Regulatory news

Guidance

EU: Good pharmacogenomic practice
European Union – The EMA has released its new Guideline on good pharmacogenomic practice, which will come into effect on 1 September 2018. The guideline describes requirements for choosing appropriate genomic methodologies during the development and the life cycle of a medicine. It discusses the characteristics of a robust clinical genomic dataset and highlights the key scientific and technological aspects to consider when determining and interpreting genomic biomarker data and translating them into clinical practice. The guideline is also expected to be a useful reference in the context of future legislation on companion diagnostics, in-house testing and medical devices in Europe.

U.S.: Genomic-based tests
United States of America – The FDA has finalized two guidance texts to drive the design, development and validation of in vitro diagnostics (IVDs) that use next generation sequencing (NGS) technologies. These diagnostics can look at millions of DNA changes in a single test, and have led to the identification of many new genetic variants. The first guidance relates to the use of FDA-recognized databases to support the clinical validation of new NGS tests, enabling developers to identify an efficient path for marketing clearance or approval of their products.(1) The second guidance provides recommendations for designing, developing, and validating NGS-based tests intended to aid clinicians in the diagnosis of symptomatic individuals with suspected germline diseases. It does not address tests intended for use in the sequencing of healthy individuals.(2)
► FDA News release, 12 April 2018.
(1) FDA. Use of Public Human Genetic Variant Databases to Support Clinical Validity for Genetic and Genomic-Based In Vitro Diagnostics. 13 April 2018.
(2) FDA. Considerations for Design, Development, and Analytical Validation of Next Generation Sequencing (NGS) – Based In Vitro Diagnostics (IVDs) Intended to Aid in the Diagnosis of Suspected Germine Diseases. 13 April 2018.

UK: Data integrity
United Kingdom – The MHRA has published its final guidance on data governance systems across all good practice sectors, including good laboratory practice, good clinical practice, good manufacturing practice, good distribution practice and good pharmacovigilance practice. This new guidance was created in response to fundamental failures identified by MHRA and international regulatory partners during inspections, many of which have resulted in regulatory action. It addresses the new technologies used to generate regulatory data—for example electronic data capture, automation of systems and use of remote technologies—and the increased complexity
of supply chains and ways of working, for example via third party service providers.  
MHRA. ‘GXP’ Data Integrity Guidance and Definitions. Revision 1: March 2018.

Pre-market assessment

Australia: New regulatory pathways

Australia – The TGA has established two new pre-market pathways for medicines, following recommendations of the national medicines and medical devices regulation review.

Firstly, a new provisional approval pathway for prescription medicines has been introduced. Approval through this pathway is on the basis of preliminary clinical data and is limited to six years. The pathway applies to new medicines as well as new uses for existing medicines. To be eligible, a product must target a serious condition, compare favourably with existing medical products and offer a major therapeutic advance. Furthermore there must be evidence of a plan to submit comprehensive clinical data.(1) In April 2018, olaratumab(rmc) (Lartruvo*) was the first medicine to be accepted for evaluation through this pathway.(2)

Secondly, the TGA has published its Assessed listed medicines evidence guidelines, along with guidance for completing applications. This new route sits between the pathways for “listed medicines” (complementary medicines with low risk) and “registered medicines” (fully reviewed products with higher risk). Assessed listed medicines can only contain certain defined low-risk ingredients but are used for at least one “intermediate level indication” requiring some proof of efficacy. Applicants must submit scientific evidence of the product’s efficacy to the TGA for assessment, whereas they can self-certify the quality and safety of the product.(3)

These initiatives are part of a series of reforms undertaken in response to the regulatory review. Another new pathway for medicines—priority review—came into effect on 1 July 2017, and the first medicine, alectinib (Alecensa*) was registered via this route in February 2018.(4) An expedited approval pathway for needed novel medical devices started in 2018.(5) An overview of changes delivered and upcoming reforms in response to the medicines and medical devices regulation review is available on the TGA website.(6)

(2) TGA News, 16 April 2018.  
(3) TGA. Assessed listed medicines pathway for complementary medicines. 27 March 2018.  
(4) TGA News, 6 February 2018.  

