



Drug Information Bulletin

Drug Information Centre (DIC)

Indian Pharmaceutical Association

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Editorial

Access to essential medicines is a problem throughout the globe especially in the developing and under developed countries. India is not an exception, where only 35-50 percent of its population has access to essential medicines, though India is the third largest producer of medicines and is exporting to about 170 countries. Experts believe there are several complex reasons behind it. One of them is irrational use of medicines. Prescribing in generic name is considered as one of the important tools for improving rational use of medicines.

In India Central Government, several State Governments and some agencies have instructed the doctors under Govt. sector to prescribe in generic name but unfortunately it has not been strictly implemented.

Though a small fraction of our population is covered by govt. sector health facilities and mostly depends on private health care facilities, it was noticed that recently a few state Govt.s have taken stringent measures for its implementation. It is expected that it may bring tangible change in the health care system.

Suspension on Pioglitazone withdrawn in India

Govt. of India has withdrawn the suspension on the manufacture for sale, sale and distribution of Pioglitazone and all formulations containing Pioglitazone for human use vide GSR.520 (E) dated 31st July 2013 with the following conditions-

1. The Drug should not be used as first line of therapy for children.

2. The manufacturer should clearly mention following box warning in bold red letters.

Advice for healthcare professionals:

- Patients with bladder cancer or with a history of bladder cancer, and those with uninvestigated haematuria, should not receive pioglitazone.
- Prescribers should review the safety and efficacy of pioglitazone in individuals after 3-6 months of treatment to ensure that only patients who are deriving benefit

continue to be treated. Pioglitazone should be stopped in patients who do not respond adequately to treatment (e.g. reduction in glycosylated hemoglobin, HbA1c).

- Before starting pioglitazone, the following known risk factors for development of bladder cancer should be assessed in individuals: age, current or past history of smoking, exposure to some occupational or chemotherapy agents such as cyclophosphamide, or previous irradiation of the pelvic region.
- Use in elderly patients should be considered carefully before and during treatment because the risk of bladder cancer increases with age. Elderly patients should start on the lowest possible dose and be regularly monitored because of the risks of bladder cancer and heart failure associated with Pioglitazone.

The notification is available at <http://www.cdsc.nic.in/GRIjuly13.pdf>

New Drug: Pertuzumab

Approved indication: metastatic breast cancer

Perjeta (Roche)

vials containing 30 mg/mL for infusion

Australian Medicines Handbook section 14.2.1

The human epidermal growth factor receptor 2 (HER2) is over expressed in up to 30% of people with breast cancer. This leads to an aggressive phenotype which is associated with reduced survival.

Adding an anti-HER2 antibody, such as trastuzumab, to chemotherapy has been found to improve prognosis.

Pertuzumab is another humanised monoclonal antibody specific for HER2. It inhibits dimerization of HER2 with other HER receptors on the cell surface and blocks intracellular signalling. This results in cell growth arrest, apoptosis and cell-mediated cytotoxicity. Because pertuzumab binds to a different epitope, it can be used to complement trastuzumab treatment.

In a phase III trial (CLEOPATRA) in patients with HER2-positive metastatic breast cancer, intravenous pertuzumab or placebo was added to trastuzumab plus docetaxel. Pertuzumab significantly prolonged progression-free survival by 6.1 months compared to placebo. 1 In an interim analysis, more patients had died in the placebo group than in the pertuzumab group.2

The most common adverse events with pertuzumab, trastuzumab and docetaxel included diarrhoea (66.8% of patients), alopecia (60.9%), neutropenia (52.8%), nausea (42.3%), fatigue (37.6%), rash (33.7%), decreased appetite (29.2%), mucosal inflammation (27.8%) and asthenia (26%). Febrile neutropenia was also reported and was more common with pertuzumab than with placebo (13.8% vs 7.6%).

Severe febrile neutropenia (grade 3 or more) was more frequent in Asian patients, particularly those receiving pertuzumab compared to placebo (26% vs 12%).1

Some patients died as a result of adverse events – the proportion of deaths was similar with pertuzumab and placebo (2% vs 3%). Febrile neutropenia and infections were the most common cause of death.2

Like other drugs that block HER2, pertuzumab can cause heart failure. For this reason, patients with a left ventricular ejection fraction of less than 50% were excluded from the CLEOPATRA trial.

The addition of pertuzumab to trastuzumab did not appear to increase left ventricular systolic dysfunction compared to placebo (4.4% vs 8.3%).¹ Left ventricular ejection fraction needs to be assessed before and regularly during treatment. If it is low (<40%) or has declined from baseline (40–45% and ≥10% below baseline), consider discontinuing or withholding pertuzumab and trastuzumab.

Pertuzumab is given as a slow intravenous infusion over one hour every three weeks. Infusion and hypersensitivity reactions have occurred so patients should be monitored during and after the infusion. Pertuzumab is cleared by catabolism and has an elimination half-life of 17 days.

In studies on monkeys, pertuzumab was toxic to unborn offspring. It has therefore been classified as a category D pregnancy drug and should be avoided in pregnancy. Because IgG is secreted in breast milk, pertuzumab could also be transferred to a nursing infant.

