Tambocor™ CR 50
Tambocor™ CR 100
Tambocor™ CR 150
Tambocor™ CR 200

SCHEDULING STATUS
S4

PROPRIETARY NAMES AND DOSAGE FORM
TAMBOCOR CR 50 (capsule)
TAMBOCOR CR 100 (capsule)
TAMBOCOR CR 150 (capsule)
TAMBOCOR CR 200 (capsule)

COMPOSITION
TAMBOCOR CR 50: Each controlled release capsule contains flecainide acetate 50 mg
TAMBOCOR CR 100: Each controlled release capsule contains flecainide acetate 100 mg
TAMBOCOR CR 150: Each controlled release capsule contains flecainide acetate 150 mg
TAMBOCOR CR 200: Each controlled release capsule contains flecainide acetate 200 mg
Excipients: Erythrosine, gelatin, iron oxide black, macrogol, methacrylic acid, microcrystalline cellulose, propylene glycol, shellac, talc, titanium dioxide.

PHARMACOLOGICAL CLASSIFICATION
A 6.2 Cardiac medicines (depressants)
(Class I anti-dysrhythmic)

PHARMACOLOGICAL ACTION
Pharmacokinetics

TAMBOCOR CR capsules contain polymer-coated microgranules, allowing controlled release of flecainide acetate. Each microgranule constitutes a controlled release form of flecainide acetate, allowing prolongation of the absorption time without modifying the elimination parameters.
Absorption of flecainide acetate via the oral route is greater than 80 % of the dose administered. After administration of one flecainide acetate capsule, plasma flecainide concentrations gradually increase after a lag time of 2 to 3 hours to reach a peak between the 21st and 25th hour and remain at plateau levels until after the 30th hour. Plasma concentrations are proportional to the dose between 50 mg and 300 mg. This dose relation is maintained at steady-state for doses of 100 to 300 mg.
Absorption of flecainide acetate from capsule is not modified by food.
Steady-state is reached after five days of treatment with minimal fluctuations, and 50 % flattening of plasma concentration peaks compared to the tablet form.
Flecainide acetate is widely and rapidly distributed in the tissues.
The mean volume of distribution is 8,31 ℓ/kg.
Protein binding is low (about 40 %).
Flecainide acetate is essentially eliminated in the urine:
25 % of the dose is eliminated after 24 hours in the unchanged form. Haemodialysis does not appear to be an effective way to eliminate flecainide acetate. Flecainide acetate is also eliminated by metabolism, especially via the cytochrome 2D6 pathway.
The apparent plasma elimination half-life is about 12 to 14 hours; it is not modified with the flecainide acetate capsule form.
No enzyme induction or inhibition phenomena have been observed after prolonged dosing.

Pharmacodynamics
Flecainide acetate is a class I anti-dysrhythmic (local anaesthetic) agent. Flecainide acetate possesses a negative inotropic effect.

Flecainide acetate:

- prolongs intra-atrial, nodal and intraventricular conduction times
- slightly increases atrial and ventricular effective refractory periods
- increases the effective refractory period of the atrioventricular node
- increases the refractory period of retrograde and anterograde accessory pathways
- does not induce any significant modifications of heart rate except in patients with sinus node dysfunction

There is a marked linear relationship between plasma flecainide acetate concentrations and widening of the QRS complex, a marker of the anti-dysrhythmic effect.

INDICATIONS

Treatment with **TAMBOCOR CR** should be initiated in a hospital for control of the following dysrhythmias:

- Sustained ventricular tachydysrhythmias
- AV nodal reciprocating tachycardia; Wolff-Parkinson-White Syndrome and similar conditions with accessory pathway and anterograde or retrograde conduction
- Paroxysmal atrial fibrillation in patients with disabling symptoms. Dysrhythmias of recent onset will respond more readily

In addition, **TAMBOCOR CR** is indicated in premature ventricular contractions and/or non-sustained ventricular tachycardia which are causing disabling symptoms.
TAMBOCOR CR can be used for the maintenance of normal rhythm following conversion by other means.

CONTRAINDICATIONS

TAMBOCOR CR must never be used in:

- Patients who are hypersensitive to flecainide acetate or any of the excipients of **TAMBOCOR CR**
- Myocardial infarction (old or acute)
- Heart failure, regardless of the type of dysrhythmia
- Complete left bundle branch block, bifascicular block, 2nd and 3rd degree atrioventricular block, sinus node dysfunction and atrial disease, in the absence of pacing
- Patients with long standing atrial fibrillation and haemodynamically significant valvular heart disease

TAMBOCOR CR is generally not recommended in combination with class I anti-dysrhythmics.

WARNINGS AND SPECIAL PRECAUTIONS

Warning:
TAMBOCOR CR was tested in a multicentre randomised double-blind trial (CAST trial) in patients with asymptomatic, non-life-threatening ventricular dysrhythmia with a history of myocardial infarction more than 6 days and less than 2 years before inclusion. The incidence of mortality and nonfatal cardiac arrests was higher with flecainide than in the placebo control group.
No controlled trial has demonstrated a beneficial effect of **TAMBOCOR CR** in terms of survival or sudden death.

Special Precautions:
Pro-dysrhythmic effects:

TAMBOCOR CR can induce a more severe form of dysrhythmia, increase the frequency of a pre-existing dysrhythmia or worsen the severity of symptoms.
Spontaneous variations of the dysrhythmia specific to the patient may be difficult to distinguish from deterioration induced by administration of a medicinal product. Treatment should be stopped in the case of more numerous or polymorphous ventricular premature complexes.

