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PSG NEWS DIGEST

A newsletter from Drug Information Centre, Department of Pharmacy Practice

FROM THE PHYSICIAN'S DESK

Sirolimus - A spin off

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National Aeronautics and Space Organization (NASA) developed digital image processing to enhance pictures of the moon. This contributed to MRI and CT of today. Similarly Sirolimus which was usedin immunosuppression is being used in complicated vascular anomalies and hyperinsulinemic hypoglycemia.

We share our experience with this drug.

Case I: There was a newborn who presented with persistent hyperinsulinemic hypoglycemia (PHHI) of infancy. As it was responsive to thiazide and as octreotide could not be used safely in the newborn period because of the risk of NEC, 85% pancreatectomy was performed. It was genetically proven ABCC8 gene deficiency. Baby had hypoglycemia in spite of that. Baby was started on sirolimus and sugars normalized.

PHHI - Persistent hyperinsulinemic hypoglycemia occurs in the neonate due to inappropriate secretion of insulin in spite of low blood sugar. The treatment for this condition is usually increasing the glucose infusion and starting thiazide. If hypoglycemia does not respond, then injection octreotide may be tried but due to the risk of necrotizing enterocolitis, it is used as a last resort. 95 to 98% pancreatectomy is usually performed with success. But in a recent study in the operated patients, it was noted 59% of them post operatively had hypoglycemia and in addition needed medical management and all of them had developed diabetes mellitus by adolescence. A possible mechanism of beta cell hyperplasia and secretion of insulin could be due to the activation of mTOR pathway. It has been noted that insulinoma has an activation of mTOR pathway and sirolimus (mTOR inhibitor) has been used in this condition. The activation of mTOR pathway in PHHI and the success with insulinoma has prompted the use of sirolimus with success by Senniappa et al. The protocol was taken from their article.

Dosage and monitoring: Sirolimus was started at 0.5mg/m2 of BSA in single dose. The desired trough level was 5 to 15ng/ml and the level should be measured every 5 days. Monthly CBC, serum lip levels, RFT and LFT were done. Sirolimus has been in use in renal transplant patients and they have noted stomatitis, increased risk of infection, changes in RFT, LFT, abnormalities in triglyceride levels, fatigue and pneumonitis.

Case II : Another 6 month old was brought with an increasing swelling involving the right side of face and neck and had a platelet count of 8,000. Clinical examination, blood investigations and MRI was diagnostic of Kaposi haemangioendothelioma (KHE) with Kasabach Meritt syndrome. He was started on Vincristine and steroid. But as the response was not satisfactory, he was started on sirolimus - 0.5mg/m2 and the coagulopathy settled and the swelling started regressing in size. He has normal blood picture and there is a minimal diffuse swelling.

Blatt et al and Hammil et al report successful use of sirolimus in KHE and complicated vascular anomalies. There are pre-clinical and clinical data supporting the essential regulatory function of the PI3K/Akt/mTOR pathway in vascular growth and organization, and this suggests a therapeutic target for patients with complicated vascular anomalies. The use of sirolimus is now being tested in a large prospective clinical trial. Sirolimus is now being used with increasing success in refractory KHE.

CDSCO Approved Drugs From September to November 2016

Drug Name	Indication
Midodrine Hydrochloride 2.5 mg Tablet	For the treatment of symptomatic orthostatic hypotension
Phospholipids Fraction from Bovine Lung (surfactant) 50 mg/vial	Preventive use in premature neonates with a high risk of respiratory Distress Syndrome
Eplerenone Tablets 25mg/50mg (Additional Indication)	Indicated as an adjunct to standard therapy, to reduce the risk of CV mortality and morbidity in adult patients with NYHA class II (chronic) heart failure and left ventricular systolic dysfunction (LVED≤30%)
Eltrmbopag Olamine 25mg and 50mg (Additional Indication)	Indicated for the treatment of patients with Severe Aplastic Anaemia (SAA) who have had an insufficient response to immunosuppressive therapy.
Afatinib Tablets (Freebase) 20mg/30mg/40mg/50mg (Additional Indication)	Indicated for the treatment of locally advanced or metastatic, NSCLC of squamous histology progressing on or after platinum based chemotherapy.
Dolutegravir 50 mg Tablet & Bulk (Dolutegravir Sodium)	Indicated in combination with other antiretroviral agents for the treatment of HIV-1 infection in adults weighing more than 40 kg.
Alcaftadine Eye Drops 0.25% w/v & Bulk	For the prevention of itching associated with allergic conjunctivitis in patients between the age group 10 to 60 years