EU: Two years of PRIME Scheme

European Union – The EMA has published a report looking back on two years’ experience with the its PRIME (PRIority Medicines) Scheme, which aims to support and optimize product development for unmet medical needs. Of 177 medicines submitted 36 have been accepted as eligible to the scheme, including 30 intended to treat rare diseases and 16 intended to treat children. The EMA has provided scientific advice for 22 of the 36 medicines, often with input from health technology assessment bodies that make recommendations on financing or reimbursement of medicines in national healthcare systems.  
► EMA News, 7 May 2018.
Medical devices

IMDRF meeting held
Shanghai, China – The International Medical Device Regulators Forum (IMDRF) held its 13th management committee meeting in Shanghai, China, on 20–22 March 2018. The IMDRF is currently working on a unique device identification (UDI) application guide, personalized medical devices, standards for improving the quality of international medical device standards for regulatory use, adverse event terminology, good regulatory review practices, patient registries and regulated product submission. Clinical evaluation of medical devices was adopted as a new work item.

At a one-day open stakeholder forum held on the second meeting day some 500 participants discussed issues of current interest, particularly the use of artificial intelligence in the field of medical devices.

The IMDRF management committee is composed of regulatory representatives of the IMDRF members, i.e. Australia, Brazil, Canada, China, Europe, Japan, Russia, Singapore, South Korea, and the United States of America. WHO and the Regulatory Harmonization Steering Committee of APEC’s Life Sciences Innovation Forum are IMDRF observers. The next committee meeting will be held in Beijing, China, on 18–20 September 2018.

IMDRF Meetings [webpage].

Canada: Disinfectants and sterilants reclassified
Canada – Health Canada has announced a reclassification of high-level disinfectant and sterilant solutions (as defined by the Agency on its website) intended for use on medical devices. Only those products that meet the definition of an antimicrobial agent will continue to be regulated under the Food and Drug Regulations; the others will be subject to the requirements of the Medical Devices Regulations (MDR).

The reclassification is part of Health Canada’s initiatives to align its regulatory requirements with those of the United States. Manufacturers of non-antimicrobial disinfectants and sterilants licensed as medicines have a transition period of 18 months to apply for Class II medical device licences. Health Canada intends to pursue an amendment to the MDR that would reclassify these products under the higher risk Class III category.


Databases

Japan: Medicines use in children
Japan – The PMDA has provided an update on the use of its Pediatric Medical Data Collecting System, which was established in 2012 for the collection and analysis of data on the safe use of medicines in children. The system utilizes a large network of institutions and has accumulated electronic medical records of approximately 250 000 patients.

A project started in 2017 to organize and analyse these data alongside information from the literature and from other regulatory authorities. A preliminary analysis focusing on four selected medicines has now been completed. The diuretics spironolactone and furosemide were found to be frequently co-prescribed, and although the package insert states only a dosage for adults they were often used in children as well. The antiepileptic levetiracetam has a dosage specified for children from age four, but was found to be given to younger children too; a clinical investigation of its
use in these children is under way. Aspirin is indicated for Kawasaki disease, a rare condition which affects mainly children under five and is more common in Japan than in other parts of the world. Only 20% of the cases in the database had a diagnosis of Kawasaki disease; about a third of the remaining ones had a diagnosis related to thrombosis.

The analysis will be expanded and refined by inclusion of body weight data, more intensive collection of data on prescribed doses, and extraction of adverse event data.

► PMDA. Pharmaceuticals and Medical Devices Safety Information No. 353, May 2018:3-7.

U.S.: Mobile app launched
United States of America – The FDA has announced the availability of its Drugs@FDA Express mobile application. The new mobile app is a streamlined version of the Agency’s Drugs@FDA webpage. It allows users to search on their mobile devices for certain information on FDA-approved medicines based on product name, active ingredient or application number using a single search box. The app will also display the most recent product approvals within seven days, and a number of useful links and contact information.

