Regulatory news

Pre-market assessment

China: Regulatory reforms

China – The State Council of China has proposed a number of reforms to the regulatory review and approval system to encourage innovation in medicines and health products. The resources for clinical trials in China will be strengthened, and there will be provisions for acceptance of clinical trial data generated in other countries. Reforms will be introduced to speed up the review and approval for urgently needed health products to meet public health needs. Furthermore, measures are to be introduced to promote drug innovation, with a system linking the review and approval of drugs with their patents, and improving the protection of clinical trial data. (1, 2, 3)

(2) Speech Made by Minister Bi Jingquan at the National Videophone Conference on Deepening the Review and Approval System Reform and Encouraging the Drug and Medical Device Innovation (10 October 2017). Posted on 12 October 2017 at: http://eng.cfda.gov.cn/WS03/CL0757/178430.html

U.S.: Promoting competition for complex products

United States of America – The FDA Commissioner Scott Gottlieb has announced measures to encourage the development and authorization of complex generic medicines, i.e. products with one or more features that are difficult to copy such as complex active ingredients, sites of action, or drug-device combinations. New draft guidance has been issued on pre-approval meeting requests and on the appropriateness of submitting applications for certain peptide products. Workshops will also be held on specific topics to support product development. Additional measures will follow.

These efforts are intended to promote competition for needed complex products to contain the cost of pharmaceuticals.


Europe: Regulators and funders meet

European Union – At a meeting held in September 2017 the EMA and healthcare payer organizations discussed ways to improve access of patients to new medicinal products. The meeting was complementary to the EMA’s existing cooperation with health technology assessment (HTA) bodies. The aim is to minimize delays between regulatory approval of a safe and effective medicine, and the pricing and reimbursement negotiations that will determine patients’ real access to it. (1)

In November 2011 the EMA and the European Network for Health Technology Assessment (EUnetHTA) published a joint three-year work plan outlining key areas of collaboration. The two organizations will explore their concepts of unmet medical need and therapeutic innovation and of the benefits and added therapeutic value of orphan medicines. (2)

**Australia: Parallel submissions**

Australia – Registration submissions for medicines and vaccines that meet certain requirements may now be made under the Therapeutics Goods Administration (TGA) and Pharmaceutical Benefits Advisory Committee (PBAC) arrangements that enable the processes of registration and of reimbursement evaluation and assessment to be undertaken in parallel. Submissions for vaccines must be accompanied by advice from the Australian Technical Advisory Group on Immunisation (ATAGI), and must address any matters raised in that advice.


**EU: Access to clinical data**

European Union – One year after its move to publish clinical data submitted in support of marketing authorization applications, the EMA has provided an overview of the response to this flagship policy. As of 20 October 2017 the published data have attracted a total of 3,641 users, of which 697 registered for “non-commercial research purposes”. In an online survey, 62% of respondents found the data useful, and 87% said that the information is presented in an understandable format, despite the redaction or anonymization of certain information in line with European legislation on personal data protection.


**Third tripartite meeting on evaluation of antibiotics**

Kyoto – At a tripartite meeting held in Kyoto, Japan, on 24 October 2017 representatives of EMA, FDA and PMDA have taken further steps to align their approaches to the evaluation of antibiotics. The discussions focused on clinical trial design for certain indications such as uncomplicated gonorrhoea or uncomplicated urinary tract infections, and on streamlining the development of new antibacterial agents for children.

This was the third tripartite meeting on convergence of regulatory requirements for antimicrobial agents. Earlier meetings took place in September 2016 and in April 2017.


**EU: Ten years of paediatric regulation**

European Union – Ten years after the Paediatric Regulation came into force the European Commission has published a report (1) on progress made with making children’s medicines available. The report concludes that there has been an encouraging increase of new research and new products, but that this is not evenly spread over all therapeutic areas and often linked to research priorities in adults. The report also finds that the paediatric use marketing authorization (PUMA) concept, with its specific reward to incentivize the development of paediatric indications for off-patent products, has failed to deliver. (1)

In December 2017 the European Commission announced an evaluation of the legislation on medicines for children, jointly with the legislation on medicines for rare diseases and special populations. (2)

► European Commission. Medicines for Children [website].


