RANCANGAN LEAFLET

Cordarone®
Amiodarone HCl
150 mg / 3 ml

sanofi

QUALITATIVE AND QUANTITATIVE COMPOSITION :

	per ml /Inj.
Amiodarone (INN) hydrochloride	50 mg
Excipient: polysorbate 80, benzyl alcohol, Water for injection preparation q.s	1 ml

PHARMACEUTICAL FORM
Ampoules containing 3 ml of solution for injection.

CLINICAL PARTICULARS

Therapeutic indications
Serious rhythm disorders when the oral route is not appropriate, namely
- atrial rhythm disorders, with rapid ventricular rhythm;
- Wolf-Parkinson-White syndrome tachycardia;
- documented symptomatic and disabling ventricular rhythm disorders.

PHARMACOLOGICAL PROPERTIES

Pharmacodynamic Properties
Antiarrhythmic properties
- Prolongs phase 3 of the cardiac cell action potential without modifying its height or ascension rate (Vaughan Williams class III). Phase 3 of the action potential is prolonged by slowing the potassium current, without modifying the sodium or calcium current;
- Bradycardiac effect by reducing sinus code automatically. This effect is not antagonized by atropine;
- Non competitive alpha-and beta-adrenergic effect;
- Slowed sinoatrial, atrial and nodal conduction, which is more pronounced the more rapid the rhythm;
- No change in ventricular conduction.
- Prolonged refractory periods and reduced myocardial excitability on atrial, nodal and ventricular levels;
- Slowed conduction and prolonged refractory periods in the atrioventricular accessory channels.
- No negative inotropic effect

Pharmacokinetics properties

The amiodarone injected diminishes very rapidly in the blood as the tissues become impregnated and drug flows to the receptor sites: the effects reach a maximum after approximately 15 minutes and decrease over a period of 4 hours.
Amiodarone is mainly metabolized by cytochrome CYP3A4, and also by cytochrome CYP2C8. Amiodarone and its metabolite, desethylamiodarone, are potential in vitro inhibitors of cytochromes CYP1A1, CYP1A2, CYP2C9, CYP2C19, CYP2D6, CYP3A4, CYP2A6, CYP2B6 and CYP2C8. Amiodarone and desethylamiodarone can also inhibit transport proteins such as P-gp and organic cation transporter 2 (OCT2). One study showed a 1.1% increase in creatinine concentration (an OCT2 substrate).

In vivo data describe an interaction between amiodarone and CYP3A4, CYP2C9, CYP2D6 and P-gp substrates.

Preclinical safety data

In a 2-year carcinogenicity study in rats, amiodarone caused an increase in the number of thyroid follicular tumors (adenomas and/or carcinomas) in both sexes at clinically relevant exposures.
Since mutagenicity findings were negative, an epigenetic rather than genotoxic mechanism has been suggested to explain induction of this type of tumor.
Studies in mice did not show any carcinomas, but dose-dependent thyroid follicular hyperplasia was observed. These effects on the thyroid in rats and mice were probably due to the effects of amiodarone on the synthesis and/or release of thyroid hormones. These findings have little relevance to humans.

DOSAGE AND ADMINISTRATION

Because of the formulation of the product, do not use concentrations of less than 2 ampoules in 500 ml. Use only isotonic glucose solution.
Do not add any other products to the infusion solution.

Amiodarone must be administered by the central venousroute.

Intravenous infusion

Initial treatment: generally 5 mg/kg in glucose solution, preferably using an electric syringe, administered over 20 minutes to 2 hours and repeated 2 or 3 times per 24 hours period. The short action of the drug requires continuation of the infusion.

Maintenance treatment: 10 to 20 mg/kg/day (generally 600 to 800 mg/24 hours, up to 1.2 g/24 hours) in 250 ml of glucose solution over a few days.

Replace by the oral route (3 tablets per day) from the first day of infusion. The dosage may be increased to 4 or even 5 tablets per day.

CONTRAINDICATION

This drug is contra-indicated in the following situations:

- Sinus bradycardia and sinoatrial heart block without a prosthesis;
- Sinus disease without a prosthesis (possible sinus arrest);
- High-degree conduction disorders without a prosthesis;
- Hyperthyroidism because of possible exacerbation by amiodarone;
- Known hypersensitivity to iodine or amiodarone;
- 2nd to 3rd trimesters of pregnancy;
- Circulatory collapse;
- Severe hypotension;
- in children aged less than 3 years due to the presence of benzyl alcohol;
- breast-feeding women;
- combination with drugs liable to induce torsades de pointes:
- class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide, etc).
- class III antiarrhythmics (sotalol, dofetilide, ibutilide, etc.).
- sultopride
- other drugs such as bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, sparfloxacin, vincamine IV, etc. (see interactions with other drug and other forms of interaction)

This drug is GENERALLY INADVISABLE in combination with:

- diltiazem injection,
- halofantrine, pentamidine, moxifloxacin,
- certain neuroleptics (thioridazine, chlorpromazine,levomepromazine, trifluoperazine, cyamemazine, sulpiride, amisulpride, tiapride, pimozide,haloperidol, droperidol),
- beta-blockers other than sotalol and esmolol (see 4.5 Interactions with other drugs and other forms of interaction).