History of heart failure:
Because of its negative inotropic action, **TAMBOCOR CR** must be prescribed under strict surveillance of cardiac function in patients with a history or symptoms suggestive of heart failure.

Electrocardiographic changes:
TAMBOCOR CR must be administered cautiously in patients with pre-existing conduction disorders.
It should be stopped if atrioventricular block, permanent complete branch block or sinoatrial block occur during treatment. The dosage should be decreased in the case of widening of QRS complexes by more than 25 % of baseline values.

In the case of modification of the dosage of **TAMBOCOR CR** or concomitant treatment able to affect cardiac conduction, patients, especially those with pre-existing conduction disorders, should be closely monitored by electrocardiogram.

Electrolyte disorders:
Hypokalaemia, hyperkalaemia or hypomagnesaemia can potentiate the pro-dysrhythmic effects of class I anti-dysrhythmic and must therefore be corrected before administration of **TAMBOCOR CR.**

Renal insufficiency, elderly:
In patients with renal insufficiency and/or elderly subjects, the rate of elimination of **TAMBOCOR CR** can be decreased, resulting in a risk of plasma and tissue accumulation of the medicinal product which can be responsible for adverse effects.
This risk justifies dosage adjustment.

Elderly patients:
The rate of flecainide elimination from plasma may be reduced in elderly people and doses may need to be adjusted accordingly. The occurrence of cardiac arrest and symptomatic conduction disturbances is higher in the elderly.

Children:
TAMBOCOR CR is not recommended in children under 18 years of age, as there is insufficient evidence of its use in this age group.

Hepatic impairment:
Insufficient efficacy and safety data are available to recommend the use of **TAMBOCOR CR** in patients with liver function impairment.

INTERACTIONS
Class I anti-dysrhythmics: **TAMBOCOR CR** must not be coprescribed with other class I anti-dysrhythmics, apart from exceptional cases, because of the increased risk of adverse cardiac effects (automatism, conduction, prodysrhythmic effects, inotropism).
Other classes of anti-dysrhythmics: combination with anti-dysrhythmics of other classes is only exceptionally indicated and is usually very delicate, requiring close clinical and ECG monitoring.
Combination with medicinal products possessing negative inotropic or bradycardic properties and/or slowing atrioventricular conduction or intraventricular conduction (beta-blockers, amiodarone, digitalis glycosides, verapamil and diltiazem, tricyclic antidepressants, local anaesthetics) requires close clinical and ECG surveillance, particularly in the elderly and at the beginning of treatment.
Cimetidine: Early studies suggest co-administration of flecainide and cimetidine results in an increase of plasma flecainide levels probably due to a decrease in biotransformation of flecainide in the presence of cimetidine. Cimetidine can cause plasma flecainide to double, making reduction of flecainide dosage of up to 50 % advisable.

PREGNANCY AND LACTATION
Safety in pregnancy and lactation has not been established.
It should not be administrated in the case of suspected pregnancy or during the first three months of pregnancy.

DOSAGE AND DIRECTIONS FOR USE
Adults:
The controlled-release form of **TAMBOCOR CR** is administrated as a once-daily dose.

1. Documented supraventricular tachycardia:
   The recommended starting dosage is 100 mg per day.
   An increase of the dosage should be considered only after a period of 4 to 5 days.
   The optimal dosage is 200 mg per day.
   The maximum dosage is 300 mg per day.
2. Documented ventricular tachycardia:
   The usual dosage is 200 mg per day.
   An increase of the dosage should only be considered after a period of 4 to 5 days.
   The maximum dosage is 300 mg per day.
3. High-risk patients:
   [e.g. elderly, history or symptoms suggestive of heart failure, severe renal insufficiency (creatinine clearance less than or equal to 30 mℓ/min/m^2)]
   The initial dose must not exceed 100 mg per 24 hours: it ranges from 50 to 100 mg/24 hours depending on the patient's state.

The dosage can be increased or decreased by steps of 50 mg per day, bearing in mind that a minimum period of 4 to 5 days is necessary to establish new steady-state plasma levels after each modification. Patients should be monitored by clinical examination and by electrocardiogram.
Note: If a patient is changed over from **TAMBOCOR TABLETS** to **TAMBOCOR CR**, the dosage should be based on the total daily dose (e.g. 2 x 100 mg **TAMBOCOR TABLETS** to **TAMBOCOR CR 200**).

SIDE EFFECTS
The following side effects have been observed during treatment with **TAMBOCOR CR** with the following frequencies: Very common (≥ 1/10); common (≥ 1/100, < 1/10); uncommon (≥ 1/1 000, < 1/100); rare (≥ 1/10 000, < 1/1 000).

Nervous system disorders:
Very common: Giddiness, dizziness, and light-headedness which are usually transient have been reported. During long term oral therapy peripheral neuropathy, paraesthesia and ataxia have been reported.

Eye disorders:
Very common: Visual disturbances, such as double vision and blurring of vision may occur.
Uncommon: Corneal deposits have been reported.

Cardiac disorders:
Common: Pro-dysrhythmic effects may occur in any patient but very common in patients with structural heart disease and/or significant left ventricular impairment.
In patients with atrial flutter the use of **TAMBOCOR CR** has been associated with 1:1 AV conduction following initial arterial slowing with resultant ventricular acceleration. This has been seen to be very common following the use of the injection for acute conversion. This effect is usually short lived and abates quickly following cessation of therapy.