(2) European Commission. Evaluation of the legislation on medicines for children and rare diseases (medicines for special populations).
Post-market monitoring

Operation Pangea X
A total of 123 countries participated in the “Pangea X” international week of action. Operation Pangea is an annual campaign coordinated by Interpol to combat the illegal trade in medicinal products via the internet. This year, regulatory authorities around the world seized more than USD51 million worth of potentially dangerous medicines and ordered the closure of 3,584 illegal websites. House searches were also conducted and some 400 arrests made. A wide range of products were confiscated, such as erectile dysfunction pills, pain reduction pills, epilepsy medication, anti-psychotic medication and nutritional products, but also antibiotics, which is a cause for concern given the serious and growing threat of antimicrobial resistance. A focus of this year’s Operation Pangea was the fight against illegal trading in fentanyl and its derivatives.

Since its start in 2008 with just eight countries, Operation Pangea has grown exponentially over the past 10 years. This year’s operation saw the highest ever participation of African countries.

Smart Safety Surveillance in LMICs
United Kingdom – The MHRA has announced that it will join the “Project Smart Safety Surveillance” (also known as “Project 3-S”) launched by WHO and the Gates Foundation to help low- and middle-income countries (LMICs) to identify, assess and manage the risks associated with new products. The MHRA’s participation will be for a three-year period, during which three pilots will be run in different LMIC settings.

U.S.: New adverse event dashboard
United States of America – The FDA has launched a new search tool that improves public access to data on adverse events associated with medicines and biologic products submitted to the FDA’s Adverse Event Reporting System (FAERS). The Agency is hoping that the increased transparency will spur the submission of more detailed and complete reports on adverse events from health care professionals and the public.

Australia: Black triangle scheme
Australia – The TGA has launched its “Black Triangle Scheme” as a simple means to encourage practitioners and patients to report adverse events that may be associated with the use of certain new medicines. A black triangle symbol will appear on product information, patient leaflets and Australian Public Assessment Reports (AusPARs) for the medicines included in the scheme. The scheme will apply to newly registered prescription medicines, except biosimilar medicines and generic versions of previously approved prescription medicines. It also excludes seasonal influenza vaccines, as these are monitored through the AusVaxSafety programme.

EU: Updated pharmacovigilance guidelines
European Union – The EMA has published the following updated pharmacovigilance guideline on its website: Revision 3 of...
Module VIII on post-authorization safety studies, Revision 1 of Module IX on signal management and its addendum on methods (finalized post-public consultation), Revision 1 of Module XV on safety communication and related templates (finalized post-public consultation), Revision 4 of Annex I on definitions, and an updated Annex V on abbreviations.


**EU: Improved Eudravigilance system launched**

European Union – The EMA has launched a new and improved version of EudraVigilance, the European information system of suspected adverse reactions to medicines in the European Economic Area (EEA). The system offers improved features for reporting and public access to data. The reports of individual cases of suspected adverse reactions will be made available to the WHO Uppsala Monitoring Centre (UMC) directly from EudraVigilance.

With the launch, further legal obligations for marketing authorization holders became applicable to the mandatory reporting through EudraVigilance. Spontaneous reporting by patients and healthcare professionals through local reporting systems, as well as reporting of adverse reactions during clinical trials, remain unchanged.


Public access to EudraVigilance data: www.adrreports.eu

**Variations**

**Australia: Automated notifications**

Australia – An online notification process for very low risk changes to all registered medicines is being introduced in Australia. Manufacturers can submit an online form requesting such changes, along with legal assurances that the conditions for the specific variation are met. Upon payment of fees the requests will be automatically processed and the changes to the medicine can be implemented.

The process started in July 2017 with non-prescription medicines, and was extended to prescription medicines in December 2017. Additional types of variations that could be processed through this route have been proposed for both prescription and non-prescription medicines; however they will first need to be included in the relevant Regulations.

► TGA notice, 2 November 2017.


**Labelling**

**U.S.: Antimicrobials**

United States of America – A new, dedicated FDA web page will list updated, FDA-recognized “breakpoints” for antimicrobial active ingredients, showing whether specific bacteria or fungi are susceptible to antibacterial or antifungal medicines. Under the new approach manufacturers will reference the FDA web page in their product information, instead of updating it continuously with new breakpoint information from susceptibility testing.

► FDA News release, 13 December 2017.
**EU: Excipients**

**European Union** – The European Commission has adopted a revised annex to the guidelines on declaring excipients in the labelling and package leaflet of medicinal products for human use. Five new excipients need to be declared, and new safety warnings are to be included for ten excipients that were previously listed in the annex.

The revised requirements apply to both centrally and nationally authorized products. For new marketing authorization applications they will be effective from the day of its publication. For authorized medicines, marketing authorization holders should submit revised wording in line with the new requirements at the earliest opportunity, or submit a variation within three years after the publication of the revised annex.