SPECIAL WARNINGS AND PRECAUTIONS FOR USE

Warning

Injectable amiodarone must be administered by the central venous route. In fact, administration by the peripheral venous route can cause local effects such as superficial phlebitis. Injectable amiodarone must be used exclusively as an infusion. In fact, even a very slow injection may exacerbate hypotension, heart failure or severe respiratory failure (see undesirable effects).

Cardiac Disorders:

Onsets of new arrhythmias or worsening of treated arrhythmias, sometimes fatal, have been reported. It is important, but difficult, to differentiate a lack of efficacy of the drug from a proarrhythmic effect, whether or not this is associated with a worsening of the cardiac condition. Proarrhythmic effects are more rarely reported with amiodarone than with the other antiarrhythmic agents, and generally occur in the context of QT prolonging factors

such as drug interactions and / or electrolytic disorders. Despite QT interval prolongation, amiodarone exhibits a low torsadogenic activity.

Severe skin disorders
Life-threatening or even fatal cutaneous reactions such as Stevens-Johnson syndrome or toxic epidermal necrolysis may occur. If patients experience signs or symptoms indicative of these conditions (e.g. progressive skin rash with blisters or mucosal lesions), amiodarone treatment should be discontinued immediately.

Severe bradycardia and conduction disorders

Cases of severe, potentially life-threatening bradycardia and conduction disorders have been observed with medicinal products containing sofosbuvir in combination with amiodarone.

Bradycardia has usually occurred within a few hours to a few days, but cases with a longer time to onset have been observed, mostly up to 2 weeks after the initiation of anti-HCV treatment.

Amiodarone should only be used in patients treated with medicinal products containing sofosbuvir in case of intolerance or contraindication to other antiarrhythmics.

If concomitant use of amiodarone is deemed necessary, it is recommended that patients undergo inpatient cardiac monitoring for the first 48 hours of co-administration, and following that outpatient monitoring or heart rate self-monitoring should be performed daily for at least the first 2 weeks of treatment.

In view of the long half-life of amiodarone, cardiac monitoring as described above should also be performed in patients who have stopped amiodarone in the last few months and who are to start treatment with medicinal products containing sofosbuvir.

All patients who are currently using or have recently used amiodarone in combination with medicinal products containing sofosbuvir should be warned of the symptoms of bradycardia and conduction disorders, and they should be advised of the need for urgent medical attention if they experience these symptoms.

Precautions for use
Electrolyte disturbances, particularly hypokalaemia: it is important to take account of situations that may be associated with hypokalaemia as these may predispose to the onset of pro-arrhythmic effects.
The hypokalaemia should be corrected before amiodarone is administered.
Regular monitoring of liver function (transaminases) is helpful in the detection of amiodarone-induced hepatic disorders (see undesirable effects).
Cordarone injection should only be administered in a specialist hospital environment and under continuous monitoring (ECG, BP).

Anaesthesia

Prior to any surgery, the anaesthetist should be informed that the patient is receiving amiodarone.

Long-term treatment with amiodarone may add, in terms of undesirable effects, to the haemodynamic risk inherent to local or general anesthesia.

This in particular concerns its bradycardiac and hypertensive effects, the reduction in cardiac output and conduction disorders

In addition, a few cases of acute respiratory distress have been observed immediately following surgery in patients receiving amiodarone. In consequence, close monitoring is recommended during artificial ventilation in such patients.

Transplantation

In retrospective studies, amiodarone use in the transplant recipient prior to heart transplant has been associated with an increased risk of primary graft dysfunction (PGD).

PGD is a life-threatening complication of heart transplantation that presents as left, right or biventricular dysfunction occurring within the first 24 hours of transplant surgery for which there is no identifiable secondary cause (see Undesirable Effects). Severe PGD may be irreversible.

For patients who are on the heart transplant waiting list, consideration should be given to use an alternative antiarrhythmic drug as early as possible before transplant.

