KMCH INSTITUTE OF HEALTH SCIENCES AND RESEARCH

(A unit of Kovai Medical Centre and Hospital Limited)

Coimbatore,Tamilnadu

SERIES 1

AUG 2019

DEPARTMENT OF PHARMACOLOGY- NEW DRUG UPDATE

Imipenem + Cilastatin + Relebactam

- It's a triple drug combination of Imipenem, Cilastatin, Relebactam.
- **Approved by US-FDA on 16th July 2019 (Brand name: RECARBRIO)**

Mechanism of Action

- **Imipenem-** a beta lactam antibiotic, which inhibits bacterial cell-wall synthesis by binding to penicillin-binding proteins(PBP 2 and PBP1B) in Enterobacteriaceae and Pseudomonas aeruginosa.
- **Cilastatin-** a renal dehydropeptidase inhibitor limits the renal metabolism of Imipenem.
- **Relebactum-** a betalactamase inhibitor,which protects Imipenem from degradation by certain serine beta lactamases such as Sulhydryl variable (SHV), Temoneira (TEM), Cefotaximase-Munich (CTX-M), *Enterobacter cloacae* (P99), Pseudomonas-derived caphalosporinase (PDC) & *Klebsiella-pneumoniae* carbapenemase (KPC).

Indications

- Complicated intra-abdominal infections
- Urinary tract infections

Dosage and Administration

RECARBRIO 1.25 grams (Imipenem 500mg, Cilastatin 500mg, Relebactam 250 mg) can be administered **as intravenous (IV) infusion** over 30 minutes every 6 hours in patients 18 years of age & older with Creatinine Clearance (CrCl) ≥ 90 mL/min.

Warnings

- History of hypersensitivity Reactions
- ↑ **Risk for seizure** when used concomitantly with,
  a) Ganciclovir
  b) Valproic acid

Adverse Effects

- Diarrhea
- Nausea
- Headache
- Vomiting
- ↑**ALT, AST**
- Phlebitis/infusion site reactions
- Pyrexia
- Hypertension

Bibliography

FDA approves new treatment for complicated urinary tract and complicated intra-abdominal infections". Food and Drug Administration. July 17, 2019.

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SERIES 2

SEP 2019

DEPARTMENT OF PHARMACOLOGY- NEW DRUG UPDATE

1. Istradefylline

- **Date of FDA Approval:** August 27, 2019
- **Indication**: Adjunctive treatment to levodopa/carbidopa in adult patients with **Parkinson's disease** experiencing "OFF" episodes.
- **Formulation**: Tablet
- **Dose:** 20 mg orally once daily; max of 40 mg orally once daily
- **Mechanism of action:** Adenosine A2A receptor Antagonist

2. Lefamulin

- **Date of FDA Approval:** August 19, 2019
- **Indication**: **Community-acquired bacterial pneumonia**
- **Formulation**: Tablet and Injection
- **Dose**: 150 mg IV / 600 mg orally twice daily x 5 -7 days
- **Mechanism of action**: First-in-class, semi-synthetic pleuromutilin antibiotic, Inhibits protein synthesis by binding to 50S of the bacterial ribosome.

3. Upadacitinib

- **Date of FDA Approval**: August 16, 2019
- **Indication:** Treatment of adult patients with **moderate to severe rheumatoid arthritis**.
- **Formulation**: Extended-Release Tablet
- **Dose**: 15 mg orally once daily
- **Mechanism of action**: Janus kinase (JAK) inhibitor

4. Fedratinib

- **Date of FDA Approval**: August 16, 2019
- **Indication**: Intermediate-2 or high-risk primary or secondary **myelofibrosis (MF)**
- **Formulation:** Capsule
- **Dose:** 400 mg orally once daily
- **Mechanism of action:** Highly selective Janus kinase 2 (JAK2) inhibitor

5. Entrectinib

- **Date of FDA Approval:** August 15, 2019
- **Indication:** ROS1-positive, metastatic **non-small cell lung cancer** (NSCLC) & neurotrophic tyrosine receptor kinase (NTRK) gene fusion-positive **solid tumors**.
- **Formulation**: Capsule
- **Dose:** 600 mg orally once daily
- **Mechanism of action:** Selective tyrosine kinase inhibitor

