Regulatory news

Pre-marketing assessment

**EMA launches adaptive licensing pilot project**

**European Union** – The European Medicines Agency (EMA) is piloting its adaptive licensing approach, also called staggered approval or progressive licensing. This approach aims to improve timely access for patients to new medicines. It builds on existing regulatory processes, including scientific advice, centralized approval for compassionate use, conditional marketing authorization (for medicines addressing life-threatening conditions), patients’ registries and pharmacovigilance tools that allow collection of real-life data and development of risk management plans.

The pilot phase will enable the Agency to further refine how the adaptive licensing pathway should be designed for different types of products and indications. EMA is inviting companies to submit ongoing medicines development programmes at an early stage of clinical development for consideration as prospective pilot cases.

► [EMA Press release, 19 March 2014](#).

**EMA and TGA strengthen collaboration on orphan medicines**

**European Union / Australia** – The European Medicines Agency (EMA) and the Australian Therapeutic Goods Administration (TGA) have announced that they have agreed to share full assessment reports related to marketing authorizations of orphan medicines received in parallel by EMA and TGA. Both regulators will still reach their own conclusions. This collaboration will enable wider use of the limited number of studies conducted on medicines used to treat rare diseases.

► [EMA News, 7 April 2014](#).

**MHRA introduces early access to medicines scheme**

**United Kingdom** – The U.K. Medicines and Healthcare products Regulatory Agency (MHRA) has launched its Early Access to Medicines Scheme (EAMS) and invites applications from the pharmaceutical industry and research organizations. The scheme aims to give patients with life-threatening or seriously debilitating conditions access to medicines that do not yet have a marketing authorization and for which there are no suitable alternative licensed treatments.

The scheme has two parts: Firstly, medicines with early indications of potential will be given a promising innovation medicine (PIM) designation based on assessment of clinical data. Secondly, medicines with a favourable benefit-risk profile will receive a positive scientific opinion which is published on the MHRA’s website. These opinions will support prescribers in deciding whether to use an unlicensed medicine for conditions where there are no or inadequate treatment options available.

► [MHRA Press release, 7 April 2014](#).
EMAs draft guidelines for parallel scientific advice with health-technology-assessment bodies

European Union – The European Medicines Agency (EMA) has invited comments on a draft best practice guidance document that aims to facilitate an early dialogue on new medicines between regulators, health technology assessment (HTA) bodies and medicines developers.

HTA bodies – such as the UK’s National Institute for Health and Care Excellence (NICE) – advise healthcare systems on the usefulness of new medicines in their respective territories. The draft guidance proposes phases and timelines of the EMA-HTA parallel scientific advice process. The aim of this process is to facilitate agreement upon a development plan that generates data for both the EMA’s benefit-risk assessment and HTA bodies’ determination of added value. Strong interaction between all stakeholders is critical for innovation to reach patients in a faster and more transparent way.

Comments on the draft guidance will be considered at the EU together with results of two other projects: the EMA’s ongoing parallel scientific advice pilot running since 2010, and the European Commission’s Shaping European Early Dialogues for health technologies (SEED) consortium.

EU votes in new rules for clinical trials

European Union – The European Parliament has voted strongly in favour of new rules on clinical trials across Europe, with strengthened rules for transparency. Since May 2011 clinical trials authorized in the EU are published in an official EU register. The Regulation requires that the results of all clinical trials, including those with unfavourable outcomes, are made public. It is expected to come into effect in mid-2016 at the earliest.

The European Medicines Agency (EMA) has welcomed the EU Regulation. In parallel EMA has conducted a final round of stakeholder consultations on its policy on proactive release of clinical trial data, with discussions on possible data redactions on the grounds of confidentiality, and the best ways of making the data accessible.

Health Action International (HAI) Europe has welcomed the Regulation and points to the importance of continued work and
supportive EMA procedures to ensure full clinical trial data transparency in the EU.

HAI Europe statements, 3 April and 22 May 2014.
EMA News, 8 April 2014.
EMA Press release, 28 May 2014.

EMA and FDA propose joint clinical investigation mechanism for rare children’s disease

European Union/United States of America – The European Medicines Agency (EMA) and the United States Food and Drug Administration (FDA) have released a draft joint proposal to facilitate the clinical investigation of new medicines for the treatment of Gaucher disease in children.

Gaucher disease is a rare condition in children that can be extremely severe. There is a high unmet need for medicines to treat children with neurological symptoms, in particular for new routes of administration to reduce the treatment burden. Recruitment of children for clinical trials on this rare condition is difficult and poses a burden on patients and their families.

The joint proposal aims to evaluate multiple medicines more quickly in fewer patients using two complementary approaches: extrapolating efficacy from adults to children through modelling and simulation, and conducting multi-arm, multi-company clinical trials on several new medicines at the same time, with the same control arm serving more than one medicine under evaluation.

