5 Central Nervous System

ANTIEPILEPTIC DRUGS

Ca Channel Blockers

1. **Valproate**

MOA –
- Blocks Ca/Na channels
- Increases GABA

Uses –
- ✓ DOC – GTCS/MS (JME)
- ✓ DOC – Mixed Seizure Syndrome (LGS/DS)
- ✓ DOC – Rapid Cyclers
- ✓ DOC – Rheumatic Chorea

S/E –

New – NTD (Most Teratogenic drug for epilepsy and BPD)
V – Vomiting, Nausea (MC)
A – Alopecia
L – Liver toxicity
P – Pancreatitis
O – Obesity
I – Increased ammonia
C – Carnitine antidote for hepatotoxicity/hyperammonemia
Tablet – Tremor

2. **Ethosuximide**

MOA – Blocks Ca channel
Use – DOC Absence Seizure

---

5. **Lamotrigine**
- MOA – Blocks Na/Ca channels, Decreases glutamate
- Use – GTCS/MS(JME)/PS/LGS
- S/E – SJS (Started at low doses)

6. **Topiramate**
- MOA – Blocks Na channels/ CA/AMPA/Kainate, Opens K channels
- Use – GTCS/PS/LGS
- Migraine prophylaxis, Obesity

S/E-
R – Renal Stones
A – Angle closure glaucoma
M – Metabolic Acidosis
Ate less – Weight loss

Na Channel Blockers

1. **Phenytoin (Diphenyl Hydantoin)**

Uses –
Oral – GTCS/PS
IV – Status Epilepticus

S/E –
H – Hirsutism/Hyperplasia of gums/Hyperglycemia
Y – lymphadenopathy
D – Diplopia, Vitamin D decreased (Hypocalcemia)
A – Ataxia
N – Nystagmus
T – Teratogenic (Facial clefts)
O – Osteomalacia
I – Increased bleeding in newborn (Prevent – Vitamin K to mother)
N – Neutropenia, Anemia (Due to folic acid deficiency)

2. **Carbamazepine**

Uses –
- ✓ DOC – Partial Seizure
- GTCS
- ✓ DOC – Trigeminal Neuralgia

S/E –
H – Hyponatremia (Delayed S/E, MC in elderly)
Hypersensitivity
E – Eosinophilia
A – Ataxia
Agranulocytosis
Aplastic anemia
D – Diplopia
S – SJS (Associated with HLA-B-1502 gene)

3. **Oxcarbazepine/ Eslicarbazepine acetate**
- Prodrugs of eslicarbazepine
- Cause lesser hypersensitivity but more hyponatremia than carbamazepine
- Uses same as carbamazepine

4. **Lacosamide**
- Causes slow inactivation of sodium channels
- Used in PS

Increase GABA Effect

1. **Tiagabine**
- Inhibits GABA reuptake
- Use – Partial Seizure

2. **Vigabatrin**
- MOA – Inhibits GABA Transaminase – Inhibits GABA metabolism
- Use –
- ✓ DOC – Infantile Spasm with Tuberous Sclerosis
- ❑ Partial Seizure
- S/E – Visual field defects

3. **Pregabalin/Gabapentin**
- GABA analogs
- MOA – Bind to presynaptic $\alpha_2\delta_1$ subunit of presynaptic voltage gated calcium channels
- Uses –
- ✓ DOC – Restless Leg Syndrome
- ✓ DOC – Post Herpetic Neuralgia
- ✓ DOC – Spinal cord injury pain
- ❑ PN, PS

Decrease Glutamate Effect

1. **Perampanel/Telampanel**
- AMPA blocker
- Use- PS

Miscellaneous

1. **Levetiracetam**
- Binds to SV2A on vesicle – Modulates release of neurotransmitters
- Use –
- ❑ GTCS/MS(JME)/PS
- ✓ DOC – Epilepsy in pregnancy (Levetiracetam > Lamotrigine)

2. **ACTH**
- ✓ DOC – Infantile/Salam spasm without Tuberous Sclerosis (West Syndrome)

OTHER ANTIBIOTICS

Drugs Acting on Cell Membrane

1. Polymyxins
- MOA – Form pseudopore after binding to cell membrane – Bactericidal
- Spectrum – Gram-negative

A. Polymyxin B
- Use – Topical – Skin infections
- Oral – GIT infections – Shigella

B. Polymyxin E – Colistin
- Use – IV
- ❑ MDR gram negatives – Pseudomonas, Enterobacter etc.
- ❑ NDM1 Beta lactamase producing bacteria
- S/E – Nephrotoxicity, Neuromuscular toxicity
- C/I – With aminoglycosides

2. Lipopeptide (Daptomycin)
- Use – IV
- ✓ DOC – VRSA
- ❑ MRSA, VRE
- S/E – Myopathy
- C/I – Pneumonia

MUST KNOW

DOC in VRSA pneumonia is Linezolid.