Respiratory, thoracic and mediastinal disorders:
Very rare: pulmonary fibrosis, interstitial lung disease or pneumonitis

Gastrointestinal disorders:
Rare: Nausea and vomiting.

Hepato-biliary disorders:
Rare: Elevated liver enzymes and jaundice have been reported in association with **TAMBOCOR CR** treatment.

Skin and subcutaneous tissue disorders:
Rare: Photosensitivity has been reported.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT
Overdose with **TAMBOCOR CR** requires surveillance in hospital in a specialised unit. It is marked by electrocardiographic changes, particularly widening of the QRS complex, and development of cardiogenic shock. Treatment is essentially symptomatic.
It can be accompanied by neurosensory, neuropsychiatric and cardiac symptoms.

IDENTIFICATION
TAMBOCOR CR 50: White opaque cap and a white opaque body, with 3M 50 printed in black ink.
TAMBOCOR CR 100: Light grey cap and an opaque white body, with 3M 100 printed in black ink.
TAMBOCOR CR 150: Opaque grey cap and an opaque grey body, with 3M 150 printed in black ink.
TAMBOCOR CR 200: Light grey cap and an opaque pink body, with 3M 200 printed in black ink.

PRESENTATION
Blister packs of 15, 30 and 60 capsules.
Blisters are made of clear UPVC / PVDC with aluminium foil backing.

STORAGE INSTRUCTIONS
Store in a cool, dry place at or below 25 °C. Protect from light.
Keep blisters in the carton until required for use.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBER
TAMBOCOR CR 50: 37/6.2/0198
TAMBOCOR CR 100: 37/6.2/0199
TAMBOCOR CR 150: 37/6.2/0200
TAMBOCOR CR 200: 37/6.2/0201

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION
iNova Pharmaceuticals (Pty) Ltd, 15E Riley Road, Bedfordview, 2007, South Africa.

DATE OF PUBLICATION OF THIS PACKAGE INSERT
2 March 2012

Tambocor™ CR 50
Tambocor™ CR 100
Tambocor™ CR 150
Tambocor™ CR 200

SCHEDULING STATUS
S4

PROPRIETARY NAME, STRENGTH AND PHARMACEUTICAL FORM
TAMBOCOR CR 50 (flecainide acetate 50 mg capsule)
TAMBOCOR CR 100 (flecainide acetate 100 mg capsule)
TAMBOCOR CR 150 (flecainide acetate 150 mg capsule)
TAMBOCOR CR 200 (flecainide acetate 200 mg capsule)

Read all of this leaflet carefully before you start taking TAMBOCOR CR

- Keep this leaflet. You may need to read it again.
- If you have further questions, please ask your doctor or your pharmacist.
- **TAMBOCOR CR** has been prescribed for you personally and you should not share your medicine with other people. It may harm them, even if their symptoms are the same as yours.

WHAT TAMBOCOR CR CONTAINS
TAMBOCOR CR 50: The active substance is flecainide acetate 50 mg.
TAMBOCOR CR 100: The active substance is flecainide acetate 100 mg.
TAMBOCOR CR 150: The active substance is flecainide acetate 150 mg.
TAMBOCOR CR 200: The active substance is flecainide acetate 200 mg.
The other ingredients are erythrosine, gelatin, iron oxide black, macrogol, methacrylic acid, microcrystalline cellulose, propylene glycol, shellac, talc, titanium oxide.

WHAT TAMBOCOR CR IS USED FOR
TAMBOCOR CR is a cardiac medicine (Class I anti – dysrhythmic [local anaesthetic]).
TAMBOCOR CR is used to regulate the rate and rhythm of the heart.

BEFORE YOU TAKE TAMBOCOR CR
Do not take TAMBOCOR CR if:

- you are hypersensitive (allergic) to flecainide acetate or any of the other ingredients of **TAMBOCOR CR**
- you suffer from kidney disease, heart failure or heart block (missed heart beats)
- you have ever had a heart attack, or wear a heart pacemaker, or suffer from liver disease or heart valve disease

Please tell your doctor if you suffer from high blood pressure or angina.
This medication should not be used by children under 18 years old.

Take special care with TAMBOCOR CR:

- if you have pre-existing dysrhythmia (irregular heart beat)
- if you have a history of heart failure
- if you have kidney disease
- if you have pre-existing conduction disorders in the heart
- if you have too little or too much potassium in the blood
- if you have too little magnesium in the blood

Pregnancy and breastfeeding
Do not use **TAMBOCOR CR** if you are pregnant or breastfeeding.
If you are pregnant or breastfeeding your baby while taking **TAMBOCOR CR**, please consult your doctor, pharmacist or other healthcare professional for advice.

Taking other medicines with TAMBOCOR CR
If you are taking other medicines on a regular basis, including complementary or traditional medicines, the use of **TAMBOCOR CR** with these medicines may cause undesirable interactions.
Please consult your doctor, pharmacist or other healthcare professional, for advice if you are taking:

- Any other medicine used to regulate rate and rhythm of the heart
- Medicines that slow down heart rate and/or conduction such as beta-blockers, amiodarone, digitalis glycosides, verapamil, diltiazem, tricyclic antidepressants, local anaesthetics
- Cimetidine (medicine used to treat stomach ulcers)

HOW TO TAKE TAMBOCOR CR
Do not share medicines prescribed for you with any other person.
Your doctor will decide how you should take **TAMBOCOR CR**.
If you have the impression that the effect of **TAMBOCOR CR** is too strong or too weak, tell your doctor or pharmacist.