Reference: *http://www.cdsco.nic.in/forms/list.aspx?lid=2034&Id=11*

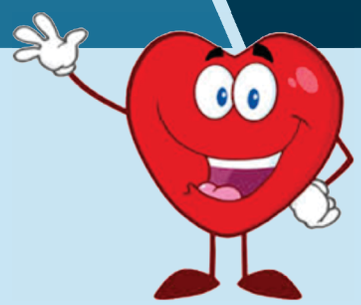
FDA Approved Drugs from September to November 2016

Drug Name	Indication
Yosprala *(Aspirin and omeprazole)*	For the prevention of cardiovascular and cerebrovascular events.
Exondys 51 *(Eteplirsen)*	For the treatment of Duchenne muscular dystrophy with mutated DMD gene amenable to exon 51 skipping
Zinplava *(Bezlotoxumab)*	For the treatment of recurrent Clostridium difficile infection in patients receiving antibacterial treatment.
Carnexiv *(Carbamazepine)*	Replacement therapy when oral administration is not feasible, in adults with seizures.
Lartruvo *(Olaratumab)*	For the treatment of soft tissue sarcoma
Soliqua 100/33 *(Insulin glargine and lixisenatide injection)*	For the treatment of inadequately controlled type II diabetes
Xultophy 100/3.6 *(Insulin degludec and liraglutide injection)*	For the treatment of inadequately controlled type II diabetes
Vemlidy *(Tenofovir Alafenamide)*	For the treatment of chronic hepatitis B

Reference : *http://www.centerwatch.com/drug-information/fda-approved-drugs/*

News Room

DURLAZA- EXTENDED RELEASE ASPIRIN FORMULATION



Current medical guidelines recommend once-daily, low-dose aspirin (75 to 162 mg) for patients who have an increased risk of experiencing a CV event. However, traditional aspirin formulations may not provide anticlotting effects throughout a full 24-hour period.

Limited 24-Hour Platelet Inhibition With Traditional Aspirin

Although traditional immediate-release and enteric-coated aspirin formulations provide peak plasma aspirin concentrations 40 minutes to 3 hours after administration, this peak is followed by a rapid decline of plasma aspirin concentrations in accordance with aspirin's short half-life (20 minutes). This means that with once-daily aspirin dosing, new platelets that are being generated (~4 billion per hour) may not be exposed to aspirin and thus would not be inhibited during an entire 24-hour period. Therefore, the antiplatelet effects of aspirin may not provide adequate coverage in high-risk populations that exhibit rapid platelet turnover.

DURLAZATM (aspirin): 24-Hour Aspirin Coverage With Once-Daily Administration

DURLAZA is an extended-release aspirin formulation for the secondary prevention of CVD events and CVD-related mortality and employs 24-hour extended-release microcapsule technology.

Dose : Higher aspirin dose (162.5 mg) is required to provide antiplatelet effects at steady state similar to those observed with a low dose (81 mg) of immediate-release aspirin.

Highlights of DURLAZA

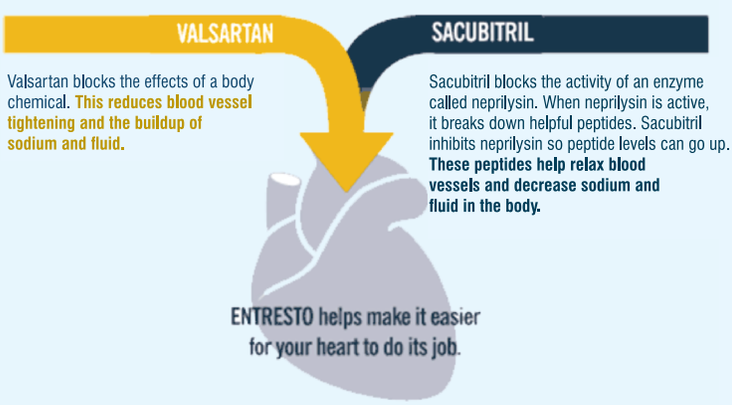
- Once daily administration with extended time period of protection from clot-forming activity in the body.
- Not useful for analgesia or situations in which rapid onset of action is required (eg, planned cardiac procedures).
- Important safety considerations: Should not be taken with alcohol, increases the risk of bleeding.
- **First approved prescription aspirin product**