DRUG INTERACTIONS

Interactions with other drugs and other forms of interaction.

Many antiarrhythmics depress cardiac automaticity and conduction and contractility.

Combining antiarrhythmics of different classes may be therapeutically beneficial, but generally requires GREAT CARE and close clinical and ECG monitoring.

Combinations of antiarrhythmics liable to induce torsades de pointes (e.g. amiodarone) are CONTRA-INDICATED.

Combining antiarrhythmics belonging to the same class is INADVISABLE, except in exceptional circumstances, because of the enhanced risk of undesirable cardiac effects.

Combination with drugs that exert negative inotropic or bradycardiac effects, and/or with drugs that slow AV conduction requires GREAT CARE and close clinical and ECG monitoring.

Effect of amiodarone on other medicinal products

Amiodarone and/or its metabolite, desethylamiodarone, inhibit CYP1A1, CYP1A2, CYP3A4, CYP2C9, CYP2D6 and P-glycoprotein and may increase exposure of their substrates.

Given the long-acting effect of amiodarone, these interactions may be observed for several months after treatment discontinuation.

Contra-indicated combinations

+ Drugs liable to induce torsades de pointes:
  - class Ia antiarrhythmics (quinidine, hydroquinidine, disopyramide),

- class III antiarrhythmics (dofetilide, ibutilide, sotalol),
- other drugs such as bepridil, cisapride, diphemanil, erythromycin IV, mizolastine, vincamine IV,
- sultopride
- Enhanced risk of ventricular rhythm disorders, particularly torsades de pointes

+ Sparfloxacin
Risk of torsades de pointes by lengthening of the QT interval (addition of the electrophysiological effects).

Inadvisable combinations

+ Sofosbuvir

Co-administration of amiodarone with treatments containing sofosbuvir may result in severe symptomatic bradycardia. Use only if no alternative treatment is available. Close monitoring is recommended when these medicinal products are co-administered (see section **SPECIAL WARNINGS AND PRECAUTIONS FOR USE**).

+ Neuroleptics liable to induce torsades de pointes:
certain phenothiazine neuroleptics (chlorpromazine, cyamemazine, levomepromazine, thioridazine, trifluoperazine), benzamides (amisulpride, sulpiride, tiapride), butyrophenones (droperidol, haloperidol), other neuroleptics (pimozide).
Enhanced risk of ventricular rhythm disorders, particularly torsades de pointes.

+ Halofantrine, moxifloxacin, pentamidine
Enhanced risk of ventricular rhythm disorders, particularly torsades de pointes. If possible, discontinue the non anti-infective drug that induces torsades de pointes. If such a combination is unavoidable, prior control of the QT interval and ECG monitoring are essential.

+ Diltiazem injection
Risk of bradycardia and AV block. If such a combination is unavoidable, start close clinical and continuous ECG monitoring.

+ Beta-blockers other than sotalol and esmolol
Contractility, automaticity and conduction disorders (suppression of compensatory sympathetic mechanisms).

Combination requiring precautions for use

+ Oral anticoagulants
Increased anticoagulant effect and risk of bleeding.
More frequent control of prothrombin levels and INR monitoring. Adjust the dosage of the oral anticoagulant during treatment with amiodarone and after its withdrawal.

+ Cyclosporin
Increased blood levels of cyclosporine due to reduced hepatic metabolism, with possible nephrotoxic effects.
Assay blood levels of cyclosporine, check kidney function and adjust the dosage during treatment with amiodarone and after its withdrawal.

+ **Diltiazem per os**
  Risk of bradycardia and AV block, particularly in the elderly. Clinical and ECG monitoring.
+ **Digitalis drugs**
  Reduced automaticity (excessive bradycardia) and AV conduction disorders. If digoxin is used, blood digoxin levels rise because of reduced digoxin clearance.
  Clinical and ECG monitoring, and measurement of blood digoxin and digoxin dose adjustment, if necessary.
+ **Esmolol**
  Contractility, automaticity and conduction disorders (suppression of compensatory sympathetic mechanisms). Clinical and ECG monitoring.
+ **Hypokalaemic agents: hypokalaemic diuretics (alone or in combination), stimulant laxatives, glucocorticoids (systemic route), tetracosactide, amphotericin B (IV route).**
  Enhanced risk of ventricular rhythm disorders, particularly torsades de pointes (hypokalaemia is a predisposing factor).
  Clinical and ECG monitoring, and laboratory tests.
+ **Phenytoin**
  Increased phenytoin plasma concentrations with signs of overdose, particularly neurological signs (reduced hepatic metabolism of phenytoin).
  Clinical monitoring, measurement of plasma phenytoin concentrations and possible adjustment of its dosage.
+ **Bradycardiac agents: bradycardiac calcium channel blockers (diltiazem, verapamil), beta-blockers (except sotalol), clonidine, guanfacin, digitalis drugs, mefloquine, anticholinesterases (donezepil, galantamine, rivastigmine, tacrine, ambemonium, pyridostigmine, neostigmine).**
  Enchanced risk of ventricular rhythm disorders, particularly torsades de pointes.
  Clinical and ECG monitoring.
+ **Statins**
  The risk of muscular toxicity (e.g. rhabdomyolysis) is increased by concomitant administration of amiodarone with statins metabolized by CYP3A 4 such as simvastatin, atorvastatin and lovastatin.
  It is recommended to use a statin not metabolized by CYP 3A4 when given with amiodarone.

