TABLE 9-2 SELECTED CHARACTERISTICS OF ANTIARRHYTHMIC DRUGS

DRUG	EFFECT ON SURFACE ECG	EFFECT ON LV FUNCTION	IMPORTANT DRUG INTERACTIONS	EFFECT ON PACING AND DEFIBRILLATION THRESHOLDS	MAJOR ROUTE OF ELIMINATION
Quinidine	Prolongs QRS and QT	Negative inotrope	Increases digoxin level and warfarin effect Cimetidine increases quinidine level Phenobarbital, phenytoin, and rifampin decrease quinidine level	Increases PT and DT at high doses	Liver and kidney
Procainamide	Prolongs PR, QRS, and QT	Negative inotrope	Cimetidine, alcohol, and amiodarone increase procainamide level	Increases PT at high doses	Liver and kidney
Disopyramide	Prolongs QRS and QT	Negative inotrope	Phenobarbital, phenytoin, and rifampin decrease disopyramide level	Increases PT at high doses	Liver and kidney
Lidocaine	Shortens QT	None	Propranolol, metoprolol, and cimetidine increase lidocaine level	Increases DT	Liver
Mexiletine	Shortens QT	None	Increases theophylline level Phenobarbital, phenytoin, and rifampin decrease mexiletine level	Various effects	Liver
Flecainide	Prolongs PR and QRS	Negative inotrope	Increases digoxin level	Increases PT; variable effect on DT	Liver and kidney
Propafenone	Prolongs PR and QRS	Negative inotrope	Increases digoxin, theophylline, and cyclosporine levels; increases warfarin effect Phenobarbital, phenytoin, and rifampin decrease propafenone level Cimetidine and quinidine increase propafenone level	Increases PT; variable effect on DT	Liver
Dronedarone	Prolongs PR and QT; slows sinus rate	Negative inotrope	CYP3A inhibitors (ketoconazole, clarithromycin, calcium-channel blockers) increase dronedarone levels; additive effect with drugs that prolong QT (macrolides, class I and III antiarrhythmics) increasing risk of TdP; increases dabigatran levels	Little effect	Liver
Amiodarone	Prolongs PR and QT; slows sinus rate	None	Increases digoxin and cyclosporine levels; increases warfarin effect	Increases DT	Liver
Sotalol	Prolongs PR and QT; slows sinus rate	Negative inotrope	Additive effects with other β-blockers	Decreases DT	Kidney
Ibutilide	Prolongs PR and QT	None	Additive effect on QT prolongation with class IA and other class III anti-arrhythmic agents	Decreases DT	Liver
Dofetilide	Prolongs QT	None	Verapamil, diltiazem, Cimetidine, and ketoconazole increase dofetilide level	Decreases DT	Liver and kidney

DT, Defibrillation threshold; ECG, electrocardiogram; LV, left ventricle; PT, pacing threshold; TdP, torsades de pointes.

Class III Antiarrhythmic Agents

Class III antiarrhythmic agents are a heterogeneous group of drugs that block the potassium rectifier currents responsible for phase 3 cardiac repolarization, prolonging the cardiac action potential duration and refractory period. These agents demonstrate reverse-use dependence, with more potent potassium-channel blockade at slower heart rates. Prolonging the action potential duration can be therapeutic or proarrhythmic (e.g., TdP). This class represents the dominant category of antiarrhythmic agents in use.

Amiodarone is an iodinated compound available orally and parentally. With oral administration, it is slowly absorbed. Deposition of amiodarone in body fat stores prolongs the time to reach steady-state levels. The elimination half-life of the drug is 35 to 100 days. Amiodarone's pharmacology is complex, with class I through IV activity, although its primary therapeutic mechanism is prolongation of the action potential duration. It is effective in treating SVTs and VTs. It is hepatically metabolized and proven safe to use in the setting of congestive heart failure. Amiodarone is commonly used to treat atrial and ventricular arrhythmias in patients with structural heart disease and renal failure. Amiodarone is superior to other parental antiarrhythmic agents used to treat cardiac arrest and recurrent VT or ventricular fibrillation (VF). Widespread use of amiodarone has been limited by significant side effects necessitating drug discontinuation in