**Canada: Prescription opioids**

**Canada** – Health Canada has convened a scientific advisory panel on opioid use and contraindications, and is working with manufacturers to update the product information of all prescription opioid products in line with the panel’s recommendations. The revised product information will recommend a limited quantity and duration of opioid prescriptions for acute pain, and a daily threshold dose of 50–90 morphine milligram equivalents per day for chronic pain except in cancer patients and palliative care and will include clearer warnings on the risks of opioids generally and in special patient groups.

► Health Canada Information update, 8 December 2017.

**Product-specific frameworks**

**Canada: Antimicrobials**

**Canada** – The Government of Canada has released its *Tackling Antimicrobial Resistance and Antimicrobial Use: A Pan-Canadian Framework for Action*. The Framework was developed jointly with provinces and territories and other key partners in the human and animal health sectors to guide collective action in four areas: surveillance, stewardship, infection prevention and control, and research and innovation. A Pan-Canadian Action Plan will be developed to put the Framework into use.(1)

In November 2017 two new rules to fight the growing problem of antimicrobial resistance came into force. Firstly, livestock owners may no longer import antimicrobials that are important to human health, but only medicines that do not pose a risk to human health or food safety, and only in limited quantities. Secondly, a new programme will facilitate importation and sale of low risk veterinary health products such as vitamin and mineral supplements.(2)


**EU: Advanced therapies**

**European Union** – The European Commission (EC)’s Directorate-General for Health and Food Safety (DG SANTE) and the European Medicines Agency (EMA) have published an action plan aiming to streamline regulatory procedures for advanced therapy medicinal products (ATMPs) and address the specific requirements of developers better. The plan contains 19 actions in different key areas. These include the proposed development
of an EC guideline on good manufacturing practices for advanced therapies, dialogue with national regulatory authorities about the interplay between the legislation on genetically modified organisms and that on medicines, and clarification of expectations for investigational ATMPs.\(^{(1)}\)

ATMPs are medicines for human use that are based on genes or cells. They offer ground-breaking opportunities for the treatment of diseases and injuries. They are particularly important for severe, untreatable or chronic diseases for which conventional approaches have proven to be inadequate.

In November 2017 the European Commission published a set of guidelines on good manufacturing practice (GMP) for ATMPs. The new guidelines address the novel and complex manufacturing scenarios for these products and foster a risk-based approach to manufacture and testing.\(^{(2)}\)

\(\text{► }\) EMA News, 20 October 2017.


**U.S.: Regenerative medicine products**

**United States of America** – The FDA has announced a comprehensive policy framework for the development and oversight of regenerative medicine products, including novel cellular therapies. The framework is outlined in a suite of four guidance documents, of which two are final and two are drafts for public comment. The new guidance describes what products are regulated as medicines, devices, and/or biological products and proposes a science-based process for evaluating the safety and effectiveness of regenerative therapies while supporting development in this area. It also sets out a risk-based framework for enforcement actions against products that raise potential significant safety concerns.

\(\text{► }\) FDA News release, 16 November 2017.

**Australia: Autologous products**

**Australia** – The TGA will introduce changes to the regulation of autologous human cell and tissue products, including so-called “autologous stem cell” therapies. The level of oversight will be determined by the risk posed to patient safety. Certain products will be in the remit of the TGA, while others will fall under the Biologicals Regulatory Framework. Detailed guidance on the new approach is being drafted. The changes are expected to commence in early 2018, with a transition period for implementation.

Autologous human cell and tissue products have previously been outside TGA’s regulatory oversight because historically they have been seen as an extension of medical practice. The new approach will bring Australia into closer alignment with other regulators.

\(\text{► }\) TGA Media release, 24 October 2017.

**Medical devices**

**India: Classification list**

**India** – The Drug Controller General of India has published a list of medical devices and in vitro diagnostics together with their risk classifications that will apply under the Medical Devices Rules, 2017. Four classes for medical devices are defined, with more stringent regulatory controls in place for products classified as having a higher risk in terms of public health.

The Rules will enter into force on 1 January 2018. The list will be updated from time to time.

\(\text{► }\) CDSCO Notice, 1 November 2017.
UK: Guide to new EU requirements

United Kingdom – The MHRA has launched an interactive guide to introduce manufacturers to their obligations under the new EU regulations for medical devices and in vitro diagnostic devices.