PREGNANCY AND LACTATION

Pregnancy :

Studies in animals have not shown any teratogenic effects. Thus, no malformations are expected in humans since substances responsible for such malformations have been shown to produce teratogenic effects in animals in animals during well conducted studies in two different animal species.

In clinical practice, the information currently available is insufficiently pertinent to evaluate whether amiodarone causes malformations when administered in the first trimester of

pregnancy.
Since the foetal thyroid gland begins to bind iodine only from week 14 of amenorrhoea, no effects are expected on the foetal thyroid in the event of prior administration.
The use of an iodine overload when the product is given beyond this period may give rise to laboratory signs of foetal hypothyroidism or even clinical goiter.

In consequence, this drug is contra-indicated from the 2nd trimester of pregnancy.

Lactation :
Amiodarone, its metabolite and iodine pass into breast milk at concentrations greater than those in maternal plasma. If the mother is receiving treatment with this drug, breast-feeding is contra-indicated because of the risk of hypothyroidism in the infant.

EFFECT ON ABILITY TO DRIVE AND USE MACHINES
Not relevant

UNDESIRABLE EFFECTS
The adverse effects are presented by system organ class and according to frequency, as follows:
Very common (≥10%); common (≥ 1%, < 10%); uncommon (≥ 0.1%, < 1%); rare (≥ 0.01%, < 0.1%); very rare (< 0.01%); not known (cannot be estimated from the available data).

General disorders and administration site conditions:
- Locally: possible inflammatory reaction such as superficial phlebitis when administeredby direct peripheral route (see paragraph Warnings), hair loss.

Vascular disorders:
- *Very rare:* Hot flushes
- *Common:* Generally moderate and transient fall in blood pressure. Cases of severe hypotension or circulatory collapse have been reported, particularly after overdose or following excessively rapid administration.

Skin and subcutaneous tissue disorders:
- *Very rare:* sweating
- Not known : Eczema, urticarial, severe skin reactions sometimes fatal including toxic epidermal necrolysis/Stevens- Johnson syndrome, Bullous dermatitis and Drug reaction with eosinophilia and systematic symptoms

Gastrointestinal disorders:
- *Very common:* nausea
- *Not known:* Pancreatitis/ acute pancreatitis

Cardiac disorders:
- Bradycardia. In certain cases, particularly in elderly subjects, marked bradycardia more rarely sinus arrest) have been observed
- Rare pro-arrhythmic effect.

- *Not known*: Torsades de pointes

Hepato-biliary disorders:

Cases of hepatic disorders have been reported; these cases were diagnosed by elevated serum transaminases. The frequency was as follows:
Very rare:

- Generally moderate and isolated elevation in transaminases (1.5 to 3 fold normallevels) regressing after dosage reduction, or even spontaneously.
- Acute hepatic disease (a few isolated cases) with elevated blood transaminases and/or jaundice, occasionally with a fatal outcome, requiring treatment discontinuation.
- Chronic hepatic disease during prolonged treatment (oral route). The histology here corresponds to pseudoalcoholic hepatitis. Because the clinical and laboratory picture is very discrete (inconstant hepatomegaly, elevated transaminases (1.5 to 5 fold normal values), regular monitoring of liver function is required. Even a moderate rise in blood transaminases, occurring after treatment lasting more than 6 months,should be suggestive of a chronic liver disorders. The clinical disorders and laboratory abnormalities usually regress after treatment discontinuation. A few cases of irreversible progression have been reported.

Respiratory, thoracic and mediastinal disorders:

- *Very rare:* A few cases of acute respiratory distress generally associated with interstitial pneumonitis have been observed, sometimes with a fatal outcome and sometimes immediately following surgery (a possible interaction with high doses of oxygen has been suggested). Discontinuation of amiodarone should be envisaged and the pertinence of corticosteroid administration considered.
- *Very rare:* Pulmonary fibrosis
- Bronchospasm and/or apnoea in the event of severe respiratory failure, particularyin asthmatics.

