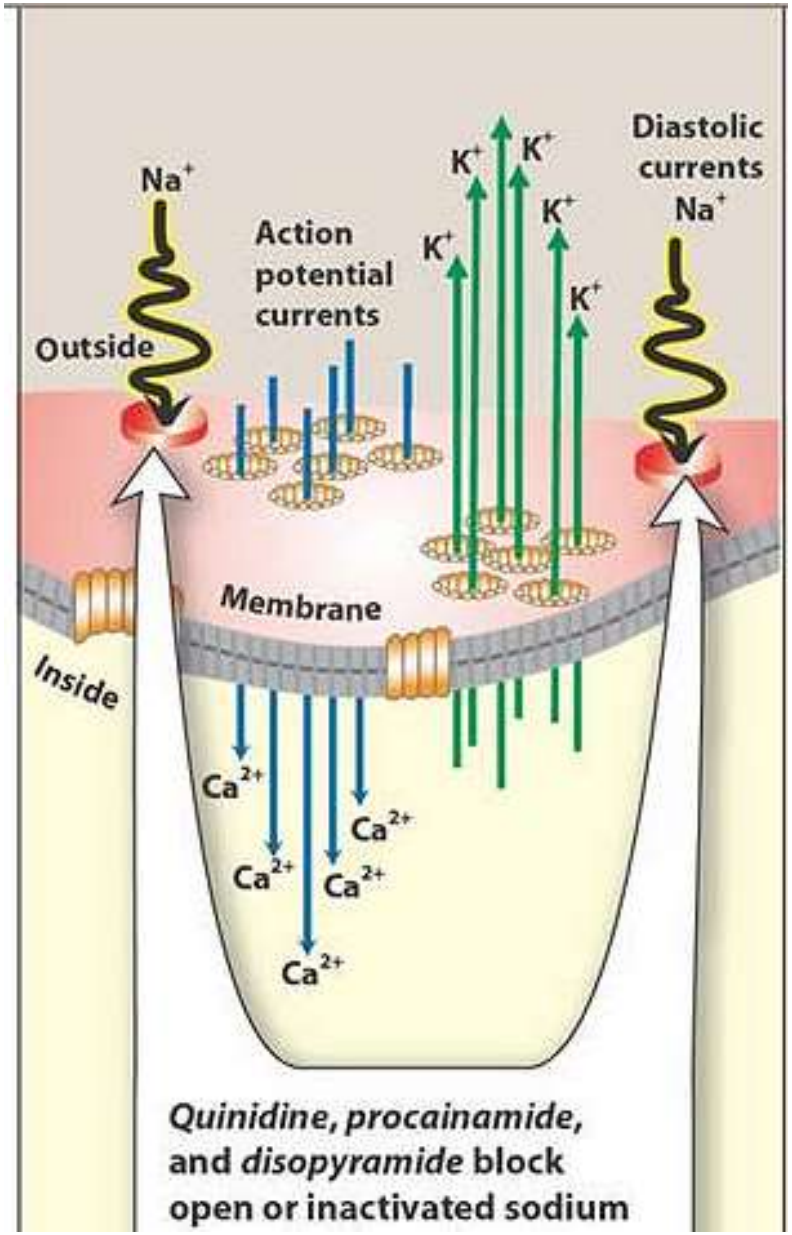
Classification of antiarrhythmics

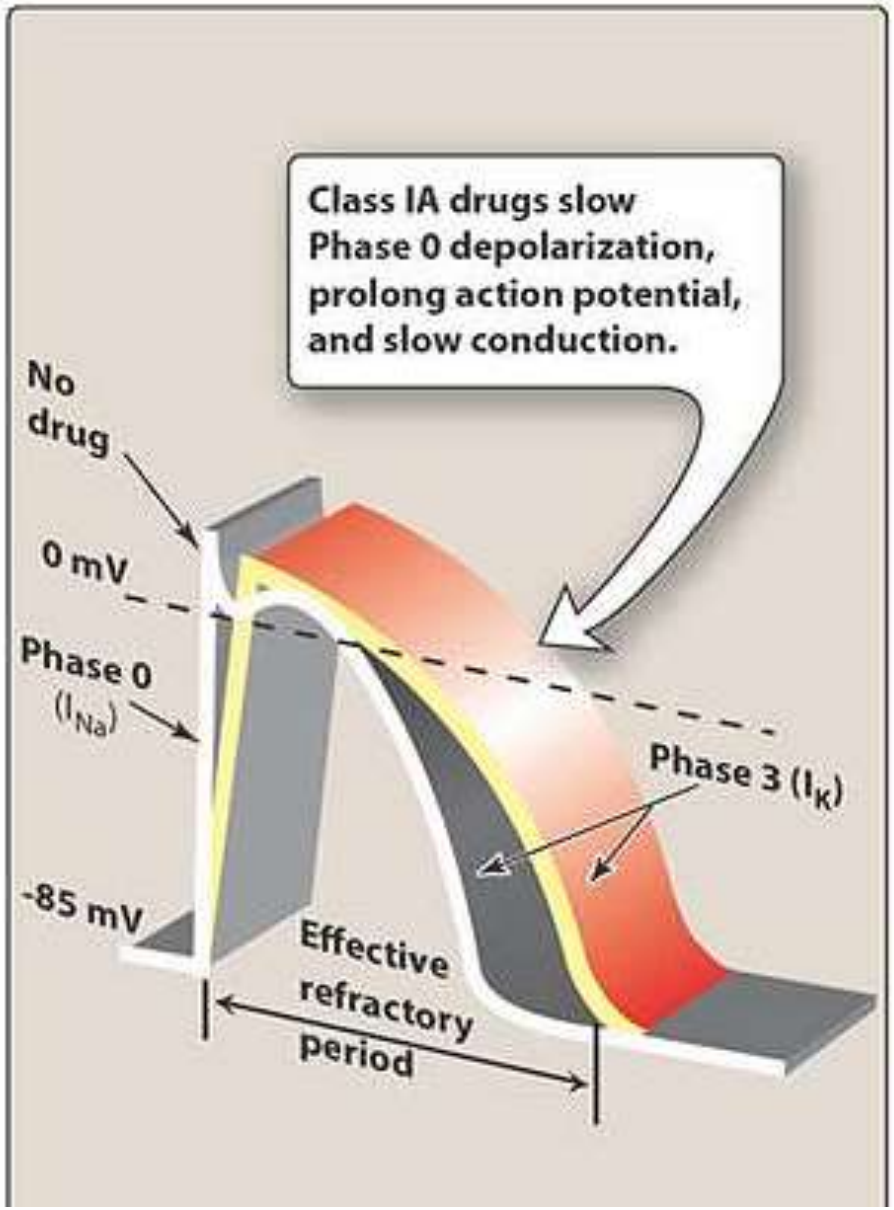
- Class I: Sodium channel blockers
- Class II: β-Adrenergic blockers
  - Propranolol, acebutolol, esmolol
- Class III: Potassium channel blockers
  - Amiodarone, bretylium, sotalol
- Class IV: calcium channel blockers
  - Verapamil, diltiazem
- Miscellaneous
  - PSVT: Adenosine, Digoxin
  - AV block: Atropine

Class I: Sodium channel blockers

- IA: Prolong repolarization
  - Quinidine, procainamide, disopyramide, morcizine
- IB: Shorten repolarization
  - Lignocaine, mexiletine, phenytoin
- 1C: Little effect on repolarization
  - Encainide, flecainide, propafenone

Class IA


Na+
Outside
Action potential currents
K+
K+
K+
K+
K+
Diastolic currents
Na+
Membrane
Inside
Ca2+
Ca2+
Ca2+
Ca2+
Ca2+
Quinidine, procainamide, and disopyramide block open or inactivated sodium