The new regulations are being phased in since 25 May 2017 and will apply across EU Member States from 26 May 2020 and 2022 respectively. They introduce stronger requirements for traceability of products throughout the supply chain with a unique device identification (UDI) system, new standards for clinical evidence, more rigorous vigilance reporting requirements and clearer requirements on post-market surveillance.


Collaboration

EU-FDA mutual recognition agreement on inspections

The EU-FDA mutual recognition agreement on good manufacturing practice (GMP) inspections came into force on 1 November 2017. This is an unprecedented step, as the FDA has never before recognized another country’s inspectorate. The mutual recognition agreement will enable more efficient global pharmaceutical manufacturing inspections.

In June 2017, the European Commission had determined that the FDA’s GMP inspections are at a level equivalent to the EU, and in October 2017 the FDA completed its capability assessments of 8 European national regulatory authorities; the others will be assessed by July 2019. The agreement initially covers inspections of sites manufacturing medicinal products for human use.

Veterinary products will be added by July 2019, and vaccines and plasma-derived medicinal products by July 2022.


Singapore joins ICH

Geneva – At the ICH meeting held in Geneva in November 2017 the Health Sciences Authority (HSA) of Singapore has been accepted as a new regulatory member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). The ICH Assembly also approved the Instituto Nacional de Vigilancia de Medicamentos y Alimentos of Colombia (INVIMA) and the Bill & Melinda Gates Foundation as new observers.


IGDRP and IPRF merge

The International Generic Drug Regulators Programme (IGDRP) and the International Pharmaceutical Regulators Forum (IPRF) have agreed to consolidate their operations. Together they will form a the International Pharmaceutical Regulators Programme (IPRP), to be officially launched on 1 January 2018. IPRP aims to provide a regulatory hub for information exchange and cooperation on all medicinal products in order to maximize synergies and simplify the numerous forms of international regulatory collaboration.

► IPRF News, 8 December 2017.
► IGDRP News, 8 December 2017.
**Regulatory summit and ICMRA meeting**

Japan – From 23–26 October 2017 the international Summit of Heads of Medicines Regulatory Agencies and the meeting of the International Coalition of Medicines Regulatory Authorities (ICMRA) were held in Kyoto, Japan. At the meeting, the ICMRA launched its Strategic Priority on Innovation (SPI), identifying the issues that the Coalition aims to address. An overview is provided in a formal concept note.

- (1) PMDA Notice, 27 October 2017.
- (2) ICMRA, Strategic Priority on Innovation – Concept Note. 11 December 2017.

**Generic work-sharing trial**

The regulatory authorities of Australia, Canada, Singapore and Switzerland (ACSS) have invited marketing authorization applications for assessment under their newly launched Generic Medicines Work Sharing Trial. Applications should be submitted simultaneously to at least two, but preferably more, of the ACSS Consortium members.

- TGA, ACSS - Generic Medicine Work Sharing Trial. 6 December 2017.

**Under discussion**

European Union – The EMA has opened two public consultations related to herbal medicines: A Draft procedure for the review and revision of European Union herbal monographs and European Union list entries and a Concept paper on the development of a reflection paper on new analytical methods/technologies in the quality control of herbal medicinal products.

- (1) EMA Consultation, 27 October 2017.
- (2) EMA Consultation, 31 October 2017.

European Union – The EMA has released a new guideline to support and facilitate the development of vaccines and medicines to prevent and treat infections caused by respiratory syncytial virus (RSV).

  Closing date: 30 April 2018.

European Union – The EMA is seeking feedback from all stakeholders (patients and consumers, healthcare professionals, pharmaceutical industry and national competent authorities) on their use of electronically or digitally delivered medicinal product information. A mapping of ongoing initiatives will be used in a workshop to be held in 2018 to develop key principles for the use of electronic formats.

  Closing date: 28 February 2018.
United States of America – The FDA has published two draft guidance documents for industry related to its new framework on regenerative medicine products.

Closing date: 15 February 2018.

United States of America – The FDA has held a public hearing about potential pathways for approval of a device intended to be used with a medicine that is already on the market, when the marketing authorization holder of the medicine does not wish to pursue the new use. Such so-called devices referencing drugs could advance public health by offering new uses with approved drugs. Independently of the public hearing, comments can be submitted to the public docket.

► FDA. Devices Referencing Drugs; Public Hearing; Request for Comments [webpage].
Closing date: 15 January 2018.

