Package leaflet: Information for the user

Tambocor 10mg/ml Solution for the injection or infusion
Flecainide acetate

Read all of this leaflet carefully before you start taking this medicine because it contains important information for you.
- **K**eep this leaflet. You may need to read it again
- If you have any further questions, ask your doctor or nurse.
- If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet.

The name of your medicine is Tambocor 10mg/ml Solution for injection, which will be called Tambocor throughout this leaflet.

What is in this leaflet:

1. WHAT TAMBOCOR IS AND WHAT IT IS USED FOR

Tambocor contains the active ingredient flecainide, which belongs to a group of medicines called anti-arrhytmics, which control the speed and rhythm of the heart.

Tambocor is used to treat:
- Arrhythmias (irregular heart beat)
- Tachycardia (too fast heartbeat)
- Wolff-Parkinson-White Syndrome (a special kind of heartbeat irregularity with a disorder of conduction)
- Atrial fibrillation and atrial flutter (rapid contraction of muscles in the heart)

2. WHAT YOU NEED TO KNOW BEFORE YOU USE TAMBOCOR

Do not use Tambocor:
- If you are allergic to Flecainide or any of the other ingredients of this medicine (listed in section 6). An allergic reaction may include rash, itching, difficulty breathing or swelling of the face, lips, throat or tongue.
- If you are taking a similar anti-arrhythmic drug (other class 1 anti-arrhythmics, e.g. disopyramide, procainamide, quinidine, lidocaine, mexiletine, propafenone)
- If you have had heart problems such as heart failure, heart attack, heart valve or conduction problems – your doctor will study your medical history
- If you have been told you have an electrolyte imbalance (altered blood salts)

Warning and precautions
Talk to your doctor or pharmacist before using Tambocor.
Tell your doctor if you have any of the following conditions:
- Liver disease
- You have a pacemaker

- You have heart disease
- You have or have had heart failure
- Your have an enlarged heart
- You have ever had a heart attack
- You have had angina
- You have or have had irregular heartbeats following heart surgery

You will be monitored to check your fluid balance and salts.

Children
Tambocor is not recommended in children under 18years old as there is not enough evidence of its use in this age group.

Other medicines and Tambocor
Tell your doctor or pharmacist if you are taking, have recently taken or might take any other medicines.

You should tell your doctor if you are taking or have taken any of the following medicines as they may interact with Tambocor:

- Digoxin (used to treat heart failure)
- Drugs that affect the heart such as beta blockers or verapamil (used to treat high blood pressure)
- Other anti-arrrhythmic drugs, such as amiodarone
- Antidepressants such as fluoxetine, amitryptiline, desipramine and reboxetine
- Drugs for epilepsy such as phenytoin, phenobarbital, carbamazepine
- Clozapine (used to treat mental illness)
- Antihistamines (used to treat hayfever and allergies) such as mizolastine or terfenadine
- Quinine (used to treat and prevent malaria
- Ritonavir (used to treat HIV [AIDS])
- Diuretics (water tablets)
- Cimetidine (an ulcer healing drug)
- Bupropion (an anti- smoking aid)
- Terbinafine (an antifungal drug)

It may still be all right for you to be given Tambocor and your doctor will be able to decide what is suitable for you.

Pregnancy and breastfeeding
You should not take Tambocor while pregnant or breast-feeding unless your doctor tell you to.
If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your doctor or pharmacist for advice before taking this medicine.

Driving and using machines
It is advisable not to drive, operate machinery or do anything that requires you to be alert until you know how Tambocor affects you. This is because Tambocor can cause blurred vision or dizziness in some people.

Tambocor contains sodium
This medicine contains 38 mg sodium (main component of cooking/table salt) per ampoule. This is equivalent to 1.9 % of the recommended maximum daily intake of sodium for an adult.

3. HOW TO USE TAMBOCOR

Always use this medicine exactly as your doctor has told you. Check with your doctor if you are not sure. Tambocor will be administered by a doctor in the hospital. Tambocor is only administered intravenously (into the vein).
Your doctor has chosen the dose which best suits your condition. It may be given directly from the syringe or through a drip (infusion). Your doctor or nurse will monitor this for you.
Tambocor may be administered by slow injection into a vein at a dose of 2 mg per kg or body weight for 10 minutes or more. If you have a history of heart failure Tambocor will be administered for 30 minutes with maximum dose of 150 mg.

