Regulatory news

**Medicines regulation**

**New biosimilar regulations in Australia**

Australia – The TGA has published version 2.0 of its biosimilar regulations. A new section has been added on adverse event reporting requirements, including the information that should be provided to identify the biosimilar linked to each incident, namely: its brand identity, its non-proprietary name (i.e. the Australian biological name), its AUST R and batch numbers, and its expiration date and dosage form.

The new guidance also defines the data requirements for registration of new biosimilars in terms of laboratory and clinical studies demonstrating their comparability (biosimilarity) to the reference biological medicine already registered in Australia. The guidance further states when and how companies can compare their biosimilars to products that are not registered in Australia.

The new version of the regulations is largely based on EMA guidance documents.

► Asia Regulatory Roundup, 22 December 2015.


**EMA launches PRIME scheme for medicines targeting unmet needs**

European Union – The EMA has launched its new PRIME (PRIority MEdicines) scheme to accelerate access to medicines that offer a major therapeutic advantage over existing treatments, or benefit patients with no treatment options. Through PRIME, EMA offers early, proactive and enhanced support to medicine developers to optimize the generation of robust data on a medicine’s benefits and risks and enable accelerated assessment of medicine applications.

PRIME builds on the existing regulatory framework and available tools. This means that a PRIME medicine is expected to benefit from accelerated assessment at the time of an application for marketing authorization. To be accepted for PRIME, a medicine has to show its potential to benefit patients with unmet medical needs based on early clinical data. While PRIME is open to all companies, micro-, small- and medium-sized enterprises (SMEs) and applicants from the academic sector can apply earlier on the basis of compelling non-clinical data and tolerability data from initial clinical trials.

► EMA Press release, 7 March 2016.

**EMA guidance for industry on clinical studies and clinical data publication**

European Union – The European Medicines Agency (EMA) has informed applicants for centralized marketing authorization that if a pivotal clinical study is found to be non-compliant with good clinical practice (GCP) during the assessment, it cannot be replaced by another study. A new application must be submitted which is supported by appropriate GCP-compliant data from a
pivotal study. With this position the EMA aims to reinforce the application of GCP during the conduct of clinical trials. (1)

The EMA has also issued guidance for pharmaceutical companies to operationalize its new policy on proactive publication of clinical data, which entered into force on 1 January 2015. The guidance includes recommendations on how to anonymize clinical reports and how to identify and redact commercially confidential information. (2)

► (1) EMA News, 30 November 2015.
► (2) EMA News, 3 March 2015.

**EMA increases access to reports on adverse reactions**

**European Union** – The EMA has adopted a revised access policy for its EudraVigilance database, which holds the reports of suspected adverse reactions to medicines authorized in the European Economic Area (EEA).

Under the revised policy, the Uppsala Monitoring Centre (UMC) of WHO will be provided with individual case safety reports originating from within the EEA on a daily basis in accordance with a data transfer agreement concluded in December 2015. Medicines regulatory authorities in countries outside the EEA can obtain data in line with the WHO dataset upon request. Academia can obtain extended access to data sets for specific research activities, and marketing authorization holders will be given enhanced access to reports on their medicines in support of their pharmacovigilance obligations.

The changes will come into effect in the third quarter of 2017 together with a series of technical improvements to the EudraVigilance system.

► EMA Press release, 18 December 2015

**Safety features on packaging to be introduced in Europe**

**European Union** – Following the approval of a new regulation of the Falsified Medicines Directive the EMA and the European Commission have published an implementation plan to guide applicants and marketing-authorization holders in meeting the new requirements.

The Delegated Regulation introduces two safety features – a unique identifier (a two-dimension barcode) and an anti-tampering device – to be placed on the packaging of most medicines for human use. Marketing authorization holders are required to place the safety features on the packaging of most prescription medicines and certain non-prescription medicines no later than 9 February 2019.


**International Health Regulations**

**Poliovirus spread: continued public health emergency**

**Geneva** – The International Health Regulations (IHR) Emergency Committee unanimously agreed that the international spread of polio remains a Public Health Emergency of International Concern and recommended the extension of the temporary recommendations for a further three months. The recommendations essentially aim to ensure vaccine coverage to eradicate polio globally, including in vulnerable areas.

► WHO Statement, 1 March 2016.
Zika virus disease a public health emergency

Geneva – On 1st February 2016 the WHO Director-General declared a Public Health Emergency of International Concern related to the recent increase of Zika virus infection in Brazil. The concern relates to the increased number of infants born with microencephaly and of other neurologic disorders observed in Brazil in connection with the spread of the virus during 2015. A similar cluster was observed in French Polynesia in 2014.

