Dofetilide (doe-fet-il-ide)

**Class (Therapeutic):** antiarrhythmics (class III)

**Pregnancy Category:** C

**Indications:**
- Maintenance of normal sinus rhythm (delay in time to recurrence of atrial fibrillation/atrial flutter [AF/AFl]) in patients with AF/AFl lasting more than one week, and who have been converted to normal sinus rhythm. Conversion of AF and AFl to normal sinus rhythm.

**Action:**
- Blocks cardiac ion channels responsible for transport of potassium. Increases monophasic action potential duration. Increases effective refractory period.

**Therapeutic Effects:**
- Prevention of recurrent AF/AFl.
- Conversion of AF/AFl to normal sinus rhythm.

**Pharmacokinetics:**
- **Absorption:** Well absorbed (90%) following oral administration.
- **Distribution:** Unknown.
- **Metabolism and Excretion:** 80% excreted by kidneys via cationic renal secretion, mostly as unchanged drug; 20% excreted as inactive metabolites; some metabolism in the liver via cytochrome P450 system (CYP3A4 isoenzyme).
- **Half-life:** 10 hr.

**TIME/ACTION PROFILE (blood levels)**

<table>
<thead>
<tr>
<th>ROUTE</th>
<th>ONSET</th>
<th>PEAK</th>
<th>DURATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>PO</td>
<td>within hours</td>
<td>2–3 hr†</td>
<td>12–24 hr</td>
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†Steady state levels are achieved after 2–3 days.

**Contraindications/Precautions**

- **Contraindicated in:** Hypersensitivity; Congenital or acquired prolonged QT syndrome; Baseline QT interval or QTc of >440 msec (500 msec in patients with ventricular conduction abnormalities); Creatinine clearance < 30 mL/min; Concurrent use of verapamil, cimetidine, ketoconazole, itraconazole, trimethoprim, megestrol, prochlorperazine, hydrochlorothiazide, or other QT-interval prolonging drugs.

**Use Cautiously in:**
- Underlying electrolyte abnormalities (risk of serious arrhythmias; correct prior to administration; Creatinine clearance 20–60 mL/min (slow **↑** recommended). Severe hepatic impairment: Do not use only when potential benefits to patient outweigh potential risks to fetus. **Pedi:** Safety not established.

**Adverse Reactions/Side Effects**

- **CNS:** Dizziness, headache.
- **CV:** Ventricular arrhythmias (including torsade de pointes), chest pain, QT interval prolongation.

**Interactions**

- **Drug-Drug:** Hydrochlorothiazide, verapamil, cimetidine, ketoconazole, trimethoprim, megestrol, prochlorperazine ↑ dofetilide levels and the risk of QT interval prolongation with arrhythmias; concurrent use is contraindicated. QT interval prolonging drugs ↑ the risk of torsade de pointes due to ↑ risk of arrhythmias. Hypokalemia or hypomagnesemia from potassium-depleting diuretics ↑ the risk of arrhythmias; correct abnormalities prior to administration. Concomitant use of digoxin ↑ the risk of arrhythmias.

**Route/Dosage**

- **Dosing should be adjusted according to renal function and assessment of QT interval.**

**PO (Adults):**
- Starting dose — 500 mcg twice daily; maintenance dose — 250 mcg twice daily (not to exceed 500 mcg twice daily).

**PO (Renal Impairment):**
- CCr 40–60 mL/min: Starting dose — 250 mcg twice daily; maintenance dose — 125 mcg twice daily.
- CCr 20–40 mL/min: Starting dose — 125 mcg twice daily; maintenance dose — 62.5 mcg twice daily.

**Renal Impairment**

**PO:**
- CCr < 30 mL/min: Starting dose — 500 mcg twice daily, maintenance dose — 250 mcg twice daily, maximum dose — 250 mg twice daily (not to exceed 1000 mg per day).

**Overdosage:**
- Mild: supportive care.
- Severe: supportive care; atropine, lidocaine, procainamide, or isoproterenol; synchronized cardioversion; defibrillation; cardioselective beta-blockers; use of intravenous magnesium for every 4 hours; dialysis.
NURSING IMPLICATIONS

Assessment

- Monitor ECG, pulse, and BP continuously during initiation of therapy and for at least 3 days, then periodically during therapy. Evaluate QTc prior to initiation of therapy and every 3 mo during therapy. If QTc exceeds 440 msec (500 msec in patients with ventricular conduction abnormalities), discontinue doxilide and monitor patient until QTc returns to baseline.
- Assess the patient’s medication history including OTC, Rx, and natural/herbal products, with emphasis on those that interact with doxilide (see Interactions).
- Lab Test Considerations: Creatinine clearance must be calculated for all patients prior to administration and every 3 mo during therapy.

Potential Nursing Diagnoses

- Decreased cardiac output (Indications)

Implementation

- Doxilide must be initiated or reinitiated in a setting that provides continuous ECG monitoring and has personnel trained in the management of serious ventricular arrhythmias and pharmacists trained to dispense doxilide. Due to the potential for life-threatening ventricular arrhythmias, doxilide is usually used for patients with highly symptomatic AF/AFl.
- Patients with AF should be anticoagulated according to usual protocol prior to electrical or pharmacological cardioversion.
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- Make sure patient has an adequate supply of doxilide prior to discharge to prevent interruption of therapy.
- PO: Administer at the same time each day without regard to food.

Patient/Family Teaching

- Instruct patient to take medication as directed, even if feeling well. If a dose is missed, do not double next dose. Take next dose at usual time.
- Instruct patient to read the patient package insert prior to initiation of therapy and re-read it each time therapy is renewed. Emphasize the need for compliance with therapy, the potential for drug interactions, and the need for periodic monitoring to minimize the risk of serious arrhythmias.
- Instruct patient or family member on how to take pulse. Advise patient to report changes to pulse rate or rhythm to health care professional.
- Warmside detection. Caution patient to avoid driving or other activities requiring alertness until response to medication is known.
- Advise patient of importance of routine follow-up exams to monitor progress.
- Emphasize the importance of routine follow-up exams to monitor progress.
- Advise patient to consult health care professional immediately if they faint, become dizzy, or have fast heartbeats. If health care professional is unavailable instruct patient to go to nearest hospital emergency department, take remaining doxilide capsules, and show them to the doctor or nurse. If symptoms associated with altered electrolyte balance such as excessive or prolonged diarrhea, sweating, or vomiting or loss of appetite or thirst occur health care professional should also be notified immediately.
- Advise patient to inform health care professional of all Rx or OTC medications, vitamins, or herbal products being taken and to consult health care professional before taking any Rx, OTC, or herbal products.
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