Professional Information Leaflet

Tambocor 10 mg/ml Solution for Injection

(Flecainide acetate)

Presentation:
Each 15 ml ampoule contains 15 ml of flecainide acetate 10 mg/ml, solution for injection. The other ingredients are sodium acetate, glacial acetic acid and water for injection.

Therapeutic Indications:
Serious sustained life-threatening ventricular arrhythmias that have not responded to other drugs.

Directions for Use:
Tambocor injection may be given as a bolus injection in an emergency or for rapid effect, or as a slow intravenous infusion when prolonged administration is required.

a) Bolus injection: Administer 2 mg/kg over not less than ten minutes, or in divided doses. Alternatively dilute with 5% glucose and give as a mini-infusion. Continuous ECG monitoring is recommended. Stop the injection when the arrhythmia is controlled.
For sustained ventricular tachycardia, or people with a history of cardiac failure (who may become decompensated during administration) give the initial dose over 30 minutes and monitor the ECG carefully.
The maximum recommended bolus dose is 150 mg.

b) Intravenous infusion: The recommended procedure is to start with a slow injection of 2 mg/kg over 30 minutes, then continue intravenous infusion at the following rates:
First hour: 1.5 mg/kg per hour.
Second and later hours: 0.1 - 0.25 mg/kg per hour.
The maximum recommended infusion duration is 24 hours; if exceeded, and in patients receiving high doses, monitor plasma levels.
The maximum cumulative dose over the first 24 hours should not exceed 600 mg.
In severe renal impairment (creatinine clearance < 35 ml/min/1.73 sq.m.) reduce the above dosage recommendations by half.

Oral maintenance dosing should be started as soon as possible after stopping the infusion.

Children:
Not recommended in children under 12 years.

Elderly Patients:
The rate of elimination of flecainide may be reduced, so dose adjustment may be necessary.

Contraindications:
- Cardiac failure.
- History of myocardial infarction with either asymptomatic ventricular ectopics, or asymptomatic non-sustained ventricular tachycardia.
- Long-standing atrial fibrillation where there has been no attempt to convert to sinus rhythm.
- Haemodynamically significant valvular heart disease.
- Unless pacing rescue is available, do not give to patients with sinus node dysfunction, atrial conduction effects, second degree or greater atrio-ventricular block, bundle branch block or distal block.

Precautions:
- Correct any electrolyte disturbances before using Tambocor injection.
- Plasma elimination of flecainide may be markedly slower in patients with significant hepatic impairment. Do not use, unless the potential benefits clearly outweigh the risks. Careful plasma monitoring is recommended.
- Decreased endocardial pacing sensitivity may occur; this effect is reversible and more marked on the acute pacing threshold than on the chronic.
- Use with caution in all patients with permanent pacemakers or temporary pacing electrodes. Do not administer to patients with existing poor thresholds, or non-programmable pacemakers, unless suitable pacing rescue is available.
- Flecainide's minor negative inotropic effect may become important in patients predisposed to cardiac failure. Difficulty in defibrillating some patients has been reported. The majority of these cases had pre-existing heart disease with cardiac enlargement, a history of myocardial infarction, arteriosclerotic heart disease and cardiac failure.
- Use cautiously in patients with acute onset atrial fibrillation following cardiac surgery.

Use in Pregnancy and Lactation:
Flecainide crosses the placenta; however, the safety of Tambocor injection in pregnancy has not been established.
Flecainide is excreted in human milk and appears in concentrations which reflect those in maternal blood. The risk of adverse effects to the nursing infant is very small.

Drug Interactions:
Flecainide is a class I antiarrhythmic. Possible interactions include:
- Additive effects with other antiarrhythmic drugs or with drugs affecting the metabolism of flecainide.
- Cardiac glycosides: flecainide can cause plasma *Digoxin* to rise by about 15%. *Digoxin* plasma level in digitalised patients should be measured not less than six hours after any *Digoxin* dose, before or after administration of flecainide.
- Class II antiarrhythmics: additive negative inotropic effects of beta-blockers and other cardiac depressants with flecainide should be recognised.
- Class III antiarrhythmics: reduce the dose of flecainide by 50% in the presence of *Amiodarone* to avoid additive effects. Monitor patients for adverse events and plasma level monitoring is strongly recommended.
- Class IV antiarrhythmics: use of flecainide with other sodium channel blockers is not recommended.
- Antidepressants: flecainide increases plasma flecainide concentration. *Tricyclics* increase the

risk of arrhythmias. *Reboxetine* manufacturer advises caution.
- Antiepileptics: Known enzyme inducers (*Phenytoin, Phenobarbital, Carbamazepine*) increase the rate of flecainide elimination by approximately 30%.
- Antipsychotics: *Clozapine* increases the risk of arrhythmias.
- Antihistamines: *Mizolastine* and *Terfenadine* increase the risk of ventricular arrhythmias.
- Antimalarials: *Quinine* increases plasma flecainide concentration.
- Antivirals: plasma flecainide concentrations are increased by *Ritonavir*, *Lopinavir* and *Indinavir* to increase risk of ventricular arrhythmias. Avoid concomitant use.
- Diuretics: Hypokalaemia may cause cardiac toxicity.
- *Cimetidine:* Increases plasma flecainide by approximately 30%.
- Anti-smoking aids: *Bupropion* may increase flecainide plasma concentration by inhibitory effects on CYP2D6, the isoenzyme responsible for flecainide metabolism.
- Tambocor injection is compatible with oral anticoagulants.