European Union – The EMA has launched a public consultation on supplementary protection certificates (SPCs) and patent research exemptions. SPCs are a unique intellectual property right that constitute an extension of up to 5 years to the term of a patent right of 20 years to offset the time spent on pre-approval testing and clinical trials. Aspects under consideration include the creation of a European SPC title, an update of the scope of EU patent research exemptions, and the introduction of an SPC manufacturing waiver.

► EMA Consultation, 12 October 2017.
Closing date: 4 January 2018.

United States of America – The FDA has released draft guidance delineating its new Breakthrough Devices Program. Building on the Expedited Access Pathway (EAP) programme, this new pathway is intended to speed up patients’ access to medical devices that more effectively diagnose or treat life-threatening or irreversibly debilitating diseases or conditions, including technologies that have no alternative or that offer a significant advantage over FDA-cleared or approved alternatives.

Closing date: 26 December 2017.
See also: FDA Statement, 24 October 2017.

European Union – The European Commission (EC) has published a proposed amendment to its Regulation No 847/2000 on orphan drug products with regard to the definition of the concept of similar medicinal products. The update is proposed in the light of major developments in the field of biological medicines, especially with regard to advanced therapy medicinal products.

► EC Draft regulation, 30 October 2017.
Closing date: 27 November 2017.

Australia – The TGA has proposed a set of reforms for evaluation of complementary medicines. Among other things it is proposed to introduce a third assessment pathway that would be sitting between the existing listed medicine (low risk) and registered medicine (higher risk) pathways, and to use reports from comparable overseas regulators in assessing ingredients and products under the new pathway.

► TGA Consultation, 26 September 2017.
Closing date: 7 November 2017.
Approved

**Semaglutide**

**Product name:** Ozempic®

**Dosage form:** Injection for subcutaneous use

**Class:** Glucagon-like peptide 1 (GLP-1) receptor agonist

**Approval:** FDA

**Use:** Adjunct to diet and exercise to improve glycaemic control in adults with type 2 diabetes mellitus

**Benefits:** Ability to reduce HbA1c levels.

**Safety information:** In rodents, semaglutide causes thyroid C-cell tumors. Semaglutide is contraindicated in patients with a personal or family history of medullary thyroid carcinoma and in patients with multiple endocrine neoplasia syndrome type 2 (MEN 2).

► FDA prescribing information, revised 12/2017.

**Vestronidase alfa for rare enzyme disorder**

**Non-proprietary name in the U.S.:** Vestronidase alfa-vjbk

**Product name:** Mepsevii®

**Dosage form:** Injection for intravenous use

**Class:** Recombinant human lysosomal beta glucuronidase, enzyme replacement therapy; **ATC code:** A16AB18

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

**Use:** Treatment of mucopolysaccharidosis type VII (MPS VII), also known as Sly syndrome, an extremely rare, progressive genetic condition that affects most tissues and organs.

**Benefits:** First approved treatment for MPS VII.

1 This FDA-approved biological is one of the first to receive a four-letter suffix to its nonproprietary name in the U.S. Previously, such suffixes were only added to the names of biosimilars.


**Safety information:** Anaphylaxis has occurred with administration of vestronidase alfa-vjbk as early as the first dose. Appropriate support should be readily available, and patients should be observed closely during and for 60 minutes after infusion. In case of anaphylaxis, infusion should be stopped immediately.(1,2)


(2) Prescribing information for Mepsevii; revised 11/2017.

**Rurioctocog alfa pegol for haemophilia A**

**Product name:** Adynovi®

**Dosage form:** Powder and solvent for solution for injection

**Class:** Recombinant human factor VIII; **ATC code:** B02BD02

**Approval:** EMA

**Use:** Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia A (congenital factor VIII deficiency)

**Benefits:** Ability to prevent and control bleeding when used on demand and during surgical procedures.

► EMA/CHMP Summary of opinion, 9 November 2017.

**Emicizumab for haemophilia A**

**Nonproprietary name in the U.S.:** Emicizumab-kxwh

**Product name:** Hemlibra®

**Dosage form:** Subcutaneous injection

**Class:** Systemic haemostatic; **ATC code:** B02BX06

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

**Use:** To prevent or reduce the frequency of bleeding episodes in adults and children with haemophilia A who have developed Factor VIII inhibitors.

See Footnote 1

2 See Footnote 1
Approved

**Benefits**: Fewer bleeding episodes and patient-reported improvement in haemophilia-related symptoms and physical functioning.

