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NEWS LETTER OF CLINICAL PHARMACY

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Vision

St.Peter's is committed to generate, disseminate and preserve knowledge and work with pioneers of this knowledge, and to be the most sought after institute globally in the field of pharmaceutical sciences by creating world class pharmacy professionals and researchers.

Mission

To achieve academic excellence with integrity and creating opportunities for leadership and responsibilities through groundbreaking performance in the field of Pharmaceutical Sciences by educating students with pharmaceutical needs of the society and to advance the knowledge through research and to serve the profession and community.

FDA APPROVED DRUG LIST:

Drug name	Category	MOA	Approval of drug	Treatment	Complications	Precautions
Ubrelvy	Calcitonin gene-related peptide antagonist	It is a Calcitonin gene related peptide receptor antagonist.	23/12/2019	To treat acute treatment of migraine with or without aura in adults.	Sleepiness, dry mouth, nausea, allergic reactions.	Should not take ubrelvy if you are taking medicines known as strong CYP3A4 inhibitors, such as: ketoconazole, clarithromycin, itraconazole
Dayvigo	Orexin receptor antagonist	In the treatment of insomnia is presumed to be through antagonism of orexin receptors. The orexin neuropeptide signaling system plays a role in wakefulness.	20/12/2019	To treat insomnia.	Inability to walk and talk, weak feeling in legs, unusual thoughts or behaviour.	Patients should be advised not to consume alcohol in combination with dayvigo because of additive effects.
Caplyta	Atypical antipsychotics	Its MOA is currently unknown. Its efficacy may be mediated through a combination of antagonist activity at central serotonin 5-HT2A receptors and post synaptic antagonist activity at central dopamine D2 receptors, according to the release.	20/12/2019	To treat schizophrenia.	Drowsiness, dizziness, lightheadedness, dry mouth, nausea.	It carries a black box warning foe adverse cerebrovascular reaction, in elderly patients who have dementia- related psychosis. Should avoid caplyta with CYP3A4 inducers.
Padcev	Anti-cancer chemotherapy drug	It is an ADC. The antibody is a human IgG1 directed against Nectin-4, an adhesion protein located on the surface of the cells. The small molecule, MMAR, is a microtubule disrupting agent attached to the antibody via protease- cleavable linker.	18/12/2019	To treat refractory bladder cancer.	Numbness or tingling in the hands or feet, muscle weakness,	Inform doctor if you have diabetes before starting treatment with padcev. Isn’t safe for people with liver damage.

Vyondys 53	Anti-sense Oligonucleotides	It is designed to bind to exon 53 of dystrophin pre mRNA resulting in exclusion of this exon during mRNA processing in patients with genetic mutations that are amenable to exon 53 skipping.	12/12/2019	To treat certain patients with Duchenne muscular dystrophy.	Headache, fever, falls, abdominal pain, runny or stuffy nose, cough, vomiting, nausea.	Possible risk of kidney problems. Allergic reactions may occur. Should not be used in pregnancy and breast feeding.
Oxbryta	Hbs polymerization inhibitor	It binds directly to hemoglobin S, allowing oxygen affinity to normalize and inhibit polymerization.	25/11/2019	To treat sickle cell disease.	Fever, low energy. A skin rash, headache, nausea.	Allergic reactions may occur. Should not be used in pregnancy and breast feeding.
Xcopri	Anti-epileptic drug	It is used to reduce repetitive neuronal firing by inhibiting voltage gated sodium currents. It is a positive allosteric modulator of GABA A ion channels.	21/11/2019	To treat partial onset seizures.	Drowsiness, dizziness, tiredness, nausea, vomiting, constipation	May cause kidney problems, liver problems, mental/mood disorders.
Fetroja	Cephalosporin antibacterial drug	It is a cyclosporin antibacterial with activity against gram negative aerobic bacteria. It functions as a siderophore and binds to extracellular free ferric iron.	14/11/2019	To treat patients with complicated urinary tract infections who have limited or no alternative treatment options.	Diarrhoea, infusion site reactions, constipation, rash, candidiasis, cough, elevations in liver tests.	May cause severe allergic reactions, liver problems, kidney problems, seizures.
Brukinsa	Bruton's tyrosine kinase inhibitor	It is a small molecule inhibitor of BTK. It forms a covalent bond with a cysteine residue in the BTK active site, leading to inhibition of BTK activity.	14/11/2019	To treat certain patients with mantle cell lymphoma, a form of blood cancer.	Decreased neutrophil and platelet count, upper respiratory tract infection.	Inform doctor your medical history especially of: bleeding/blood problems, heart problems, high blood pressure, liver problems
Reblozyl	Erythroid maturation agent	It regulates the maturation of RBCs. It does this by blocking a signalling pathway called Smad3/3 that slows down the maturation of RBCs.	8/11/2019	For the treatment of anemia in adult patients with beta thalassemia who require regular RBC transfusions	Headache, bone pain, joint pain, fatigue, cough, abdominal pain.	May cause allergic reactions, risk for blood clots, hypertension, not safe for pregnancy, breast feeding.