► FDA In Brief. 22 March 2018.

Collaboration

Treaty for African Medicines Agency signed
Geneva – The ministers of health of African Union member states have unanimously adopted the Treaty for the establishment of the African Medicines Agency (AMA). This Agency will promote the harmonization of policies, standards and guidelines for medical products regulation and advocate for the use of the AU Model Law on Medical Products Regulation. The AMA will provide a common framework for regulatory actions, with centres of regulatory excellence that can give guidance and technical assistance to countries that lack regulatory capacity and resources. The Treaty is to be sent to the African Union’s Specialised Technical Committee on Justice and Legal Affairs later in 2018.(1)

The AMA is modelled on the setup of the EMA, a unique regulatory network of national competent authorities in the Member States of the European Economic Area (EEA) working together with the EMA and the European Commission. The future AMA builds on the successes of long-standing efforts for regulatory strengthening, through the WHO-supported African Medicines Regulatory Harmonisation (AMRH) Programme, and through the African Vaccine Regulatory Forum (AVAREF), which was instrumental in coordinating clinical trials for an Ebola vaccine and could be transitioned into a centre for assessment of multi-country clinical trials for a wide range of new medicines and medical devices. These achievements will greatly help the formidable task of setting up a regulatory network among 54 African member states serving a total population of over 1 billion people.(2)


API inspection programme
The partners in the International Active Pharmaceutical Ingredient (API) Inspection Programme have published their report
on activities in 2011–16. In that period, they conducted 1333 GMP inspections in 20 countries outside their own territories. Between them, the partners inspected a total of 458 sites of common interest, of which 226 (49%) were located in India, and 165 (36%) in China. Non-compliances were found at 28% of all sites. Of the 1333 inspections, 131 were conducted by the WHO Prequalification Team.

The collaboration started as a pilot in 2008 and became a full programme in January 2011. It allows the EMA, national regulators of five European countries, the U.S. FDA, Australia’s TGA, Health Canada and Japan’s MHLW and PMDA, as well as the European Directorate for the Quality of Medicines (EDQM) and WHO, to share information on inspections of foreign API manufacturing sites. Since 2011 the membership, the number of sites of common interest, the level of information shared, and overall inspection coverage have all increased. The partners will now seek ways to improve their electronic information exchange platforms and programme reviews further.

► EMA News, 12 April 2018.


PIC/S updates

Geneva – The Pharmaceutical Inspection Co-operation Scheme (PIC/S) held meetings of its Committee and Executive Bureau in Geneva on 16-18 April 2018. The PIC/S Committee adopted a new PIC/S guidance on reliance in GMP inspections of foreign manufacturing sites and revised Chapters 3, 5 and 8 of the PIC/S GMP guide, to enter into force on 1 July 2018. From the same date PIC/S will also adopt the EU guidelines on GMP excipient risk assessment, exposure limits and good distribution practices for active pharmaceutical ingredients. Furthermore, the Committee has adopted an aide-memoire on cross-contamination in shared facilities. A revised draft guidance on data integrity will be implemented for a trial period while being published for external consultation.


9th Meeting of World Pharmacopoeias

Hanoi, Viet Nam – Thirteen national, regional and international pharmacopoeias representing 50 pharmacopoeial authorities around the world gathered in Da Nang, Viet Nam on 18–19 April 2018 to attend the 9th International Meeting of World Pharmacopoeias (IMWP). This event has been convened by WHO since 2012, with the first eight meetings focusing on the development of good pharmacopoeial practices. The 2018 meeting focused on creating new collaboration models and improving information-sharing. The participants agreed to establish a pharmacopoeial alert system to exchange information on issues detected with products covered by monographs that necessitate urgent action by a pharmacopeia. The delegations also agreed to use the annual IMWP as a discussion forum to inform each other of recent challenges and to share solutions.