Antifolate Drugs

Sulfonamides
- MOA – Block DHPS – Bacteriostatic
- Sulfadiazine + Pyrimethamine – TOC Toxoplasmosis (Spiramycin – Pregnancy)
- Trimethoprim + Sulfamethoxazole (Cotrimoxazole) - Cidal
- ❑ Ratio of TMP:SMX = 1:5
- ❑ Uses – DOC -
- ❑ Cautery- Cystitis, Cyclosporiasis, Cepacia.B
- ❑ P-Pneumocystis
- ❑ I-Isosporiasis
- ❑ N-Nocardiosis
- ❑ S-Sarcocystosis, Stenotrophomonas (Add Ticarcillin)
- ❑ Sulfadiazine – Topical – DOC in burn patients
- ❑ Sulfasalazine – Rheumatoid arthritis, Ulcerative colitis

S/E –

Folic – Fetus – After birth kernicterus

Acid – Acute intermittent porphyria

Makes - Methemoglobinemia

R – Rash

B – Bone marrow suppression

C – Crystalluria

DNA Gyrase Inhibitors

1. Fluoroquinolones – Cidal

A. Norfloxacin

Use – UTI, Traveler's diarrhea

B. Ciprofloxacin
- Use – DOC
- ✓ Traveler's diarrhea
- ✓ Typhoid carrier
- ✓ Shigella
- ✓ Pyelonephritis
- ✓ Contact of meningococcal meningitis

C. Ciprofloxacin, Levofloxacin – Pseudomonas

D. Ofloxacin, Moxifloxacin – Leprosy and TB

E. Gemifloxacin, Moxifloxacin, Levofloxacin – Respiratory quinolones – Pneumonia

S/E –

P – Peripheral neuropathy

Q – QT prolongation

R – Rash – Photosensitivity

S – Seizure

T – Tendinitis

C/I – Pregnancy and Children – Cartilage growth defect

MUST KNOW

Moxifloxacin – Longest acting, Max QT prolongation, Max seizure.

ANTIFUNGAL DRUGS

1. Amphotericin B
- MOA – Sequesters ergosterol in cell membrane
- Route – IV with 5% D (Carrier)
- Use – DOC
- ✓ Systemic fungal infections
- ✓ Kala-azar
- ✓ Mucormycosis
- ✓ Cryptococcal meningitis
- ✓ Talaromyces
- S/E -
- ❑ Hypokalemia – Prevented by KCl
- ❑ Nephrotoxicity – Prevented by preloading NaCl and combining liposome.

2. Azoles
- MOA – Inhibit ergosterol synthesis in cell membrane – By inhibiting 14-α-Sterol demethylase
- Uses-
- ❑ Fluconazole – DOC – Candida (Only mucocutaneous infection e.g., vaginal and only against albicans species)
- ❑ Itraconazole – DOC – Endemic mycoses, Dermatophytes, Sporotrichosis
- ❑ Voriconazole – DOC Invasive Aspergillosis
- ❑ Posaconazole–Mucormycosis, GVHD
- ❑ Isavuconazole – Mucormycosis, Invasive Aspergillosis

3. Terbinafine
- MOA – Inhibits ergosterol synthesis – By inhibiting Squalene Epoxidase
- Use – Dermatophytes

4. Echinocandins (Caspofungin, Micafungin, Anidulafungin) –
- Block β-Glucan-Synthase
- Use – Aspergillus, Candida-DOC for systemic and non-albicans infection