Class IA drugs slow Phase 0 depolarization, prolong action potential, and slow conduction.
No drug
0 mV
Phase 0 (I_{Na})
Phase 3 (I_K)
-85 mV
Effective refractory period

Quinidine

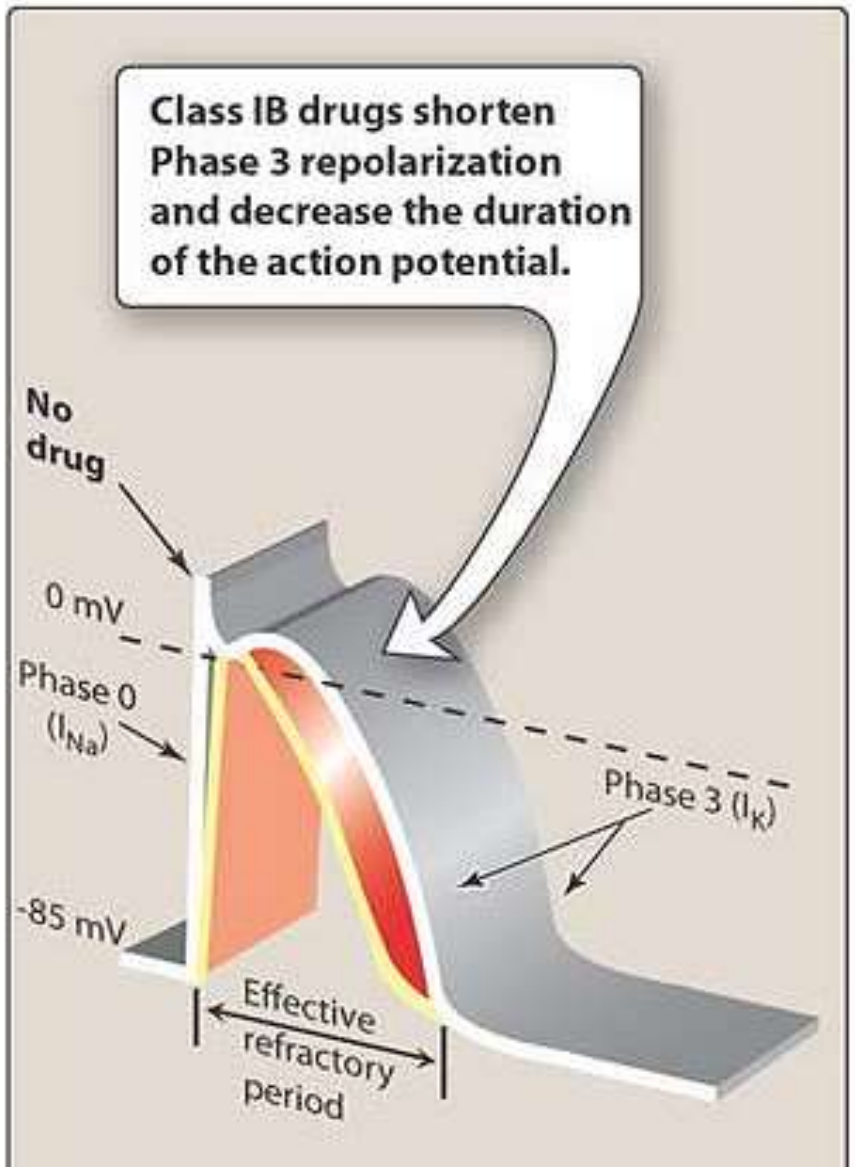
- D- isomer of quinine obtained from cinchona bark
- MOA: blocks sodium channels
  - ↓ automaticity , conduction velocity and prolongS repolarization
  - ↓phase 0 depolarization , ↑ APD & ↑ERP
- Other actions:
  - ↓ BP (α block), skeletal muscle relaxation
- Uses: Atrial and ventricular arrhythmias
- Adverse effects:
  - Arrhythmias and heart block , hypotension, QT prolongation
  - GIT , thrombocytopenia, hepatitis , idiosyncratic reactions
  - High doses – cinchonism like quinine