The document is released for public consultation until 31 August 2014.
► EMA News, 14 May 2014.

Post-marketing control

EU adopts specifications for post-marketing efficacy studies

European Union – The European Commission has adopted legislation that specifies the situations where medicines regulatory authorities can require an efficacy study for a medicine after it has been granted a marketing authorization. The act will enter into force on 30 April 2014.

Post-authorization studies aim to address concerns about the efficacy of a medicine in certain situations, such as everyday medical practice, in specific populations, or over time. Such studies already existed previously, however, new pharmacovigilance legislation came into force in the EU in July 2012 to extend the legal framework in which they can be required.
► EMA News, 11 April 2014.

EMA reports on implementation of new pharmacovigilance legislation

European Union – The European Medicines Agency (EMA) has presented the European Commission with its report on the first year of implementing the EU’s new pharmacovigilance legislation on monitoring the safety of medicines and reducing their risks.

The report reveals positive first-year results in collection and analysis of data, timeliness and transparency. Patient reports of suspected adverse drug reactions increased by over 60% compared with the previous year. Product information was updated as a consequence of signals of new or changing safety issues with certain medicines, and a number of major public health reviews were initiated. Thousands of individuals
were trained in pharmacovigilance, and a catalogue with training material for the implementation of the new legislation has been published.

► EMA News, 2 May 2014.

Guidance

**EMA recommendations on seasonal influenza vaccine composition**

**European Union** – The European Medicines Agency (EMA) has issued its annual recommendations for the influenza virus strains that should be included in vaccines for the 2014/2015 season. For trivalent vaccines these include an A/California/7/2009 (H1N1)pdm09-like virus; an A/Texas/50/2012 (H3N2)-like virus and a B/Massachusetts/2/2012-like virus. Quadrivalent vaccines containing two influenza-B viruses should also include a B/Brisbane/60/2008-like virus. The annual recommendations are made on the basis of observations by the World Health Organization.


**MHRA confirms position on statins**

**United Kingdom** – The UK Medicines and Healthcare products Regulatory Agency (MHRA) has confirmed its position on the use of statins, advising that their benefits strongly outweigh the risks.

The MHRA statement follows recent controversial media coverage about side effects associated with statins. The MHRA advises that large clinical trials have shown that statins reduce the risk of heart attacks, strokes and the need for heart surgery, and that most side effects are mild.

► MHRA News, 16 May 2014.

Approvals

**Miltefosine for leishmaniasis**

**United States of America** – The U.S. Food and Drug Administration (FDA) has approved miltefosine (Impavido®) to treat leishmaniasis, a disease transmitted to humans through sand fly bites primarily in tropical and subtropical regions.

Miltefosine was approved for oral treatment of visceral, cutaneous and mucosal leishmaniasis in patients 12 years of age and older. The medicine was granted fast track designation, priority review, and orphan product designation. The medicine should not be taken during pregnancy. Women should use effective contraception during and for five months after treatment with miltefosine.

► FDA News release, 19 March 2014.

**Apremilast for psoriatic arthritis**

**United States of America** – The U.S. Food and Drug Administration (FDA) has approved apremilast (Otezla®) to treat adults with active psoriatic arthritis (PsA), a form of arthritis that affects some people with psoriasis. Currently approved treatments for PsA include corticosteroids, tumor necrosis factor blockers, and an interleukin-12/interleukin-23 inhibitor. Compared to placebo, apremilast was shown to have benefits in treating tender and swollen joints and improving physical function.

Patients treated with apremilast should be monitored for unexplained or clinically significant weight loss and for signs of depression. The FDA is requiring a pregnancy exposure registry as a post-marketing requirement to assess the risks of apremilast to pregnant women.

► FDA News release, 21 March 2014.
Vintafolide for ovarian cancer, with diagnostic medicines etarfolatide and folic acid

European Union – The European Medicines Agency (EMA) has recommended approval of vintafolide (Vynfinit®) to treat a sub-type of platinum-resistant ovarian cancer for which there are limited approved treatment options.

The medicine was recommended for approval together with two companion diagnostic medicines, etarfolatide (Folcepri®) and folic acid (Neocepri®), that will help identify patients who may benefit from treatment with vintafolide. All three medicines have an orphan designation and were recommended for conditional marketing authorizations.


Siltuximab for Castleman’s disease

European Union/United States of America – The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have both approved siltuximab (Sylvant®) for the treatment of adult patients with multicentric Castleman’s disease.

Siltuximab is the first medicine approved to treat this rare disorder, which is characterized by non-cancerous growth of the lymph nodes and related tissues. Affected patients have an increased risk of infection, kidney failure and certain cancers. Castleman’s disease is chronically debilitating and life-threatening, especially for patients with more than one affected lymph node.

