Regulatory Action and News

Operation Pangea VI: combating sale of unapproved medicines

**United States of America** — The Food and Drug Administration and international regulatory and law enforcement agencies have taken action against more than 9600 web sites that illegally sell potentially dangerous, unapproved prescription medicines to consumers. This action includes issuance of regulatory warnings and seizure of offending web sites and over 41 million US dollars’ worth of illegal medicines worldwide. The action occurred as part of the 6th annual International Internet Week of Action (IIWA), a global cooperative effort to combat the online sale and distribution of potentially counterfeit and illegal medical products. The goal of Pangea VI — which involves law enforcement, customs, and regulatory authorities from 99 countries — was to identify the makers and distributors of illegal drug products and medical devices and remove these products from the supply chain.

As part of this international effort, the FDA Office of Criminal Investigations, in coordination with the United States Attorney’s Office for the District of Colorado, seized and shut down 1677 illegal pharmacy web sites. The effort ran from 18–25 June 2013.

Many of these web sites appeared to be operating as a part of an organized criminal network that falsely purported to be “Canadian Pharmacies.” These web sites displayed fake licences and certifications to convince U.S. consumers to purchase drugs they advertised as “brand name” and “FDA approved.” The drugs collected as part of Operation Pangea were not from Canada, and were neither brand name nor FDA approved.

These web sites also used certain major U.S. pharmacy retailer names to trick consumers into believing an affiliation existed.

**Reference:** *FDA News Release, 27 June 2013* at [http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm358794.htm](http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm358794.htm)

SARA: System for Australian Recall Actions

**Australia** — The Therapeutic Goods Administration (TGA) recently launched the System for Australian Recall Actions (SARA) — an online, searchable data base of recall actions for therapeutic goods undertaken in Australia.

Health professionals are encouraged to use SARA, along with other resources on the TGA website, such as the Database of Adverse Event Notifications and the alerts web page, to access valuable information on medicines safety.

A recall action is a regulatory action taken for a therapeutic good supplied in Australia to resolve issues or deficiencies relating to safety, quality, efficacy or performance. Recall actions can be recalls, recalls for product correction or hazard alerts. Not all recall actions result in a product being removed from the market, for example hazard alerts may be issued in cases involving implantable devices, and corrections may be undertaken for products that have software issues.

SARA includes recall actions for a range of therapeutic goods including prescription medicines, over-the-counter medicines, complementary medicines, medical devices including
in vitro diagnostic medical devices, and biologicals.

The data base holds information on all recall actions that have been undertaken in Australia since 1 July 2012.

SARA has been launched as part of the TGA's commitment to improve transparency, as well as trust and confidence in the safety and quality of therapeutic goods and regulatory processes.


Oral ketoconazole: suspension of marketing authorization

European Union — The European Medicines Agency’s Committee on Medicinal Products for Human Use (CHMP) has recommended that the marketing authorizations of oral ketoconazole-containing medicines should be suspended throughout the European Union (EU). The CHMP concluded that the risk of liver injury is greater than the benefits in treating fungal infections.

Patients currently taking oral ketoconazole for fungal infections should make a non-urgent appointment with their doctor to discuss suitable alternative treatments. Doctors should no longer prescribe oral ketoconazole and should review treatment options.

The EU-wide review of oral ketoconazole was triggered by the suspension of the medicine in France. Having assessed the available data, the CHMP concluded that liver injury with oral ketoconazole was higher than with other antifungals. The CHMP was concerned that reports of liver injury occurred early after starting treatment with recommended doses and it was not possible to identify measures to adequately reduce this risk. The Committee also concluded that the clinical benefit of oral ketoconazole is uncertain as data on its effectiveness are limited and do not meet current standards, and alternative treatments are available.

Topical formulations of ketoconazole can continue to be used as the amount of ketoconazole absorbed throughout the body is very low with these formulations.

References


Advanced therapy approved for metastatic prostate cancer

European Union — The European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) has recommended granting a marketing authorization for a new advanced-therapy medicinal product (ATMP). Provenge® is recommended for the treatment of asymptomatic or minimally symptomatic metastatic castrate-resistant prostate cancer in male adults in whom chemotherapy is not yet clinically indicated.