**Safety information**: Severe blood clots (thrombotic microangiopathy and thromboembolism) have been observed in patients who were also given activated prothrombin complex concentrate as rescue treatment for bleeds for 24 hours or more while taking emicizumab-kxwh.

► (1) FDA Press release, 16 November 2017.

Non-live recombinant zoster vaccine (adjuvanted)

**Product name**: Shingrix®

**Dosage form**: Suspension for intramuscular injection

**Class**: Viral vaccine

**Approval**: Health Canada

**Use**: Prevention of H. zoster infection in adults.

**Benefits**: In a pooled analysis of clinical studies, the vaccine demonstrated efficacy against H. zoster of greater than 90% in adults aged 50 and older and in those aged 70 and older. Efficacy was sustained during the four-year follow-up period.

**Notes**: Canada is the first country to approve this vaccine. It is also under review in the U.S., the EU, Australia and Japan.


**Padeliporfin for prostate cancer**

**Product name**: Tookad®

**Dosage form**: Powder for solution for injection

**Class**: Sensitizer used in photodynamic/radiation therapy; **ATC code**: L01XD07

**Approval**: EMA

**Use**: Treatment of adults with previously untreated, unilateral, low-risk adenocarcinoma of the prostate.

**Benefits**: Higher probability of negative biopsy at 24 months, and delayed disease progression, compared with active surveillance.

Safety information: For hospital use only.


**Dolutegravir and rilpivirine for HIV infection**

**Product name**: Juluca®

**Dosage form**: Fixed-dose combination tablet

**Class**: Antiviral combination for treatment of HIV infection; **ATC code**: J05AR21

**Approval**: FDA

**Use**: Treatment of adults with HIV-1 infections whose virus has been suppressed on a stable regimen for at least six months, with no history of treatment failure and no known substitutions associated with resistance to dolutegravir or rilpivirine.

**Benefits**: As effective as other HIV regimens and potentially less toxic due to the reduced number of active ingredients.

**Notes**: This is the first FDA-approved complete treatment regimen containing only two antiretrovirals.


**Letermovir to prevent CMV after stem cell transplant**

**Product name**: Prevymis®

**Dosage form**: Concentrate for solution for infusion; film-coated tablets

**Class**: Antiviral medicine; **ATC code**: J05AX18

**Approval**: EMA (orphan designation)

**Use**: Prophylaxis of cytomegalovirus (CMV) reactivation and disease in adult CMV-seropositive recipients of an allogeneic haematopoietic stem cell transplant.

**Benefits**: Better tolerated than other antiviral agents approved for the same indication.


**Copanlisib for relapsed follicular lymphoma**

**Product name**: Aliqopa®

**Dosage form**: Injection
**Class:** Kinase inhibitor  
**Approval:** FDA (accelerated approval, priority review; orphan drug designation)  
**Use:** treatment of adults with relapsed follicular lymphoma who have received at least two prior systemic therapies.  
**Benefits:** Complete or partial shrinkage of tumours in clinical trials.  
**Safety information:** Serious side effects include infections, hyperglycaemia, hypertension, non-infectious pneumonitis, neutropenia and severe skin reactions. Copanlisib should not be used in pregnant or breastfeeding women.  

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**Abemaciclib for certain breast cancers**  
**Product name:** Verzenio®  
**Dosage form:** Oral tablet  
**Class:** Inhibitor of cyclin-dependent kinases 4 and 6 (CDK4 and CDK6)  
**Approval:** FDA (priority review, breakthrough therapy)  
**Use:** Treatment of adults with hormone receptor-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer that has progressed after endocrine therapy.  
**Benefits:** Longer median progression-free survival in clinical trials.  
**Safety information:** Serious side effects include diarrhoea, neutropenia, elevated liver blood tests and deep venous thrombosis/pulmonary embolism. Abemaciclib may cause harm to a developing foetus.  

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**Acalabrutinib for mantle cell lymphoma**  
**Product name:** Calquence®  
**Dosage form:** Capsules for oral use  
**Class:** Kinase inhibitor  
**Approval:** FDA (accelerated approval, priority review, breakthrough therapy, orphan drug designation)  
**Use:** Treatment of adults with mantle cell lymphoma who have received at least one prior therapy.  
**Benefits:** Complete or partial response observed in 81% of patients in initial study.  
**Safety information:** Serious side effects include bleeding, infections and atrial fibrillation. Additional cancers have occurred in some patients taking acalabrutinib. Women who are breastfeeding should not take acalabrutinib because it may cause harm to a newborn baby.  