Immune system disorders:

- *Very rare:* Anaphylactic shock.
- *Not known:* angioneurotic edema

Nervous system disorders:

- *Very rare:* Benign intracranial hypertension (pseudotumor cerebri).

Endocrine disorder

- *Not known:* Hyperthyroidism
- *Very rare:* Syndrome of inappropriate antidiuretic hormone secretion (SIADH)

Musculoskeletal and Connective Tissue Disorders

- Not known : back pain

Blood and lymphatic system disorders

- Not known: Neutropenia, agranulocytosis

Psychiatric disorder

- *Not known:* **Confusional state/delirium, hallucination**

Reproductive system and breast disorders

- *Not known:* Libido decreased

Eye Disorder

Not known : Optic neuropathy/neuritis that may progress to blindness

Injury, poisoning and procedural complications

- *Not known: Potentially fatal primary graft dysfunction post cardiac transplant (See Precaution).*

Overdosage

No information regarding amiodarone overdose by the IV route is available.
As regards the oral form, few cases concerning the acute administration of high doses amiodarone have been documented.

A few cases of sinus bradycardia, ventricular rhythm disorders, particularly torsades de pointes and liver damage have been reported. Treatment must be symptomatic. Given the kinetic profile of the product, cardiac monitoring in particular, over a sufficiently long period of time, is recommended.
Amiodarone and its metabolites are not dialysable.

SHELF-LIFE

24 months

SPECIAL PRECAUTIONS FOR STORAGE

Ampoules should be stored below 25°C

HARUS DENGAN RESEP DOKTER

Reg. No. : DKI1077402943A1
Pack size : Box of 6 ampoules of 3 ml

Manufactured by:
Sanofi Winthrop Industrie
Carbon Blanc – FRANCE

Registered by:
PT Kalventis Sinergi Farma,
Jakarta - Indonesia

sanofi

INFORMASI UNTUK PENGGUNA

Cordarone® 150 mg/3 mL larutan untuk injeksi intravena (IV) dalam ampul

Amiodarone hidroklorida

Bacalah dengan cermat seluruh isi leaflet ini sebelum Anda memulai penggunaan obat ini, karena terdapat informasi penting yang perlu Anda ketahui.
- Simpanlah leaflet ini. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, silakan tanyakan kepada dokter atau apoteker Anda.
- Obat ini hanya boleh digunakan atas resep untuk Anda saja. Jangan memberikannya kepada orang lain, karena hal ini dapat membahayakan mereka, meskipun gejala penyakitnya serupa dengan yang Anda alami.
- Jika Anda mengalami efek samping apa pun, segera bicarakan dengan dokter atau apoteker Anda. Ini mencakup kemungkinan efek samping yang tidak tercantum dalam brosur ini. Lihat bagian 4, Efek Samping yang Mungkin Terjadi

Isi dari brosur ini mencakup informasi berikut:

1. Penjelasan tentang Cordarone® 150 mg/3 mL injeksi dan fungsinya.
2. Hal-hal yang perlu Anda ketahui sebelum menggunakan Cordarone® 150 mg/3 mL injeksi.
3. Petunjuk penggunaan Cordarone® 150 mg/3 mL injeksi.
4. Daftar efek samping yang mungkin timbul.
5. Panduan menyimpan Cordarone® 150 mg/3 mL injeksi.
6. Informasi tentang isi kemasan dan aspek lainnya.

1. Penjelasan tentang Cordarone® 150 mg/3 mL injeksi dan fungsinya

Golongan Farmakoterapi: Anti aritmia kelas III, kode ATC : C01BD01
Obat ini digunakan untuk mengatasi masalah detak jantung yang serius ketika pengobatan melalui rute oral tidak memberikan hasil yang memadai:
- Gangguan irama jantung pada atrium, yang ditandai oleh detak jantung ventrikel yang cepat.
- Wolf-Parkinson-White syndrome tachycardia, yaitu kondisi detak jantung yang cepat yang terkait dengan sindrom Wolf-Parkinson-White. Ini adalah gangguan jantung yang melibatkan jalur listrik tambahan dalam jantung, yang dapat menyebabkan detak jantung yang lebih cepat dari normal.
- Gangguan irama jantung pada ventrikel yang menyebabkan gejala yang tercatat dan menghambat aktivitas sehari-hari.

