Side Effects
Side effects observed with amiodarone are often related to too high a dosage. They may be prevented or reduced to a minimum by determining the lowest effective dosage.

Ophthalmological
Corneal microdeposits, which appear in the majority of patients. Formed of complex lipid deposits, they are always reversible upon termination of treatment. A few cases of optic neuritis with blurred vision and impaired visual acuity have been reported. The causal relationship with amiodarone has not currently been established.

Dermatological
Photosensitivity. Patients should avoid sun exposure (and as a rule UV rays exposure). Skin rashes, usually of specificity, including exceptional cases of exfoliative dermatitis have been reported with no clearly-established causal relationship to amiodarone. Slate-grey or bluish pigmentations of the skin may occur in case of prolonged treatments with high daily doses. Such pigmentations slowly disappear following treatment discontinuation (10 to 24 months later).

Thyroid Gland
Apart from any clinical evidence of thyroid dysfunction, “dissociated” thyroid hormone levels are usual (increased levels of T4, normal or slightly decreased T3): they should not lead to discontinuation of treatment.

Hypothyroidism: clinical signs (usually slight): weight gain, apathy, drowsiness; a clear increase in serum ultrasensitivity TSH (TSHu) confirms the diagnosis. Cessation of treatment restores normal thyroid function within 1 to 3 months. In lifethreatening situations, amiodarone may be continued in combination with thyroid replacement therapy by L-thyroxine. TSHu levels provide a guide to L-thyroxine dosage.

Hyperthyroidism: giving rise to few symptoms (unexplained light weight loss, decreased effectiveness
in angina and/or arrhythmia); psychiatric aspect in elderly patients; sharply reduced TSHu confirms the diagnosis. Amiodarone should be withdrawn. Clinical recovery usually occurs within 3 to 4 weeks. In severe cases, the inconstant efficacy of synthet-
ic antithyroid drugs may require the concomitant administration of corticosteroids (1 mg/kg) for a suf-ficient course (3 months).

In patients with increased risk of thyroid dysfunction (family history of thyroid disease, doubtful personal history) regular assessment of thyroid function tests is recommended.

**Pulmonary**
Cases of diffuse interstitial pulmonary fibrosis have been reported. Onset of exertional dyspnea, whether alone or in combination with deterioration of general health (fatigue, weight loss, fever) requires that a chest x-ray be performed.

Early withdrawal of amiodarone, with or without con-comitant corticosteroid therapy, leads to regression of disturbances.

Clinical symptoms usually disappear within 3 to 4 weeks, but functional and radiological improvement occurs slowly (several months).

**Neurological**
Sensitive motor peripheral neuropathy and/or myop-athy, usually reversible on treatment discontinuation. Other disturbances reported: extrapyramidal tremor, cerebellar ataxia, exceptional benign intracranial hypertension, and nightmares.

**Hepatic**
Regular monitoring of liver function tests (transami-nases) is recommended during the course of therapy. The following adverse reactions have been reported:

*At the Beginning of Treatment:* Elevation of serum transaminases, isolated and usually moderate (1.5 to 3 times normal values) returning to normal with dose reduction, or even spontaneously.

Acute liver disorders exceptionally (a few isolated cases) with elevated serum transaminases and/or jaundice. Regression of such conditions always occurs when treatment is withdrawn.

During Lengthy Treatments: A few rare cases of chronic liver disease have been reported. Histological findings reveal lesions resembling pseudo-alcohol-ic hepatitis. The subtle clinical signs and biological changes (possible hepatomegaly, elevated transami-nases 1.5 to 5 times normal) justify regular monitoring of liver function tests. Elevated serum transaminases, even moderate, developing after treatment for longer than 6 months should suggest this diagnosis. Clinical and biological abnormalities usually regress upon cessation of treatment. A few cases of irreversible progression have been reported.

**Cardiac**
Bradyarrhythmia, which generally is moderate and dose-related. In some cases (sinus node dysfunc-tion, elderly subjects) marked bradycardia or more exceptionally sinus arrest have been reported. There have been rare instances of conduction disturbances (sinoatrial block, AV block of various degrees). Amiodarone has a weak arrhythmia-induc-ing potential, less than that observed with most of the other anti-arrhythmic drugs, and it occurs generally in case of certain drug associations (see Drug Interactions) or electrolytic disorders.

