St. Peter's Institute of Pharmaceutical Sciences	#2-4-1211, Vidyanagar, Hanamkonda, Telangana - 506001 India **Website:** www.stpeters.co.in, **Email :** spipswgl@gmail.com

NEWS LETTER OF CLINICAL PHARMACY

Volume (2) issue (2)-April-June 2019

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.

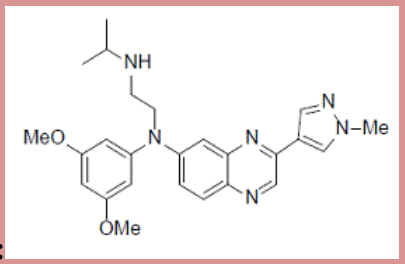
Mission

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.

DRUG MONOGRAPH ON BALVERSA(ERDAFITINIB)

Balversa:Erdafitinib is the active ingredient in it and it is the first-ever fibroblast growth factor receptor (FGFR) kinase inhibitor indicated for patients with locally advanced or metastatic urothelial carcinoma, with susceptible FGFR3 or FGFR2 genetic alterations, that has progressed during or following platinum-containing chemotherapy, including within 12 months of neoadjuvant or adjuvant platinum-containing chemotherapy.

- **Chemical name:**N-(3,5 dimethoxyphenyl)-N'-(1-methylethyl)-N-[3-(1-methyl-1H-pyrazol-4-yl) quinoxalin-6-yl]ethane-1,2diamine

structuralformula : 

- C25H30N6O2 (446.55g/mol), Fibroblast growth factor receptor (FGFR) tyrosine kinase inhibitor

FDA Approval: It was approved by FDA on 12th April, 2019

Available Dosage Forms: Tablets: 3 mg, 4 mg, and 5 mg.

Indications: Balversa is a kinase inhibitor indicated for the treatment of adult patients with locally advanced or metastatic urothelial carcinoma

- **Mechanism of action:**
  Erdafitinib is a kinase inhibitor that binds to and inhibits enzymatic activity of FGFR1, FGFR2, FGFR3 and FGFR4 based on in vitro data. Erdafitinib also binds to RET, CSF1R, PDGFRA, PDGFRB, FLT4, KIT, and VEGFR2.

Pharmacodynamics:Erdafitinib should be increased to the maximum recommended dose to achieve target serum phosphate levels of 5.5– 7.0 mg/dL in early cycles with continuous daily dosing.

- Pharmacokinetics:

• Absorption: Steady-state maximum observed plasma concentration (Cmax) = 1,399 ng/mL (51%), area under the curve (AUC tau) = 29,268ng•h/mL (60%), and minimum observed plasma concentration (Cmin) were and 936 ng/mL (65%)

• Volume of distribution: 26 to 29 L in patients.

• Protein binding:99.8%,

- Metabolism: By the cytochrome CYP2C9 and CYP3A4 isoenzymes. The contribution of CYP2C9 and CYP3A4 in the total clearance of Erdafitinib is estimated to be 39% and 20% respectively.

- Elimination:69% of the dose was recovered in feces (19% as unchanged) and 19% in urine (13% as unchanged)

- Half – life:59 hours

- Clearance:0.362 L/h, while the oral clearance = 0.26 L/h.

➢ **Adverse reactions:**

Ocular disorders, Hyperphosphatemia, Expanded serum phosphate fixations, Stomatitis, dry mouth, onycholysisetc

➢ **Drug Interactions:** There are 84 major and 122 minor drug interactions Ex**:** Alprazolam, Buspirone, Ketoconazole etc.
➢ **Contraindications:** No contraindications
➢ **Storage:** Store at 20°C – 25°C (68°F – 77°F); excursions permitted between 15°C and 30°C(59°F and 86°F)