2. Hal-hal yang perlu Anda ketahui sebelum menggunakan Cordarone® 150 mg/3 mL injeksi.

Jangan menggunakan injeksi Cordarone® 150mg/3ml dalam kondisi berikut:
- Jika Anda alergi terhadap iodin.

- Jika Anda alergi terhadap bahan aktif Amiodaron atau bahan lain yang ada dalam produk Cordarone® 150mg/3ml. Lihat bagian 6 untuk daftar lengkap bahan-bahannya.
- Jika Anda mengidap hipertirodisme (gangguan kelenjar tiroid).
- Anda mengalami masalah khusus dengan detak jantung atau gangguan pada sistem yang mengirimkan sinyal untuk membuat jantung berkontraksi.
- Anda pernah pingsan dan tekanan darah Anda turun.
- Anda memiliki tekanan darah yang sangat rendah (tekanan darah rendah).
- Detak jantung Anda terlalu lambat.
- Anak-anak berusia kurang dari 3 tahun, karena obat ini mengandung benzil alcohol

Peringatan dan Perhatian

- Obat ini hanya boleh digunakan di rumah sakit khusus dengan pengawasan terus menerus, kecuali dalam situasi darurat yang mengancam jiwa.
- Masalah detak jantung, tekanan darah rendah, atau gagal jantung dapat memburuk dengan suntikan Cordarone®, meskipun diberikan dengan sangat lambat.
- Suntikan juga dapat menyebabkan masalah pernapasan dan/atau hati. Oleh karena itu, tes darah mungkin diperlukan selama pengobatan untuk memeriksa cara kerja hati Anda.
- Obat ini harus digunakan dengan hati-hati jika Anda memiliki gangguan elektrolit, terutama kekurangan kalium.
- Jika Anda akan menjalani operasi, beritahu dokter anestesi Anda bahwa Anda menggunakan obat ini.
- Jika Anda mengalami reaksi kulit yang parah, seperti ruam melepuh disertai pengelupasan kulit yang dapat menyebar dengan cepat ke seluruh tubuh dan mengancam jiwa, segera hentikan pengobatan dan konsultasikan dengan dokter.
- Jika Anda berada dalam daftar tunggu untuk transplantasi jantung, dokter Anda mungkin mengubah pengobatan Anda. Penggunaan amiodarone sebelum transplantasi jantung menunjukkan peningkatan risiko komplikasi yang mengancam jiwa (disfungsi cangkok primer) di mana jantung yang ditransplantasikan berhenti bekerja dengan baik dalam waktu 24 jam setelah operasi.

Obat-obatan lain dan Cordarone® 150 mg/3 ml injeksi

Jangan menggunakan Cordarone® 150mg/3ml injeksi jika Anda sedang mengonsumsi obat-obat berikut:

- Obat untuk mengobati gangguan jantung, seperti quinidine, hydroquinidine, disopyramide, dofetilide, ibutilide, sotalol;
- Obat-obatan lain, seperti:
  - bepridil,
  - cisapride,
  - diphemanil,
  - erythromycin IV,
  - mizolastine,
  - vincamine IV,
  - sultopride,
  - sparfloxacin

Kecuali ada instruksi khusus dari dokter Anda, jangan menggunakan obat ini jika Anda sedang menggunakan obat-obatan berikut:

- Injeksi diltiazem.
- Obat antiparasit tertentu: halofantrine, pentamidine, dan moxifloxacin.
- Beberapa obat neuroleptik (jenis obat yang digunakan untuk mengobati gangguan mental atau kejiwaan) tertentu (seperti thioridazine, chlorpromazine, levomepromazine, trifluoperazine, cyamemazine, sulpiride, amisulpride, tiapride, pimozide, haloperidol, droperidol),
- Beta bloker selain sotalol dan esmolol

Beritahu dokter Anda jika Anda sedang mengonsumsi obat-obat berikut:

- Anda sedang mengonsumsi atau telah mengonsumsi obat yang mengandung sofosbuvir untuk pengobatan hepatitis C dalam beberapa bulan terakhir. Kombinasi ini dapat membahayakan jiwa karena dapat menyebabkan perlambatan detak jantung. Dokter Anda mungkin akan mempertimbangkan pengobatan alternatif jika Anda menggunakan obat ini. Jika terpaksa Anda harus menggunakan Cordarone® bersama dengan sofosbuvir, pemantauan jantung tambahan mungkin diperlukan.
- Antikoagulan oral
- Cyclosporin
- Diltiazem oral
- Obat digitalis
- Esmolol
- Agen hipokalemia: diuretik hipokalemia (sendiri atau dalam kombinasi), obat pencahar stimulan, glukokortikoid (melalui rute sistemik), tetrakosaktida, amphotericin B (melalui rute intravena).
- Phenytoin
- Agen bradikardia: penghambat saluran kalsium yang menurunkan denyut jantung (diltiazem, verapamil), beta bloker (kecuali sotalol), clonidine, guanfacin, obat digitalis, mefloquine, antikolinesterase (donepezil, galantamine, rivastigmine, tacrine, ambemonium, pyridostigmine, neostigmine).
- Statin