If given by intravenous infusion the maximum total dose given in the first 24 hours should not exceed 600 mg. In patients with severe renal impairment the dose should be reduced by half.
Dosage in renal impairment:
The maximum initial dosage should be 100 mg daily.

Use in Children
Tambocor is not recommended in children under 18 years old as there is not enough evidence of its use in this age group.

Older people and people with liver or kidney problems
Older patients may require a lower dose.
If you have liver or kidney disease you may need a reduced dose.

If you use more Tambocor than you should:
It is unlikely that you will be given the wrong dose of Tambocor as treatment is usually given in hospital.

If you have any further questions on the use of this medicine, ask your doctor or nurse.

4. POSSIBLE SIDE EFFECTS

Like all medicines, this medicine can cause side effects, although not everybody gets them.
All medicines can cause allergic reactions, although serious allergic wheeziness, difficulty in breathing, swelling of the eyelids, face or lips, rash or itching (especially affecting your whole body).

The following side effects have been reported:
Weakness, tiredness, fever, swelling, missed heart beats, slow heart beat, heart failure, chest pain, low blood pressure, heart attack, fast or irregular heart beat, rash, hair loss, light sensitivity, feeling sick, vomiting, tummy pain, anorexia (loss of appetite), increased appetite, constipation, diarrhoea, indigestion, flatulence (wind).
Also, raised liver enzymes and changes in the numbers of blood cells (your doctor can detect these with a blood test), yellow eyes and skin, itching, liver failure, dizziness, light-headedness, headache, muscle weakness and cramps, muscle pain, pins and needles, lack of co-ordination, joint pain, flushing, numbness, and increased sweating.

Sleepiness, fainting, ringing in the ears, tremor, spinning sensation, double vision, blurring of vision, breathlessness, inflammation of lungs, depression, anxiety, confusion, hallucination and sleeplessness.
Extremely rare cases of vision disorder caused by particles in the front of the eye (corneal deposits) have also been reported.
If you get any side effects, talk to your doctor or nurse. This includes any possible side effects not listed in this leaflet.

Reporting of side effects
If you get any side effects, talk to your doctor, pharmacist or nurse. This includes are possible side effects not listed in this leaflet. You can also report side effects directly via HPRA Pharmacovigilance, Website: www.hpra.ie. By reporting side effects you can help provide more information on the safety of this medicine.

5. HOW TO STORE TAMBOCOR

Keep this medicine out of the sight and reach of children. Do not store above 30°C. Do not freeze. Keep ampoules in the outer carton.

Do not use Tambocor after the expiry date which is stated on the container after ''EXP''. The expiry date refers to the last day of that month.

Do not throw away any medicines via wastewater or household waste. Ask your pharmacist how to throw away medicines you no longer use. These measures will help protect the environment.

6. CONTENTS OF THE PACK AND OTHER INFORMATION

What Tambocor contains
Each 15ml ampoule contains 150 mg (10 mg/ml) of the active ingredient flecainide acetate, as a solution for injection. The other ingredients are: sodium acetate, glacial acetic acid, water for injections.

What Tambocor looks like and contents of packs
Tambocor is a clear, colourless solution and is available in packs of 5 ampoules.

Marketing Authorisation Holder and Manufacturer

Marketing Authorisation Holder
Mylan IRE Healthcare Limited,
Unit 35/36, Grange Parade,
Baldoyle Industrial Estate,
Dublin 13,
Ireland

Manufacturer
Cenexi
52, rue Marcel et Jacques Gaucher
94120 Fontenay-Sous-Bois, France

This leaflet was last revised in July 2020

** HCP **

Tambocor
10mg/ml Solution for injection or infusion
Flecainide acetate

The following information is intended for medical or healthcare professionals only:
Presentation
Each ampule contains 15ml of flecainide acetate 10mg/ml, solution for injection. This is clear, colourless solution which also contains sodium acetate, glacial acid and water for injections.