If you take more TAMBOCOR CR than you should
In the event of overdosage, consult your doctor or pharmacist. If neither is available, contact the nearest hospital or poison control centre.

If you forget to take TAMBOCOR CR
Do not take a double dose to make up for forgotten individual doses.

POSSIBLE SIDE EFFECTS
TAMBOCOR CR can have the following side effects, including:

- feeling dizzy
- giddy or lightheaded
- weak or tired
- swelling
- double vision or blurring of vision
- feeling sick and vomiting
- yellowing of the skin (jaundice)
- sensitivity to the effects of sunlight

Not all side effects reported for **TAMBOCOR CR** are included in this leaflet. Should your general health worsen or if you experience untoward effects while taking this medicine, please consult your doctor, pharmacist or other healthcare professional for advice.
If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

STORING AND DISPOSING OF TAMBOCOR CR
Store the capsules in a cool, dry place at or below 25 °C. In order to protect from light, keep blister pack in the outer carton.
Keep all medicines out of the reach and sight of children. Return all unused medicine to your pharmacist. Do not dispose of unused medicine in drains or sewerage systems (e.g. toilets).

PRESENTATION OF TAMBOCOR CR
Blister packs of 15, 30 and 60 capsules.
Blisters are made of clear UPVC / PVC with aluminium foil backing.

IDENTIFICATION OF TAMBOCOR CR
TAMBOCOR CR 50: White opaque cap with a white opaque body, with 3M 50 printed in black ink.
TAMBOCOR CR 100: Light grey cap with opaque white body, with 3M 100 printed in black ink.
TAMBOCOR CR 150: Opaque grey cap and an opaque grey body, with 3M 150 printed in black ink.
TAMBOCOR CR 200: Light grey cap and an opaque pink body, with 3M 200 printed in black ink.

REGISTRATION NUMBER
TAMBOCOR CR 50: 37/6.2/0198
TAMBOCOR CR 100: 37/6.2/0199
TAMBOCOR CR 150: 37/6.2/0200
TAMBOCOR CR 200: 37/6.2/0201

NAMES AND ADDRESS OF REGISTRATION HOLDER
iNova Pharmaceuticals (Pty) Ltd, 15E Riley Road, Bedfordview, 2007, South Africa.

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Customer	iNova Pharma		colours used:
Description	Tambocor CR 50, 100, 150 + 200 mg Lft	■	PANTONE BLACK
Part No	6204 2564 1		
Leaflet Size	190 mm x 594 mm		
Drawing Ref	PE00228 v1	■	KEYLINE
Text Size	11.5 point on 9 pt leading		
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Date	11.05.2016		***SOUTH AFRICA***

Antony Whitton
Digitally signed by Antony Whitton
DN: cn=Antony Whitton, o, ou=Technically approved, email=awhitton@mmm.com, c=GB
Date: 2016.05.12 12:25:06 +01'00'

Tambocor™ CR 50
Tambocor™ CR 100
Tambocor™ CR 150
Tambocor™ CR 200

SKEDULERINGSTATUS
S4

EIENDOMSNAME EN DOSEERVORM
TAMBOCOR CR 50 (kapsule)
TAMBOCOR CR 100 (kapsule)
TAMBOCOR CR 150 (kapsule)
TAMBOCOR CR 200 (kapsule)

SAMESTELLING
TAMBOCOR CR 50: elke kapsule vir gekontroleerde vrystelling bevat 50 mg flekaïniedasetaat
TAMBOCOR CR 100: elke kapsule vir gekontroleerde vrystelling bevat 100 mg flekaïniedasetaat
TAMBOCOR CR 150: elke kapsule vir gekontroleerde vrystelling bevat 150 mg flekaïniedasetaat
TAMBOCOR CR 200: elke kapsule vir gekontroleerde vrystelling bevat 200 mg flekaïniedasetaat
Onaktiewe bestanddele: Eritrosien, gelatien, swart ysteroksied, makrogol, metakrielsuur, mikrokristallyne sellulose, propileenglikol, skilferlak, talk, titaandioksied.

FARMAKOLOGIESE KLASSIFIKASIE
A 6.2 Hartmedisyne (onderdrukkers)
(klas I-antidisritmiese middel)

FARMAKOLOGIESE WERKING
Farmakokinetika

TAMBOCOR CR-kapsules bevat polimeerbedekte mikrogranules, wat gekontroleerde vrystelling van flekaïniedasetaat bewerkstellig. Elke mikrogranule bestaan in 'n vorm vir gekontroleerde vrystelling van flekaïniedasetaat wat verlenging van die absorpsietyd sonder verandering in die eliminasie moontlik maak.

Absorpsie van flekaïniedasetaat na orale dosering bedra meer as 80 % van die toegediende dosis. Na toediening van een kapsule flekaïniedasetaat styg die konsentrasie van flekaïnied na 'n tydsverloop van 2 tot 3 uur geleidelik om tussen die 21ste en 25ste uur 'n piek te bereik en dit bly tot na die 30ste uur op platovlakke. In die dosisgebied van 50 tot 300 mg is die plasmakonsentrasies in verhouding tot die dosis. Hierdie verhouding word by gelykvlakke vir dosisse van 100 tot 300 mg volgehou.