- Procainamide:
  - Derivative of procaine
  - No vagolytic or α-blocking action unlike quinidine
  - Better tolerated
  - Adverse effects:
    - Nausea, vomiting and hypersensitivity reactions
    - Higher doses can cause hypotension, heart block and QT prolongation
- Disopyramide:
  - Significant anticholinergic properties:
    - Dry mouth, blurred vision, constipation, urinary retention

Class IB drugs

Lignocaine, phenytoin, mexiletine

Block sodium channels also shorten repolarization



Lignocaine

- Local anaesthetic
- Raises threshold for action potential, ↓automaticity
- Suppress electrical activity of arrhythmogenic tissues, normal tissues less effected
- High first pass metabolism so given parenterally
- Use: ventricular arrhythmias
- Adverse effects:
  - Drowsiness, hypotension, blurred vision, confusion and convulsions

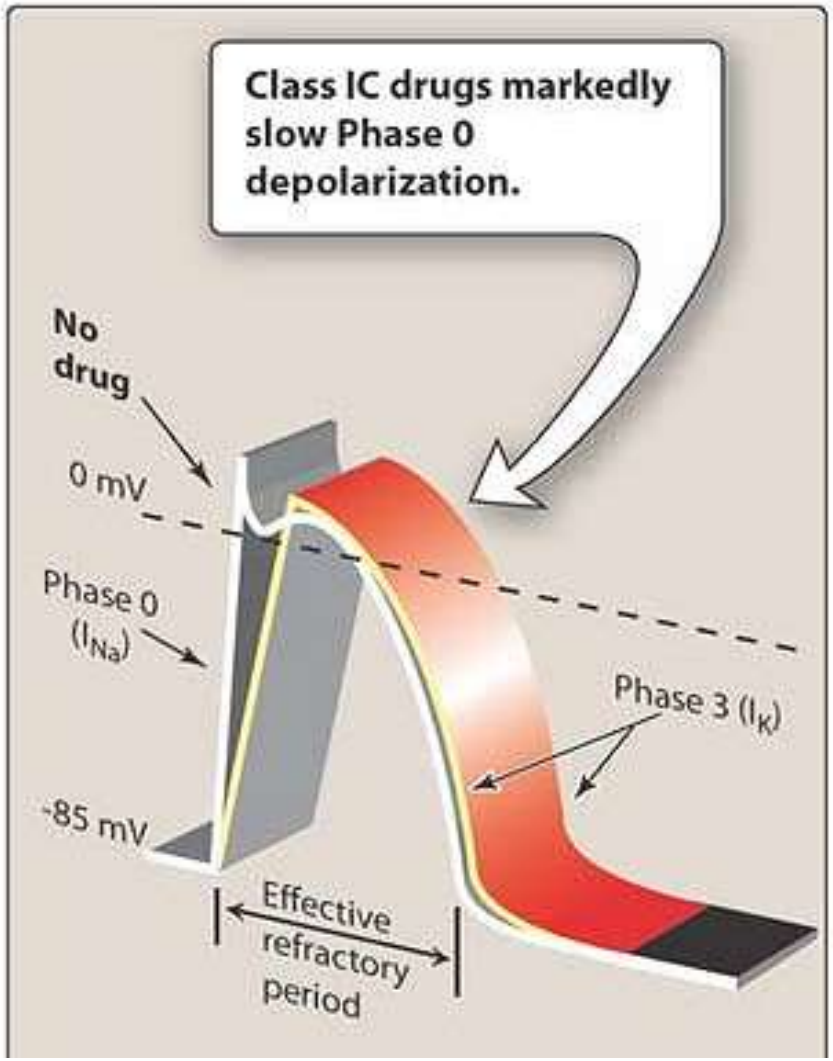
- Phenytoin:
  - Antiepileptic also useful in ventricular arrhythmias (not preferred) and digitalis induced arrhythmias
- Mexiletine:
  - Can be used orally causes dose related neurological adverse events like tremors and blurred vision
  - Nausea is common
  - Used as alternative to lignocaine in ventricular arrhythmias