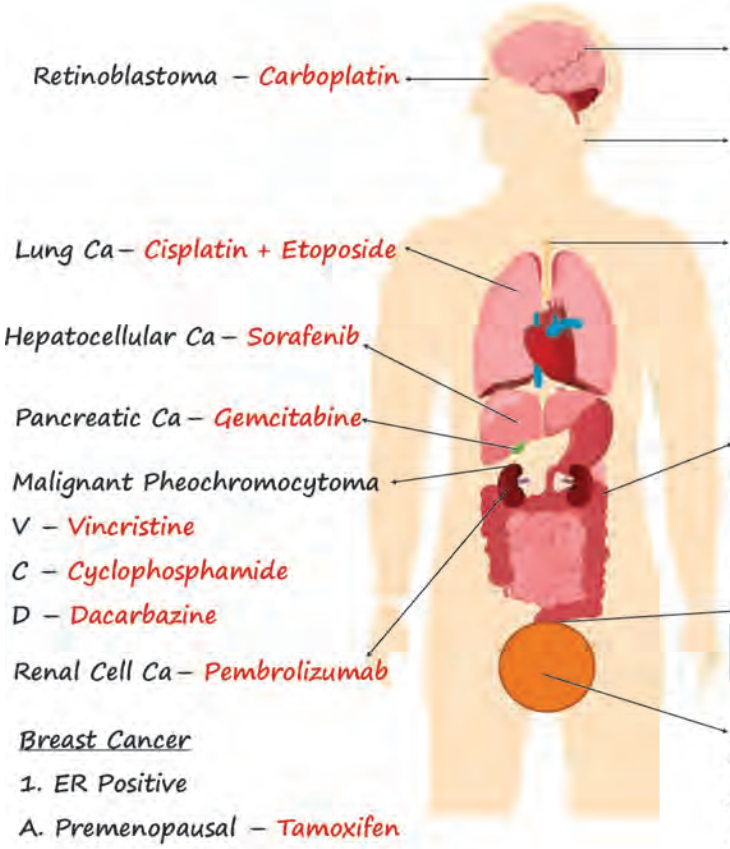
5. Griseofulvin - Blocks microtubules
- Route – Oral – With fatty food
- ✓ DOC – Tinea Capitis

6. Flucytosine –
- Prodrug of 5FU – Blocks DNA synthesis
- Use – Cryptococcal Meningitis

7. New drugs
- Tavaborole and Efinaconazole solution - Used in onychomycosis
- Oteseconazole and Ibrexafungerp used in recurrent vaginal candidiasis

7 Anticancer Drugs

DRUGS OF CHOICE



Retinoblastoma – Carboplatin

Brain Tumor – Temozolomide

Head and Neck Ca – Cisplatin

Lung Ca – Cisplatin + Etoposide

Esophageal/Gastric Ca – Cisplatin

MUST KNOW

To make a regimen for head and neck Ca, Esophageal Ca and Gastric Ca - Add 5 Fluorouracil to Cisplatin

Hepatocellular Ca – Sorafenib

Pancreatic Ca – Gemcitabine

Colorectal Ca – 5 Fluorouracil

MUST KNOW

To make a regimen for colorectal Ca - Add Oxaliplatin and/or irinotecan and Folinic Acid - Regimens - FOLFOX, FOLFIRI, FOLFIRINOX

Malignant Pheochromocytoma

V – Vincristine

C – Cyclophosphamide

D – Dacarbazine

Anal Ca – 5 fluorouracil

MUST KNOW

To make a regimen, add Mitomycin-C

Renal Cell Ca – Pembrolizumab

Urogenital Cancers – Cisplatin – To make regimen, add another drug

Ovary Ca – Cisplatin + Paclitaxel

Bladder Ca – Cisplatin + Gemcitabine

Cervical Ca - Cisplatin

Testicular Ca – B –Bleomycin

E – Etoposide

P – Platinum Compound (Cisplatin)

Breast Cancer

1. ER Positive
   - A. Premenopausal – Tamoxifen
   - B. Postmenopausal – Letrozole
2. Her-2 Positive – Trastuzumab
3. Triple Negative – 5 Fluorouracil + Epirubicin + Cyclophosphamide followed by Paclitaxel

BONE MARROW CANCERS

Leukemia

1. ALL – VPAD

Vincristine + Prednisolone + Asparaginase + Daunorubicin

2. AML –

Cytarabine + Daunorubicin/ Idarubicin

3. CLL – FCR

Fludarabine + Cyclophosphamide + Rituximab

4. CML

DOC – Imatinib – 1st gen

↓Resistance

Dasatinib

Nilotinib

Bosutinib – 2nd gen

↓Resistance

Ponatinib – 3rd gen

(BCR/ABL TKI (Enz Site))

↓ Resistance (T-315 I Mutation)

Asciminib – BCR/ABL TKI (Allost Site)

