Regulatory news

Pre-market assessment

Assessment of generics in China: Demonstrating interchangeability

In 2016 the State Council of the Government of China launched a policy requiring that all oral solid preparations of generic medicines on the National Essential Drugs List (2012) approved before 1st October 2007 should be evaluated by the end of 2018, with a possibility to extend the deadline until the end of 2021 in case of special circumstances, for example if clinical trials are required. (1) More details about this policy are found in a recently published commentary, the abstract of which is reproduced below. (2)

Generic drugs should be interchangeable with originators in terms of quality and efficacy. With relative lower prices, generic drugs are playing an important role in controlling health expenditures and ensuring access. However, the widespread understanding of “cheap price equals low quality” has a negative impact on the acceptance of generic drugs. In China, medical doctors doubt the efficacy and quality of generic drugs manufactured domestically. To address these concerns, the Chinese State Council released a policy in 2016 to ensure the interchangeability by re-evaluating the quality and efficacy of generic drugs. It intends to make up a missed lesson in the regulation to be in line with internationally accepted practices. Generic drugs firms, depending on the availability of appropriate comparators, should conduct either comparative bioequivalence studies or full scale clinical trials. The re-evaluation will be implemented in a stepwise approach with the essential medicines covered in the first step. The policy could achieve several benefits by increasing confidence on the Chinese produced generic drugs, upgrading regulatory standards, streamlining the Chinese generic drug industry and creating a healthy competition market. Nevertheless, enormous challenges remain in enlarging the capacity to review applications, selecting appropriate comparators, ensuring the capacity of domestic clinical research sites, and achieving the acceptance of re-evaluated generic drugs.


New fast-track pathway in India: WHO-recommended combinations

India – The Drugs Controller General of India has issued a notice outlining a fast-track regulatory approval pathway for combination products recommended in WHO guidelines and which are used to treat HIV infection and subtypes of hepatitis B and C relevant to the Indian population. The fast-track provisions apply regardless of whether the specific combination product has been previously approved elsewhere. The fast-track provisions apply regardless of whether the specific combination product has been previously approved elsewhere.

The new pathway includes provisions for waiving clinical trial requirements and for early submission of abbreviated data with a commitment that complete data will be submitted prior to approval. The rationale is that combinations recommended in WHO treatment guidelines are considered to have...
a positive risk-benefit balance, and that they are falling under the category of “extreme urgency” as defined in national regulations. 

**Australian orphan drug programme: Reforms and transition arrangements**

Australia – The TGA has announced updates to its orphan drug programme to align it with the practices of other regulatory authorities and to target the most important unmet needs. The changes take into account feedback received in two public consultations. The threshold and eligibility criteria will be adjusted so that more conditions may qualify as orphan diseases, and the validity period of orphan drug designation will be limited to 6 months, with a possibility of extension to 12 months with written justification. The changes are effective from 1 July 2017. (1) Transition arrangements are in place for existing designations made at a time when their status would not lapse. (2)

 ► (1) TGA. Submissions received and TGA response: Orphan drug program. 18 April 2017.
 (2) TGA. Reform of the Orphan Drug Program - Transition arrangements.

**EU Priority medicines scheme: One year on**

European Union – The EMA has met with stakeholders to look back on one year’s experience with its PRIME (PRIority MEdicines) scheme. Of 96 requests processed, 20 were approved including 8 for orphan medicines. Among the requests that were not granted, approximately 70% lacked sufficiently robust data, about 40% had an insufficient justification of therapeutic advantage, and about 20% were at an advanced stage of development process was already so that the use of the scheme would not have been effective.

The PRIME scheme was launched in March 2016 to provide early support to developers of medicines targeting unmet treatment needs. It assists applicants in optimizing development plans, collecting robust data and submitting high quality applications enabling timely authorization of needed products.


**EU medical devices regulation: Strengthened rules**

European Union – The European Parliament has adopted two new regulations on medical and in vitro diagnostic medical devices. The new rules will impose tighter controls on high-risk devices such as implants, on clinical trials and on the independent notified bodies that can approve the marketing of medical devices. The new rules will also cover certain previously unregulated aesthetic products. A new system for risk classification in line with international guidelines will apply to in vitro diagnostic medical devices (IVDs). The rules will also improve the traceability of medical devices in the supply chain by using a unique identification number reflected in the new European database of medical devices (EUDAMED). Manufacturers will be obliged to collect data about their performance and EU countries will coordinate more closely in the field of market surveillance.

Medical devices such as diagnostics, companion tests and delivery devices are playing an increasingly important role in guiding and supporting the use of medicines. The new rules address the need for revision of the existing regulatory framework and for stronger market surveillance in the area of medical devices.
The rules were adopted by the European Parliament in April 2017, for publication in the Official Journal in May. They will become effective after a transitional period of three years from publication for medical devices and five years from publication for in vitro diagnostics.