Directions for use

a) Bolus injection: Tambocor can be given in an emergency or for rapid effect by a slow injection of 2mg/kg over not less than ten minutes or in divided doses. If preferred the dose may be diluted with 5% glucose and given as a mini infusion. Continuous ECG monitoring is recommended in all patients receiving the bolus dose. The injection should be stopped when there is control of the arrhythmia. It is recommended that Tambocor should be administered more slowly to patients in sustained ventricular tachycardia with careful monitoring of the electrocardiogram. Similar caution should apply to patients with a history of cardiac failure, who may become decompensated during the administration. For such patients it is recommended that the initial dose is given over 30 minutes. The maximum recommended bolus dose is 150mg.
b) Intravenous infusion: When prolonged parenteral administration is required, it is recommended that therapy is initiated by slow injection of 2mg/kg over 30 minutes and continued by intravenous infusion at the following rates:
First hour: 1.5mg/kg per hour.
Second and later hours: 0.1-0.25 mg/kg per hour.
It is recommended that the infusion duration should not exceed 24 hours.
However, where this is considered necessary, or for patients receiving the upper end of the dose range, plasma level monitoring is strongly recommended. The maximum cumulative dose given in the first 24 hours should not exceed 600mg.
In patients with severe renal impairment (creatinine clearance of less than 35 ml/min/1.73 sq.m.), each of the above dosage recommendations should be reduced by half.
Transition to oral dosing should be accomplished as soon as possible by stopping the infusion and administering the first required oral dose. Oral maintenance is then continued as indicated in the relevant oral dosage instructions.

Children: Tambocor is not recommended in children under 18, as there is insufficient evidence of its use in this age group.
Older patients: The rate of flecainide elimination from plasma may be reduced in older people. This should be taken into consideration when making dose adjustments.
Plasma Levels
Based on PVC suppression, it appears that plasma levels of 200-1000 ng/ml may be needed to obtain the maximum therapeutic effect. Plasma levels above 700-1000 ng/ml are associated with increased likelihood of adverse experiences.
Dosage in impaired renal function
In patients with significant renal impairment (creatinine clearance of 35ml/min/1.73 sq.m. or less) the maximum initial dosage should be 100mg daily (or 50mg twice daily). When used in such patients, frequent plasma level monitoring is strongly recommended.
Therapeutic indications
Tambocor is indicated when rapid control of the following arrhythmias is the main clinical requirement:

a) Ventricular tachyarrhythmias.

b) AV nodal reciprocating tachycardia when patients have been unresponsive to betablockers or calcium channel blockers.
c) Wolff-Parkinson White Syndrome and similar conditions with accessory pathways.

Contra-indications and warnings
Contra-indications
Tambocor is contra-indicated in

1) Cardiac failure or left ventricular dysfunction.
2) Patients with a history of myocardial infarction who have either asymptomatic ventricular ectopics or asymptomatic nonsustained ventricular tachycardia.
3) Patients with severe ischaemic heart disease.
   Unless pacing rescue is available Tambocor should not be given to patients with sinus node dysfunction, atrial conduction defects, second degree or greater atrioventricular block, bundle branch block or distal block.
4) Patients with a presence of cardiogenic shock
5) Known Brugada syndrome
6) Use of flecainide with other sodium channel blockers is not recommended. Tambocor is contra-indicated in patients with known hypersensitivity to amide drugs.

Precautions
Electrolyte disturbances should be corrected before using Tambocor. This medicinal product contains 1.6mmol (or 37.7 mg) sodium per ampoule. To be taken into consideration by patients on a controlled sodium diet. Since flecainide elimination from the plasma can be markedly slower in patient with significant hepatic impairment, flecainide should not be used in such patients unless the potential benefits clearly outweigh the risks. Plasma level monitoring is strongly recommended in these circumstances. This product should be used with caution in patients with severe hepatic disease. ECG monitoring should be maintained during intravenous administration.
Flecainide has been shown to increase mortality risk of post-myocardial infarction patients with asymptomatic ventricular arrhythmia. Flecainide, like other antiarrhythmics, may cause proarrhythmic effects, i.e it may cause the appearance of a more sever type of arrhythmia, increase the frequency of an existing arrhythimia or the severity of the symptoms. Flecainide should be avoided in patients with structural heart disease or abnormal left ventricular functions. Treatment for patients with other indications should continue to be initiated in hospital. Continuous ECG monitoring is recommended in all patients receiving bolus injection. Severe bradycardia or pronounced hypotension should be corrected before using flecainide. The rate of flecainide elimination from plasma may be reduced in older people. This should be taken into consideration when making dose adjustments.
Tambocor is known to increase endocardial pacing thresholds – i.e. to decrease endocardial pacing sensitivity. This effect is reversible and is more marked on the acute pacing threshold than on the chromic. Tambocor should thus be used with caution in all patients with permanent pacemakers or temporary pacing electrodes and should not be administered to patients with existing poor thresholds or non-programmable pacemakers unless suitable pacing rescue is available.
Generally, a doubling of either pulse width or voltage is sufficient to regain capture, but it may be difficult to obtain ventricular thresholds less than 1 volt at initial implantation in the presence of Tambocor. Intravenous administration of this compound may lead to bradycardia and hypotension.
The minor negative inotropic effect of flecainide may assume importance in patients predisposed to cardiac failure. Difficulty has been experienced in defibrillating some patients.
Most of the cases reported has pre-existing heart disease with cardiac enlargement, a history of myocardial infarction, arteriosclerotic heart disease and cardiac failure.
A Brugada syndrome may be unmasked due to flecainide therapy. In the case of the development of ECG changes during treatment with flecainide that may indicate Brugada syndrome, consideration to discontinue the treatment should be made.
Tambocor was included in the National Heart Lung and Blood Institute's Cardiac Arrhythmia Suppression Trial (CAST), a long-term, multi-centre, randomized, double-blind study in patients with asymptomatic non-life-threatening arrhythmias who had had a myocardial infarction more than six