Absorpsie van flekaïniedasetaat vanaf die kapsule word nie deur voedsel beïnvloed nie.

Gelykvlakke met minimale wisseling word na vyf dae bereik met pieke van plasmakonsentrasies 50 % laer as met tablette.

Flekaïniedasetaat versprei wyd en vinnig in die weefsel in. Die gemiddelde volume van verspreiding is 8,31 ℓ/kg. Binding aan proteïene is laag (ongeveer 40 %).

Flekaïniedasetaat word hoofsaaklik in die urien uitgeskei:

25 % van die dosis word binne 24 uur onveranderd in die urien uitgeskei. Dit lyk nie asof hemodialise 'n effektiewe manier is om flekaïniedasetaat te verwyder nie.
Flekaïniedasetaat word ook metabolies, veral deur die sitochroom 2D6-weg, uitgeskei.

Die oënskynlike eliminasiehalfleeftyd uit die plasma is ongeveer 12 tot 14 uur; dit is nie anders vir flekaïniedasetaat in die kapsulevorm nie.

Geen induksie of remming van ensieme is na langdurige dosering waargeneem nie.

Farmakodinamika
Flekaïniedasetaat is 'n klas I-antidisritmiese middel (lokale anestetikum). Flekaïniedasetaat het 'n negatiewe inotropiese effek.

Flekaïniedasetaat:

- verleng intra-atriale, nodale en intraventrikulêre geleidingstyd
- verleng atriale en ventrikulêre effektiewe refraktoriese periodes
- verleng die effektiewe refraktoriese periode van die atrioventrikulêre node
- verleng die refraktoriese periode van retrograde en anterograde bykomende weë
- induseer nie enige beduidende veranderinge in harttempo nie, behalwe in gevalle van pasiënte met sinusnodedisfunksie

Daar is 'n merkbare lineêre verband tussen die plasmakonsentrasies van flekaïniedasetaat en die verwyding van die QRS-kompleks wat 'n merker van die antidisritmiese effek is.

INDIKASIES

Behandeling met **TAMBOCOR CR** moet in die hospitaal begin in die behandeling van die volgende tipes disritimeë:

- Volgehoue ventrikulêre tagidisritmie
- AV-nodale resiprokatiewe tagikardie; Wolff-Parkinson-Whitesindroom en soortgelyke toestande met geleiding deur die bykomende weg en anterograde of retrograde geleiding
- Paroksismale atriale fibrillasie in pasiënte met stremmende simptome. Disritimeë wat pas tevore begin het, sal meer geredelik reageer

Daarby is **TAMBOCOR CR** aangedui vir premature ventrikulêre kontraksies en/of nie-volgehoue ventrikulêre tagikardie wat stremmende simptome veroorsaak.

TAMBOCOR CR kan gebruik word om normale ritme na omskakeling op ander maniere te onderhou.

KONTRA-INDIKASIES

TAMBOCOR CR moet nooit vir die volgende gebruik word nie:

- Pasiënte wat hipersensitief vir flekaïniedasetaat of enige van die hulpstowwe in **TAMBOCOR CR** is
- Miokardiale infarksie (oud of akuut)
- Hartversaking, onafgesien van die tipe disritmie
- Volledige linkerbondeltakblok, bifassikulêre blok, 2de- en 3de-graadse atrioventrikulêre blok, sinusnodedisfunksie en atriale siekte sonder 'n pasaangeër
- Pasiënte met 'n jare lange atriale fibrillasie en hemodinamies beduidende hartklepsiekte

Oor die algemeen word **TAMBOCOR CR** nie in kombinasie met klas I-antidisritmiese middels aanbeveel nie.

WAARSKUWINGS EN SPESIALE VOORSORGMAATREËLS

Waarskuwing:
TAMBOCOR CR is in 'n ewekansige, multisentrum, dubbelblinde proef (die CAST-proef) getoets in pasiënte met asimptomatiese, nie-lewensbedreigende ventrikulêre disritmie met 'n geskiedenis van miokardiale infarksie van meer as 6 dae en minder as 2 jaar voor insluiting in die proef. Die voorkoms van sterftes en nie-dodelike hartarres was hoër met flekaïenied as in die plasebogroep.
Geen gekontroleerde proef het 'n voordelige effek van **TAMBOCOR CR** in terme van oorlewing of skielike dood aangetoon nie.

Spesiale voorsorgmaatreëls:
Prodisritmiese effekte:

TAMBOCOR CR kan 'n erger vorm van disritmie induseer, die frekwensie van bestaande disritmie verhoog of die graad van simptome vererger.

Dit kan moeilik wees om spontane variasie in disritmie van 'n spesifieke pasiënt te onderskei van agteruitgang vanweë toediening van die medisinale produk. Behandeling moet gestaak word in geval van meer dikwelse of polimorfe ventrikulêre premature komplekse.

Geskiedenis van hartversaking:

Vanweë die negatiewe inotropiese werking moet **TAMBOCOR CR** met streng monitering van hartfunksie voorgeskryf word aan pasiënte met 'n geskiedenis of simptome aanduidend van hartversaking.

Veranderings in elektrokardiogram:

TAMBOCOR CR moet versigtig toegedien word aan pasiënte met bestaande versteurings in geleiding.