FDA APPROVED DRUGS LIST : APRIL –JUNE 2019

Brand name	**Active Ingredient**	**Company**	**Date of Approval**	**Category**	**MOA**	**Indications**
Evenity	Romosozumab-aqqg	AmgenandUCB	09-04-2019	Monoclonal antibody	It is a monoclonal antibody that blocks the effects of the protein sclerostin. It mainly acts by increasing new bone formation	To treat osteoporosis in postmenopausal women at high risk of fracture
Balversa	Erdafitinib	TheJanssenPharmaceutical Companiesof Johnson& Johnson	12-04-2019	Tyrosine kinaseinhibitor	Fibroblast growth factor receptor (FGFR)kinase inhibitor that binds to and inhibits enzymatic	For the treatment of adult patients with locally advanced ormetastaticurothelial carcinoma

					activity of FGFR1,FGFR 2, FGFR3andFG FR4	
Skyrizi	Risankizumab -rzaa	BoehringerIng elheim andAbbVie	23-04-2019	Monoclon alantibody	Prevent the release of pro-inflammatory cytokines and chemokines that often lead to inflammatory skin symptoms, such as redness,pain, and plaques	For the treatment of moderate-to-severe plaque psoriasis in adults
Vyndaqel	Tafamidismeg lumine	Pfizer	03-05-2019	Transthyre tin stabilizers	It binds to transthyretintetr amers at the thyroxin binding sites, reducing the availability of monomers for amyloidogenesis	To treat cardiomyopathyo f wild type or hereditary transthyretin-mediated amyloidosis in adults
Piqray	Alpelisib	Novartis Pharmaceutica ls	24-05-2019	Kinaseinhi bitors	Alpelisib inhibits(PI3K), with thehighestspecifi city forPI3Kα	For the treatment of post menopausal women, and men with hormone receptor (HR)-positive, human epidermal growth factor receptor 2(HER2)-negative,breast cancer
Polivy	Polatuzumab vedotin-piiq	Genentech	10-06-2019	Antineopl asticAgent	Polivy binds to CD79b and destroys these B-cells through the delivery of an anti-cancer agent, which is thought to minimize the effects on normal cells	To treat adults with relapsed or refractory diffuse large B-cell lymphoma

TREATMENT GUIDELINES: INFECTIVE ENDOCARDITIS

Management of Infective Endocarditis:

1. Introduction:

Infective endocarditis (IE) is one of the most challenging syndromes in the landscape of infectious diseases. It is infection of the endothelial surfaces of the heart or iatrogenic foreign bodies like prosthetic valves and other intracardiac devices.

Table 1: Empirical antibiotic therapy for IE (pending blood culture results)

Native valve(IE)	Etiologies (usual)	Suggested regimens (primary)	Adjunct Diagnostic or Therapeutic Measures or comments
Empirical Treatment awaiting cultures (No h/o skin/soft tissue infection or abscesses, no h/o IV drug abuse, no h/o CVC line or recent cardiac/prosthetic valve replacement)	VGS, Enterococci, NVS, Streptococcus gallolyticus	Ampicillin-sulbactam 3g q6h (Ampicillin-150mg/kg/day or Sulbactam 50 mg/kg/day) in 4 divided doses or Ampicillin 2 g IV in q4h Or 200 mg/kg/day in six divided doses Plus Ceftriaxone 2 g IV q24h Paed Dose: 50-100 (60 mg/kg/day) in two divided doses Plus Gentamicin 1 mg/kg q8h	Gentamicin used for synergy, peak levels need not exceed 4 mcg/ml. • Advantage of Ampicillinsulbactam (AS) over CP/Ampicillin: AS Covers βlactamase producing Enterococci & HACEK Group of organisms • Combination of ceftriaxone with Gentamicin does not cover Enterococcus, Nutritionally variant Streptococci 157 (Abiotrophica&Granulicatella)
Native Valve IE (Risk factors for S. aureus)	MSSA, CA-MRSA, HA-MRSA***	Vancomycin 25 mg/kg loading dose followed by 30per/kg per 24 hIV in 2-3 equally divided doses. Alternative Therapy: Daptomycin 6 mg/kg q24h (for Right-sided IE) Or 8-10 mg/kg q24h (For left- sided IE) For Possible MSSA: Flucloxacillin or Cefazolin	Vancomycin trough levels -1 hour before the 4rth dose of vancomycin Recommended Vancomycin. trough levels in serious MRSA infections- 15- 20 µg/ml. Nephrotoxicity (0- 12%) which is associated with vancomycin trough levels greater than or equal to 15 µg/mL, in those receiving high dose vancomycin (greater or equal to 4 g/day), concomitant use of nephrotoxic agents, and duration of vancomycin therapy

PVE pending blood cultures or with negative blood cultures		Ceftriaxone 2 g IV q24h Paed Dose: 50-100 (60 mg/kg/day) in two divided doses AND Vancomycin (25 mg/kg loading dose followed by 30-60 mg/kg per 24 h IV) AND Gentamicin 1mg/kg q12h AND Rifampicin 300-600 mg q12H po/IV	Use lower dose of rifampicin in severe renal impairment.