**Adverse events reporting**

**Pharmacovigilance in Europe: Updates and system upgrade**

*European Union – The following revised guidance has been published on the Agency’s Good Pharmacovigilance Practice (GVP) website: Module II – Pharmacovigilance system master file (Rev 2), which completes the transition to the 2010 EU pharmacovigilance legislation including the “Article 57” database for medicinal products, and a major revision of Module V – Risk management systems along with consequent revisions of Module XVI – Risk minimisation measures. The GVP introductory cover note has been updated accordingly. (1)

In addition, the EMA's experience with its coordinated "single assessments" of manufacturers' periodic safety update reports (PSUR) is reflected in two new documents: an explanatory note on the GVP Module VII addressing issues that have been raised by companies, and a question-and-answer document that guides assessors throughout the evaluation process. In the single assessment process the EMA's Pharmacovigilance Risk Assessment Committee (PRAC) reviews all PSURs for medicines containing the same active substance(s) together. Each review is led by an assessor from one nominated national authority. The recommendations are legally binding in all EU Member States. Before the introduction of this process in 2015, marketing authorization holders submitted their PSURs for nationally authorized medicines separately to each national authority. (2)

In May 2017 a new and improved version of EudraVigilance successfully passed an independent audit leading to a positive recommendation by the PRAC. EudraVigilance is the European information system of suspected adverse reactions to medicines. The enhanced system will be launched in November 2017. (3)

► (1) EMA. Good pharmacovigilance practices [website].

(2) EMA News, 6 April 2017.

(3) EMA News, 22 May 2017.

**Adverse events of illicit drugs in UK: New reporting scheme**

*European Union – The MHRA has launched a pilot scheme for reporting adverse events observed in people using illicit drugs, particularly new psychoactive substances. The scheme's reporting form is intended to be used by health professionals working in services such as emergency departments, general practice, drug treatment services, sexual health services and mental health services.

The pilot scheme was created following a marked increase in hospital admissions for poisoning by psychostimulants with abuse potential. The data from the pilot are intended to support provision of clinical guidance to professionals.

Supply

GMP for compounded medicines
Australia – The TGA has published new guidance text to assist companies and pharmacists in the interpretation of the PIC/S good manufacturing practice (GMP) requirements for compounded medicinal products. The text provides point-by-point annotations to the main chapters of the PIC/S GMP guide as well as its annexes on manufacturing sterile products and on computerized systems.

Compounding is the preparation of a medicine under the supervision of a pharmacist to meet the specific needs of a patient when no suitable authorized dosage form is available. The guidance provides valuable detail on how to implement good practices in compounding to ensure patient safety.


Reporting of shortages in Canada: Now mandatory via new website
Canada – Pharmaceutical companies are now required by law to report medicines shortages and discontinuances on a new, independent website1. The following must be reported: an anticipated drug shortage; a discontinuation of a drug six months in advance; and any previously unreported shortage within five days of learning about it.

The new website replaces the industry-run website2 where manufacturers have been voluntarily reporting medicines shortages and discontinuances since 2012. The new system offers enhanced notification features and a mobile application. It also provides updated information for health care providers and patients, including tools and guidance to help manage shortages.


Dispensing categories in Switzerland: Revision to encourage self-medication
Switzerland – Changes have been made in Swiss regulations to encourage self-medication without jeopardizing patient safety. Dispensing category C (in-pharmacy sales only) will be abolished. Drugstores will be able to dispense all medicinal products that do not require a prescription (category D), and certain products currently in that category will be reassigned to category E (sale in all shops). Swissmedic is re-evaluating the products concerned, with a focus on the risks of abuse and possible interactions. The Agency is also re-defining the lists of products that can be dispensed by various types of professional therapists. The project is expected to be concluded by 2019.

► Swissmedic Announcement, 10 April 2017.

Antimicrobial resistance

India national action plan
India – The Union Minister of Health and Family Welfare of India has announced the finalization of India’s comprehensive and multi-sectoral National Action Plan to combat antimicrobial resistance (AMR). The announcement was made at the Inter-Ministerial Consultation on AMR containment, where representatives of various Ministries under the Government of India signed a declaration, pledging to strategize collectively to prevent and contain AMR.


1 www.DrugShortagesCanada.ca
2 www.drugshortages.ca
**New investments in Canada**

Canada – Health Canada has announced new rules for veterinary drugs to combat antimicrobial resistance. The new rules impose stricter quality requirements for active pharmaceutical ingredients and restrict the personal importation of certain products. They also require manufacturers, importers and compounders to report annual sales of medically important antimicrobials, and they simplify the importation of low-risk veterinary health products, including those that may be used as alternatives to antimicrobials.(1)

Furthermore, the Government of Canada has announced funding of 1.39 million Canadian Dollars (approximately 1 million USD) from the Canadian Institutes of Health Research to support five research teams whose work will advance innovations in point-of-care diagnostics, with the goal of implementing the best diagnostic tools in health care settings and appropriate use of antibiotics.