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**Benralizumab for eosinophilic asthma**  
**Product name:** Fasenra®  
**Dosage form:** Solution for injection in pre-filled syringes  
**Class:** Anti-eosinophil, humanized monoclonal antibody; ATC code: R03DX10  
**Approval:** EMA  
**Use:** Add-on maintenance treatment in adult patients with severe eosinophilic asthma that is inadequately controlled despite high-dose inhaled corticosteroids plus long-acting beta-agonists.  
**Benefits:** Significant reductions in annual exacerbation rates of eosinophilic asthma, especially in patients with more than 300 eosinophils per microlitre of blood before treatment.  
▶ EMA/CHMP Summary of opinion, 9 November 2017.

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**Latanoprostene bunod for glaucoma**  
**Product name:** Vyzulta®  
**Dosage form:** Ophthalmic solution 0.024%, for topical ophthalmic use  
**Class:** Prostaglandine analog  
**Approval:** FDA  
**Use:** Reduction of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.
Approved

**Benefits**: Sustained lowering effect on intraocular pressure.

► [Prescribing information for Vyzulta®, Revised 11/2017](#)

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**Gene cell therapy**

**Axicabtagene ciloleucel** for certain B-cell lymphomas

**Product name**: Yescarta®

**Dosage form**: Cell suspension for infusion, for autologous use

**Class**: Autologous chimeric antigen receptor (CAR) T cell therapy

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

**Use**: Treatment of adult patients with certain types of large B-cell lymphoma who have not responded to or who have relapsed after at least two other kinds of treatment. The product is not indicated for the treatment of patients with primary central nervous system lymphoma.

**Benefits**: Ability to induce complete remission lasting several months.

**Safety information**: Severe side effects include cytokine release syndrome (CRS) and neurologic toxicities, both of which can be fatal or life-threatening. Other side effects include serious infections, low blood cell counts and a weakened immune system.

► **FDA News release, 18 October 2017.**

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**Biosimilars**

**Insulin lispro**

**Product name**: Admelog®

**Reference product**: Humalog®

**Approval**: FDA (abbreviated approval as a “follow-on product” through the 505(b)(2) pathway)

**Use**: To improve control in blood sugar levels in adults and children aged 3 years and older with type 1 diabetes mellitus, and adults with type 2 diabetes mellitus.

► **FDA News release, 11 December 2017.**

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**Trastuzumab**

(1)

**Product name**: Ontruzant®

**Reference product**: Herceptin®

**Approval**: EMA

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

► **EMA/CHMP Summary of opinion, 14 September 2017.**

(2)

**Nonproprietary name in the U.S.**: Trastuzumab-dkst

**Product name**: Ogivri®

**Reference product**: Humira®

**Approval**: FDA

**Use**: Treatment of patients with breast or metastatic stomach cancer (gastric or gastroesophageal junction adenocarcinoma) whose tumours overexpress the HER2 gene (HER2+)

► **FDA News release, 1 December 2017.**

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**Bevacizumab**

**Product name**: Mvasi®

**Reference product**: Avastin®

**Approval**: EMA

**Use**: Treatment of certain advanced, metastatic or recurrent cancers.

► **EMA/CHMP Summary of opinion, 9 November 2017.**

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**Filgrastim (South Africa)**

**Product**: Filgrastim from Teva Pharmaceutical Industries (Teva)

**Reference product**: Neupogen®

**Approval**: Medicines Control Council (MCC), South Africa
Use: 1. peripheral blood stem cell harvesting in autologous stem cell harvesting in haematological malignancies; 2. chemotherapy-induced febrile neutropenia
Note: This is the first non-originator biological medicine approved in South Africa.
► GaBI News, 1 December 2017.

**Adelimumab**
- **Product name:** Cyltezo®
- **Reference product:** Humira®
- **Approval:** EMA
- **Use:** Treatment of rheumatoid arthritis, juvenile idiopathic arthritis, axial spondyloarthritis, psoriatic arthritis, psoriasis, paediatric plaque psoriasis, hidradenitis suppurativa, Crohn's disease, ulcerative colitis and uveitis.
- **Benefits:** Ability to reduce eosinophil infiltrations into the oesophageal mucosa and reduce symptoms such as dysphagia and pain during swallowing.
- **Note:** Budesonide as inhalation spray has been used off-label to treat patients with eosinophilic oesophagitis and the effects of this use have been extensively described in scientific literature.
► EMA/CHMP Summary of opinion, 14 September 2017.