The 10th International Meeting of World Pharmacopoeias meeting will be held in New Delhi, India, in February 2019.

► WHO Representative Office, Viet Nam.

International meeting of world pharmacopoeias says collaboration is key to improving access to essential medicines. 11 May 2018.
**Under discussion**

**European Union** – The European Medicines Agency (EMA) has released a draft revised guideline on the *clinical evaluation of vaccines*. The proposed revision addresses advances in science and technology and adds considerations on priming and boosting strategies and on developing vaccines for emerging pathogens for which it might be problematic to conduct clinical trials outside of outbreaks.

▶ EMA News, 26 April 2018.
  Closing date: 30 October 2018.

**European Union** – The European Commission has proposed a set of recommendations on strengthening EU cooperation to fight vaccine-preventable diseases. The proposal comes as recent data point to vaccination gaps in Europe, for example with regard to measles and influenza.

  The Commission’s proposal will be discussed by the European Council, with the aim of seeing a Council recommendation adopted before the end of 2018, with an immediate entry into force.

**Canada** – The government of Canada has published its proposed *pathogens of interest list* for public comment. The list largely adopts the *Global Priority List of Antibiotic-Resistant Bacteria* issued by WHO in 2017. It names the bacterial pathogens that may cause serious, life-threatening infections in the Canadian population and for which new therapies need to be developed.

  Closing date: 1 July 2018.

**United States of America** – The FDA has released a draft guidance documents on postmarketing safety reporting requirements for combination products, *i.e.* products composed of two or more different types of medical products (medicine, medical device and/or biological product). In addition, the Agency has published an immediately-in-effect guidance titled *Compliance Policy for Combination Product Postmarketing Safety Reporting*.

▶ FDA. Postmarketing Safety Reporting for Combination Products [webpage].
  FDA Federal Register Notice, 21 March 2018.
  Closing date: 19 June 2018.

**Australia** – The TGA has published a proposal that would require medicine sponsors to report all medicines shortages in confidence to the TGA. Shortages classified under a revised protocol as of “extreme” or “high” patient impact would be mandatorily published via the Medicines Shortages Information Initiative on the TGA website.

▶ TGA Consultation, 27 March 2018.
  Closing date: 30 April 2018.

**European Union** – The European Commission (EC) is seeking comments on a one-health approach to counteracting the threat from infectious diseases. The roadmap document proposes a strategy with three pillars to protect European citizens from emerging and highly pathogenic agents.

▶ EC Initiative, 26 March 2018.
  Closing date: 23 April 2018.
Approved

**Fostamatinib for thrombocytopenia**
**Product name:** Tavalisse®
**Dosage form:** Tablets
**Class:** Tyrosine kinase inhibitor;  
**ATC code (temporary):** B02BX09
**Approval:** FDA
**Use:** Treatment of adult patients with chronic immune thrombocytopenia (ITP) who have had an insufficient response to a previous treatment.
**Benefits:** Ability to achieve a stable platelet count to reduce the risk of bleeding.
**Safety information:** The main adverse effects include hypertension, liver toxicity, diarrhoea and neutropenia. Fostamatinib can cause foetal harm.
► FDA Prescribing information for Tavalisse®. Revised: 04/2018

**Avatrombopag to treat thrombocytopenia before procedures in certain patients**
**Product name:** Doptelet®
**Dosage form:** Tablets
**Class:** Thrombopoietin receptor agonist;  
**ATC code:** B02BX05
**Approval:** FDA (priority review; orphan designation)
**Use:** Treatment of thrombocytopenia in adults with chronic liver disease who are scheduled to undergo a medical or dental procedure
**Benefits:** Ability to increase platelet count, reducing the need for platelet transfusion or rescue therapy.
**Safety information:** Medicines of this class have been associated with thrombotic and thromboembolic complications in patients with chronic liver disease.
► FDA News release, 21 May 2018.