**Tripartite alignment on requirements for antibacterials**

European Union, Japan, United States of America – The EMA, the PMDA and the FDA have agreed to align their data requirements for certain aspects of the clinical development of new antibiotics. The Agencies will update their respective guidance documents, and will provide advice to individual medicine developers.

The agreement was reached at the second tripartite meeting to discuss regulatory approaches for the evaluation of antibacterial agents, held in Vienna on 26–27 April 2017. A first tripartite meeting on the subject had taken place in September 2016; a third is planned for October 2017. The alignment aims to stimulate the development of new treatments to fight antimicrobial resistance and protect global public health.

► EMA News, 12 June 2017.

EMA. Second tripartite meeting held between EMA, PMDA and FDA to discuss regulatory approaches for the evaluation of antibacterial agents (webpage).

**Collaboration**

**EU and African regulators meet**

Malta – A workshop jointly organized by the EMA and the Maltese Presidency of the EU on 2–3 March 2017 has brought together scientific experts from EMA’s Committee for Medicinal Products for Human Use (CHMP) and regulators from across Africa. The participants discussed how to promote reliance on the scientific output of the CHMP, in particular the Agency’s “Article 58” procedure for global health products intended for use outside the EU. This procedure aims to increase access to high quality, safe and effective medicines by patients in low- and middle-income countries.

This was the first time that CHMP experts met with non-EU regulators in such a forum. The workshop was organized with support from the Bill & Melinda Gates Foundation and WHO. It is in line with the World Health Assembly Resolution WHA67.20, which calls for regulatory systems strengthening.(1)

London – On 18–19 May 2017 a delegation from the East African Community (EAC) visited the EMA to gather information and experience to support the potential
creation of a networking medicines agency for the EAC. The EAC has six partner States: Burundi, Kenya, Rwanda, South Sudan, Tanzania and Uganda. Participants discussed the structure and operations of EMA that could serve as a model for regional collaboration in the regulatory assessment of medicines. (2)
► (1) EMA News, 10 March 2017.
(2) EMA News, 23 May 2017.

Report on EMA–FDA assessment pilot
European Union – The EMA and the US FDA have released the report on their joint pilot programme for the parallel assessment of applications containing Quality by Design (QbD) elements as reflected in ICH Q8, Q9 and Q10 guidelines. The pilot demonstrated a solid alignment between the two Agencies on the implementation of QbD-related concepts, and has opened up a platform for continuous dialogue.

Launched in 2011 and subsequently extended, the pilot programme concluded in April 2016. Two applications for marketing authorization, three variation applications and nine scientific advice applications were evaluated under this programme. The pilot led to the adoption of three sets of Question-and-Answer documents that also addressed comments from the Pharmaceuticals and Medical Devices Agency (PMDA) of Japan, which participated as an observer.
► Report from the EMA-FDA QbD pilot program, 19 April 2017.

Swiss–Austrian agreement
Vienna – A memorandum of understanding (MoU) has been signed by the Swiss Agency for Therapeutic Products (Swissmedic) and the Austrian Agency for Health and Food Safety (AGES). The MoU provides a formal basis for intensifying collaboration and for working together on bilateral initiatives. Swissmedic now has cooperation agreements with the medicines regulatory authorities in all German-speaking countries.
AGES Press release, 15 March 2017 (German).

MedDRA expands global reach
Montreal, Canada – Over 5 000 organizations in 103 countries now subscribe to MedDRA, the Medical Dictionary for Regulatory Activities. This reflects the successful adoption of MedDRA as a worldwide standard in the protection of public health.

MedDRA was developed by ICH in the 1990s to facilitate sharing of regulatory information internationally. The update was presented at the MedDRA Management Board meeting, held in Montreal, Canada on 27–28 May 2017. The Board noted the successful collaboration between the MedDRA Maintenance and Support Services Organization (MSSO) and the WHO Collaborating Centre for International Drug Monitoring (the Uppsala Monitoring Centre) in expanding the MedDRA user base, and acknowledged the significant work of the CIOMS SMQ Implementation Working Group in developing Standardised MedDRA Queries (SMQs).
► ICH. Press release, 12 June 2017.

EMA and academia
European Union – The EMA has developed a framework and action plan to formalize and further develop its interactions with the academic community. The aim is to increase academia’s engagement in the
European regulatory system in order to foster technological advances and to ensure that the best scientific expertise is available on time to support regulatory processes and decision-making.

A new webpage has also been published with information on EMA’s activities that are most relevant to academia.

EMA. Academia [webpage].

