs, a dose reduction should be considered.

Note: In patients with flutter, treatment should be initiated with careful monitoring (preferably under hospitalization).

When prescribing propafenone it should be taken into account that there is no evidence that antiarrhythmic treatment with Class I antiarrhythmics improves survival.

It is recommended that therapy be initiated with 150 mg propafenone given every eight hours (450 mg/day). Dosage may be increased at a minimum of 3 to 4 day intervals to 300 mg every 12 hours (600 mg/day). If necessary, 300 mg every 8 hours (900 mg/day) may be administered until optimum clinical response is obtained.

Occasionally, it may be necessary to increase the daily dose to 900 mg of propafenone hydrochloride. The daily dose should be reduced accordingly for patients with a lower body weight.
Dose increases should not be attempted until the patient has been receiving treatment for 3-4 days.

The individual maintenance dose should be determined under cardiological surveillance including ECG monitoring and repeated blood pressure control (titration phase).

The usefulness and safety of dosages exceeding 900 mg per day have not been established.

As with other antiarrhythmic agents, in the elderly or in patients with marked previous myocardial damage, the dose of Rythmex should be increased slowly and gradually during the initial phase of treatment, whereby monitoring of plasma concentrations of the drug may be appropriate. The first dose increase should take place after 5 to 8 days at the earliest.

Patients with Hepatic/Renal Impairment
In patients whose liver and/or kidney function is impaired, there may be drug accumulation after standard therapeutic doses. Nonetheless, patients with these conditions can still be titrated on propafenone hydrochloride under ECG and clinical monitoring.

Because of its bitter taste and its surface anaesthetic action, the tablets should be swallowed whole together with some liquid after meals.

Overdosage

Manifestations: The symptoms of overdosage, which are usually most severe within 3 hours of ingestion, may include

Myocardial Symptoms:
The effects of propafenone hydrochloride overdose in the myocardium manifest as impulse generation and conduction disorders such as PQ prolongation, QRS widening, suppression of sinus node automaticity, AV block, ventricular tachycardia, ventricular flutter and ventricular fibrillation. Reduction of contractility (negative inotropic effect) can cause hypotension which, in severe cases, can lead to cardiovascular shock.

Non-cardiac symptoms
Headache, dizziness, blurred vision, paraesthesia, tremor, nausea, constipation and dry mouth may occur frequently. In extremely rare cases, convulsions have been reported on overdose. Death has also been reported.

In severe cases of poisoning, clonic-tonic convulsions, paraesthesia, somnolence, coma and respiratory arrest may occur.

Treatment: Defibrillation as well as infusion of dopamine and isoproterenol have been effective in controlling rhythm and blood pressure.
In the rare instances where SA-, AV- or IV-blocks appear, the following countermeasures should be instituted:

In addition to general emergency measures, the patient's vital parameters should be monitored in an intensive care setting, and rectified, as appropriate.

Countermeasures in the case of SA- or AV-block: atropine 0.5 - 1 mg total dose intravenously or orciprenaline 0.5 - 1 mg intravenously with subsequent drip infusion 5 - 50 μg/minute, depending on effective ventricular rate.

Countermeasure in the case of IV-block: electrotherapy.

Convulsions have been alleviated with intravenous diazepam.

In cases of severe hypotension and bradycardia (generally, unconscious patients) : 0.5 - 1.0 mg atropine intravenously or 0.5 - 1.0 mg adrenaline intravenously, if necessary adrenaline drip infusion.

General supportive measures such as mechanical respiratory assistance and external cardiac massage may be necessary.

Owing to high protein binding (greater than 95%) and the large volume of distribution, hemodialysis is ineffective and attempts to achieve elimination via hemoperfusion are of limited efficacy.

Registration Numbers

Rythmex: 150 mg: 103 99 27103 00; 103 99 27103 12.
Rythmex: 300 mg: 104 01 27104 00; 104 01 24104 12.

Storage

Store this medicine in a dry place below 30°C.

Manufacturer

Teva Pharmaceutical Industries Ltd,
P.O.Box 3190, Petach Tikva 49131