Omacetaxine – BCR/ABL Protein Inhib

Lymphoma

1. Hodgkin's – ABVD – Adriamycin, Bleomycin, Vinblastine, Dacarbazine
2. Non-Hodgkin's

A. Low Grade – FCR – Fludarabine, Cyclophosphamide, Rituximab

B. High grade – RCHOP – Rituximab, Cyclophosphamide, Hydroxydaunorubicin, Oncovin, Prednisolone

ANTICANCER DRUGS

Non-Cell Cycle Specific Drugs

1. Alkylating Agents

A. Nitrogen Mustards
- Cyclophosphamide – Activated into 4-hydroxycyclophosphamide
- Ifosfamide
- Mechlorethamine
- Melphalan
- Chlorambucil

B. Nitrosoureas
- Carmustine, Lomustine, Somustine
- Streptozocin

C. AA acting by methylation
- Procarbazine – S/E – Disulfiram like reaction
- Dacarbazine
- Temozolomide
- Miscellaneous
- Busulfan
- Thiotepa

2. Platinum Compounds

A. Cisplatin

B. Carboplatin

C. Oxaliplatin

3. Antitumor Antibiotics

A. Doxorubicin

B. Daunorubicin

C. Idarubicin

D. Epirubicin

E. Mitoxantrone

F. Bleomycin

Cell Cycle Specific Drugs

S-Phase Inhibitors

1. Antimetabolites

A. DHFR Inhibitors (Antifolate)
- Methotrexate
- PemetrexedPralatrexate
- Raltitrexed

B. Purine Analogs
- 6 Mercaptopurine
- 6 Thioguanine
- Fludarabine
- Cladribine
- Pentostatin

C. Pyrimidine Analogs
- 5 Fluorouracil
- Capecitabine
- Gemcitabine
- Cytarabine (Ara-c)

2. Topoisomerase Inhibitors

A. Topoisomerase-1 Inhibitors
- Irinotecan
- Topotecan

B. Topoisomerase-2 Inhibitors
- Etoposide
- Teniposide

3. Hydroxyurea – DOC – Sickle Cell Disease

4. Histone Deacetylase Inhibitors
- Romidepsin
- Belinostat
- Panobinostat

M-Phase Inhibitors

1. Vinka Alkaloids – Inhibit microtubule polymerization
- Vincristine, Vinblastine, Vinorelbine

2. Taxanes – Promote microtubule polymerization
- Paclitaxel, Docetaxel

3. Ixabepilone – Stabilizes microtubules

Miscellaneous Drugs

1. Retinoic Acid – DOC – Promyelocytic leukemia

2. Asparaginase
- Use – Leukemia
- S/E – Hyperglycemia, Hyperlipidemia, Hypersensitivity, Hypercoagulation, Hemorrhage

3. Proteasome Inhibitors
- Bortezomib, Carfilzomib – Used in multiple myeloma

4. FLT-3 Kinase Inhibitors
- Midostaurin, Gilteritinib – Used in AML

5. MAPK Inhibitors – Used in malignant melanoma

A. BRAF Inhibitors – Vemurafenib, Dabrafenib

B. MEK 1/2 Inhibitors – Trametinib, Cobimetinib

6. PI-3 Kinase Inhibitors – Idelalisib, Duvelisib - Used in CLL, NHL

7. CDK 4/6 Inhibitors – Palbociclib, Abemaciclib, Rivociclib – Used in ER positive breast cancer

8. Immune Checkpoint Inhibitors

New – Nivolumab - Used in Hodgkin's lymphoma
Star – Dostarlimab
Drugs – Durvalumab
Acting – Avelumab
At – Atezolizumab
Immune – Ipilimumab
Check – Cemiplimab
Point – Pembrolizumab – Used in uterine cancer

9. PARP Inhibitors –
- Olaparib, Niraparib – Used in BRCA positive ovarian, fallopian tube and primary peritoneal cancer
- Talazoparib – BRCA positive breast cancer

DRUGS USED IN OSTEOPOROSIS

Drugs Inhibiting Bone Resorption – Common S/E - Hypocalcemia

1. Bisphosphonates
- Oral – Alendronate, Risedronate
- IV – Pamidronate, Zoledronate

MUST KNOW

Zoledronate is most potent and longest acting.