**Transparency and databases**

**Publication of clinical study reports: Release of EMA documents halted**

Luxembourg – The EU Court of Justice of the European Union has dismissed two appeals by the EMA against interim orders of the General Court, thus upholding the suspension of the release of clinical study reports on two medicines.

This follows court cases brought against EMA in December 2015 by the two pharmaceutical companies manufacturing the respective products. Both companies argue that the release of the documents would infringe their right to protect commercially confidential information contained in their marketing authorization applications. The two cases are still ongoing. Meanwhile the EMA will respect the interim orders and will not release the documents concerned. The Agency will continue to process requests for access to other documents made under the terms of the EU’s Transparency Regulation.

The EMA’s policy on access to documents, which entered into force in 2010, is the EU’s central instrument to achieve transparency in regulatory decision-making. In October 2016, EMA launched its policy on the proactive publication of clinical study reports that support applications for marketing authorization for medicines.


**India builds centralized regulatory portal**

India – The Drug Controller of India has requested pharmaceutical manufacturers to register their sites on the online “SUGAM” portal. Companies are required to register only once and can then enter information on all their facilities, even if they are located in different States.

The portal was launched in November 2015 and is intended for filing, tracking and processing of applications for various types of services rendered by the Central Drugs Standard Control Organization (CDSCO) of India. The latest phase includes modules for manufacturing facilities, approved pharmaceutical products as well as retail and wholesale licences.

► CDSCO. Notice, 3 April 2017.

**Ingredients catalogue in Australia**

Australia – The TGA has published an online catalogue of ingredients approved for use in listed medicines. The catalogue provides a single, searchable online source of information on excipients and associated requirements, increasing transparency for industry and consumers and reducing complexities for business. The catalogue is can be accessed through the Ingredient Table search facility on the TGA’s Business Services website.

► TGA News, 4 April 2017.
Under discussion

European Union – The EMA has published draft guidance on the type and format of data on antimicrobial use by animal species. The guidance is intended for EU member states that might provide such data to EMA from their national data collection systems on a voluntary basis.

► EMA Consultation, 24 March 2017.
Closing date: 24 September 2017.

Health Canada is proposing regulations that would make a warning sticker and patient information handout mandatory with all prescription opioids at the time of sale. Final publication of the regulations would mark the first time the Canadian government requires a warning sticker and patient handout with a dispensed medicine.

Closing date: 31 August 2017.

The EMA has released a draft guideline outlining the practical arrangements for notification of serious breaches of clinical trials authorized in the EU. It aims to provide advice on what should be classified as a serious breach and what should be reported.

► EMA Consultation, 23 May 2017.
Closing date: 22 August 2017.

European Union – The EMA has proposed a concept paper to clarify the regulatory expectations for data to support the approval of novel medicines to treat influenza. Several new antiviral agents are being developed for this indication.

► EMA Consultation, 4 May 2017.
Closing date: 31 July 2017.

Canada – The Government of Canada has launched a consultation on proposed amendments to the Patented Medicines Regulations. The amendments are intended to provide new regulatory tools and information to protect Canadian consumers from high prescription drug prices.

Closed 28 June 2017.

United States of America – The FDA has solicited input on its proposal for the future of patient engagement so that the perspectives of patient communities can be better captured. For this purpose the Agency is considering to establish a new Office of Patient Affairs.

► FDA Notice in the Federal Register, 14 March 2017.
Closed 12 June 2017.

London, UK – The EMA has released a draft concept paper in view of updating its 2006 guidance on the role of pharmacokinetics in developing medicines for children. The proposed revision reflects scientific advances and the experience gained over the last decade.

► EMA Consultation, 4 May 2017.
Closing date: 31 July 2017.

United States of America – The FDA has extended the period for comments on its draft guidance on the data and information
expected for a **biological product** to meet the standard for **interchangeability**.

   Extended until 19 May 2017.

**Australia** – The TGA has released a consultation document on proposed options for the future regulation of so-called “**low risk**” products, such as antiperspirants, over-the-counter (OTC) products, disinfectants, sunscreens, class I medical devices, vitamins and minerals, and homoeopathic products.

► TGA Consultation, 31 March 2017.

The TGA has also informed the public about a new notifications process to be introduced for “**very low risk**” variations of registered medicines.

► Notifications process: requests to vary registered medicines where quality, safety and efficacy are not affected. Version 1.0, June 2017 (pending legislative amendments). 8 June 2017.

**Canada** – Health Canada has proposed to permit **emergency imports** of bulk quantities of foreign-authorized medications, *i.e.* medications that have been authorized in the U.S., the EU or Switzerland, but not yet in Canada. The permits would be valid for one year, renewable. The most immediate need is expected to be for medicines to treat opioid use disorder.

   Comment period: 15 days.