6. Pitolisant

- **Date of FDA Approval:** August 14, 2019
- **Indication**: **Excessive daytime sleepiness** in adult patients with narcolepsy.
- **Formulation**: Tablet
- **Dose**: Initiate with 8.9 mg orally once daily
- **Mechanism of action:** Histamine-3 (H_3) receptor antagonist/inverse agonist

7. Pretomanid

- **Date of FDA Approval**: August 14, 2019
- **Indication:** Part of a combination regimen with Bedaquiline & Linezolid for adults with **pulmonary extensively drug resistant (XDR),** treatment-intolerant or nonresponsive **multidrug-resistant (MDR) tuberculosis (TB)**
- **Formulation**: Tablet
- **Dose**: Pretomanid 200 mg orally once daily x 26 weeks
- **Mechanism of action**: It act as a bacterial respiratory poison and inhibits bacterial cell wall mycolic acid biosynthesis.

8. Pexidartinib

- **Date of FDA Approval**: August 2, 2019
- **Indication:** **Tenosynovial giant cell tumor (TGCT)** in adults.
- **Formulation:** Capsule
- **Dose:** 400 mg orally twice daily on an empty stomach
- **Mechanism of action:** Tyrosine kinase inhibitor

References

1.https://www.drugs.com/newdrugs.html
2.https://www.medscape.com/drugs

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SERIES 3

OCT 2019

DEPARTMENT OF PHARMACOLOGY- NEW DRUG UPDATE

1. Smallpox and Monkeypox Vaccine (Jynneos)

Date of FDA Approval: September 24, 2019

Indication: Prevention of Smallpox and Monkeypox (Orthopoxvirus)

Formulation: Subcutaneous Suspension

Dose: 0.5 mL subcutaneously x 2 doses 4 weeks apart

Mechanism of action: Attenuated, live, nonreplicating Smallpox and Monkeypox Vaccine that elicits humoral and cellular immune responses

2. Semaglutide (Rybelsus)

Date of FDA Approval: September 20, 2019

Indication: Type 2 Diabetes mellitus

Formulation: Tablet

Dose: 3 mg orally once daily for 30 days

Mechanism of action: Glucagon-like Peptide-1 (GLP-1) receptor agonist - reduces blood glucose by stimulating insulin secretion and lowering glucagon secretion, in a glucose-dependent manner.

3. Tenapanor (Ibsrela)

Date of FDA Approval: September 12, 2019

Indication: Irritable Bowel Syndrome with constipation (IBS-C)

Formulation: Tablet

Dose: 50 mg orally twice daily

Mechanism of action: First-in-class, Inhibits Sodium / Hydrogen Exchanger 3 (NHE3), an antiporter on the apical surface of enterocyte of the small intestine and colon primarily responsible for the absorption of dietary sodium

4. Glucagon (Gvoke)

Date of FDA Approval: September 10, 2019

Indication: Severe hypoglycemia in diabetes patients

Formulation: Ready-to-use, auto-injector and pre-filled syringe for subcutaneous injection

Dose:
For adults and pediatric patients aged 12 years and older - 1 mg.
For children aged 2 to < 12 years: < 45 kg - 0.5 mg, ≥ 45 kg - 1 mg

Mechanism of action: Glucagon increases blood glucose concentration by activating hepatic glucagon receptors

References

1.https://www.drugs.com/newdrugs.html
2.https://www.medscape.com/drugs

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SERIES 4

NOV 2019

DEPARTMENT OF PHARMACOLOGY- NEW DRUG UPDATE

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Innovation drives progress.

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4. Minocycline
5. Lasmiditan
6. Asenapine
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8. Brolucizumab-dbll
9. Teriparatide
10. Trifarotene

- *Newer drugs*
- *Existing drugs with change in formulation*

1. DIROXIMEL FUMARATE

DIROXIMEL FUMARATE is similar to dimethyl fumarate, in efficacy, but its unique chemical structure is less likely to cause GI irritation. It acts by regulating cell signalling pathways causing beneficial immune & neuroprotective effects.

DIROXIMEL FUMARATE used in **relapsing forms of multiple sclerosis (MS)** in adults with active secondary progressive disease, clinically isolated syndrome & relapsing-remitting MS

Dosage & administration: Available as delayed release capsule 231 mg to be taken orally twice daily for 7 days. Maintenance dose of 462mg twice daily for 7days.

Adverse effects: Flushing, abdominal pain, diarrhea and nausea.