Class I C drugs

Encainide, Flecainide, Propafenone

Have minimal effect on repolarization
Are most potent sodium channel blockers

- Risk of cardiac arrest , sudden death so not used commonly
- May be used in severe ventricular arrhythmias

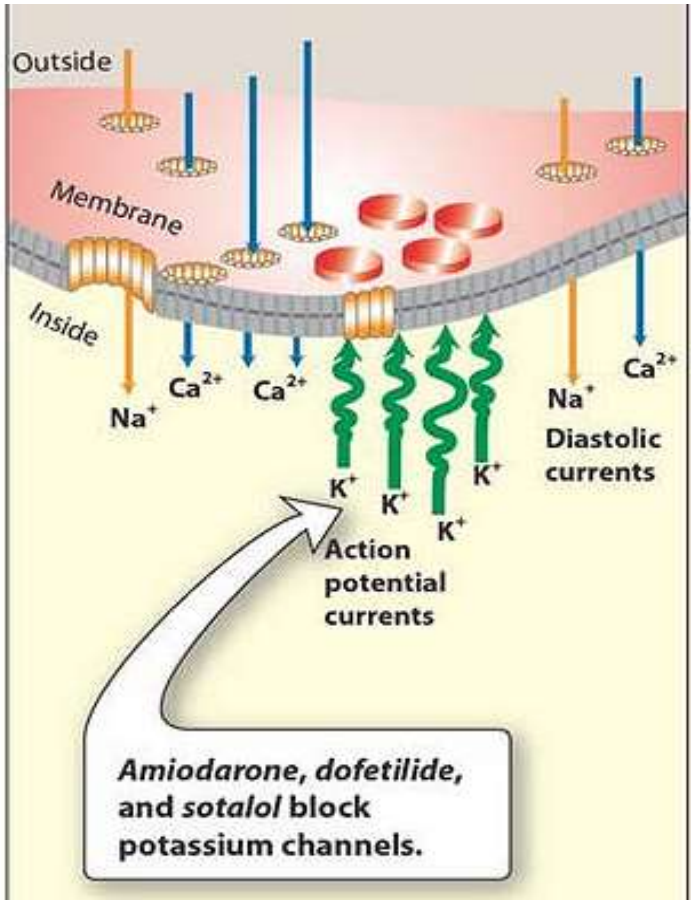


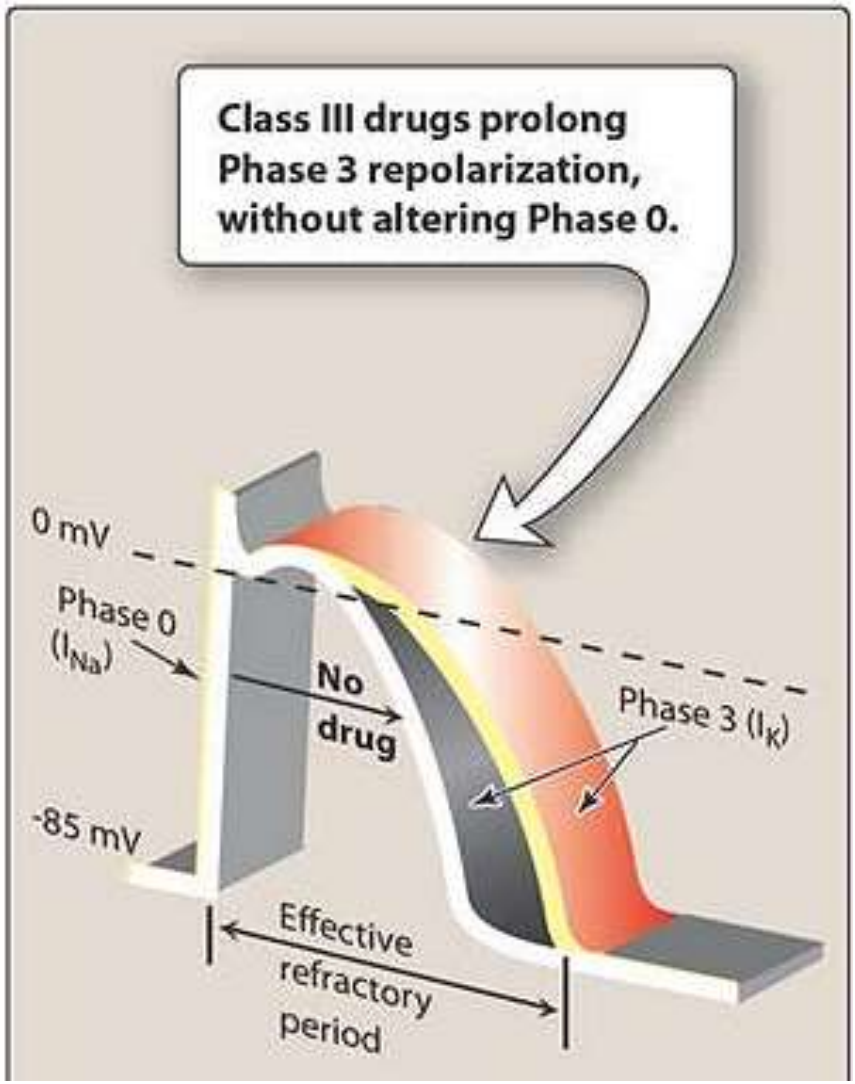
Class II drugs

- Supress adrenergically mediated ectopic activity
- Antiarrhythmic action due to of β blockade
- Depress myocardial contractility, automaticity and conduction velocity
- Propranolol:
  - Treatment & prevention of supraventricular arrhythmias especially associated with exercise, emotion or hyperthyroidism
- Esmolol:
  - IV short acting can be used to treat arrhythmias during surgery , following MI & other emergencies

Class III drugs

↑APD & ↑RP by blocking the K^+ channels





Amiodarone

- Iodine containing long acting drug
- Mechanism of action: (Multiple actions)
  - Prolongs APD by blocking K^+ channels
  - blocks inactivated sodium channels
  - β blocking action , Blocks Ca^{2+} channels
  - ↓ Conduction, ↓ectopic automaticity
- Pharmacokinetics:
  - Variable absorption 35-65%
  - Slow onset 2days to several weeks
  - Duration of action : weeks to months
  - Many drug interactions