**Australia** – The TGA has invited comments from interested parties on its proposed **provisional approval registration process** and post-market requirements for provisionally registered medicines. This follows a recommendation from the Review of Medicines and Medical Devices regulation to implement expedited pathways in Australia. A consultation paper on the proposed eligibility criteria and designation process for the two proposed expedited pathways (priority review and provisional approval) was published by the TGA in October 2016.

   Closed 1 May 2017.

**Australia** – The TGA has sought comments on its proposed changes that will **strengthen safety monitoring** for medicines available in Australia. The changes will apply to medicines only and will be implemented progressively from late 2017 onward.

   Closed 1 May 2017.

**India** – The Ministry of Health and Family Welfare has launched a public consultation on the development of an **electronic platform for tracking the supply of medicines in India**. All manufacturers, wholesalers and distributors will be required to register on this portal and enter batch numbers, quantities supplied and expiry dates of all medicines supplied, sold or returned to the manufacturers. This tracking system is intended to complement the bar coding, which has been introduced for export purposes.


**Canada** – The Government of Canada has proposed amendments to the Protecting Canadians from Unsafe Drugs Act (Vanessa’s Law). Under the amended regulations, Health Canada would be able to require companies to conduct new tests and studies. Companies would also have to notify Health Canada of any drug safety-related actions required by a regulator in another jurisdiction.

### Approved

**Naldemedine** for constipation caused by opioids
- **Product name:** Symproic®
- **Dosage form:** Tablet
- **Class:** Opioid antagonist
- **Approval:** FDA
- **Use:** Treatment of opioid-induced constipation in adults with chronic non-cancer pain.
- **Benefits:** Increase in number of spontaneous bowel movements, compared to placebo.

**Cerliponase alfa** for a rare neurodegenerative disorder in children
- **Product name:** Brineura®
- **Dosage form:** Solution for intracerebroventricular infusion
- **Class:** Enzyme replacement therapy; **ATC code:** A16AB
- **Approval:** EMA (marketing authorization under exceptional circumstances, accelerated assessment; orphan designation) FDA (priority review, breakthrough therapy; orphan drug designation)
- **Use:** Treatment of neuronal ceroid lipofuscinosis type 2 (CLN2) disease in children.
- **Benefits:** Ability to slow the progression of motor and language decline.
- **Note:** This is the first EMA- and FDA-approved medicine for CLN2 disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency, a very rare neurodegenerative genetic disorder that usually leads to the death of the child between the ages of eight and twelve years.

**Nonacog beta pegol** for haemophilia B
- **Product name:** Refixia®
- **Dosage form:** Powder and solvent for solution for injection
- **Class:** Recombinant coagulation factor IX; **ATC code:** B02BD
- **Approval:** EMA (orphan designation)
- **Use:** Treatment and prophylaxis of bleeding in patients 12 years and above with haemophilia.
- **Benefits:** Ability to prevent and treat bleeding in patients with haemophilia B.
- **Note:** This is the first EMA- and FDA-approved medicine for CLN2 disease, also known as tripeptidyl peptidase 1 (TPP1) deficiency, a very rare neurodegenerative genetic disorder that usually leads to the death of the child between the ages of eight and twelve years.

**Dupilumab** for atopic dermatitis
- **Product name:** Dupixent®
- **Dosage form:** Subcutaneous injection
- **Class:** Antibody binding to the interleukin-4 receptor alpha subunit (IL-4Ra) protein; **ATC code (temporary):** D11AH05
- **Approval:** FDA (priority review, breakthrough therapy)
- **Use:** Treatment of adults with moderate to severe eczema (atopic dermatitis) not controlled adequately by topical therapies. Can be used with or without topical corticosteroids.
- **Benefits:** Greater efficacy than placebo to clear skin and reduce itch.

**Abaloparatide** for osteoporosis
- **Product name:** Tymlos®
- **Dosage form:** Injection for subcutaneous use
- **Class:** Human parathyroid hormone related peptide analog
- **Approval:** FDA
- **Use:** Treatment of postmenopausal women with osteoporosis at high risk of fractures.
- **Benefits:** Ability to reduce the risk of vertebral and nonvertebral fractures.
- **Safety information:** A dose-dependent increase in the incidence of osteosarcoma was found in animal studies. This medicine is not recommended in patients at increased risk for osteosarcoma. Cumulative use with other parathyroid hormone analogs for more than...
Inotuzumab ozogamicin for acute lymphoblastic leukaemia

**Product name:** Besponsa®

**Dosage form:** Powder for concentrate for solution for infusion

**Class:** Specific humanised immunoglobulin class G subtype 4 (IgG4) antibody; **ATC code:** L01XC26

**Approval:** EMA (orphan designation)

**Use:** Treatment of adults with relapsed or refractory CD22-positive B cell precursor acute lymphoblastic leukaemia.

**Benefits:** Ability to increase the proportion of patients who have complete remission and molecular remission and to delay the progression of disease.

► FDA Prescribing information, revised 04/2017. Available from: Drugs@FDA. FDA Approved Drug Products.