Dit moet gestaak word as atrioventrikulêre blokkering, permanente volledig takblokkering of sinoatriale blokkering tydens behandeling voorkom. As die QRS-komplekse met meer as 25% vanaf die basislynwaardes verwyd, moet die dosis verlaag word.

As die dosis van **TAMBOCOR CR** verander word of as middels wat hartgeleiding beïnvloed saam gegee word, moet pasiënte, en veral dié met versteurings in geleiding, noukeurig met elektrokardiografie gemonitor word.

Versteurings in elektrolietbalans:
Hipokalemie, hiperkalemie of hipomagnesemie kan die pro-disritmiese effekte van klas I-antidisritmiese middels versterk en moet dus reggestel word voordat **TAMBOCOR CR** toegedien word.

Swak nierfunksie, bejaardes:
Die tempo van uitskeiding van **TAMBOCOR CR** kan stadiger wees in pasiënte met swak nierfunksie en/of in bejaardes en dit hou 'n risiko vir die opbou van die medisinale produk in plasma en weefsel in wat newe-effekte kan veroorsaak. Hierdie risiko regverdig verlaging van die dosis.

Bejaarde pasiënte:
Die tempo van uitskeiding van flekaïnied uit die plasma kan stadiger in bejaardes wees en dit mag nodig wees dat die dosisse dienooreenkomstig aangepas moet word. Die voorkoms van hartarres en simptomatiese versteurings in geleiding is hoër in bejaardes.

Kinders:
TAMBOCOR CR word nie vir gebruik deur kinders jonger as 18 jaar aanbeveel nie omdat daar nie genoeg getuienis vir gebruik deur hierdie ouderdomsgroep is nie.

Swak lewerfunksie:

Daar is nie genoeg data oor die effektiwiteit en veiligheid om **TAMBOCOR CR** vir pasiënte met swak lewerfunksie aan te beveel nie.

INTERAKSIES

Klas I-antidisritmiese middels: Vanweë die hoër risiko vir nadelige effekte op die hart (outomatisme, geleiding, prodisritmiese effekte, inotropie) moet **TAMBOCOR CR**, behalwe in uitsonderlike gevalle, nie saam met klas I-antidisritmiese middels voorgeskryf word nie.

Ander klasse antidisritmiese middels: kombinasie met ander klasse antidisritmiese middels is slegs in uitsonderlike gevalle aangedui en is gewoonlik baie delikaat waarvoor noukeurige monitering van kliniese beeld en EKG nodig is.

Noukeurige monitering van kliniese beeld en EKG, en veral vir bejaardes en aan die begin van behandeling, is ook nodig tydens kombinasie met medisinale produkte wat negatiewe inotropiese eienskappe besit of bradikardiese effekte uitoefen en/of atrioventrikulêre of intraventrikulêre geleiding vertraag (beta-blokkeerders, amiodaroon, digitalisglikosiede, verapamil en diltiasem, trisikliese antidepressante, lokale verdowers)

Simetidien: Vroeë studies toon dat toediening van flekaïnied en simetidien vlakke van flekaïnied in die plasma verhoog, waarskynlik vanweë 'n verlaging in die biotransformasie van flekaïnied in teenwoordigheid van simetidien. Simetidien kan maak dat die plasmavlakke van flekaïenied verdubbel sodat dit raadsaam is om die dosis van flekaïnied met tot 50 % te verminder.

SWANGERSKAP EN BORSVOEDING

Die veiligheid tydens swangerskap en borsvoeding is nie bepaal nie. Dit moet nie in geval van vermoedelike swangerskap of tydens die eerste drie maande van swangerskap gegee word nie.

DOSIS EN GEBRUIKSAANWYSINGS
Volwassenes:

TAMBOCOR CR vir gekontroleerde vrystelling word een keer per dag toegedien.

1. Gedokumenteerde supraventrikulêre tagikardie:~
   Die aanbevole aanvangsdosis is 100 mg per dag.
   'n Verhoging in die dosis moet eers na 'n periode van 4 tot 5 dae oorweeg word.
   Die optimale dosis is 200 mg per dag.
   Die maksimum dosis is 300 mg per dag.
2. Gedokumenteerde ventrikulêre tagikardie:
   Die gewone dosis is 200 mg per dag.
   'n Verhoging in die dosis moet eers na 'n periode van 4 tot 5 dae oorweeg word.
   Die maksimum dosis is 300 mg per dag.
3. Hoë risiko pasiënte:
   [bv. bejaardes, geskiedenis of simptome aanduidend van hartversaking, erge swak nierfunksie (kreatinienopruiming minder of gelyk aan 30 mℓ/min/m^2)]
   Die aanvangsdosis moet nie meer as 100 mg in 24 uur wees nie: dit wissel van 50 tot 100 mg/24 uur afhangende van die pasiënt se toestand.
   Die dosis kan met hoeveelhede van 50 mg per dag verhoog of verlaag word terwyl in gedagte gehou word dat 'n minimum periode van 4 tot 5 dae na elke aanpassing in die dosis nodig is om nuwe gelykvlakke in die plasma te bereik.
   Pasiënte moet met kliniese ondersoek en elektrokardiografie gemonitor word

Opmerking: As 'n pasiënt van **TAMBOCOR tablette** na **TAMBOCOR CR** oorgeskakel word, moet die dosis op die totale daaglikse dosis gebaseer wees (bv. 2 x 100 mg **TAMBOCOR tablette** na **TAMBOCOR CR 200**).