In combination with trastuzumab plus docetaxel, pertuzumab appears to extend progression-free survival of people with HER2-positive metastatic breast cancer. However patients must have a positive HER2 tumour status to receive treatment. Pertuzumab is specifically indicated for those who have not previously received anti-HER2 therapy or chemotherapy for metastatic disease.

References:

1. Baselga J, Cortés J, Kim SB, Im SA, Hegg R, Im YH; CLEOPATRA Study Group. Pertuzumab plus trastuzumab plus docetaxel for metastatic breast cancer. *N Engl J Med* 2012;366:109-19 .
2. Swain SM, Kim SB, Cortés J, Ro J, Semiglazov V, Campone M, et al. Pertuzumab, trastuzumab, and docetaxel for HER2-positive metastatic breast cancer (CLEOPATRA study): overall survival results from a randomised, double-blind, placebo-controlled, phase 3 study. *Lancet Oncol* 2013;14:461-71 .

Ref. Australian Prescriber

List of new molecular entity approved by CDER, USFDA during 2012

During this year 39 new molecule was approved, one third of which was indicated for sort of cancer. Only four is aninfective.

| No. | Drug Name | Active Ingredient | Date | What it's used for |
|-----|--|-------------------|----------|---|
| 39. | Fulyzaq ⁵ | crofelemer | 12/31/12 | To treat HIV/AIDS patients whose diarrhea is not caused by an infection from a virus, bacteria, or parasite. Press Release ⁶ |
| 38. | Sirturo ⁷ | bedaquiline | 12/28/12 | As part of combination therapy to treat adults with multi-drug resistant pulmonary tuberculosis (TB) when other alternatives are not available. Press Release ⁸ |
| 37. | Eliquis ⁹ | apixaban | 12/28/12 | To reduce the risk of stroke and dangerous blood clots (systemic embolism) in patients with atrial fibrillation that is not caused by a heart valve problem. Press Release ¹⁰ |
| 36. | Juxtapid ¹¹ | lomitapide | 12/21/12 | To reduce low-density lipoprotein (LDL) cholesterol, total |

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| | | | | cholesterol, apolipoprotein B, and non-high-density lipoprotein (non-HDL) cholesterol in patients with homozygous familial hypercholesterolemia (HoFH). Press Release ¹² |
| 35. | Gattex ¹³ | teduglutide | 12/21/12 | To treat adults with short bowel syndrome (SBS) who need additional nutrition from intravenous feeding (parenteral nutrition). Press Release ¹⁴ |
| 34. | Signifor ¹⁵ | pasereotide | 12/14/12 | To treat Cushing's disease patients who cannot be helped through surgery Press Release ¹⁶ |
| 33. | raxibacumab ¹⁷ | raxibacumab | 12/14/12 | To treat inhalational anthrax, a form of the infectious disease caused by breathing in the spores of the bacterium Bacillus anthracis. Press Release ¹⁸ |
| 32. | Iclusig ¹⁹ | ponatinib | 12/14/12 | To treat adults with chronic myeloid leukemia (CML) and Philadelphia chromosome positive acute lymphoblastic leukemia (Ph+ ALL), two rare blood and bone marrow diseases. Press Release ²⁰ |
| 31. | Cometriq ²¹ | cabozantinib | 11/29/12 | To treat medullary thyroid cancer that has spread to other parts of the body (metastasized). Press Release ²² |
| 30. | Xeljanz ²³ | tofacitinib | 11/6/12 | To treat adults with moderately to severely active rheumatoid arthritis (RA) who have had an inadequate response to, or who are intolerant of, methotrexate. Press Release ²⁴ |
| 29. | Synribo ²⁵ | omacetaxine mepesuccinate | 10/26/12 | To treat adults with chronic myelogenous leukemia (CML), a blood and bone marrow disease. Press Release ²⁶ |
| 28. | Fycompa ²⁷ | perampanel | 10/22/12 | To treat partial onset seizures in patients with epilepsy ages 12 years and older. Press Release ²⁸ |
| 27. | Jetrea ²⁹ | ocriplasmin | 10/17/12 | To treat an eye condition called symptomatic vitreomacular adhesion (VMA). Press Release ³⁰ |
| 26. | Stivarga ³¹ | regorafenib | 9/27/12 | To treat patients with colorectal cancer that has progressed after treatment and spread to other parts of the body (metastatic). Press Release ³² |
| 25. | Choline C 11 Injection ³³ | Choline C 11 Injection | 9/12/12 | A Positron Emission Tomography (PET) imaging agent used to help detect recurrent prostate cancer. Press Release ³⁴ |
| 24. | Aubagio ³⁵ | teriflunomide | 9/12/12 | For the treatment of adults with relapsing forms of multiple sclerosis (MS). Press Release ³⁶ |
| 23. | Bosulif ³⁷ | bosutinib | 9/4/12 | To treat chronic myelogenous leukemia (CML), a blood and bone marrow disease that usually affects older adults. Press Release ³⁸ |