The Emergency Committee convened under the International Health Regulations (2005) has recommended that aggressive measures should be taken to reduce the risk of infection with Zika virus, particularly among women of childbearing age. No travel or trade restrictions have been recommended. In the longer term, research and development will be intensified for Zika virus vaccines, therapeutics and diagnostics. (1)

European Union – In response to the WHO announcement, the EMA has set up a task force to provide advice on any scientific and regulatory matters for the research and development of medicines or vaccines against the Zika virus. (2)

The International Coalition of Medicines Regulatory Authorities (ICMRA) has pledged its support to WHO in countering the Zika outbreak (3). ICMRA brings together 21 medicines regulators from every region in the world. Its members are working together to fight against Zika virus disease, building on ICMRA’s collaborative work on Ebola.


Blood safety

FDA updates blood donor deferral policies

United States of America – The FDA has provided guidance on blood donor deferral to reduce the risk of human immunodeficiency virus (HIV) transmission and Zika virus transmission.

To reduce the risk of HIV transmission, men who have sex with men will be deferred for 12 months since the last sexual contact with another man, instead of indefinitely. This deferral period is more aligned with that recommended for other at-risk individuals and that recommended in other countries (1).

To reduce the risk of Zika virus transmission the FDA has recommended that donors at risk for Zika virus infection be deferred for four weeks if they have had symptoms suggestive of Zika virus infection or have potentially been exposed to the virus by travelling to an area with active Zika virus transmission or through sexual contact. The FDA recommends that whole blood and blood components for transfusion be obtained from areas without active transmission. (2)

The FDA has also issued new recommendations to reduce the risk of Zika virus transmission from human cells, tissues and cellular and tissue-based products, for immediate implementation. (3)

►(1) FDA News release, 21 December 2015.
(2) FDA News release, 16 February 2016.
(3) FDA News release, 1 March 2016.
Approved

Sebelipase alfa for lysosomal acid lipase (LAL) deficiency

Product name: Kanuma®
Dosage form: Concentrate for solution for intravenous infusion
Class: rhLAL protein, enzyme; ATC code: A16AB14
Approval: FDA (orphan drug; breakthrough therapy)
Use: Treatment of patients with LAL deficiency, also known as Wolman disease and as cholesteryl ester storage disease (CESD). LAL deficiency is a rare inherited genetic disorder that can lead to serious and life-threatening organ damage.
Benefits: Increased survival of infants with rapidly progressing Wolmans disease at 12 months of age; improvement in disease-related parameters in CESD patients.
Notes: The product is produced in the egg whites of genetically engineered chickens. The U.S. Center for Veterinary Medicine (CVM) determined that the rDNA construct is safe for the animals and is stable in the genome of the chicken over several generations. Neither the chicken nor the eggs are allowed in the food supply. The product was approved in the EU in August 2015.

Benefits: Ability to decrease the elevated pressure in the vessels supplying blood to the lungs.

Albutreponacog alfa for Haemophilia B

Product name: Idelvion®
Dosage form: Powder and solvent for solution for injection
Class: Antihaemorrhagic, blood coagulation factor IX; ATC code: B02BD04
Approval: FDA (non-proprietary name: Coagulation factor IX (recombinant), albumin fusion protein); EMA (orphan designation)
Use: Treatment and prophylaxis of bleeding in patients with Haemophilia B
Benefits: Ability to stop and prevent bleeding.

Recombinant von Willebrand factor for control of bleeding episodes

Product name: Vonvendi®
Dosage form: Lyophilized powder for solution for intravenous injection
Class: Blood coagulation factor; recombinant von Willebrand factor (first-in-class approved by FDA); ATC code: B02BD10
Approval: FDA (orphan product designation)
Use: On-demand (as needed) treatment and control of bleeding episodes in adults diagnosed with von Willebrand disease.
Benefits: Additional therapeutic option for the treatment of bleeding episodes in patients with von Willebrand disease
► FDA News release, 8 December 2015.

Selexipag for pulmonary arterial hypertension

Product name: Utravi®
Dosage form: Tablets
Class: Oral IP prostacyclin receptor agonist; ATC code: B01AC27
Approval: FDA (orphan drug designation); EMA (orphan medicinal product designation)
Use: Treatment of adults with pulmonary arterial hypertension

Benefits: Ability to decrease the elevated pressure in the vessels supplying blood to the lungs.
Approved

**Emtricitabine/tenofovir alafenamide for HIV infection**

**Product name:** Descovy®

**Dosage form:** Film-coated tablets

**Class:** Fixed-dose combination of two antiretrovirals, reverse transcriptase inhibitors; **ATC code:** J05AR17

**Approval:** EMA

**Use:** In combination with other antiretroviral agents, for the treatment of adults and adolescents infected with human immunodeficiency (HIV) virus type 1

**Benefits:** Lower impact on renal safety and bone mineral density compared with tenofovir disoproxil-containing regimens.