**Tildrakizumab for psoriasis**
**Non-proprietary name in the U.S.:** Tildrakizumab-asmn
**Product name:** Ilumya®
**Dosage form:** Injection
**Class:** Interleukin-23 antagonist;
**ATC code:** L04AC17
**Approval:** FDA
**Use:** Treatment of adults with moderate-to-severe plaque psoriasis who are candidates for systemic therapy or phototherapy.
**Benefits:** Significant clinical improvement in skin clearance compared to placebo.
**Safety information:** Tildrakizumab may increase the risk of infections. The medicine should not be administered to patients with active tuberculosis.
► FDA. Prescribing information for Ilumya®. Revised: 03/2018.

**Erenumab for prevention of migraine**
**Non-proprietary name in the U.S.:** Erenumab-aooe
**Product name:** Aimovig®
**Dosage form:** Subcutaneous injection for once-monthly self-administration
**Class:** Calcitonin gene-related peptide receptor antagonist (first-in-class);  
**ATC code:** N02CX07
**Approval:** FDA; EMA
**Use:** Preventive treatment of migraine in adults. In the EU the medicine is indicated only in adults who have at least 4 migraine days per month.
**Benefits:** More effective than placebo in reducing the number of days with migraine.
EMA Press release, 1 June 2018.

**Lofexidine for opioid use disorder**
**Product name:** Lucemyra®
**Dosage form:** Tablets
**Class:** Central alpha-2 adrenergic agonist;  
**ATC code:** N07BC04
**Approval:** FDA (priority review, fast track designation)
**Use:** Mitigation of opioid withdrawal symptoms to facilitate abrupt opioid discontinuation
in adults. The product is only approved for treatment for up to 14 days.

**Benefits:** Reduces the release of norepinephrine, the actions of which in the autonomic nervous system are believed to play a role in many of the symptoms of opioid withdrawal.

**Safety information:** The main risks include hypotension, bradycardia, and syncope, QT prolongation, and an increased risk of opioid overdose after opioid discontinuation. Safety and efficacy have not been established in people under 17 years of age.

**Note:** This is the first FDA-approved non-opioid treatment for the management of opioid withdrawal symptoms.

► FDA News release, 16 May 2018.

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**Pegvaliase for phenylketonuria**

**Product name:** Palynziq®

**Non-proprietary name in the U.S.:** Pegvaliase-pqpz

**Dosage form:** Injection for subcutaneous use

**Class:** Phenylalanine-metabolizing enzyme

**Approval:** FDA

**Use:** Treatment of adult patients with phenylketonuria who have uncontrolled blood phenylalanine concentrations greater than 600 micromol/L on existing management.

**Benefits:** Ability to reduce blood phenylalanine concentrations.

**Safety information:** Risk of anaphylaxis, especially during upward titration of the dose within the first year of treatment.


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**Inotersen for a rare hereditary deficiency**

**Product name:** Tegsedi®

**Dosage form:** Solution for injection

**Class:** Antisense oligonucleotide

**Approval:** EMA (accelerated assessment; orphan designation)

**Use:** Treatment of stage 1 or stage 2 polyneuropathy in patients with hereditary transthyretin amyloidosis (hATTR). Efficacy in stage 3 polyneuropathy has not yet been demonstrated.

**Benefits:** Clinically relevant effects on the neurological manifestations of hATTR and on patients’ quality of life.

**Notes:** hATTR is diagnosed in about three of every 10 million people in Europe every year. Current therapeutic options are liver transplant, treatment with the nervous system medicine tafamidis, and off-label use of a non-steroidal anti-inflammatory drug.

► EMA Press release, 1 June 2018.

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**New formulation**

**Fosnetupitant and palonosetron injection**

**Product name:** Akynzeo®

**Newly approved dosage form:** Intravenous injection

**Approval:** FDA

**Use:** Prevention of acute and delayed nausea and vomiting associated with initial and repeat courses of cancer chemotherapy.

**Note:** An oral fixed-dose combination of palonosetron and netupitant was approved by the FDA in 2014.

► FDA Product information for Akynzeo®, revised 04/2018.