Date of FDA Approval: Oct 29,2019

2.ELEXACAFTOR+TEZACAFOR+ IVACAFTOR & IVACAFTOR

ELEXACAFTOR, TEZACAFTOR & IVACAFTOR combined therapy ↑quantity & function of F508del-Cystic fibrosis transmembrane conductance regulator (CFTR) protein at the cell surface, resulting in ↑CFTR activity as measured by CFTR mediated chloride transport.

ELEXACAFTOR+TEZACAFTOR+ IVACAFTOR & IVACAFTOR is indicated in **cystic fibrosis**

Dosage & administration: Per orally 2 fixed-dose tablets (Elexacaftor100 mg, Tezacaftor 50 mg and Ivacaftor 75 mg) once in the morning, one Ivacaftor 150-mg tablet in the evening, 12 hours apart. Should be taken orally with fat-containing food

Adverse effects: Headache, upper respiratory tract infection , diarrhea

Date of FDA Approval: Oct 21, 2019

3. PHENYLEPHRINE HYDROCHLORIDE

PHENYLEPHRINE HYDROCHLORIDE is an alpha-1 adrenergic receptor agonist causing vasoconstriction, used for the treatment of **hypotension** during anesthesia

Dosage & administration: PHENYLEPHRINE is available as a ready to use injection. IV bolus: 40-100 mcg. If BP < target, start a continuous IV infusion at a dose of 10-35 mcg/min; not to exceed 200 mcg/min

Adverse effects: Nausea, vomiting, headache, exacerbation of angina, heart failure, pulmonary arterial hypertension, peripheral & visceral ischemia, skin & subcutaneous necrosis, bradycardia

Date of FDA Approval: Oct 21, 2019

4. MINOCYCLINE

MINOCYCLINE, a broad spectrum antibiotic, acts topically by an unknown mechanism and it is indicated in **inflammatory lesions of non-nodular moderate-to-severe acne vulgaris**

Dosage & administration: Topical Foam 4%. Apply to acne-affected areas once daily at night, repeat until it resolves.

Adverse effects: Headache, rarely systemic side effects similar to oral minocycline

Date of FDA Approval: Oct 18, 2019

5. LASMIDITAN

LASMIDITAN is a serotonin (5-HT) 1F receptor agonist, indicated for **Acute migraine with or without aura in** adults

Dosage & administration: 50 mg, 100 mg, or 200 mg tablet

Adverse effects: Dizziness, fatigue, paresthesia, sedation, nausea and/or vomiting, and muscle weakness

Date of FDA Approval: Oct 11, 2019

6. ASENAPINE

ASENAPINE acts by an unknown mechanism, probably via combined antagonist activity at dopamine D_2 and serotonin type 2 ($5\text{-}HT_2$) receptor, indicated in **Schizophrenia**

Dosage & administration: Transdermal System. Apply 3.8 mg/24 hours patch initially & ↑ 5.7 mg/24 hr or 7.6 mg/24 hr after 1 week

Adverse effects: Restlessness, difficulty moving, muscle stiffness, tremors, skin irritation, weight gain

Date of FDA Approval: Oct 11, 2019

7. AFAMELANOTIDE

AFAMELANOTIDE is a First-in-class. Selective agonist of the melanocortin 1 receptor (MC1R), acts by ↑the levels of melanin in the skin & shields against UV radiation and sunlight, used to Prevent **Phototoxicity in Erythropoietic Protoporphyria**

Dosage & administration: Available as a Subcutaneous Implant - 16mg implanted SC every 2 months

Adverse effects: Implant site reaction, nausea, oropharyngeal pain, cough, fatigue, dizziness, skin hyperpigmentation, somnolence, melanocytic nevus, respiratory tract infection, non-acute porphyria, skin irritation.