NEWE-EFFEKTE
Die volgende newe effekte is met die volgende frekwensies tydens behandeling met **TAMBOCOR CR** waargeneem:

baie algemeen (≥ 1/10); algemeen (≥ 1/100, < 1/10); soms (≥ 1/1 000, < 1/100); selde (≥ 1/10 000, < 1/1 000).

Versteurings in senustelsel:
Baie algemeen: Dronkheid, duiseligheid en lighoofdigheid wat gewoonlik tydelik is, is aangemeld. Tydens orale behandeling oor die lang termyn is perifere neuropatie, parestesie en ataksie aangemeld.

Oogversteurings:
Baie algemeen: Versteurings in visie, soos dubbelvisie en dowwe visie kan voorkom.
Soms: Neerslag op die korneas is ook aangemeld.

Hartversteurings:
Algemeen: Prodisritmiese effekte kan in enige pasiënt voorkom, maar is baie algemeen in pasiënte met strukturele hartsiekte en/of beduidende verswakte linkerventrikelfunksie.
By pasiënte met atriale fladder mag **TAMBOCOR CR** die atriale tempo vertraag met 1:1 AV geleiding wat die ventrikulêre tempo aansienlik sal versnel. Dit is baie algemeen na inspuiting vir akute oorskakeling waargeneem. Hierdie effek is gewoonlik kort en klaar vinnig na staking van behandeling op.

Respiratoriese, bors en mediastinale versteurings:
Uiters selde: longfibrose, interstisiële longsiekte of pneumonitis

Gastro-intestinale versteurings:
Selde: Naarheid en braking

Hepatobilière versteurings:
Selde: Hoër vlakke lewerensieme en geelsug is met gebruik van **TAMBOCOR CR** aangemeld.

Versteurings van die vel en subkutane weefsel:

Selde: Fotosensitiwiteit is aangemeld.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VIR DIE BEHANDELING DAARVAN

Monitering in 'n gespesialiseerde eenheid in 'n hospitaal is na oordosering met **TAMBOCOR CR** nodig. Dit word gekenmerk deur veranderings in die elektrokardiogram en veral 'n verwyding van die QRS-kompleks en die ontwikkeling van kardiogeniese skok. Behandeling is grootliks simptomaties.

Dit kan met neurosensoriese en neuropsigiatriese simptome en effekte op die hart gepaardgaan.

IDENTIFIKASIE

TAMBOCOR CR 50: Wit ondeursigtige doppie en 'n wit ondeursigtige romp met 3M 50 in swart ink daarop gedruk.
TAMBOCOR CR 100: Liggrys doppie en 'n wit ondeursigtige romp met 3M 100 in swart ink daarop gedruk.
TAMBOCOR CR 150: Grys ondeursigtige doppie en 'n grys ondeursigtige romp met 3M 150 in swart ink daarop gedruk.
TAMBOCOR CR 200: Liggrys doppie en 'n pienk ondeursigtige romp met 3M 200 in swart ink daarop gedruk.

AANBIEDING
Stulppakke met 15, 30 of 60 kapsules.
Stulppakke is van helder UPVC / PVDC met aluminiumrugkante gemaak.

BERGINGSINSTRUKSIES
Bêre op 'n koel, droë plek teen of benede 25 ºC. Beskerm teen lig.
Hou die stulpstroke in die karton totdat dit benodig word.

HOU BUITE BEREIK VAN KINDERS.

REGISTRASIENOMMERS
TAMBOCOR CR 50: 37/6.2/0198
TAMBOCOR CR 100: 37/6.2/0199
TAMBOCOR CR 150: 37/6.2/0200
TAMBOCOR CR 200: 37/6.2/0201

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE REGISTRASIESERTIFIKAAT
iNova Pharmaceuticals (Edms) Bpk, Rileyweg 15E, Bedfordview, 2007, Suid-Afrika

DATUM VAN PUBLIKASIE VAN HIERDIE VOUBILJET
2 Maart 2012

Tambocor™ CR 50
Tambocor™ CR 100
Tambocor™ CR 150
Tambocor™ CR 200

SKEDULERINGSTATUS
S4

EIENDOMSNAAM, STERKTE EN FARMASEUTIESE VORM
TAMBOCOR CR 50 (flekaïniedasetaat 50 mg kapsule)
TAMBOCOR CR 100 (flekaïniedasetaat 100 mg kapsule)
TAMBOCOR CR 150 (flekaïniedasetaat 150 mg kapsule)
TAMBOCOR CR 200 (flekaïniedasetaat 200 mg kapsule)

Lees hierdie hele voubiljet aandagtig deur voordat jy begin om TAMBOCOR CR te neem

- Hou hierdie voubiljet. Dit mag nodig wees om dit weer te lees.
- Indien jy enige verdere vrae het, raadpleeg asseblief jou dokter of apteker.
- **TAMBOCOR CR** is voorgeskryf vir jou persoonlike gebruik en moet nie met ander mense gedeel word nie. Dit mag hulle nadelig beïnvloed, al ervaar hulle dieselfde simptome as joune.