- MOA – Block farnesyl pyrophosphate synthase – Induces osteoclast apoptosis
- Use –
✓ DOC – Osteoporosis (Oral drugs)
✓ DOC – Paget's disease and Hypercalcemia of malignancy (IV drugs)
- S/E –
❑ Esophagitis – Prevented by – Taking drugs with a full glass of water on empty stomach – Not lie down for 30 minutes
❑ Osteonecrosis of jaw
❑ Bone fracture – Femoral chalk stick fracture
- C/I – Renal failure

2. Denosumab
- MOA – Blocks RANK Ligand
- Use – Postmenopausal osteoporosis with high risk of fracture

3. Raloxifene – SERM – Used in postmenopausal osteoporosis

4. Calcitonin – Used in Postmenopausal osteoporosis, Hypercalcemia and Paget's disease

Drugs Increasing Bone Formation – Anabolic Drugs

1. PTH Analog – Teriparatide

2. PTHrP Analog - Abaloparatide
- Use –
- Postmenopausal osteoporosis with very high risk of fracture
❑ Bisphosphonates induced fracture
- S/E – Osteosarcoma – Max duration of use – 2 years
- C/I – Paget's disease

3. Romosozumab
- MOA – Blocks Sclerostin
- Use – Postmenopausal osteoporosis with very high risk of fracture
- Duration of use – Only 1 year – Effect decreases after 1 year
- S/E –

Arthralgia

MUST KNOW

Strontium Ranelate both inhibits resorption and stimulates formation.

THYROID DISORDERS

Hyperthyroidism

1. Thioamide Drugs

- MOA – Block Thyroid Peroxidase – Block synthesis of T3/T4
- Use –

Hyperthyroidism

✓ DOC – Methimazole in general population, 2nd and 3rd trimesters of pregnancy and lactation

✓ DOC – Propylthiouracil in 1st trimester of pregnancy

Thyroid Storm

✓ DOC – Propylthiouracil

(1st drug used though is propranolol in thyroid storm)

- S/E –

❑ Common – Rash and Agranulocytosis

❑ Methimazole – Teratogenic – Choanal/ Esophageal atresia and Cutis aplasia

❑ Propylthiouracil – Hepatotoxic

2. Potassium Iodide/Lugol's Iodine

- MOA –

❑ Block release of T3/T4

❑ Make thyroid gland small and firm

❑ Decreases blood vessels in thyroid-decreases bleeding during Sx

- Use – Prior to thyroid surgery

Hypothyroidism

1. T4 Salt – Levothyroxine

- Use –

✓ DOC – Replacement – Taken on empty stomach

❑ Thyroid Ca – To decrease TSH

❑ Myxedema coma

- S/E –

❑ Thyrotoxicosis

❑ Osteoporosis

❑ Atrial fibrillation – Decrease dose in arrhythmia

2. T3 salt – Liothyronine

Use –

Myxedema coma

---

3. Inhibitors of 5-deiodinase

PTU, β Blockers, Steroids, Amiodarone

4. Radioactive Iodine (I131)

- Use –

❑ Hyperthyroidism in elderly/patients with arrhythmia

❑ Thyroid Ca

- S/E – 2° Cancer
- C/I – Pregnancy

STEROIDS

MUST KNOW

- Learn about steroid use in clinical subjects.
- Side-effects of steroids are nothing but presentation of Cushing's disease.

Steroids	Potency	Half-life
Hydrocortisone	1	8-12 hours
Prednisone Prednisolone	4	12-36 hours
Methylprednisolone	5	12-36 hours
Triamcinolone	5	12-36 hours
Dexamethasone Betamethasone	50	36-72 hours

ANTIAGGREGANTS

1. Aspirin (Oral)

- MOA – Blocks COX-1 – Decreases synthesis of Thromboxane-A2
- Use – Prophylaxis of MI and stroke

2. P2Y12 Inhibitors

A. Irreversible (Oral)

- Clopidogrel
  - Use – Prophylaxis of MI
  - Variable effect due to CYP2C19 polymorphism
  - C/I – With Omeprazole – Decreases effect
- Ticlopidine
  - Toxic – Less used
  - S/E – Agranulocytosis, TTP-HUS, GIT upset
- Prasugrel
  - Fastest acting and most efficacious
  - Use – PCI in MI
  - S/E – Increased intracranial bleed
  - C/I – Cerebrovascular disorders – Stroke/TIA

B. Reversible

- Cangrelor
  - Adenosine analog – Short acting and IV route
  - Use – PCI in MI
- Ticagrelor
  - Not an adenosine analog – Long acting and Oral route
  - Use - Prophylaxis of MI and Stroke

3. Vorapaxar (Oral)

- MOA – Blocks protease activated receptor
- Use – Prophylaxis of MI (Not stroke)
- S/E – Increased intracranial bleed
- C/I – Cerebrovascular disorders – Stroke/TIA

4. GP IIb/IIIa Blockers (IV)

- Abciximab, Tirofiban , Eptifibatide
- Use –
  - PCI in MI
  - Acute Coronary syndrome