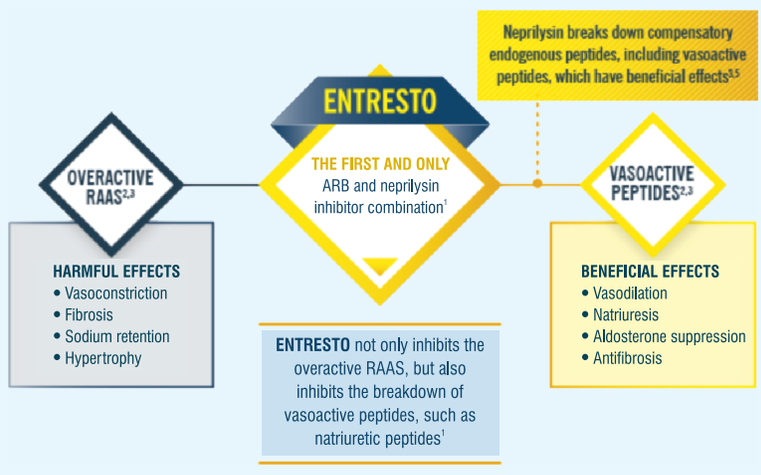
Overall, aspirin is a key therapy for the secondary prevention of CVD, and once-daily DURLAZA provides an important opportunity to potentially overcome some of the issues concerning 24-hour antiplatelet coverage with traditional OTC aspirin formulations in high-risk populations.

Reference: *http://www.pharmacytimes.com/publications/issue/2015/october2015/r735_october2015*

A Break Through Heart Failure Treatment

Entresto™
(sacubitril/valsartan) tablets
24/26mg · 49/51mg · 97/103mg





Reference : *http://www.entresto.com/index.jsp*

Reported Adverse Reactions

DRUG (ORAL)	ADVERSE REACTION	DRUG (PARENTERAL)	ADVERSE REACTION
Amlodipine	Hypotension	Atropine	Delirium
Aspirin	Haematuria	Ceftriaxone	Headache
Atorvastatin	Sleep disturbance	Cerebroprotein hydrolysate	Fever
Carbamazepine	Toxic epidermalnecrolysis	Fosphenytoin	Ataxia
Glipizide	Giddiness	Enoxaparin	Dysnoea
Leflunomide	Exfoliative dermatitis	Haloperidol	Involuntary movements
Levetiracetam	Agitation/Dryness of mouth	Iron sucrose	Pain, burning sensation
Metoproteronol	Tremor	Ketorolac	Heartburn/ Rashes
Nicorandil	Headache	Levofloxacin	Erythema
Phenytoin	Bradycardia	Mannitol	Hyponatremia
Rifampicin	Acute interstitial nephritis	Methyprednisolone	Myopathy/Sleep disturbance
Silodol	Abdominal pain	Paclitaxel	Tachypnea and Tachycardia
Sulfasalazine	Skin lesions	Sodium Valproate	Diarrhoea
Ticagrelor	Anemia/Episodic dysnoea	Thiamine	Allergic skin reaction
Trimethoprim/Sulfamethoxazole	Leukopenia	Tramadol	Breathing difficulty
Zolpidem	Hallucination Delirium	Vincristine	Restlessness, Agitation
Diclofenac transdermal patch: *Allergy, Redness, Itching.*			

Reference: *Peripheral Pharmacovigilance centre, Department of Pharmacology, PSGIMS&R, Coimbatore.*

Department Activities

Mrs. Rama P. was awarded the best oral presentation entitled "Assessment of comorbidity and drug-drug interaction in Cancer patients" in the International Conference on 'Clinical Pharmacy Practice Skills- Recent Perspectives' held at Faculty of Pharmacy, Sri Ramachandra University, Porur, Chennai during 7th to 9th September 2016.

The faculties of Department of Pharmacy Practice attended a workshop on "Effective use of moodle-A learning Module" on the 2nd and 7th of November 2016.

Diabetes Camp: On the 14th of November 2016, World Diabetes Day, a diabetes awareness program was organized by the Department of Pharmacy Practice, PSG College of Pharmacy at the PSG Urban Health Centre, Pioneer Mill Road, Coimbatore. People living in and around the vicinity of the health centre were informed of the camp through distribution of flyers in the preceeding week. Seventeen Pharm.D interns & M Pharm Pharmacy Practice students accompanied by a member of our faculty conducted the programme which included registration, blood sugar monitoring, blood pressure monitoring and BMI measurement for diabetes risk assessment. Further, patients were counseled based on their individual test results. 119 people attended the camp out of which 1 was newly diagnosed as type II diabetes mellitus and 4 as pre diabetes, 29 were known cases of DM, 25 individuals were at high risk and 32 were at medium risk for DM. A video presentation was made to the public to create awareness regarding the symptoms, causes, complications and life style modifications in Diabetes Mellitus.

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