Durvalumab for bladder cancer

**Product name:** Imfinzi®

**Dosage form:** Injection for intravenous use

**Class:** Programmed death-ligand 1 (PD-L1) blocking antibody; **ATC code (temporary):** L01XC28

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

**Use:** In combination with an aromatase inhibitor as initial endocrine-based therapy, treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

**Benefits:** Improvement in investigator-assessed progression-free survival. Overall survival data are immature.

Safety information: Ribociclib can cause QT interval prolongation, hepatobiliary toxicity, neutropenia, and harm to an unborn child.


Midostaurin for acute myeloid leukaemia

**Product name:** Rydapt®

**Dosage form:** Capsules

**Class:** Kinase inhibitor; **ATC code:** L01XE39

**Approval:** FDA, fast track designation (for the AML indication), priority review (for the mastocytosis indication), breakthrough therapy

**Uses:**
- Treatment of newly diagnosed, FLT3 mutation-positive acute myeloid leukaemia (AML), in combination with standard cytarabine and daunorubicin induction and cytarabine consolidation.
- Treatment of aggressive systemic mastocytosis, systemic mastocytosis with associated haematological neoplasm, or mast cell leukaemia.

**Benefits:** In AML: longer survival and longer progression-free survival period than with chemotherapy alone (a specific median survival rate could not be reliably estimated).


Ribociclib for breast cancer

**Product name:** Kisqali®

**Dosage form:** Tablets

**Class:** Cyclin-dependent kinase 4/6 inhibitor; **ATC code (temporary):** L01XE42

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

**Use:** Treatment of postmenopausal women with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative advanced or metastatic breast cancer.

**Benefits:** Improvement in investigator-assessed progression-free survival. Overall survival data are immature.

Safety information: Ribociclib can cause QT interval prolongation, hepatobiliary toxicity, neutropenia, and harm to an unborn child.


Brigatinib for certain lung cancers

**Product name:** Alunbrig®

**Dosage form:** Tablets
**Approved**

**Class**: Tyrosine kinase inhibitor;  
**ATC code (temporary)**: L01XE43  
**Approval**: FDA (accelerated approval)  
**Use**: Treatment of patients with anaplastic lymphoma kinase (ALK)-positive metastatic non-small cell lung cancer who have progressed on or are intolerant to crizotinib.  
**Benefits**: Ability to shrink tumours in approximately half of the patients enrolled in the clinical study.  
► *FDA Prescribing information, April 2017. Available from: Drugs@FDA: FDA Approved Drug Products*

**Niraparib for certain recurrent cancers**  
**Product name**: Zejula®  
**Dosage form**: Capsules  
**Class**: Poly ADP-ribose polymerase (PARP) inhibitor; **ATC code (temporary)**: L01XX54  
**Approval**: FDA (fast-track, priority review, breakthrough therapy; orphan drug designation)  
**Use**: Maintenance treatment of adult patients with recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer, whose tumours have completely or partially shrunk in response to platinum-based chemotherapy.  
**Benefits**: Longer progression-free survival than with placebo.  
► *FDA News release, 27 March 2017.*

**Ocrelizumab for multiple sclerosis**  
**Product name**: Ocrevus®  
**Dosage form**: Intravenous infusion  
**Class**: Selective immunosuppressant; **ATC code**: L04AA36  
**Approval**: FDA (breakthrough therapy, fast-track designation, priority review)  
**Use**: Treatment of adults with relapsing forms of multiple sclerosis and primary progressive multiple sclerosis.  
**Benefits**: Longer time to the worsening of disability, compared to placebo.  
**Safety information**: Ocrelizumab should not be given to patients with active hepatitis B virus infection.  
**Notes**: This is the first FDA-approved treatment of primary progressive multiple sclerosis. Ocrelizumab is also under review by EMA (1) and Health Canada. (2)  
(1) EMA. Applications for new human medicines under evaluation by the Committee for Medicinal Products for Human Use. March 2017.  
(2) Health Canada. Drug and health product submissions under review (SUR).*

**Sarilumab for rheumatoid arthritis**  
**Product name**: Kevzara®  
**Dosage form**: Solution for subcutaneous injection  
**Class**: Interleukin inhibitor, specific human monoclonal antibody (IgG1 subtype); **ATC code**: L04AC14  
**Approval**: EMA  
**Use**: Treatment of moderately to severely active rheumatoid arthritis in adult patients who have responded inadequately to, or who are intolerant to one or more disease-modifying anti rheumatic drugs (DMARDs).  
**Benefits**: Ability to reduce the signs and symptoms of rheumatoid arthritis and to improve physical function.  
► *EMA/CHMP Opinion, 21 April 2017.*