**Others**
Benign digestive disorders (nausea, vomiting, dys-geusia) which usually occur with loading dosage and disappear with dose reduction. A few isolated cases, of various clinical features, have been observed in a context suggesting a hypersensitivity reaction: vas-culitis, renal involvement with moderate elevation of creatinine levels, and thrombopenia. A few cases of epididymitis have been reported. The relationship with amiodarone has not been established.

Particular to I.V. administration: Hot flushes, sweat-ing, nausea (intravenous injection). Decrease in blood pressure, usually moderate and transient. Cases of severe hypotension or collapse have been reported following overdosage or a too rapid injection.

Moderate bradycardia. In some cases, and especially in elderly patients, marked bradycardia, or more exceptionally sinus arrest, requires the discontinua-tion of therapy. Occurrence of arrhythmia, or aggra-
Precautions
Electrolytic disturbances, especially hypokalemia; these disturbances could enhance proarrhythmic effects and have to be rebalanced before using Cordarone. Undesirable effects (see Side Effects) are related in most cases with drug overloading; therefore careful attention should be paid in determining the minimum effective maintenance dosage in order to avoid or minimize undesirable effects. Patients should be instructed to avoid sun exposure or to use protective measures during therapy. In patients with personal or family history of thyroid disorders, caution should be exercised when administering Cordarone if it is necessary; the minimum effective dosage should be used and careful clinical and biological monitoring should be undertaken.

Amiodarone intravenous should only be used in a special care unit under continuous monitoring (ECG, blood pressure).

Caution should be exercised in case of hypotension, severe respiratory failure, decompensated myocardopathy or severe heart failure.

Pregnancy and Lactation
Pregnancy: In view of its effects on the fetal thyroid gland, amiodarone is contraindicated during pregnancy, except in exceptional cases.

Lactation: Amiodarone is excreted in breast milk in significant quantities; therefore amiodarone is contraindicated in nursing mothers.

Overdosage
Little information is available regarding acute overdosage with amiodarone. Sinus bradycardia or spontaneously resolving attacks of ventricular tachycardia may occur. Most often the patient does not demonstrate clinical signs. Nevertheless, due to the pharmacokinetics of amiodarone, the patient should be monitored long enough, particularly with regard to cardiac status. Neither amiodarone or its metabolites can be dialysed.

Drug Interactions
Contraindicated
Non antiarrhythmic agents causing torsades de
levels with signs of over-dosage (particularly neurological signs); clinical monitoring should be undertaken and phenytoin dosage should be reduced as soon as overdosage signs appear; phenytoin plasma levels may be determined.

General anesthesia, oxygen therapy: Potentially severe complications have been reported in patients undergoing general anesthesia: bradycardia unresponsive to atropine, hypotension, disturbances of conduction, decreased cardiac output. A few cases of severe respiratory complications, resulting sometimes in fatalities, have been observed most often in the period immediately after surgery (acute adult respiratory distress syndrome); a possible interaction with a high oxygen concentration may be implicated. Before surgery, the anesthesiologist should be informed that the patient is taking amiodarone.

Dosage and Administration
Cordarone should only be given under close medical supervision. The dosage and mode of administration in each particular case, depends on the desired therapeutic effects, the patient’s individual response and the possible Side effects.

Tablets
Loading dose: Average dosage: 200 mg (1 tablet) three times a day for 8-10 days. Dosage and Administration may be increased to 4 or even 5 tablets daily for short periods and under ECG monitoring.

Maintenance dose: 100 - 400 mg (½ - 2 tablets) daily. The treatment should be given once or twice daily, with or just after meals. The minimum effective maintenance dosage should be used.

Ampoules
Injectable route should only be used where cardiac monitoring and defibrillation facilities are available. Cordarone I.V. must be diluted in 5% dextrose only.

Intravenous Infusion
Due to galenic reasons, concentration less than 2 vials in 500 ml should not be used. Isotonic dextrose infusion should be used exclusively. Do not mix with other preparations in infusion solution.

Loading dose: 5 mg/kg diluted in 250 ml 5% dex-
trose given over 20 minutes to 2 hours and renewed 2 to 3 times per 24 hours. Therapeutic effect appears within the first minutes and then it is progressively decreasing. Therefore, an infusion should be set up to take over.

Maintenance dose: Usual dosage is 10-20 mg/kg/24 hours (600-1200 mg/24 hours) in 250 ml 5% dextrose over few days.

It is recommended that Cordarone be infused by a central venous catheter.

Take over with oral administration from the first day of infusion.

**Packaging**

a: 150 mg/3 ml x 6

b: 200 mg x 30.