Drug Information Bulletin

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Content

Editorial

Analgin and formulations containing Analgin for human use has been banned by Government of India since 18th June 2013 will end a long battle of health activists for banning Analgin for its ADRs.

Analgin or Metamizole is banned in USA since 1977 and it is banned over 30 countries including Japan, Australia, Iran, Philippines and several EU countries, round the world. Health care organizations in India tried to impress upon the authorities for more than three decades for banning this drug due to its severe ADRs like agranulocytosis. In India FDC of Analgin with any other drug has been banned in the year of 1996 and finally it has been banned in India since 18th June 2013.

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 .

The Transparency Score (T) is explained in 'New drugs: transparency', Vol 34 No 1, Aust Prescr 2011;34:26-7.

*At the time the comment was prepared, information about this drug was available on the web site of the Food and Drug Administration in the USA (www.fda.gov).

Ref. Australian Prescriber

With calls for transparency, drug firms release clinical data

Following a lengthy effort to review data about the efficacy of Tamiflu, U.S. and British researchers have won the release of massive amounts of past clinical-trial data from the drug companies Roche and GlaxoSmithKline that were previously inaccessible or unpublished. The European Medicines Agency has published the draft of a policy that would release clinical trial data when a new drug is launched, and while some drug companies agree with the policy, the Pharmaceutical Research and Manufacturers Association of America opposes the plan, citing concerns over "commercially protected information." U.S. officials, however, say that clinical data results already appear in a government clearinghouse. The New York Times

Painkiller drug deaths up 400% among women

Women are dying from prescription painkiller overdoses at rates never seen before, according to a new CDC Vital Signs. While men are more likely to die of a prescription painkiller overdose, the percentage increase in deaths since 1999 was greater among women (400 percent in women compared to 265 percent in men). Prescription painkiller overdoses killed nearly 48,000 women between 1999 and 2010.

•About 42 women die every day from a drug overdose (including those from prescription painkillers). Since 2007, more women have died from drug overdoses than from motor vehicle crashes. More than 940,000 women were seen in emergency departments for drug misuse or abuse in 2010.

•Prescription painkillers have been a major contributor to increases in drug overdose deaths among women. More than 6,600 women died from a prescription painkiller overdose in 2010. This is about 18 women a day; which accounts for nearly half of all drug overdoses that happen each day among women. In 2010, there were more than 200,000 emergency department visits

for opioid misuse or abuse among women; about one every three minutes.

•Health care providers and women can take steps to protect against prescription painkiller overdoses. It is important that health care providers follow guidelines for responsible opioid prescribing (including screening and monitoring for substance abuse and mental health problems). They should also discuss all pain treatment options with their patients (including ones that do not involve prescription drugs). Women should only use prescription drugs as directed by a health care provider and should dispose of medications properly as soon as the course of treatment is done.

Prevent misuse and abuse by never selling or sharing prescription drugs. Get help for substance abuse problems (1-800-662-HELP) and call Poison Help (1-800-222-1222) with questions about medicines. For more information about prescription drug overdoses, please visit CDC's Injury Center.

FDA approves sublingual opioid-addiction tablet

Bloomberg News reports Orexo on Thursday announced that the US Food and Drug Administration has approved its opioid-dependence treatment, Zubsolv (buprenorphine and naloxone). The Uppsala, Sweden-based specialty pharmaceutical firm said the FDA approved the sublingual tablet to treat heroin and prescription painkiller addictions. Earlier this week Orexo announced that it had formed a partnership with Yardley, Pennsylvania-based Publicis Touchpoint Solutions "to help sell Zubsolv in the US." Reuters adds that Zubsolv will compete on the US market with Suboxone (buprenorphine and naloxone), a sublingual film, and Subutex (buprenorphine), both of which are manufactured by Berkshire, England-based Reckitt Benckiser Group Plc.

UK Home Secretary announces herbal stimulant ban

The AP reported that the "British government said Wednesday it is banning khat," despite the fact that in January, its Advisory Council on the Misuse of Drugs concluded the herbal stimulant "has no links to adverse medical effects" and recommended against banning the plant, which is "also known as cathonine." However, UK Home Secretary Theresa May pointed out on Wednesday that because the "whole of northern Europe and most other EU member states have banned khat, failure to act would put Britain at risk of becoming a trafficking hub." The stimulant, which produces a mild euphoria when chewed, is "popular in parts of the Middle East and Africa" but it is "classified as a dangerous narcotic" in the US.

According to Bloomberg News May issued a statement Wednesday to Parliament, saying khat would be "categorized as a Class C drug, meaning the penalty for possession can be up to two years in jail." Moreover, individuals convicted of "dealing a Class C drug" could see a prison term of "as much as 14 years."

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