Sampaikan kepada dokter atau apoteker Anda jika saat ini Anda sedang mengonsumsi atau baru saja mengonsumsi obat lain, termasuk obat yang bisa didapatkan tanpa resep dokter.

Kehamilan dan Menyusui

Kehamilan

Jangan mengonsumsi obat ini jika Anda sedang hamil lebih dari 3 bulan, khususnya pada trimester kedua kehamilan.

Menyusui

Jangan menyusui selama menggunakan obat ini.

Jika Anda sedang hamil, menyusui, memiliki kecurigaan sedang hamil, atau merencanakan kehamilan, segera konsultasikan dengan dokter atau apoteker sebelum menggunakan obat ini.

3. Petunjuk penggunaan Cordarone® 150 mg/3 mL injeksi

Karena formulasi produknya, pastikan untuk tidak menggunakan konsentrasi kurang dari 2 ampul dalam 500 ml. Gunakan hanya larutan glukosa isotonik.

Tidak disarankan menambahkan produk lain ke dalam larutan infus. Pastikan Amiodaron diberikan melalui jalur vena sentral.

Infus intravena:
- Pengobatan awal: dosis umumnya adalah 5 mg/kg dalam larutan glukosa. Disarankan menggunakan pompa suntik elektrik, dan berikan infus selama 20 menit hingga 2 jam. Proses ini dapat diulang 2 atau 3 kali dalam periode 24 jam. Karena efek obat yang singkat, sangat penting untuk memperhatikan dan memastikan pemberian infus yang berkelanjutan untuk menjaga tingkat obat dalam tubuh dan memastikan efek terapeutik yang diinginkan.
- Dosis pemeliharaan: berikan 10 hingga 20 mg/kg/hari (biasanya 600 hingga 800 mg/24 jam, hingga 1,2 g/24 jam) dalam 250 ml larutan glukosa selama beberapa hari.

Pada tahap selanjutnya, pertimbangkan untuk beralih ke rute oral (3 tablet per hari) sejak hari pertama infus. Dosis dapat ditingkatkan menjadi 4 atau bahkan 5 tablet per hari.

4. Daftar efek samping yang mungkin timbul

Efek samping disajikan berdasarkan kelas organ sistem dan frekuensinya, dengan rincian sebagai berikut:
- Sangat umum (≥10%);
- Umum (≥ 1%, <10%);
- Tidak umum (≥ 0,1%, <1%);
- Jarang (≥ 0,01%, < 0,1%);
- Sangat jarang (<0,01%);
- Tidak diketahui (tidak dapat diperkirakan dari data yang tersedia).

Gangguan umum dan kondisi tempat pemberian:
- Lokal: reaksi inflamasi/bengkak, rambut rontok.

Gangguan pembuluh darah:
- Sangat jarang: Kulit kemerahan disertai rasa panas
- Umum: penurunan tekanan darah atau gangguan peredaran darah

Gangguan kulit dan jaringan subkutan:
- Sangat jarang: berkeringat
- Tidak diketahui : Eksim, urtikaria, reaksi kulit yang parah terkadang berakibat fatal termasuk lesi kulit dengan penampakan kulit seperti terbakar/ruam, lepuhan di kulit, lapisan bola mata, rongga mulut, dubur, dan kelamin, lepuhan berisi cairan di kulit, serta reaksi obat dengan eosinofilia dan gejala sistematis

Gangguan saluran cerna:
- Sangat umum: mual
- Tidak diketahui: Pankreatitis/pankreatitis akut (peradangan pada pankreas)

Gangguan jantung:
- Detak jantung melambat
- Jarang: efek proaritmia (obat yang dapat memperburuk kondisi detak jantung)
- Tidak diketahui: *Torsades de pointes* (gangguan irama jantung yang bisa menyebabkan detak jantung menjadi tidak teratur)

Gangguan hepatobilier (penyakit yang terkait dengan hati dan saluran empedu):
Sangat jarang: penyakit hati akut, penyakit hati kronis

Gangguan yang terkait dengan sistem pernapasan, dada, dan mediastinum (ruang di antara paru-paru):
- Sangat jarang: gangguan pernapasan akut, fibrosis paru

- Bronkospasme (penyempitan mendadak pada saluran udara utama (bronkus) dalam paru-paru) dan/atau apnea (kondisi ketika seseorang berhenti bernapas secara sementara) jika terjadi gagal napas berat, terutama pada penderita asma.