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**Emtricitabine/rilpivirine/tenofovir alafenamide for HIV infection**

**Product name:** Odefsey®

**Dosage form:** Tablets

**Class:** Fixed dose combination of three antiretrovirals; **ATC code:** J05AR19

**Approval:** FDA

**Use:** Complete treatment regimen for HIV-1 infection in patients from 12 years of age as initial therapy in ARV treatment-naïve patients with ≤100 000 RNA copies per mL; or to replace a stable antiretroviral regimen in patients with less than 50 RNA copies per mL for at least six months, no history of treatment failure and no known substitutions associated with resistance to the individual drug components.

**Benefits:** Lower impact on renal safety and bone mineral density compared with tenofovir disoproxil-containing regimens.


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**Uridine triacetate for emergency treatment of chemotherapy overdose**

**Product name:** Vistogard®

**Dosage form:** Oral granules

**Class:** Pyrimidine analogue (**ATC code:** L01BC)

**Approval:** FDA

**Use:** Emergency treatment of overdose or life-threatening toxicity of fluorouracil or capecitabine

**Benefits:** First-of-its-kind therapy that can block cell damage and cell death caused by competitive inhibition.

**Notes:** The safety and efficacy of uridine triacetate initiated more than 96 hours following the end of treatment with fluorouracil or capecitabine have not been established. Uridine triacetate is not recommended for treating non-emergency adverse reactions associated with fluorouracil or capecitabine because it may lessen the efficacy of these drugs.

► FDA News release, 11 December 2015.
Elotuzumab for multiple myeloma

Product name: Empliciti®
Dosage form: Concentrate for solution for infusion
Class: Monoclonal antibody; ATC code (temporary): L01XC23
Approval: EMA (orphan designation)
Use: In combination with lenalidomide and dexamethasone, treatment of multiple myeloma in patients who have received at least one prior therapy
Benefits: Ability to delay the progression of disease and to increase the proportion of patients who have a response.

Alectinib for certain advanced non-small cell lung cancers

Product name: Alecensa®
Dosage form: Capsules
Class: ALK (anaplastic lymphoma kinase) blocker; ATC code (temporary): L01XE36
Approval: FDA (accelerated approval; breakthrough therapy designation, priority review status; orphan drug designation)
Use: Treatment of patients with anaplastic lymphoma kinase (ALK)-positive, metastatic non-small cell lung cancer who progressed on, or are intolerant to, crizotinib.
Benefits: New therapy for certain types of advanced metastatic non-small cell lung cancer, with ability to reduce primary tumours in the lung and brain metastases.
Safety information: Serious side effects include hepatotoxicity, interstitial lung disease, bradycardia and severe myalgia. Women treated with alectinib should use effective contraception. Patients treated with alectinib should avoid sun exposure and use a broad spectrum sunscreen.
► FDA News release, 11 December 2015.

Lesinurad for hyperuricaemia

Product name: Zurampic®
Dosage form: Film-coated tablets
Class: Selective reabsorption inhibitor of uric acid transporter 1 (URAT1);
ATC code: M04AB05
Approval: EMA, FDA
Use: Adjunctive treatment of hyperuricaemia in combination with a xanthine oxidase inhibitor in adults with gout.
Benefits: Ability to increase uric acid excretion and thereby lower serum uric acid levels.
► EMA/CHMP Summary of opinion, 17 December 2015.
FDA News release, 22 December 2015.

Brivaracetam for epilepsy

Product name: Briviact®
Dosage form: Tablets, oral solution, and solution for injection/infusion
Class: Antiepileptic; ATC code: N03AX23
Approval: FDA, EMA
Use: Adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in patients from 16 years of age with epilepsy
Benefits: Ability to reduce the frequency of partial-onset epileptic seizures.
► FDA News release, 19 February 2016.
EMA/CHMP Summary of opinion, 19 November 2015.

“InFollow-on” biological product

Insulin glargine

Product name: Basaglar®
Dosage form: Injection
Class: Long-acting human insulin analog
Approval: FDA final approval
Use: Improvement of glycaemic control in adults and paediatric patients with type 1 diabetes mellitus and in adults with type 2 diabetes mellitus
Note: Basaglar® is the first insulin product approved through an abbreviated approval
Approved pathway under the Federal Food, Drug, and Cosmetic Act. A 505(b)(2). The application submitted for its marketing authorization relied, in part, on the FDA’s finding of safety and effectiveness for Lantus® (insulin glargine injection), and demonstrated that Basaglar® was sufficiently similar to Lantus® to scientifically justify such reliance.

Basaglar® was not approved as a biosimilar product, as there was no insulin glargine “reference product” licensed under the Public Health Service Act.

► FDA News release, 16 December 2015.

### Extensions of indications

#### Nivolumab for kidney cancer

**Product name:** Opdivo®

**Approval:** EMA

**Newly approved use:** Treatment of adult patients with advanced renal cell carcinoma.


(See also the Safety news on page 49)

#### Eribulin for liposarcoma

**Product name:** Halaven®

**Approval:** FDA (orphan drug designation, priority review)

**Newly approved use:** Treatment of unresectable or metastatic liposarcoma in patients who received prior chemotherapy containing an anthracycline drug.


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