Reyvow	Serotonin (5-HT) receptor agonist	It binds with high affinity to the 5-HT1F receptor. It presumably exerts its therapeutic effects in the treatment of migraine through agonist effects at the 5-HT1F receptor; the precise mechanism is unknown.	11/10/2019	For the acute treatment of migraine with or without aura in adults.	Fast heartbeat, hallucinations, loss of coordination, severe dizziness, twitching muscles, fever.	Inform doctor your medical history especially of: slow heartbeat, liver disease, high blood pressure.

MONOGRAPH ON PEXIDARTINIB

- **Name:**Pexidartinib
- **Description:**Pexidartinib is an oral small molecule and selective tyrosine kinase inhibitor (TKI) that works by inhibiting the colony stimulating factor csf-1 receptor pathway.
- **Brand Name:**Turalio
- **Dosage form**: Capsule
- **Dose:** 200mg
- **Categories:** Amines
- **Indications:** Patients with symptomatic tenosynovial giant cell tumor (TGCT)
- **Associated Condition:** Symptomatic tenosynovial giant cell tumor.
- **Mechanism of Action:**Tenosynovial giant cell tumor (TGCT) is a rare, non- malignant neoplasm affecting the synoviumbursae (or) tendon sheath, where the synovium and tendon sheath thicken and overgrow, causing damage to surrounding tissue.Pexidartinib targets the csf1/csf1R pathway as selective csf1R inhibitors.If stimulates the auto inhibited state of the CSF1R by interacting with the juxtra membrane region of CSFIR, which is responsible for folding and inactivation of the kinase domain, and preventing the binding of CSF1R and ATP to the region without the binding of CSF1R to the receptor, cannot undergo ligand induced autophosphorylation. By inhibiting the CSF1R signaling pathway pexidartinib works to inhibit tumor cell proliferation and down modulate cells involved in the disease such as macrophage.It also inhibit the CD117 or proto- oncogene receptor tyrosine kinase 3 (FLT3) and platelet derived growth factor receptor (PDGAR) –B, which are all receptor tyrosine kinases that regulate critical cellular processes such as cell proliferation and survival.
- **Absorption:** The median Tmax was 2.5 hour and time, Cmax and AUC by 100% with a delay Tmax by 2.5 hours.
- **Volume of distribution**: 187L in rats pexidartinib was shown to penetrate into CNS.
- **Protein Binding:** about 99% bound to serum proteins alpha-1 acid glycoprotein by 89.9%.
- **Metabolism:**Pexidartinib primarily undergoes oxidation mediated by hepatic CYP3A4 and glucuronidation by UGT1A4.
- **Half Life:** The elimination half –life is about 26.6 hours.
- **Clearance:** The apparent clearance is about 5.1l/h.

- **Affected Organism**: Human and other mammals.
- **Target:** Macrophage colony – stimulating factor 1 receptor.
  Mast/stem cell growth factor receptor kit.
  Receptor type tyrosine protein kinase FLT3.
  Platelet derived growth factor receptor beta.

GUIDELINES FOR PROCUREMENT OF BIOLOGICAL MATERIALS AS A SOURCE OF STEM CELLS

Procurement of Biological Material for Research

Gametes, blastocysts, embryos, fetal and placental tissue, as well as somatic cells are commonly collected for biological materials for stem cell transplantation. Their procurement as a source of stem cells for basic or translational research is permissible subject to approval by IC-SCR and IEC. If the source of the tissue is from hospital/clinic/entity other than the institute utilizing it for research, then the IEC clearance from the source institute is mandatory.

Fetal /Placental Tissue:

- For procurement of fetal or placental tissue as a source of stem cells, the following should be adhered to:
- Termination of pregnancy (TOP) should comply with all obligations under the MTP Act. However, TOP with a view to donate fetal tissue in return for financial or any other inducement is not permissible.
- Informed consent for donation:
- Voluntary informed consent should be obtained for termination of pregnancy and for donation of the fetal material for research.
- The consent for donation of fetal tissue should be obtained in advance and not just before or at the time of the procedure.
- The parents should be given sufficient time to take decision regarding the donation. If there is disagreement between parents, the mother's wish shall prevail.
- The consent for donation should include permission for screening of the donor for transmissible diseases and obtaining family history of genetic disorders.
- The purpose and use of donated fetal tissue should be fully explained to the parents. It should not be vague and open ended. The information sheet for the purpose should be carefully scrutinized and vetted by the IC-SCR.
- The medical person responsible for care of the pregnant woman willing to undergo termination of pregnancy and the investigator using the fetal material shall not be the same.
- The donor shall not have the option to specify the use of the donated material for a particular person or in a particular manner.
- The identity of the donor should be kept confidential. Personal information of the donor, however, should be kept available for traceability in situations where the cells derived from the donated fetal tissue are proposed to be used for therapy.
- **Banking of Umbilical Cord Blood:**
- UCB is a rich source of CD34+ hematopoietic and mesenchymal (stromal) stem cells. Use of UCB derived HSCs for treatment of various haematological and immunological disorders is currently well established, particularly where an HLA-matched sibling is not available. However, there is a paucity of public funded UCB banks in India.

- UCB banks are permitted only under license and monitoring by the CDSCO. These are expected to follow the Drugs and Cosmetics (3rd Amendment) Rules, Gazette Notification No. GSR 899(E) dated 27/12/2011 for collection processing, testing, storage, banking, and release of stored units.
- (Available at: http://cdsco.nic.in/html/GSR%20899.pdf).
- Therapeutic use of stem cells derived from UCB for indications other than those listed in *Annexure III* is not permitted. These can be used only as a clinical trial after obtaining approval of IC-SCR, IEC and CDSCO.
- Cord blood banks involved in basic research or clinical trials should constitute an IC-SCR and register the same with NAC-SCRT.
- The release of UCB units for research and/or clinical trials should be to only those institutions that have a registered IC-SCR and IEC.
- **Procedure for Collection of Umbilical Cord Blood**
- Parents should be fully informed regarding risks and benefits involved. Voluntary informed consent should be obtained from both parents well before the scheduled delivery date, but in no case at the time of delivery or subsequently. If there is disagreement between parents, the mother's wish shall prevail.
- Period of preservation for self-use later in life should be clearly defined.
- SOPs for collection, transportation, processing, storage (cryopreservation) and release of UCB/cells for clinical application should be clearly laid down and approved by IC-SCR and IEC.
- Exact timing of clamping the umbilical cord should be defined in the SOPs and recorded in the case file. No harm should occur to the neonate and the mother.
- Donor families should be compensated by providing them *Donor Cards* to enable them preferential access during emergency and for any other benefits to donor/relatives in future.
- SOPs for release of UCB units should be in place.

TAKAYASU'S ARTERITIS

INTRODUCTION:

Takayasu's arteritis is a diseasenamed in honor of Japanese Ophalmologist **MikitoTakayasu** who first reported a case of the disease in 1908.

Takayasu's arteritis is a rare type of vasculitis, a group of disorders that causes blood vessel inflammation. Here the inflammation damages the large artery that carries blood from your heart to the rest of your body (aorta) and its main branches. Less commonly arteries that provide to the heart, intestine, kidneys and legs may be involved.
This disease can lead to narrowed or blocked arteries or weakened artery walls that bulge (aneurysm) and tear. It also can lead to arm or chest pain, high blood pressure and eventually heart failure or stroke. It is also called PULSELESS DISEASE because the difficulty in detecting peripheral pulses that sometimes occurs as a result of the vascular narrowing's.
The large arteries that get damaged are **carotids, subclavin, axillary, brachial, aorta, renal, lliac, femoral.**

ETIOLOGY:

The exactly what causes is still no one knows about the initial inflammation. Although the cause of Takayasu's arteritis is unknown, this condition is characterized by a segmental and patchy

granulomatous inflammation of the aorta and its major derivative branches. Here the condition is likely an autoimmune disease in which your immune system attacks your own arteries by mistake. And it may be triggered by a virus or other infection. Sometimes the condition runs in families (genetic).

SIGNS AND SYMPTOMS:

The signs and symptoms often occur in two stages.

Stage 1: Fatigue, unintended weight loss, muscle and joint aches , mild fever sometimes it is accompanied by night sweats , not everyone has these early signs and symptoms.

Stage 2: During this stage, inflammation will causes arteries to narrow so less blood and oxygen and fewer nutrients reach your organs and tissues. Therefore it includes:

Weakness or pain in limbs, a week pulse, difficulty getting a blood pressure or a difference in blood pressure between your arms, lightheadedness or dizziness, headaches or visual changes, memory problems, chest pain or shortness of breath, high blood pressure, diarrhea or blood in stool, too few red blood cells(anemia).

DIAGNOSIS: The diagnostic tests include-X-rays of your blood vessels (angiography), Magnetic resonance angiography (MRA), Computerized tomography (CT) angiography, Ultrasonography, Position emission tomography (PET)

TREATMENT:

Treatment of this disease focuses on controlling inflammation with medications and preventing further damage to your blood vessels.

