Drug Information Bulletin

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Content

Editorial

Recent grant of patent to Pneumonia vaccine Prevenar 13 developed by Pfizer by Indian patent office attract criticism as it is believed that this will restrict access to poorer section till 2026.

Industry source said that a complete course of Prevenar 13 would cost $170 in private market which is considered too costly.

This patent will also prevent Indian manufacturers to develop chipper version of the same vaccine, which not only prevent access to the Indian patient, it will also prevent access to poorer nations round the globe as Indian vaccine manufacturers are supplying their vaccine products to the poorer nations at cheaper price.

It may also be noted that Patent on Prevenar 13 was revoked by the European patent office in 2014 and it is facing challenge in Korea and US.

It is reported by health care activist groups that some Indian manufacturers and NGOs are going to filled post grant opposition in the interest of the millions of patients suffering from Pneumonia.

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New Drug: Apalutamide for prostate cancer

Approved indication: prostate cancer
Erlyand (Janssen-Cilag)
60 mg film-coated tablets

Apalutamide has been approved in Australia for non-metastatic, castration-resistant prostate cancer. It is an oral anti-androgen which binds to the androgen receptor, reducing cell proliferation and increasing apoptosis.

The approval of this drug is mainly based on a placebo-controlled phase 3 trial (SPARTAN) in 1207 men who had prostate cancer with a high risk of developing metastatic disease.[1] This was defined as a prostate-specific antigen (PSA) doubling time of 10 months or less while they were receiving androgen-deprivation therapy. Metastatic disease was ruled out with imaging before randomisation. The men were randomised to receive apalutamide (240 mg a day) or placebo in a 2:1 ratio. They also continued androgen-deprivation therapy.

The primary end point of the study was metastasis-free survival. This was defined as the time from randomisation to first detection of a distant metastasis on imaging, or death from any cause. Median metastasis-free survival was significantly longer with apalutamide compared to placebo (40.5 vs 16.2 months). Median progression-free survival was also significantly longer. At the final analysis, median overall survival had not been reached with apalutamide.[1]

Serious adverse events (grades 3–4) were more common with apalutamide than with placebo – the most frequently reported were hypertension (14.3 vs 11.8%), rash (5.2 vs 0.3%), fracture (2.7 vs 0.8%), falls (1.7 vs 0.8%), diarrhoea (1 vs 0.5%), fatigue (0.9 vs 0.3%) and weight loss (1 vs 0.3%).[1] Although not serious, hypothyroidism was much more common with apalutamide than with placebo (8.1 vs 2%) and was considered to be related to treatment.[1] Dysgeusia, pruritus, depression, heart failure and ischaemic heart disease were also more frequent with apalutamide and three patients died of myocardial infarction. Treatment had to be stopped because of an adverse event in 11% of men receiving apalutamide and 7% of men receiving placebo. About a third of the discontinuations with apalutamide were due to a rash.

There is evidence that apalutamide prolongs the QT interval so prescribers should consider an electrocardiogram and electrolyte monitoring in patients with a history of QT prolongation or who are taking other drugs that prolong the QT interval.

Two patients taking apalutamide had a seizure even though people with a predisposition to seizures were excluded from the study. Patients should be warned of this risk and apalutamide should be permanently discontinued if seizure occurs.

People on prolonged androgen-deprivation therapy have an increased risk of osteopenia and osteoporosis. As apalutamide adds to this risk, patients should be monitored for fall and fracture risk and treated if necessary.

The recommended dose of apalutamide is 240 mg taken once a day. Tablets should be swallowed whole (with or without food). Dose adjustment is not required in patients with mild or moderate hepatic or renal insufficiency (eGFR ≤29 mL/1.73 m^2). However, there is no experience of the drug in those with severe impairment.

Following administration, maximum plasma concentrations are reached within 1–5 hours. Oral bioavailability is 100% and the drug is excreted in the urine (65%) and faeces (24%). Apalutamide is metabolised by cytochrome P450 (CYP) 2C8 and 3A4 so concomitant use of strong inhibitors of these enzymes (e.g. gemfibrozil, clarithromycin) may increase apalutamide exposure. Apalutamide is a strong inducer of CYP3A4 and 2C19 and a weak inducer of CYP2C9 so it may decrease the efficacy of substrates of these enzymes such as midazolam, omeprazole and warfarin respectively. It also weakly induces P-glycoprotein, breast cancer resistance protein (BCRP) and organic anion transporting polypeptide 1B1 (OATP1B1).

Apalutamide provides a new treatment option for men with castration-resistant prostate cancer who have not yet started chemotherapy. It prolongs metastatic-free survival by a median of two years when added to androgen-deprivation

therapy. However, treatment comes with some serious adverse effects and numerous potential drug interactions.

References

1. Smith MR, Saad F, Chowdhury S, Oudard S, Hadaschik BA, Graff JN, et al. Apalutamide treatment and metastatis-free survival in prostate cancer. N Engl J Med 2018;378:1408-18.