**Avelumab for rare skin cancer**  
**Product name**: Bavencio®  
**Dosage form**: Injection  
**Class**: Programmed death ligand-1 (PD-L1) blocking antibody  
**Approval**: FDA (accelerated approval, priority review, breakthrough therapy; orphan designation)  
**Use**: Treatment of adults and children 12 years and older with metastatic Merkel cell carcinoma.  
**Benefits**: Ability to shrink tumours in approx. 33% of patients treated.  
**Note**: This is the first FDA-approved treatment option for metastatic Merkel cell carcinoma.  
► *FDA News release, 23 March 2017.*
**Autologous chondrocyte suspension** to repair cartilage defects in the knee

**Product name:** Spherox®  
**Dosage form:** Implant suspension  
**Class:** Autologous chondrocytes;  
**ATC code:** M09AX02  
**Approval:** EMA  
**Use:** Repair of certain cartilage defects of the knee.  
**Benefits:** Ability to repair symptomatic cartilage defects in the knee with defect sizes up to 10 cm².  
**Notes:** This is an advanced therapy medicinal product in the form of a suspension containing 10–70 three-dimensional spheroids/cm², each composed of a cartilage matrix with the patient's own chondrocytes, isolated from healthy cartilage and cultured in vitro. The CHMP positive opinion was based on an assessment by the Committee for Advanced Therapies.  

**Edaravone** for amyotrophic lateral sclerosis

**Product name:** Radicava®  
**Dosage form:** Intravenous infusion  
**Class:** Free radical scavenger  
**Approval:** FDA (orphan drug designation)  
**Use:** Treatment of patients with amyotrophic lateral sclerosis (ALS), also known as Lou Gehrig's disease.  
**Benefits:** Ability to slow the decline of daily functioning.  
**Notes:** This is the second FDA-approved medicine for ALS, after riluzole, which gained FDA approval in 1995. Edaravone was previously approved in Japan.  

**Valbenazine** for tardive dyskinesia

**Product name:** Ingrezza®  
**Dosage form:** Capsules  
**Class:** Vesicular monoamine transporter 2 (VMAT2) inhibitor  
**Approval:** FDA (fast track, priority review, breakthrough therapy)  
**Use:** Treatment of adult patients with tardive dyskinesia, a neurological disorder characterized by repetitive involuntary movements seen in some patients treated with certain medications.  
**Benefits:** Ability to reduce the severity of involuntary movements, compared with placebo.  

**Deutetrabenazine** for chorea

**Product name:** Austedo®  
**Dosage form:** Tablets  
**Class:** Vesicular monoamine transporter 2 (VMAT2) inhibitor  
**Approval:** FDA  
**Use:** Treatment of chorea associated with Huntington's disease.  
**Benefits:** Ability to reduce chorea in Huntington's disease patients.  
**Safety information:** This medicine increases the risk of depression and suicidal thoughts. It is contraindicated in patients who are suicidal, and in patients with untreated or inadequately treated depression.  
► FDA. Drug trials snapshots: Austedo.

**Triple combination for COPD**

**Product name:** Trimbow®  
**Dosage form:** Solution delivered by pressurized metered dose inhaler  
**Class:** Triple combination of an inhaled glucocorticoid (beclometasone dipropionate), a long-acting beta-2 receptor agonist (formoterol fumarate dihydrate) and a long-acting muscarinic antagonist (glycopyrronium bromide). ATC code: R03AL09  
**Approval:** EMA  
**Use:** Maintenance treatment of moderate to severe chronic obstructive pulmonary disease (COPD).  
**Benefits:** The product can relieve and prevent symptoms such as shortness of breath,
Approved wheezing and cough and reduce exacerbations of COPD symptoms.


**Cenegermin for a rare eye disease**

**Product name:** Oxervate®

**Dosage form:** Eye drops solution

**Class:** Recombinant form of human nerve growth factor

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

**Use:** Treatment of moderate or severe neurotrophic keratitis in adults

**Benefits:** Cenegermin can stimulate corneal healing and restore eye surface integrity in patients with neurotrophic keratitis suffering from persistent epithelial defects or corneal ulcers.

**Notes:** Neurotrophic keratitis is a rare eye disease that can lead to loss of sight. It is caused by damage to the trigeminal nerve, resulting in reduced sensation in the cornea and reduced production of substances that play a role in repairing damage and ensuring survival of cornea cells.

(1) Patients in the United Kingdom will get early access to the product under the MHRA’s early access to medicine (EAMS) scheme.

(2) MHRA. Decision, 7 June 2017.

**Biosimilars**

**Insulin lispro**

**Product name:** Insulin lispro Sanofi®

**Reference product:** Humalog®

**Approval:** EMA

**Use:** Treatment of diabetes mellitus.


**Rituximab**

**Product name:** Rixathon®

**Reference product:** Mabthera®

**Approval:** EMA


**Product name:** Riximyo®

**Reference product:** Mabthera®

**Approval:** EMA

Use: Treatment of non-Hodgkin’s lymphoma, chronic lymphocytic leukaemia, granulomatosis with polyangiitis, and microscopic polyangiitis.