FIBRINOLYTICS

1. Streptokinase

- MOA – Binds to plasminogen and uncovers tPA binding site
- Clot nonspecific – Breaks fibrin both in plasma and clot – Higher risk of bleeding
- Higher dose requirement
- Less preferred

2. TPA Analogs

- Alteplase, Reteplase, Tenecteplase – Most clot specific
- More preferred – Clot specific – Lesser bleeding risk
- Use – STEMI, Ischemic stroke, Massive pulmonary embolism
- S/E – Bleeding – Treated with Tranexamic acid (DOC) > EACA (Antifibrinolytics)

Mnemonic

- C/I –
  - B – Brain tumor/aneurysm
  - R – Recent surgery/trauma
  - A – Aortic dissection
  - I – Hypertension, H/O Intracranial bleed
  - N – Noncompressive vascular punctures

HEMATOPOIETIC AGENTS

1. Erythropoetin Analogs

- Epoetin, Darbopoetin (Longer acting – More preferred)
- Use – DOC – Anemia due to
  - ✓ Chronic Renal Failure
  - ✓ Chemotherapy, Zidovudine
  - ✓ Dialysis
- S/E – Hypertension, Thrombosis, Pure red cell aplasia, Fe deficiency

2. G-CSF Analog – Filgrastim, Lipegfilgrastim (Longer acting – More preferred)
3. GM-CSF Analog – Sargramostim
   - Both use – Neutropenia due to HIV, Chemotherapy
   - Both S/E – Bone pain
4. IL 11 Analog – Oprelvekin – Use – Chemo induced thrombocytopenia
5. Thrombopoietin agonist – Romiplostim, Eltrombopag – Used in ITP

14 18 Images/Spotters

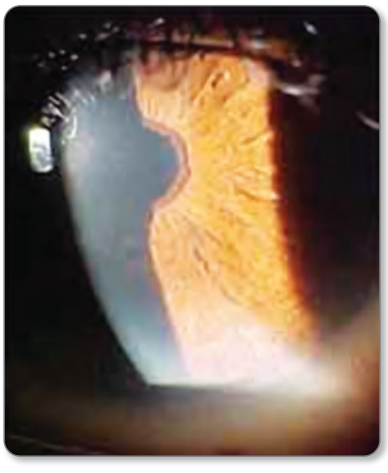
1. Physostigma Venenosum

2. Amiodarone Induced Blue Gray Pigmentation – Ceruloderma

3. Digitalis Lanata

4. Datura

5. Amiodarone Induced Whorl Like Corneal Deposits



6. Papaver Somniferum

15 New Drugs 2024

Drug	MOA	Uses
Enmetazobactam	Beta lactamase inhibitor	Used with Cefepime for complicated UTI
Tislelizumab	PD-1 Blocker	Esophageal cancer
Resmetirom	Thyroid hormone receptor beta agonist	NASH
Aprocitentan	Endothelin receptor antagonist	Mild/Moderate Hypertension
Sotatercept	Activin signaling inhibitor	PAH
Vadadustat	Hypoxia-inducible factor prolyl hydroxylase (HIF PH) inhibitor	Anemia of CKD
Nogapendekin alfa	IL-5 receptor agonist	Used with BCG for treatment of bladder cancer
Tovorafenib	BRAF inhibitor	Low grade glioma
Elafibranor	PPAR agonist – alpha, gamma, delta	Primary biliary cholangitis
Seladelpar	PPAR agonist – delta	Primary biliary cholangitis
Sofpironium	Anticholinergic	Axillary hyperhidrosis
Donanemab	Anti-beta amyloid antibody	Mild Alzheimer's disease
Palopegteriparatide	PTH analog	Hypoparathyroidism
Axatilimab	Colony stimulating factor-1 receptor (CSF-1R)-blocking antibody	Resistant chronic GVHD
Xanomeline	Cholinergic drug – Stimulates M1 and M4	Psychosis Note: Trospium is added to prevent peripheral side-effects
Sulopenem	Carbapenem	Uncomplicated UTI Note: Probenecid is added to increase half-life.
Revumenib	Menin inhibitor	Relapsed ALL
Landiolol	Beta blocker – Shortest acting– Metabolized by pseudocholinesterase – Half-life 4 minutes Esmolol – Previously shortest acting with half-life of 9 minutes	IV route – Short-term rate control in atrial fibrillation/ flutter
Olezarsen	Antisense oligonucleotide directed against ApoC-III	Familial chylomicronemia syndrome – To decrease triglycerides