WAT TAMBOCOR CR BEVAT
TAMBOCOR CR 50: Die aktiewe bestanddeel is 50 mg flekaïniedasetaat.
TAMBOCOR CR 100: Die aktiewe bestanddeel is 100 mg flekaïniedasetaat.
TAMBOCOR CR 150: Die aktiewe bestanddeel is 150 mg flekaïniedasetaat.
TAMBOCOR CR 200: Die aktiewe bestanddeel is 200 mg flekaïniedasetaat.
Die ander bestanddele is eritrosien, gelatien, swart ysteroksied, makrogol, metakrielsuur, mikrokristallyne sellulose, propileenglikol, skilferlak, talk, titaandioksied.

WAARVOOR TAMBOCOR CR GEBRUIK WORD
TAMBOCOR CR is medikasie wat vir die hart gebruik word (klas I-antidisritmiese middel [lokale verdowing]).

TAMBOCOR CR word gebruik om die tempo en ritme van die hart te reguleer.

VOOR U TAMBOCOR CR GEBRUIK
Moet nie **TAMBOCOR CR** neem indien:

- jy hipersensitief (allergies) is vir flekaïniedasetaat of enige van die ander bestanddele van **TAMBOCOR CR** nie
- jy ly aan nierversaking, hartversaking of hartblok (gemiste hartslae)
- jy al ooit 'n hartaanval gehad het, 'n pasaangeër dra, of ly aan lewersiekte of hartklepsiekte

Vertel asseblief jou dokter indien jy ly aan hoë bloeddruk of angina.
Hierdie medikasie moet nie gebruik word deur kinders jonger as 18 jaar nie.

Spesiale sorg moet geneem word met die gebruik van TAMBOCOR CR:

- indien jy voorafbestaande disritmie het (ongereelde hartklop)
- indien jy 'n geskiedenis het van hartversaking
- indien jy niersiekte het
- indien jy voorafbestaande geleidingsversteurings van die hart het
- indien jy te min of te veel kalium in jou bloed het
- indien jy te min magnesium in jou bloed het

Swangerskap en Borsvoeding
Moet nie **TAMBOCOR CR** gebruik as jy swanger is of terwyl jy borsvoed nie.
Indien jy swanger is of jou baba borsvoed tydens die gebruik van **TAMBOCOR CR**, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir advies.

Gebruik van ander medisyne tesame met TAMBOCOR CR
Indien jy ander medikasie op 'n gereelde basis neem, insluitend komplimentêre middels, aanvullings of tradisionele medisyne, kan die gebruik van **TAMBOCOR CR** saam met hierdie medisyne ongewenste interaksies veroorsaak.
Raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgdeskundige vir raad wanneer jy die volgende medisyne neem:

- Enige ander medisyne wat gebruik word om die tempo en ritme van die hart te reguleer
- Medisyne wat die hartklop verminder en/of geleiding reguleer soos beta-blokkers, amiodaroon, digitalis-glikosiede, verapamil, diltiasem, trisikliese antidepressante, lokale verdowingsmiddels
- Simetidien (medikasie wat gebruik word om maagsere te behandel)

HOE OM TAMBOCOR CR TE NEEM
Moet nie medisyne wat aan jou voorgeskryf is met enige persoon deel nie.
Jou dokter sal besluit hoe jy **TAMBOCOR CR** moet gebruik.
Indien jy onder die indruk is dat die effekte van **TAMBOCOR CR** te sterk of te swak is, laat weet asseblief jou dokter of apteker.

As jy meer TAMBOCOR CR neem as wat jy moet:
Raadpleeg jou dokter of apteker in die geval van oordosering. Indien nie een van die twee beskikbaar is nie, gaan na die naaste hospitaal of vergiftiginseenhied.

As jy vergeet om TAMBOCOR CR te neem:
Moet nie 'n dubbele dosis neem om op te maak vir die vergete individuele dosisse nie.

MOONTLIKE NEWE-EFFEKTE
TAMBOCOR CR mag die volgende newe effekte hê, insluitend:

- duiseligheid
- dronkheid en lighoofdigheid
- swakheid of moegheid
- swelling
- dubbele visie en versteurde visie
- naarheid en braking
- vergeling van die vel (geelsug)
- sensitiwiteit teenoor die effek van sonlig

Nie alle newe-effekte wat al aangemeld is gedurende die gebruik van **TAMBOCOR CR** is vervat in hierdie voubiljet nie. Indien jou algemene gesondheid agteruitgaan of as jy ongewenste effekte ervaar terwyl jy hierdie medisyne gebruik, raadpleeg asseblief jou dokter, apteker of ander gesondheidsorgdeskundige.
Indien jy enige newe-effekte ervaar wat nie in herdie voubiljet is nie, stel asseblief jou dokter of apteker in kennis daarvan.

BERGING EN VERNIETIGING VAN TAMBOCOR CR
Bêre die kapsules in 'n koel, droë plek teen of benede 25 °C. Ten einde te beskerm teen lig, hou die stulpstroke in die buitenste kartonhouer. Hou alle medisyne buite die bereik en sig van kinders. Neem alle ongebruikte medisyne na jou apteker. Moet nie ongebruikte medisyne in afvoerpype of rioolstelsels (bv. toilette) weggooi nie.

AANBIEDING VAN TAMBOCOR CR
Stulpverpakkings van 15, 30 en 60 kapsules.
Stulpverpakkings is van helder UPVC / PVDC met aluminiumrugkante gemaak.

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NAAM EN ADRES VAN DIE REGISTRASIEHOUER
iNova Pharmaceuticals (Edms) Bpk, Rileyweg 15E, Bedfordview, 2007, Suid-Afrika

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