Gangguan sistem imun:
- Sangat jarang: anafilaktik syok (reaksi alergi yang sangat serius dan cepat terjadi).
- Tidak diketahui: *Angioneurotic edema* (reaksi alergi di mana terjadi pembengkakan mendadak pada lapisan dalam kulit, jaringan subkutan, atau selaput lendir, biasanya disertai rasa gatal).

Gangguan pada sistem saraf:
- Sangat jarang: *Benign Intracranial Hypertension* (BIH), atau juga dikenal sebagai pseudotumor cerebri, adalah kondisi di mana tekanan cairan di dalam tengkorak meningkat tanpa adanya tumor atau penyebab lain yang jelas.

Gangguan endokrin:
- Tidak diketahui: *Hyperthyroidism* (kondisi di mana kelenjar tiroid menghasilkan terlalu banyak hormon tiroid).
- Sangat jarang: *Syndrome of Inappropriate Antidiuretic Hormone Secretion* (SIADH) adalah kondisi medis di mana tubuh melepaskan terlalu banyak hormon antidiuretik (ADH), yang berfungsi untuk mengatur keseimbangan air dalam tubuh.

Gangguan muskuloskeletal dan jaringan ikat:
- Tidak diketahui : nyeri punggung

Gangguan pada sistem peredaran darah dan limfatik:
- Tidak diketahui: Neutropenia (jumlah sel darah putih jenis tertentu, yang disebut neutrofil, berada di bawah batas normal), agranulositosis (kondisi di mana jumlah sel darah putih granulosit dalam tubuh sangat rendah).

Gangguan psikiatri:
- Tidak diketahui: Keadaan bingung/delirium, halusinasi.

Gangguan sistem reproduksi dan payudara:
- Tidak diketahui: Libido menurun

Gangguan Mata:
- Tidak diketahui : Neuropati/neuritis optik yang dapat berkembang menjadi kebutaan.

Cedera, keracunan dan komplikasi prosedur (komplikasi yang timbul selama atau setelah suatu prosedur medis atau bedah):
- Tidak diketahui: komplikasi yang berpotensi fatal setelah transplantasi jantung (disfungsi cangkok primer) yang menyebabkan jantung yang ditransplantasikan berhenti bekerja dengan baik (lihat bagian peringatan dan perhatian)

Pelaporan efek samping

Jika Anda mengalami efek samping apa pun, segera diskusikan dengan dokter atau apoteker Anda. Ini termasuk kemungkinan efek samping yang tidak tercantum dalam brosur ini.

Melaporkan efek samping membantu memberikan informasi tambahan tentang keamanan obat ini.

5. Panduan menyimpan Cordarone® 150 mg/3 mL injeksi

Jauhkan obat ini dari jangkauan anak-anak dan hindari terlihat oleh mereka.

Jangan menggunakan Cordarone® 150 mg/3 mL injeksi setelah tanggal kadaluwarsa yang tertera pada kotak. Tanggal kadaluwarsa mengacu pada hari terakhir bulan tersebut.

Setelah dibuka, gunakan obat segera. Simpan di bawah suhu 25°C.

Jangan membuang obat melalui saluran air atau sampah rumah tangga. Tanyakan kepada apoteker Anda cara membuang obat yang tidak lagi Anda perlukan.

Langkah-langkah ini membantu melindungi lingkungan.

6. Informasi tentang isi kemasan dan aspek lainnya

Apa kandungan Cordarone® 150 mg/3 mL larutan untuk injeksi intravena (IV) dalam ampul

- Zat aktifnya adalah:
  Amiodarone hydrochloride ..... 150 mg

  Untuk 1 ampul @ 3 mL
- Bahan lainnya adalah:

  Polysorbate 80, benzyl alcohol, water for injections.

Seperti apa Cordarone® 150 mg/3 mL injeksi dan isi kemasannya

Obat ini diberikan dalam bentuk larutan injeksi

Kotak berisi 6 ampul.
HARUS DENGAN RESEP DOKTER

No Registrasi: DKI1077402943A1
Kemasan: Dus, 6 ampul @ 3 ml

Diproduksi oleh:
Sanofi Winthrop Industrie
Carbon Blanc – France

Diregistrasikan oleh:
PT Kalventis Sinergi Farma
Jakarta – Indonesia