ATMPs are innovative medicines that are derived from gene therapy, cell therapy or tissue engineering. The CHMP recommendation follows the draft opinion of the Committee for Advanced Therapies (CAT), the Agency’s expert committee for ATMPs.

Provenge® is a cellular immunotherapy designed to induce an immune response
against prostate cancer cells. It uses immune cells that are extracted from and treated outside the patient’s body so that when they are infused back into the patient they trigger an immune response directed against an antigen found in metastasized cancer cells. Provenge® has been shown to improve the overall survival by 4.1 months over placebo in clinical trials.

28/06/2013

Dabrafenib approved for metastatic melanoma

European Union — The European Medicines Agency’s Committee for Medicinal Products for Human Use (CHMP) has recommended marketing authorization for dabrafenib (Tafinlar®) for the treatment of adult patients with advanced unresectable or metastatic melanoma expressing a BRAF V600 gene mutation.

The therapeutic landscape for the treatment of metastatic melanoma in the European Union has changed significantly in recent years with the granting of marketing authorizations for new targeted active agents: one of them, the monoclonal antibody ipilimumab, targets a molecule found on the surface of T cells and is thought to inhibit immune responses; another agent, vemurafenib, is a first-in-class protein kinase inhibitor, inhibiting the BRAF serine-threonine kinase with a genetic mutation at position 600 (BRAF V600E).

Mutations of the protein kinase BRAF have been identified in about half of patients with metastatic melanoma, with the BRAF V600E mutation found in about 80 to 90% of these. These mutations cause the cell to make an abnormal protein that promotes cancer growth. By blocking the action of this abnormal protein, BRAF inhibitors help slow down the growth and spread of tumours bearing the BRAF V600 mutation.


Calcitonin nasal spray: market withdrawal

Canada — Health Canada has advised of the market withdrawal of all synthetic calcitonin nasal spray products (Miacalcin®, Sandoz Calcitonin® and Apo-calcitonin®) with effect 1 October 2013. All three products are authorized in Canada for the treatment of post-menopausal osteoporosis in females five years post menopause with low bone mass relative to healthy pre-menopausal females.

Health Canada has concluded, in light of a newly identified risk of cancer, that the benefit-risk profile for the treatment of postmenopausal osteoporosis is no longer considered favourable. As of 3 July 2013, manufacturers have ceased the sale of synthetic calcitonin nasal spray products.


Afatinib and companion test approved for late-stage lung cancer

United States of America — The Food and Drug Administration (FDA) has approved afatinib (Gilotrif®) for patients with late stage (metastatic) non-small cell lung cancer (NSCLC) whose tumours express specific types of epidermal growth factor receptor (EGFR) gene mutations, as detected by an FDA-approved test.
Lung cancer is the leading cause of cancer-related death among men and women. About 85 percent of lung cancers are NSCLC, making it the most common type of lung cancer. EGFR gene mutations are present in about 10 percent of NSCLC, with the majority of these gene mutations expressing EGFR exon 19 deletions or exon 21 L858R substitution.

Afatinib is a tyrosine kinase inhibitor blocking proteins that promote the development of cancerous cells. It is intended for patients whose tumours express the EGFR exon 19 deletions or exon 21 L858R substitution gene mutations. Afatinib is being approved concurrently with the therascreen EGFR RGQ PCR Kit®, a companion diagnostic that helps determine if a patient’s lung cancer cells express the EGFR mutations.

In May 2013, the FDA approved erlotinib (Tarceva®) for first-line treatment of patients with NSCLC and a new indication was approved concurrently with the cobas EGFR Mutation Test® to identify patients with tumours expressing the EGFR gene mutations.

Common side effects of Gilotrif® include diarrhoea, skin breakouts that resemble acne, dry skin, pruritus, inflammation of the mouth, paronychia, decreased appetite, decreased weight, cystitis, nose bleed, runny nose, fever, eye inflammation and hypokalemia. Serious side effects include diarrhoea that can result in kidney failure and severe dehydration, severe rash, lung inflammation and liver toxicity.