days, but less than two years, previously. An excessive mortality or non-fatal cardiac arrest rate was seen in patients with Tambocor compared with that seen in a carefully matched placebo-treated group. This rate was 16/316 (5.1%) for Tambocor and 7/309 (2.3%) for its matched placebo. The average duration of treatment with Tambocor in this study was 10 months. It was noted that the increased risk from sudden cardiac death occurred in patients with a history of multiple previous myocardial infarction, usually with poor ventricular function.

Drug Interactions

Flecainide is a class I anti-arrhythmic and interactions are possible with other anti- arrhythmic drugs where additive effects may occur or where drugs interfere with the metabolism of flecainide. The following known categories of drugs may interact with flecainide.

Cardiac glycosides; Flecainide can cause the plasma digoxin level to rise by about 15%, which is unlikely to be of clinical significance for patients with plasma levels in the therapeutic range. It is recommended that the 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 anti-arrhythmics; the possibility of additive negative inotropic effects of beta-blockers, and other cardiac depressants such as verapamil, with flecainide should be recognised.

Class III anti-arrhythmics; when flecainide is given in the presence of amiodarone, the usual flecainide dosage should be reduced by 50% and the patient monitored closely for adverse effects. Plasma level monitoring is strongly recommended in these circumstances.

Class IV anti-arrhythmics; use of flecainide with other sodium channel blockers is not recommended.

Anti-depressants; fluoxetine increases plasma flecainide concentration; increased risk of arrhythmias with tricyclics; manufacturer of reboxetine advises caution.

Anti-epileptics; limited data in patients receiving known enzyme inducers (phenytoin, phenobarbital, carbamazepine) indicate only a 30% increase in the rate of flecainide elimination.

Anti-psychotics: clozapine – increased risk of arrhythmias.

Anti-histamines; increased risk of ventricular arrhythmias with mizolastine and terfenadine (avoid concomitant use).

Anti-malarials: quinine increases plasma concentration of flecainide.

Antivirals: plasma concentration increased by ritonavir, (increased risk of ventricular arrhythmias (avoid concomitant use).

Antifungals: Terbinafine may increase plasma concentrations of flecainide resulting from its inhibition of CYP2D6 activity.

Diuretics: Class effect due to hypokalaemia giving rise to cardiac toxicity.

Ulcer healing drugs: Cimetidine inhibits metabolism of flecainide. In healthy subjects receiving cimetinde (1g daily) for one week, plasma flecainide levels increased by about 30% and the half-life increased by about 10%.

Anti-smoking aids: Co-administration of bupropion with drugs that are metabolized by CYP2D6 isoenzyme including flecainide, should be approached with caution and should be initiated at the lower end of the dose range of the concomitant medication. If bupropion is added to the treatment regimen of a patient already receiving flecainide, the need to decrease the dose of the original medication should be considered.

Cardiac glycosides: Flecainide can cause the plasma digoxin level to rise by about 15%, which is unlikely to be of clinical significance for patients with plasma levels in the therapeutic range. It is recommended that the digoxin plasma level in digitalized patients should be measured not less than six hours after any digoxin dose, before or after administration of flecainide.

Dairy products (milk, infant formula and possibly yoghurt) may reduce the absorption of flecainide in children and infants.

Treatment with Tambocor is compatible with use of oral anti-coagulants.