**Product name:** Blitzima®

**Reference product:** Mabthera®

**Approval:** EMA

Use: Treatment of non-Hodgkin’s lymphoma, chronic lymphocytic leukaemia, granulomatosis with polyangiitis and microscopic polyangiitis.


**Product name:** Ritemvia®

**Reference product:** Mabthera®

**Approval:** EMA


**Etanercept**

**Product name:** Erelzi®

**Reference product:** Enbrel®

**Approval:** EMA

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

**Infliximab**

**Product name:** Renflexis® (infliximab-abda)

**Reference product:** Remicade®

**Approval:** FDA

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

► Drugs@FDA: FDA Approved Drug Products. Biologic License Application (BLA): 761054.

**Extensions of indications**

**Maraviroc for use in children**

**Product name:** Celsentri®

**Approval:** EMA

**Newly approved use:** Treatment of adolescents and children of 2 years of age and older and weighing at least 10 kg with certain types of HIV-1 infection.


**Sofosbuvir, ledipasvir and sofosbuvir for use in children and adolescents**

**Product name:**
- Sofosbuvir: Sovaldi®
- Ledipasvir/sofosbuvir: Harvoni®

**Approval:** FDA

**Newly approved use:** Treatment of certain types of hepatitis C virus infection in children 12 years of age and older or weighing at least 35 kg.


**Pembrolizumab for tumours with a certain biomarker**

**Product name:** Keytruda®

**Approval:** FDA (accelerated approval, priority review)

**Newly approved use:** Treatment of adults and children with unresectable or metastatic tumours having a biomarker referred to as microsatellite instability-high (MSI-H) or mismatch repair deficient (dMMR), including:
- solid tumours that have progressed following prior treatment and who have no satisfactory alternative treatment options and
- colorectal cancer that has progressed following treatment with certain chemotherapy drugs.

**Note:** This is the first FDA approval based on a tumour's biomarker without regard to the tumour's original location.


**Regorafenib for liver cancer**

**Product name:** Stivarga®

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

**Newly approved use:** Treatment of patients with hepatocellular carcinoma who have been previously treated with sorafenib.

**Note:** This is the first FDA-approved treatment for liver cancer in almost a decade.


**Tocilizumab for giant cell arteritis**

**Product name:** Actemra®

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

**Newly approved use:** Treatment of giant cell arteritis, a form of vasculitis impeding adequate blood flow in the inflamed arteries.

**Note:** Tocilizumab was previously FDA-approved for certain types of arthritis. The newly approved indication provides the first FDA-approved therapy specific to this type of vasculitis.


**Ivacaftor to treat additional mutations of cystic fibrosis**

**Product name:** Kalydeco®

**Approval:** FDA
Extensions of indications

**Newly approved use:** Treatment of additional gene mutations in patients with cystic fibrosis.

**Note:** The approval triples the number of rare gene mutations that the drug can treat, from 10 to 33. The agency based its decision on the results of laboratory testing, in conjunction with evidence from earlier human clinical trials. This pathway was used because many cystic fibrosis mutations have such small patient populations that clinical trial studies are not feasible.


**Early access**

**Glecaprevir/pibrentasvir for chronic hepatitis C infection**

**Dosage form:** Film-coated tablets

**Class:** Fixed-dose combination of two direct-acting antivirals

**Approval:** MHRA Early Access to Medicines Scheme (EAMS)

**Use:** Treatment of chronic hepatitis C virus (HCV) infection in adults. In the context of the EAMS, use of glecaprevir/pibrentasvir is restricted to certain patient groups.

**Benefits:** High cure rates of hepatitis C infection across HCV genotypes in patients with or without cirrhosis.

► MHRA EAMS. Decision, 10 May 2017.

**EU ruling**

**Paracetamol/ibuprofen fixed-dose combination**

The EMA’s Committee for Medicinal Products for Human Use (CHMP) has concluded that marketing authorization can be granted for the analgesic fixed-dose combination paracetamol/ibuprofen 500mg/150mg film-coated tablets in relevant EU member states.

The matter had been referred to the CHMP because no agreement could be reached during joint assessment of the application under the EMA’s “Decentralized procedure”. The CHMP concluded that this combination is more effective than the individual components, while its safety profile is similar. Using the combination may avoid having to use stronger painkillers such as opioids, which have risks of abuse and misuse. Post-marketing data show that similar combinations have not led to significant long-term use (which is not authorized for this product) or increased safety concerns.

► EMA. Questions and answers on Paracetamol/ibuprofen 500mg/150mg film-coated tablets and associated names (tablets containing 500 mg paracetamol and 150 mg ibuprofen). 19 May 2017.