Medication:

- Corticosteroids to control inflammation: The first line treatment is usually a corticosteroid such as “Prednisone”. The dosage should be lowered gradually/slowly based on disease status. The possible side effects of corticosteroids are weight gain, increased risk of infection and bone thinning so, to help prevent bone loss, you may suggested with a “Calcium supplement and Vitamin D”.

- Other drugs that suppress the immune system: if your condition doesn’t respond well to corticosteroids or you have trouble as your medication dose is lowered, you may be prescribed with drugs such as “Methotrexate”, “Azathioprine” and “Leflunomide. Some people respond well to medications that were developed for people receiving organ transplants, such as “Mycophenolatemofetil” .The most common side effect seen is increased risk of infection.

- Medications to regulate the immune system: If you don't respond to standard treatments, then suggested with drugs that correct abnormalities in the immune system (biologics),

although more research is needed. Examples of biologics include “Etanercept”, “Infliximab” and “Tocilizumab” .The most common side effect seen with these drugs is an increased risk of infection.

- Many of the patients with Takayasu's arteritis have high blood pressure. So a Careful control of blood pressure is very important. Inadequate treatment of high blood pressure may result in stroke, heart disease, or kidney failure. In some cases, it is desirable to stretch narrow vessel openings with a balloon (a technique known as "Angioplasty”) or to do a bypass operation to restore normal flow to the kidney. This may result in normal blood pressure without the need to use blood pressure drugs.

Surgery: If arteries become severely narrowed or blocked, you may need surgery to open or bypass these arteries to allow an uninterrupted flow of blood or if you develop large aneurysms, then surgery may be needed to prevent them from rupturing.

1. Bypass surgery

2. Blood vessel widening (percutaneous angioplasty)

3. Aortic valve surgery.

COVID-19 COMPLICATIONS

- COVID-19 symptoms persist for months. This virus can cause damage to the lungs, heart and brain, which increases the risk of long-term health problems.
- They are described as "long haulers" and the conditions called post-COVID-19 syndrome or "long COVID-19." These health issues are sometimes called post-COVID-19 conditions.
- Acute respiratorydistress syndrome, acute respiratory failure, disseminated intravascular coagulation, sepsis, pulmonary embolism are some of the most seen complications.
- Symptoms as fatigue, shortness of breath or difficulty breathing, cough, joint pain, chest pain, memory, concentration or sleep problems, muscle pain or headache, fast or pounding heartbeat, loss of smell or taste, depression or anxiety, fever, dizziness when you stand, worsened symptoms after physical or mental activities may last for a long time.

Organ damage caused by COVID-19:

- **Heart.** Various cases as been reported even after months showing damage to the heart muscle, even in people who experienced few/ mild COVID-19 symptoms. This might increase the risk of heart failure or other heart complications in a lifetime.
- **Lungs.** The severity of pneumonia often associated with COVID-19 can cause long-standing damage to the tiny air sacs (alveoli) in the lungs. The resulting scar tissue can lead to long-term breathing problems.
- **Brain.** COVID-19 may cause strokes even in young people; seizures and Guillain -Bare syndrome. There is also an increase in the risk of developing Parkinson's and Alzheimer's diseases.
  Few of them experience multisystem inflammatory syndrome after they had COVID-19. Thereby, some organs and tissues become severely inflamed.

Blood clots and blood vessels associated problems

COVID-19 may cause the blood cells to clump up and form clots, large clots can cause heart attacks and strokes. Much of the heart damage caused by COVID-19 is from very small clots that block tiny blood vessels in the cardiac muscle.

Other organs that are seen to be affected are lungs, legs, liver and kidneys. COVID-19 weakens blood vessels and causes them to leak, which may lead to problems with the liver and kidneys.

Problems with mood and fatigue

People having severe COVID-19 have to be treated in a hospital's ICU, with mechanical assistance like ventilators to breathe, is mostly seen to be developing post-traumatic stress syndrome, depression and anxiety.

As it's difficult to predict long-term outcomes of the new COVID-19 virus, scientists are considering that the long-term effects seen in related viruses, such as severe acute respiratory syndrome (SARS) may be same.

- According to centre for disease control and prevention, pregnant women are at higher risk of becoming seriously ill from COVID-19, because they appear to be more likely to develop respiratory and obstetric complications that can lead to miscarriage, premature delivery and intrauterine growth restriction.
- Transmitting the virus from mother to child during pregnancy isn’t likely but newborn is able to contact virus after birth.
- In case if the child shows pediatric multisystem inflammatory syndrome, it might be fatal to the child.