**Novel dosage forms**

**Orodispersible budesonide for a rare condition of the oesophagus**
- **Product name:** Jorveza®
- **Dosage form:** Orodispersible tablets
- **Class:** Locally acting corticosteroid; ATC code: A07EA06
- **Approval:** EMA (accelerated approval, orphan designation)
- **Use:** Treatment of eosinophilic oesophagitis in patients over 18 years of age.
- **Benefits:** Ability to reduce eosinophil infiltrations into the oesophageal mucosa and reduce symptoms such as dysphagia and pain during swallowing.
- **Note:** Budesonide as inhalation spray has been used off-label to treat patients with eosinophilic oesophagitis and the effects of this use have been extensively described in scientific literature.

**Aripiprazole with tracking sensor**
- **Product name:** Abilify MyCite®
- **Dosage form:** Tablet with embedded ingestible sensor
- **Class:** Antipsychotic; ATC code: N05AX12
- **Approval:** FDA
- **Use:** Treatment of schizophrenia, acute treatment of manic and mixed episodes associated with bipolar I disorder, and add-on treatment for depression in adults.
- **Benefits:** Ability to track the ingestion of a medication prescribed for a mental illness.
- **Safety information:** Aripiprazole is not approved to treat patients with dementia-related psychosis. Its safety and effectiveness in children have not been proven. Patients should be monitored for worsening and emergence of suicidal thoughts and behaviours. It has not been shown whether the product can improve patients' compliance with their treatment regimen. The system should not be used to track drug ingestion in real time or during an emergency because detection may be delayed or may not occur.

**Once-monthly buprenorphine for opioid use disorder**
- **Product name:** Sublocade®
- **Dosage form:** Drug-device combination utilizing buprenorphine and the Atrigel Delivery System in a pre-filled syringe.
- **Class:** Medicine used in opioid dependence; ATC code: N07BC
- **Approval:** FDA (fast track designation, priority review)
- **Use:** Treatment of moderate-to-severe opioid use disorder in adult patients who have initiated treatment with a transmucosal buprenorphine-containing product and have been on a stable dose of buprenorphine treatment for at least seven days.
- **Benefits:** Reduced medication burden, potentially promoting adherence.
Approved

**Safety information:** The product carries a boxed warning about the risks of intravenous self-administration, which could cause occlusion, tissue damage or embolus and could be fatal. The product is to be administered only by health care professionals and will be provided to them through a restricted programme.


**Extensions of indications**

**Sunitinib** to reduce the risk of relapsing kidney cancer

**Product name:** Sutent®

**Approval:** FDA

**Newly approved use:** Adjuvant treatment for adult patients at a high risk of kidney cancer returning after nephrectomy. First FDA-approved product for this use.

**Safety information:** Risk of severe liver damage, which may result in liver failure or death.


**Vemurafenib** for rare blood cancer

**Product name:** Zelboraf®

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

**Newly approved use:** Treatment of adult patients with BRAF V600 mutation-positive Erdheim-Chester Disease, a rare type of blood cancer.

▶ FDA News release, 6 November 2017.

**Mepolizumab** to treat a rare autoimmune disease

**Product name:** Nucala®

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

**Newly approved use:** Treatment of adult patients with eosinophilic granulomatosis with polyangiitis (EGPA), a rare autoimmune disease that causes vasculitis, an inflammation in the wall of blood vessels of the body.

▶ FDA News release, 12 December 2017.

**Diagnostics**

**Next-generation sequencing (NGS) cancer profiling tests**

(1)

**Product name:** IMPACT (Integrated Mutation Profiling of Actionable Cancer Targets) tumour profiling test (assay)

**Approval:** FDA

**Use:** This in vitro diagnostic test can identify genetic cancer mutations in 468 unique genes.

**Notes:** The FDA has announced the recent accreditation of the New York State Department of Health (NYSDOH) as a third-party reviewer of in vitro diagnostics submitted for FDA review. Along with this authorization, the FDA has established a Class II regulatory pathway for the review of other NGS-based tumour profiling tests for use in patients diagnosed with cancer.


(2)

**Product name:** FoundationOne CDx (F1CDx)*

**Approval:** FDA (breakthrough device designation)

**Use:** Detection of genetic mutations in 324 genes and two genomic signatures in any solid tumour type.

**Note:** The Centers for Medicare & Medicaid Services (CMS) at the same time proposed coverage of the F1CDx, after overlapping review by the FDA and CMS under the Parallel Review Program, which facilitates earlier access to innovative medical technologies for Medicare beneficiaries.