Both authorities had granted an orphan designation to the medicine and evaluated it by their respective accelerated priority review mechanism.

FDA News release, 20 May 2014.

Vedolizumab for ulcerative colitis and Crohn’s disease

European Union/United States of America – The European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) have both approved vedolizumab (Entvyio®) to treat moderately to severely active ulcerative colitis or Crohn’s disease in adult patients who have had an inadequate response or were intolerant to other therapies.

Ulcerative colitis and Crohn’s disease are chronic auto-immune diseases that cause considerable ill health and mortality and increase the risk of colon cancer. Vedolizumab is a monoclonal antibody that binds specifically to a key mediator of gastrointestinal inflammation, allowing for a selective, targeted activity.

FDA News release, 20 May 2014.

Empagliflozin for type 2 diabetes

European Union – The European Medicines Agency (EMA) has recommended approving empagliflozin (Jardiance®) for type 2 diabetes both for monotherapy and as an add-on agent in combination therapy. Empagliflozin blocks a protein in the kidney, reducing glucose re-absorption and leading to glucose excretion in the urine, thereby lowering blood glucose levels and improving glycaemic control.


Simeprevir for chronic hepatitis C

European Union – The European Medicines Agency (EMA) has recommended approving simeprevir (Olysio®) for the treatment of chronic hepatitis C in adult patients in combination with other medicinal products. Simeprevir is a specific inhibitor of the hepatitis C virus NS3/4A serine protease. The medicine should be prescribed by health
professionals experienced in the treatment of chronic hepatitis C.


Fluticasone furoate and vilanterol trifenatate for asthma and COPD
European Union – The European Medicines Agency (EMA) has recommended authorizing a fixed-dose combination of fluticasone furoate and vilanterol trifenatate (Revinty Ellipta®) for the treatment of asthma and of chronic obstructive pulmonary disease (COPD) in patients not adequately controlled with other therapies. The Risk Management Plan identifies pneumonia as a risk which the applicant will investigate through further post-authorization safety studies.


Generic oseltamivir for influenza
European Union – The European Medicines Agency (EMA) has recommended authorizing a generic oseltamivir product (Ebilfumin®) for the prevention and treatment of influenza. This is a generic of Tamiflu® which has been authorized in the EU since 20 June 2002.


Topiramate for migraine prevention in adolescents
United States of America – The U.S. Food and Drug Administration (FDA) has approved topiramate (Topamax®) for prevention of migraine headaches in adolescents ages 12 to 17. This is the first FDA approval of a medicine for migraine prevention in this age group. Topiramate was approved by the FDA in 1996 to prevent seizures, and in 2004 for migraine prevention in adults.

► FDA News release, 28 March 2014.

Long-acting recombinant coagulation factor IX concentrate for haemophilia B
United States of America – The U.S. Food and Drug Administration has approved a recombinant coagulation factor IX linked to Fc fusion protein (Alprolix®) to help control and prevent bleeding in adults and children with haemophilia B. The Fc protein fragment is found in antibodies, making the product last longer in circulation and requiring less frequent injections. The product received orphan-drug designation for this use by the FDA.

► FDA News release, 28 March 2014.

Albiglutide for type 2 diabetes
United States of America – The U.S. Food and Drug Administration (FDA) has approved albiglutide subcutaneous injection (Tanzeum®) to improve glycemic control in adults with type 2 diabetes. Albiglutide is a glucagon-like peptide-1 (GLP-1) receptor agonist, which mimics the action of a hormone that helps normalize blood sugar levels.

Albiglutide should not be used as first-line therapy, nor should it be used in patients with type 1 diabetes, those with diabetic ketoacidosis, or those that have an increased risk of medullary thyroid carcinoma. The FDA is requiring a number of post-marketing studies and the implementation of a Risk Evaluation and Mitigation Strategy (REMS) to manage the risks associated with albiglutine.

► FDA News release, 15 April 2014.

Two sublingual pollen extracts for allergies
United States of America – The U.S. Food and Drug Administration (FDA) has approved two sublingual allergen extract tablets for the treatment of pollen allergies in adults (Oralair® and Ragwitek®). These
are the first sublingual allergen extracts to be approved in the United States.

Treatment is initiated under the observation of a health professional four months before the start of the pollen season and continued once daily throughout the season.

► FDA News releases, 2 April 2014 and 17 April 2014.

**Ramucirumab for stomach cancer**
United States of America – The U.S. Food and Drug Administration (FDA) has approved ramucirumab (Cyramza®) to treat advanced stomach cancer. Ramucirumab is an angiogenesis inhibitor that blocks the blood supply to tumors. The medicine was reviewed under the FDA’s priority review programme and had been granted orphan product designation.