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**Extensions of indications**

**Brentuximab vedotin for Hodgkin lymphoma**

**Product name:** Adcetris®

**Approval:** FDA (priority review, breakthrough therapy)

**Newly approved use:** Treatment of adult patients with previously untreated stage III or IV classical Hodgkin lymphoma, in combination with chemotherapy.

**Safety information:** The product carries a boxed warning highlighting the risk of John Cunningham virus infection resulting in progressive multifocal leukoencephalopathy. Serious risks include peripheral neuropathy; severe allergic (anaphylaxis) or infusion-site
Approved reactions; damage to the blood, lungs and liver; serious or opportunistic infections; metabolic abnormalities (tumour lysis syndrome); serious dermatologic reactions and gastrointestinal complications. The medicine can cause harm to a developing foetus.


**Blinatumomab for acute lymphoblastic leukaemia**

**Product name:** Blincyto®

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

**Newly approved use:** Treatment of adults and children with B-cell precursor acute lymphoblastic leukaemia (ALL) who are in remission but have minimal residual disease.

**Safety information:** The medicine carries a boxed warning about cytokine release syndrome and neurological toxicities observed in some clinical trial participants at the start of the first treatment. Serious risks include infections, effects on the ability to drive and use machines, pancreatitis, and adverse events caused by preparation or administration errors. There is a risk of serious adverse reactions in children due to benzyl alcohol preservative; therefore, the drug prepared with preservative-free saline should be used for patients weighing less than 22 kg.


**Dabrafenib with trametinib for certain thyroid cancers**

**Product name:** Tafinlar® in combination with Mekinist®

**Approval:** FDA (priority review; breakthrough therapy; orphan drug designation)

**Newly approved use:** Treatment of locally advanced or metastatic anaplastic thyroid cancer with BRAF V600E mutation

**Note:** This is the first FDA-approved treatment for patients with this aggressive form of thyroid cancer.

► FDA News release, 4 May 2018.

**Fingolimod for multiple sclerosis in children**

**Product name:** Gilenya®

**Approval:** FDA (priority review, break-through therapy)

**Newly approved use:** Treatment of relapsing multiple sclerosis in children and adolescents aged 10 years and older.

**Safety information:** Fingolimod can cause slowing of the heart rate, especially after the first dose; serious infections, including progressive multifocal leukoencephalopathy (PML); and a number of other adverse effects. Patients should be monitored for infection during treatment and for two months thereafter.


**Tofacitinib for ulcerative colitis**

**Product name:** Xeljanz®

**Approval:** FDA

**Newly approved use:** Treatment of adults with moderately to severely active ulcerative colitis

**Safety information:** Increased risk of developing serious infections that may lead to hospitalization or death; as well as lymphoma and other malignancies, have been observed in patients treated with tofacitinib.

**Notes:** Tofacitinib is the first FDA-approved oral medicine for chronic use in ulcerative colitis.

► FDA News release, 30 May 2018.

**Biosimilars**

**Epoetin alfa**

**Non-proprietary name in the U.S.:** Epoetin alfa-epbx

**Product name:** Retacrit®

**Use:** Treatment of anaemia caused by chronic kidney disease, chemotherapy, or use of zidovudine in patients with HIV infection; reduction of allogeneic red blood cell transfusions in patients undergoing elective, non-cardiac, non-vascular surgery.

Trastuzumab

**Product name:** Kanjinti®

**Use:** Treatment of metastatic breast cancer, early breast cancer, and metastatic gastric cancer.

► EMA Summary of opinion, 22 March 2018.

**Product name:** Trazimera®

**Use:** Treatment of metastatic breast cancer, early breast cancer, and metastatic gastric cancer.

► EMA Summary of opinion, 31 May 2018.