Date of FDA Approval: Oct 8, 2019

8. BROLUCIZUMAB- dbll

BROLUCIZUMAB- dbll, binds to Human vascular endothelial growth factor - A (e.g., VEGF110, VEGF121 and VEGF165), thereby prevents the interaction with receptors VEGFR-1 and VEGFR-2 & suppresses endothelial cell proliferation, neovascularization and vascular permeability

BROLUCIZUMAB- dbll is used to treat **Neovascular (wet) age-related macular degeneration (AMD).**

Dosage & administration: Available as an Intravitreal Injection. 6 mg monthly for the first three doses, followed by one dose of 6 mg every 8-12 weeks

Adverse effects: Blurred vision, cataract, conjunctival hemorrhage, vitreous floaters, eye pain, endophthalmitis, retinal detachment, ↑ intra-ocular pressure & arterial thromboembolic events

Date of FDA Approval: Oct 7, 2019

9. TERIPARATIDE

TERIPARATIDE is a Parathyroid hormone analog (PTH 1-34)

TERIPARATIDE is used in **postmenopausal osteoporosis,** ↑ bone mass in men with primary **hypogonadal osteoporosis**, sustained systemic **glucocorticoid therapy induced osteoporosis**

Dosage & administration: Single-patient-use pen for subcutaneous injection at a dose of 20 mcg subcutaneously once a day

Adverse effects: Arthralgia, pain and nausea

Date of FDA Approval: Oct 4, 2019

10. TRIFAROTENE

TRIFAROTENE is an agonist of retinoic acid receptors (RARγ), stimulation of RAR results in modulation of target genes which are associated with cell differentiation and mediation of inflammation. The exact process by which trifarotene ameliorates acne is unknown

TRIFAROTENE is used to treat **Acne vulgaris** in patients aged 9 years and above

Dosage & administration: 0.005% Topical Cream. Apply a thin layer of cream to the affected areas of the face and/or trunk once a day, in the evening, on clean and dry skin

Adverse effects: Site irritation, application site pruritus (itching), and sunburn

Date of FDA Approval: Oct 4, 2019

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SERIES 5
DEC 2019

DEPARTMENT OF PHARMACOLOGY- NEW DRUG UPDATE

Innovation drives progress.

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- *Novel drugs*
- *Former drugs with formulation change*

S.No	Drug Name	Mechanism of Action	Indications	Dosage Formulation	Date of FDA Approval
1.	**Methotrexate**	Folate analog metabolic inhibitor	Rheumatoid arthritis, Juvenile idiopathic arthritis, Psoriasis	Subcutaneous Injection	November 27, 2019
2.	**Voxelotor**	HbS (sickle hemoglobin) polymerization inhibitor	Sickle cell anemia	Tablet	November 25, 2019
3.	**Riluzole**	Glutamate inhibitor	Amyotrophic lateral sclerosis patients with dysphagia	Oral Film	November 22, 2019
4.	**Cenobamate**	Selective blocker of the inactivated state of voltage-gated sodium channel	Partial-onset seizures in adult patients	Tablet	November 21, 2019
5.	**Givosiran**	Aminolevulinate synthase 1-directed small interfering RNA	Acute hepatic porphyria	Injection	November 20, 2019
6.	**Crizanlizumab-tmca**	P-Selectin inhibitor	Prevention of vaso-occlusive crises in Sickle cell disease	Injection	November 15, 2019
7.	**Adalimumab-afzb** (Biosimilar)	Tumor necrosis factor blocker	Rheumatoid arthritis , Juvenile idiopathic arthritis, Psoriatic arthritis, Ankylosing spondylitis, Crohn's disease & Ulcerative colitis, Plaque psoriasis	Injection	November 15, 2019
8.	**Zanubrutinib**	Bruton's tyrosine kinase inhibitor	Adult patients with Mantle cell lymphoma who have received at least one prior therapy	Capsule	November 14, 2019
9.	**Cefiderocol**	Siderophore cephalosporin – inhibits bacterial cell wall synthesis	Complicated urinary tract infections- in patients with limited / no alternative treatment options	Injection	November 14, 2019
10.	**Luspatercept-aamt**	First-in-class erythroid maturation agent. Recombinant fusion protein that binds several endogenous TGF-β superfamily ligands, thereby diminishing Smad2/3 signaling	Transfusion-dependent Beta-thalassemia-associated anemia	Injection	November 8, 2019
11.	**Amoxicillin, Omeprazole and Rifabutin**	Amoxicillin inhibits cell wall biosynthesis, Omeprazole inhibits proton pump, Rifabutin inhibits DNA-dependent RNA polymerase	*Helicobacter pylori* infection	Delayed-Release Capsule	November 4, 2019
12.	**Pegfilgrastim-bmez** (Biosimilar)	PEGylated growth colony-stimulating factor	Reduce the incidence of Febrile neutropenia in patients treated with chemotherapy	Injection	November 4, 2019

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