► FDA News release, 21 April 2014.

**Ceritinib for late-stage lung cancer**
United States of America – The U.S. Food and Drug Administration (FDA) has granted accelerated approval to ceritinib (Zykadia®) for patients with a certain type of late-stage non-small cell lung cancer. Ceritinib is intended to treat patients previously treated with crizotinib, the only other approved product of the class of ALK tyrosine inhibitors targeting this particular type of lung cancer. The FDA granted ceritinib breakthrough therapy designation, priority review and orphan product designation.

► FDA News release, 29 April 2014.

**Trametinib for advanced melanoma**
European Union – The European Medicines Agency (EMA)’s Committee for Medicinal Products for Human Use (CHMP) has recommended marketing authorization for trametinib (Mekinist®) for the treatment of adult patients with unresectable or metastatic melanoma.

Trametinib is the first cancer treatment that selectively targets an enzyme called MEK protein kinase, which is activated by a protein produced in patients with a BRAF V600 mutation. Together with dabrafenib, vemurafenib and imurafenib, trametinib belongs to the group of new selective treatments that have changed the therapeutic landscape for advanced melanoma.


**Vorapaxar to reduce cardiovascular risks**
United States of America – The U.S. Food and Drug Administration (FDA) has approved vorapaxar (Zontivity®) to reduce the risk of heart attack, stroke, cardiovascular death, and the need for procedures to restore the blood flow to the heart in patients with a previous heart attack or blockages in the arteries to the legs. Vorapaxar, an anti-platelet agent, is the first approved protease-activated receptor-1 (PAR-1) antagonist.

Vorapaxar increases the risk of bleeding. It must not be used in people who have had a stroke, transient ischaemic attack, or bleeding in the head. Patients should report to their health care professional any unanticipated, prolonged or excessive bleeding, or blood in their stool or urine.

► FDA News, 8 May 2014.

**Dalbavancin for skin infections**
United States of America – The U.S. Food and Drug Administration (FDA) has approved dalbavancin, (Dalvance®), for the intravenous treatment of acute skin and skin structure infections caused by susceptible bacteria like *Staphylococcus aureus* (including methicillin-susceptible and methicillin-resistant strains) and *Streptococcus pyogenes*. 
Dalbavancin is the first drug designated as a Qualified Infectious Disease Product (QIDP) to receive FDA approval. This designation is granted to antibacterial or antifungal human medicines intended to treat serious or life-threatening infections.

Ataluren for Duchenne muscular dystrophy
European Union – The European Medicines Agency (EMA) has recommended conditional approval of a first-in-class medicine for treatment of Duchenne muscular dystrophy in patients aged five years and older who are able to walk. Ataluren (Translarna®), an orphan-designated medicine for the treatment of Duchenne muscular dystrophy.

Duchenne muscular dystrophy is a genetic disease characterized by the lack of the protein dystrophin, causing loss of muscle function. There are currently no approved therapies available for this life-threatening condition.

The company will be required to provide comprehensive data from an ongoing confirmatory study.

Obinutuzumab for chronic lymphocytic leukaemia
European Union – The European Medicines Agency (EMA) has recommended approving obinutuzumab (Gazyvaro®) in combination with the cancer medicine chlorambucil for the treatment of adults with previously untreated chronic lymphocytic leukaemia.

Chronic lymphocytic leukaemia is a long-term debilitating disease as patients can develop severe infections. It remains incurable, although currently available treatments generally induce remission. Obinutuzumab has an orphan designation. It is a monoclonal antibody that targets B-lymphocytes, thereby helping the body’s immune system to kill the cancer cells.

Peginterferon beta-1a for multiple sclerosis
European Union – The European Medicines Agency (EMA) has recommended granting of a marketing authorization for peginterferon beta-1a (Plegridy®) for the treatment of relapsing remitting multiple sclerosis. The product reduces the relapse rate in relapsing-remitting multiple sclerosis. It should be prescribed by physicians experienced in the treatment of multiple sclerosis.

Simoctogog alfa for patients with haemophilia A
European Union – The European Medicines Agency (EMA) has recommended approval of simoctogog alfa (Nuwiq®) for the treatment and prophylaxis of bleeding in paediatric and adult patients with haemophilia A (congenital factor VIII deficiency). The active substance is a recombinant blood coagulation factor VIII.

Brinzolamide / brimonidine tartrate to reduce intra-ocular eye pressure
European Union – The European Medicines Agency (EMA) has recommended approval of the combination of brinzolamide and brimonidine (Simbrinza®) eye drops for the treatment of elevated intraocular pressure (IOP) in adult patients with open-angle glaucoma or ocular hypertension for whom monotherapy provides insufficient IOP reduction.