Pegfilgrastim

**Non-proprietary name in the U.S.:**

Pegfilgrastim-jmdb

**Product name:** Fulphila®

**Use:** To decrease the incidence of infection, as manifested by febrile neutropenia, in patients with non-myeloid malignancies receiving myelosuppressive anti-cancer drugs associated with a clinically significant incidence of febrile neutropenia.

► FDA News release, 4 June 2018.

Infliximab

**Product name:** Zessly®

**Use:** Treatment of rheumatoid arthritis, adult and paediatric Crohn’s disease, adult and paediatric ulcerative colitis, ankylosing spondylitis, psoriatic arthritis and psoriasis.

► EMA Summary of opinion, 22 March 2018.

Adalimumab

**Product name:** Halimatoz®

**Use:** Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, uveitis and paediatric uveitis.

► EMA Summary of opinion, 31 May 2018.

**Product name:** Hefiya®

**Use:** Treatment of juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn’s disease, paediatric Crohn’s disease, ulcerative colitis, uveitis and paediatric uveitis.

► EMA Summary of opinion, 31 May 2018.

**Product name:** Hyrimoz®

**Use:** Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, uveitis and paediatric uveitis.

► EMA Summary of opinion, 31 May 2018.

Diagnostics

**Mass spectroscopy test for Candida auris**

United States of America – The FDA has authorized the first test to identify *Candida auris*, an emerging pathogen which can cause serious infections in hospitalized patients and is frequently resistant to multiple antifungal drugs. The approval permits a new use for a mass spectrometry-based diagnostic system that has previously been authorized by the FDA to identify a wide range of pathogen species.

The FDA plans to propose exempting certain mass spectrometry microorganism identification system processes from an additional premarket review once they have achieved initial FDA authorization. This would permit easy updates to device-specific organism databases to expand the capabilities of these devices.

► FDA News release, 20 April 2018.
Negative opinions

Three medicines approved in the U.S. have received negative opinions in the European Union. In all three cases the applicants have requested a re-examination of the negative EMA opinion.

Betrixaban

Product name: Dexxience®
Dosage form: Capsules
Class: Anticoagulant, Factor Xa inhibitor
Regulatory authority: EMA
Intended use: Prevention of venous thromboembolism in adults admitted to hospital for the treatment of a recent medical illness.
Reasons for negative opinion: The EMA considered that the pivotal study was not reliable because some results of tests for blood clots were not available. In addition, patients treated with betrixaban had more episodes of bleeding than those treated with the comparator medicine. This was considered an important concern given that the medicine was expected to be used in patients with serious underlying conditions.

FDA approval of betrixaban (Bevyxxa®): 23 June 2017.

Abaloparatide

Product name: Eladynos®
Dosage form: Injection for subcutaneous use
Class: Human parathyroid hormone-related peptide analog
Regulatory authority: EMA
Use: Treatment of postmenopausal women with osteoporosis at high risk for fracture.
Reasons for negative opinion: The EMA considered that the main study did not satisfactorily show the effectiveness of abaloparatide for the intended use. The data from two study sites had to be excluded as the study had not been conducted in compliance with good clinical practice at those sites. From a safety point of view, the EMA was concerned about the medicine’s effects on the heart, such as increases in heart rate and palpitations. Because most post-menopausal women are at an increased risk of heart problems, the EMA could not identify a group of patients in whom the benefits would outweigh the risks.

► EMA. Refusal of the marketing authorisation for Eladynos (abaloparatide). 23 March 2018.

Neratinib

Product name: Nerlynx®
Dosage form: Tablets
Class: Tyrosine kinase inhibitor;
ATC code: L01XE45
Regulatory authority: EMA
Intended use: For the extended adjuvant treatment of early-stage, HER2-positive breast cancer in adult patients previously treated with trastuzumab.
Reasons for negative opinion: The EMA considered that, although more women on neratinib than on placebo lived for two years without disease progression than women (94% versus 92% respectively), it is uncertain that this difference would be seen in clinical practice. Furthermore, neratinib causes side effects in the digestive system, particularly diarrhoea, which affected most patients and might be difficult to manage.