Side effects:
- ***Body as a whole:*** Asthenia, fatigue, fever, oedema.
- ***Cardiovascular:*** Pro-arrhythmic effects - most likely in patients with structural heart disease and/or significant left ventricular impairment.
  1:1 AV conduction following initial atrial slowing with resultant ventricular acceleration may occur (most commonly seen following use of the injection for acute conversion).
  This effect is usually short lived and abates quickly once therapy is stopped. Other reported effects: AV block-second-degree and third degree, bradycardia, cardiac failure/congestive cardiac failure, chest pain, hypotension, myocardial infarction, palpitation, sinus pause or arrest and tachycardia (AT or VT).
- ***Skin and appendages:*** Allergic skin reactions, rashes, urticaria, photosensitivity.
- ***Immune system:*** Increased anti-nuclear antibodies with and without systemic inflammatory involvement.
- ***Haematological:*** Reductions in red and white blood cells and platelets reported occasionally.
- ***Psychiatric:*** Hallucinations, depression, confusion, amnesia, anxiety, insomnia.
- ***Gastrointestinal:*** Nausea, vomiting, abdominal pain, anorexia, constipation, diarrhoea, dyspepsia, flatulence.
- ***Liver and biliary system:*** Elevated liver enzymes, jaundice which is reversible on stopping treatment, hepatic dysfunction.
- ***Neurological:*** Giddiness, dizziness, light-headedness, dyskinesia, convulsions. During long term therapy peripheral neuropathy, paraesthesia, ataxia, flushing, headache, hypoaesthesia, increased sweating, somnolence, syncope, tinnitus, tremor, vertigo.
- ***Ophthalmological:*** Double vision, blurred vision, corneal deposits.
- ***Respiratory:*** Dyspnoea, pneumonitis.

Overdosage:
No specific antidote or rapid method of removing flecainide from the system is known. Forced acid diuresis may be helpful (theoretically), but dialysis and haemoperfusion are not. Injections of anticholinergics are not recommended.
Treatment of flecainide overdosage may include use of an inotropic agent, intravenous calcium, circulatory assistance (e.g. balloon pumping), mechanically assisting respiration, or temporarily inserting a transvenous pacemaker if there are severe conduction disturbances or the patient's left ventricular function is otherwise compromised.

Pharmacologic Properties

Pharmacodynamic
Tambocor is a Class 1 anti-arrhythmic (local anaesthetic) agent.
Tambocor slows conduction through the heart, having its greatest effect on His Bundle conduction. It also acts selectively to increase anterograde and particularly retrograde accessory pathway refractoriness. Its actions may be reflected in the ECG by prolongation of the PR interval and widening of the QRS complex. The effect on the JT interval is insignificant

Pharmacokinetic
Intravenous administration of 0.5 - 2.0 mg/kg to healthy subjects resulted in plasma concentrations ranging from 70 - 340 mcg/l. Protein binding ranges from 32 to 58%. The volume of distribution in healthy subjects following intravenous infusion of 2 mg/kg averaged 512 litres.

The elimination half life after IV administration to patients was 7 to 19 hours.

Handling and Storage:
Tambocor injection should be diluted with, or injected into, sterile solutions of 5% glucose. If chloride containing solutions, such as sodium chloride or Ringer's lactate are used, the injection should be added to a volume of not less than 500 ml, otherwise a precipitate will form.

Do not store above 30°C. Do not freeze. Protect from light.

Manufacturer:
3M Health Care Ltd., United Kingdom for Meda Pharma Germany.

Registration Holder:
Rafa Laboratories Ltd., P.O. Box 405, Jerusalem 91003

Registration number: 106 41 23294

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Tambocor inj PL PB0312-04

שם התכשיר	טמבוקור זריקות
מק"ט רפא	794709
מס' מהדורה	I-709004
פריסה	21x16 ס"מ לפי נספח 3 / ג' (3)
סוג הנייר	60 גרם
קיפולים	3
גודל עלון סופי לאחר קיפול	בערך 8*5 ס"מ - על החזית, יופיע שם התכשיר
שפות	1 אנגלית
צבע	שחור
אריזה	ידנית
פרמהקוד	813 (בית הדפוס ילביש את הפרמקוד ללא עלות)
דפוס	אידיאל
מידות לקוי פרמהקוד	קו דק 0.5 מ"מ; קו עבה 1.5 מ"מ; רווח בין הקווים 1 מ"מ; אורך נטו מקסימום 10 מ"מ (מינימום 8 מ"מ - עדיפות למידה מקסימלית)
הוכן ע"י	בלאו שירותים פרמצבטיים
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