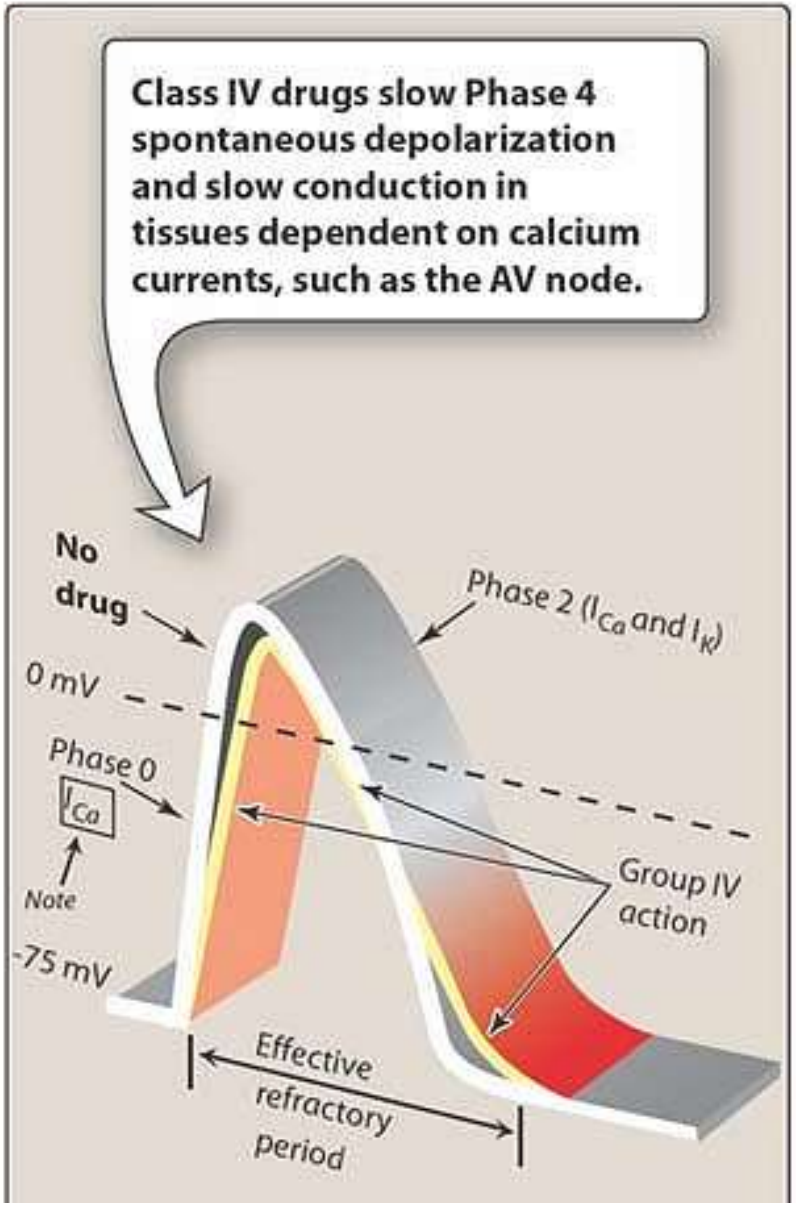
Amiodarone

- Uses:
  - Can be used for both supraventricular and ventricular tachycardia
- Adverse effects:
  - Cardiac: heart block , QT prolongation, bradycardia, cardiac failure, hypotension
  - Pulmonary: pneumonitis leading to pulmonary fibrosis
  - Bluish discoloration of skin
  - GIT disturbances, hepatotoxicity
  - Blocks peripheral conversion of T4to T3 can cause hypothyroidism or hyperthyroidism

- Bretylium:
  - Adrenergic neuron blocker used in resistant ventricular arrhythmias
- Sotalol:
  - Beta blocker
- Dofetilide:
  - Selective K^+ channel blocker, less adverse events
  - Oral use in AF to convert or maintain sinus rhythm
- Ibutilide:
  - K^+ channel blocker used as IV infusion in AF or flutter can cause QT prolongation

Calcium channel blockers (Class IV)

- Inhibit the inward movement of calcium ↓ contractility, automicity , and AV conduction.
- Verapamil & diltiazem



Verapamil

- Uses:
  - Terminate PSVT
  - control ventricular rate in atrial flutter or fibrillation
- Drug interactions:
  - Displaces digoxin from binding sites
  - ↓ renal clearance of digoxin

Other antiarrhythmics

- Adenosine :
  - Purine nucleotide having short and rapid action
  - Mechanism of action: AcetylCholine sensitive K+ channels and causes membrane hyperpolarization through interaction with A_1 type of adenosine GPCRs on SA node
  - IV suppresses automaticity, AV conduction and dilates coronaries
  - Drug of choice for PSVT
  - Adverse events:
    - Nausea, dyspnoea, flushing, headache
- Atropine: Used in sinus bradycardia
- Digitalis: Atrial fibrillation and atrial flutter
- Magnesium SO_4: digitalis induced arrhythmias