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| 22. | Xtandi ³⁹ | enzalutamide | 8/31/12 | To treat men with late-stage (metastatic) castration-resistant prostate cancer that has spread or recurred, even with medical or surgical therapy to minimize testosterone. Press Release ⁴⁰ |
| 21. | Linzess | linaclotide | 8/30/12 | To treat chronic idiopathic constipation and to treat irritable bowel syndrome with constipation (IBS-C) in adults. Press Release ⁴¹ |
| 20. | Neutroval ⁴ ₂ | tbo-filgrastim | 8/29/12 | To reduce the time certain patients receiving cancer chemotherapy experience severe neutropenia, a decrease in infection-fighting white blood cells called neutrophils. Press Release ⁴³ |
| 19. | Stribild ⁴⁴ | elvitegravir, cobicistat, emtricitabine, tenofovir disoproxil fumarate | 8/27/12 | A once-a-day combination pill to treat HIV-1 infection in adults who have never been treated for HIV infection. Press Release ⁴⁵ |
| 18. | Zaltrap ⁴⁶ | ziv-aflibercept | 8/3/12 | For use in combination with a FOLFIRI (folinic acid, fluorouracil and irinotecan) chemotherapy regimen to treat adults with colorectal cancer. Press Release ⁴⁷ |
| 17. | Tudorza Pressair ⁴⁸ | aclidinium bromide | 7/23/12 | For the long-term maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease (COPD), including chronic bronchitis and emphysema. Press Release ⁴⁹ |
| 16. | Kyprolis ⁵⁰ | carfilzomib | 7/20/12 | To treat patients with multiple myeloma who have received at least two prior therapies, including treatment with Velcade (bortezomib) and an immunomodulatory. Press Release ⁵¹ |
| 15. | Prepopik ⁵² | sodium picosulfate, magnesium oxide and citric acid | 7/16/12 | To help cleanse the colon in adults preparing for colonoscopy. Press Release ⁵³ |
| 14. | Myrbetriq ⁵ ₄ | mirabegron | 6/28/12 | To treat adults with overactive bladder. Press Release ⁵⁵ |
| 13. | Belviq ⁵⁶ | lorcaserin hydrochloride | 6/27/12 | For chronic weight management. Press Release ⁵⁷ |
| 12. | Perjeta ⁵⁸ | pertuzumab | 6/8/12 | To treat patients with HER2-positive late-stage (metastatic) breast cancer. Press Release ⁵⁹ |
| 11. | Elelyso ⁶⁰ | taliglucerase alfa | 5/1/12 | For long-term enzyme replacement therapy to treat a form of Gaucher disease, a rare genetic disorder Press Release ⁶¹ |
| 10. | Stendra ⁶² | avanafil | 4/27/12 | To treat erectile dysfunction. Press Release ⁶³ |

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| 9. | Amyvid ⁶⁴ | Florbetapir F 18 | 4/6/12 | Used as a radioactive diagnostic agent for Positron Emission Tomography (PET) imaging of the brain to estimate β -amyloid neuritic plaque density in adult patients with cognitive impairment who are being evaluated for Alzheimer's Disease (AD) and other causes of cognitive decline. |
| 8. | Omontys ⁶⁵ | peginesatide | 3/27/12 | To treat anemia, a condition in which the body does not have enough healthy red blood cells, in adult dialysis patients who have chronic kidney disease (CKD). Press Release ⁶⁶ |
| 7. | Surfaxin ⁶⁷ | lucinactant | 3/6/12 | For the prevention of respiratory distress syndrome (RDS), a breathing disorder that affects premature infants. Press Release ⁶⁸ |
| 6. | Zioptan ⁶⁹ | tafluprost | 2/10/12 | For reducing elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension. Press Release ⁷⁰ |
| 5. | Kalydeco | ivacaftor | 1/31/12 | For the treatment of a rare form of cystic fibrosis (CF) in patients ages 6 years and older who have the specific G551D mutation in the Cystic Fibrosis Transmembrane Regulator (CFTR) gene. Press Release ⁷¹ |
| 4. | Erivedge ⁷² | vismodegib | 1/30/12 | To treat adult patients with basal cell carcinoma, the most common type of skin cancer. Press Release ⁷³ |
| 3. | Inlyta ⁷⁴ | axitinib | 1/27/12 | To treat patients with advanced kidney cancer (renal cell carcinoma) who have not responded to another drug for this type of cancer. Press Release ⁷⁵ |
| 2. | Picato ⁷⁶ | ingenol mebutate | 1/23/12 | For the topical treatment of actinic keratosis. |
| 1. | Voraxaze ⁷⁷ | glucarpidase | 1/17/12 | To treat patients with toxic levels of methotrexate in their blood due to kidney failure. Press Release ⁷⁸ |

Health Camp At Tarakeswar

Dates:

22nd July, 29th July, 5th August, 12th
August 2013

Organizers:

Indian Pharmaceutical Association,
Bengal Branch
&
IPA Bengal Pharma and Health
Care Trust

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