Table 2: Antibiotic therapy for native valve IE due to VGS and group D streptococci, Streptococcus gallolyticus

Etiologies (usual)	**Suggested regimens (primary)**	**Adjunct Diagnostic or Therapeutic Measures or comments**	**Duration of antibiotic therapy**
Highly Penicillin-Susceptible VGS and S gallolyticus (bovis) (MIC ≤0.12 μg/mL)	Aqueous crystalline penicillin G (CP) sodium 20 -40 lac Units/kg/day IV 4 hrly Or 12–18 million U/24 h IV in 4-6 divided doses or continuously if possible	Ampicillin 200 mg/kg/day in six divided doses (Max dose - 2 g IV in q4h Or Ceftriaxone 50-100 (60 mg/kg/day) in two divided doses (Max dose- 2 g IV q24h) For penicillin Allergy- Vancomycin is an alternative	If only β-lactam is used – then, 4 weeks But if the combination of β-lactam with Gentamicin (3mg/kg/day) is used – then, 2 weeks is sufficient except in with known cardiac or extracardiac abscess or for those with creatinine clearance of
Relatively resistant VGS (MIC >0.12 -0.5 μg/mL)	Aqueous crystalline penicillin G (CP) sodium Plus Gentamicin	Ampicillin Or ceftriaxone Plus Gentamicin For penicillin allergy- Vancomycin is an alternative	β-lactam for 4 weeks and Gentamicin for 2 weeks
VGS isolates with a penicillin MIC ≥0.5 μg/mL &Abiotrophia and Granulicatella spp. (nutritionally variant streptococci)	Aqueous crystalline penicillin G (CP) sodium Plus Gentamicin	Ampicillin Or ceftriaxone Plus Gentamicin For penicillin allergy- Vancomycin is an alternative	β-lactam and Gentamicin for 6 weeks

DISEASE INFORMATION:SJ SYNDROME- STEVENS JOHNSON SYNDROME

- Stevens-Johnson syndrome/toxic epidermal necrolysis is a rare, potentially fatal skin reaction. Toxic epidermal necrolysis- more than 30% effected area.

Causes: Nonsteroidal anti-inflammatory drugs (NSAIDs) are a uncommon cause of SJS in grown-ups; the chance is higher for more seasoned patients, ladies, and those starting treatment.

- Drugs- Rivaroxaban, Vancomycin, Allopurinol, Valproate, levofloxacin, Diclofenac etc.

Symptoms: 1-3 days- Fever, Sore throat, Fatigue, Burning eyes. As the condition develops, skin pain can be noticed, red or purple rashes on skin will be developed, blisters on skin, and mucus membranes of eyes, nose, mouth and genitals. Shedding of the skin happens within few days after the blister formation.

Pathophysiology: The introductory step for Stevens-Johnson syndrome/toxic epidermal necrolysis may be binding of a drug-associated antigen or metabolite with the major histocompatibility complex (MHC) sort 1 or cellular peptide to create an immunogenic compound. Stevens-Johnson syndrome/toxic epidermal necrolysis is T–cell-mediated.CD8+ cells may initiate keratinocyte apoptosis. Other cells of the natural resistant framework play a role. CD40 ligand cells may initiate the discharge of TNF–alpha, nitrous oxide, interleukin 8 (IL-8), and cell attachment antibodies. TNF–alpha induces apoptosis. Both Th1 and Th2 cytokines are present. Other cells in Stevens-Johnson syndrome/toxic epidermal necrolysis incorporate macrophages, neutrophils, and characteristic executioner (NK) cells.

Diagnosis:review of medical history and physical examination, Skin biopsy is done for laboratory testing, Skin or oral culture to rule out the infection, Imaging is done such as chest x ray, Blood tests, Liver function tests, Complete blood count, Direct immune fluorescence, Renal function, Cardiac function.