Ref.: Australian Prescriber

Ministry of Health and Family Welfare, Govt. of India notified 8 devices intended for human use as drugs with effect from 1st April 2020

Ministry of Health and Family Welfare, Govt. of India notified eight devices intended for human use as drugs vide S.O. 775(E) dated 8th February 2019 with effect from 01.04.2020, which are-

(i) All implantable medical devices;
(ii) CT scan Equipment;
(iii) MRI Equipment;
(iv) Defibrillators;
(v) Dialysis Machine;
(vi) PET Equipment;
(vii) X-Ray Machine; and
(viii) Bone marrow cell separator.

Ministry of Health and Family Welfare, Govt. of India revoked banned order on FDC containing Paracetamol + Caffeine + Phenylephrine + Chlorpheniramine

Ministry of Health and Family Welfare, Govt. of India revoked banned order on FDC containing Paracetamol + Caffeine + Phenylephrine + Chlorpheniramine vide S.O. 697 (E) dated 5th February 2019.

Earlier this FDC was banned vide notification number S.O. 4616 (E) dtd 7th September 2018 with immediate effect.

List of new drugs approved in the year 2019 till date

S.No	Name of drug	Indication	Date of issue
1	Fenspiride hydrochloride film coated extended release tablet 80 mg and Fenspiride hydrochloride bulk	1. Acute Rhinosinusitis 2. Moderate persistent asthma as an add on therapy	04.02.2019
2	Bilastine tablets 20 mg and Bilastine Bulk	For symptomatic treatment of allergic rhino-conjuctivitis (seasonal and perennial) and utricaria in adults	06.02.2019
3	Iguratimod film coated tablets 25mg and Iguratimod Bulk	For the treatment of active rheumatoid arthritis symptoms	18.02.2019

The European Medicines Agency (EMA) has announced an EU-wide suspension of Fenspiride medicines due to a potential risk of heart rhythm problems

The decision is based on recent nonclinical studies (hERG channel binding and *in vitro* animal model studies) that showed that fenspiride has the potential to increase QT intervals in humans.

The medicine, used in children and adults to relieve cough caused by lung diseases, has been suspended as a precautionary measure to protect patients while The Pharmacovigilance Risk Assessment Committee (PRAC) reviews the risk of QT prolongation, which can lead to a life threatening ventricular arrhythmia known as torsades de pointes and can result in sudden cardiac death.

Cases of heart rhythm problems had been reported in patients who had taken these medicines in the past, and so to explore the potential link with fenspiride, animal studies were carried out. These show that fenspiride has the potential to prolong QT in humans.

While authorities review all the evidence, patients are advised to stop taking these medicines.

The PRAC will now examine all the available evidence and make recommendations on the action to be taken on marketing authorisations for fenspiride medicines across the EU.

Once the review is concluded, EMA will communicate further and provide updated guidance to patients and healthcare professionals.

Senator Sanders asking Catalyst to justify $375K price for rare-disease drug

U.S. Senator Bernie Sanders sent a letter to Catalyst Pharmaceuticals asking it to justify its decision to charge $375,000 annually for a medication that for years has been available to patients for free.

The drug, Firdapse, is used to treat Lambert-Eaton Myasthenic Syndrome (LEMS), a rare neuromuscular disorder, according to the letter, made available to Reuters by the senator's office. The disorder affects about one in 100,000 people in the United States.

The government is intensifying its scrutiny of the pharmaceutical industry and rising prescription drug prices, a top voter concern and a priority of President Donald Trump's administration.

Both the Democratic-led U.S. House of Representatives and the Senate, controlled by Republicans, have begun holding hearings this year on the rising costs of medicines. A sander is an independent who usually votes with Democrats.

In the letter dated Feb. 4, Sanders asked Catalyst to lay out the financial and non-financial factors that led the company to set the list price at $375,000, and say how many patients would suffer or die as a result of the price and how much it was paying to purchase or produce the drug. For years, patients have been able to get the same drug for free from Jacobus Pharmaceuticals, a small New Jersey-based drug company, which offered it through a U.S. Food and Drug Administration (FDA) program called "compassionate use."

For details: https://www.reuters.com/article/us-usa-healthcare-catalyst/senator-sanders-to-ask-why-drug-once-free-now-costs-375k-idUSKCN1PT0ZJ

EMA Seeks Comments on Revised Guidelines for Antibiotic Trials

The European Medicines Agency released revised guidelines for stakeholder comment on evaluating drugs for treating bacterial infections.

The revised draft reflects discussions between EU, U.S. and Japanese regulators on aligning data requirements so drug developers can design clinical trials that meet the needs of multiple regulatory agencies.

The revised document includes new information on developing antibacterial agents to address unmet medical needs. It also includes specific advice on EU regulatory requirements for developing medicines for the treatment of uncomplicated urinary tract infections and gonorrhea.

Ref.: FDAnews

Participants in one of the refreshers course