Side-effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (≥ 1/10), Common (≥1/ 100 to < 1/10), Uncommon (≥1/1, 000 to < 1/100,)Rare (≥ 1/10, 000 to < 1/ 1, 000), Very rare (< 1/10, 000), not known (cannot be estimated from the available data).

Blood and lymphatic system disorders:
Uncommon: red blood cell count decreased, white blood cell count decreased and platelet count decreased.

Immune system disorders:
Very rare: antinuclear antibody increased with and without systemic inflammation.

Psychiatric disorders:
Rare: hallucination, depression, confusional state, anxiety, amnesia, insomnia.

Nervous system disorders:
Very common: dizziness, which is usually transient
Rare: paraesthesia, ataxia, hypoesthesia, hyperhidrosis, syncope, tremor, flushing, somnolence, headache, neuropathy peripheral, seizure, dyskinesia.

Eye disorders:
Very common: visual impairment, such as diplopia and vision blurred
Very rare: corneal deposits

Ear and labyrinth disorders:
Rare: tinnitus, vertigo

Cardiac disorders:
Common: Proarrhythmia (most likely in patients with structural heart disease)
Frequency not known (cannot be estimated from the available data). Dose related increase inPR and QRS intervals may occur (see section 4.4). Altered pacing threshold (see section 4.4).

Uncommon: Patients with atrial flutter can develop a 1:1 AV conduction with increased heart rate.
Frequency not known: atrioventricular block-second-degree and atrioventricular block third degree, cardiac arrest, bradycardia, cardiac failure/cardiac failure congestive, chest pain, hypotension, myocardial infarction, palpitations, sinus arrest, and tachycardia (AT or VT) or ventricular fibrillation. Demasking of a pre-existing Brugada syndrome.

Respiratory, thoracic and mediastinal disorders:
Common: dyspnoea
Rare: pneumonitis
Frequency not known: pulmonary fibrosis, insterstital lung disease.

Gastrointestinal disorders:
Uncommon: nausea, vomiting, constipation, abdominal pain, increased appetite, diarrhea, dyspepsia, flatulence.

Hepatobiliary disorders:
Rare: hepatic enzymes with or without jaundice.
Frequency not known: hepatic dysfunction.

Skin and subcutaneous tissue disorders:
Uncommon: dermatitis allergic, including rash, alopecia.
Rare: serious urticarial
Very rare: photosensitivity reaction.

Musculoskeletal and connective tissue disorders:
Not known: Arthralgia and Myalgia

General disorders and administration site conditions:
Common: asthenia, fatigue, pyrexia, oedema.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via HPRA Pharmacovigilance, Website: www.hpra.ie.

Overdosage
No specific antidote is known. There is no known way of rapidly removing flecainide from the system, but forced acid diuresis may theoretically be helpful. Neither dialysis nor haemoperfusion are helpful and injections of anticholinergics are not recommended.
Treatment may include therapy with an inotropic agent, intravenous calcium, giving circulatory assistance (e.g. balloon pumping), mechanically assisting respiration or temporarily inserting a transvenous pacemaker if there are severe conduction disturbances or the patients left ventricular function is otherwise compromised. Intravenous 8.4 % sodium bicarbonate reduces flecainide activity. Intravenous fat emulsion and ECMO could be considered on a case-by-case basis

Use in Pregnancy and Lactation
There is no evidence as to drug safety in human pregnancy. Use should be avoided during pregnancy or lactation unless considered essential by the physician.
Studies in animals have shown reproductive toxicity. The relevance of these findings to humans has not been established. Data have shown that flecainide crosses the placenta to the foetus in patients taking flecainide during pregnancy.
Flecainide is excreted in human milk and appears in concentrations which reflect those in maternal blood. The case of adverse effects to the nursing infant is very small.

Requirements for handling and storage
Dilution: When necessary Tambocor 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.

When diluted the product should be used within 24 hours when stored at ambient room temperature.
Diluted Product: Chemical and physical in-use stability of the diluted solutions have been demonstrated for 24 hours at room temperature.
From a microbiological point of view, the product should be used immediately, in-use storage times and conditions prior to use are the responsibility of the user and would not normally be longer than 24 hours at 2 to 8°C, unless dilution has taken place in controlled and validated aseptic conditions.
Do not store above 30°C. Do not freeze.
Keep the ampoules in the outer carton.
The label contains an expiry date. Do not use Tambocor Injection after the expiry date which is stated on the carton and ampoule after Exp.
The expiry date refers to the last day of that month.
For single use only.
Keep out of the sight and reach of children.