Regulatory news

Ebola

Update on treatments and vaccines

The Ebola crisis has prompted an unprecedented cooperation between regulators to support WHO and to advise on possible pathways for the development, evaluation and approval of medicines to fight Ebola. Progress towards provision of treatments and vaccines is summarized below.

In August 2014, a WHO-convened panel had agreed unanimously that it is ethically acceptable to use of experimental medicines and vaccines under the exceptional circumstances of the Ebola epidemic (1). In early September, WHO convened a consultation on potential Ebola therapies and vaccines (2). The importance of supportive care and community response was stressed in this and subsequent discussions.

Treatments

In September, more than 200 experts from around the world met at WHO and agreed to prioritize convalescent blood and plasma therapies for further investigation. Many questions remain to be answered about the safety and efficacy of convalescent therapies, the feasibility of implementation in countries with shattered health systems, and the prospects of scaling up therapy to curb the fatality rate (2). To support implementation, WHO has issued new interim guidance on the use of convalescent therapies for national health authorities and blood transfusion services (3). The first clinical trials of – possibly curative – transfusions of whole blood or blood plasma from recovered patients have been scheduled to be conducted in Liberia, in line with WHO technical guidelines (4).

In September the European Medicines Agency (EMA) established an expert group to review available information on Ebola experimental treatments – excluding convalescent therapies – and invited developers to submit their data (5).

Vaccines

On 29–30 September, 70 experts attended a WHO-convened consultation on Ebola vaccines. They took stock of the many ongoing efforts to rapidly evaluate the safety and efficacy of Ebola vaccines for deployment as soon as possible to critical frontline workers and ultimately to populations at risk in mass vaccination campaigns. Two candidate vaccines have clinical-grade vials available for safety trials. (6)

In October, WHO convened industry leaders and key partners to discuss trials and production of Ebola vaccine (7). Consensus was achieved to make results available in December 2014, to begin efficacy trials at the same time, and to scale up production in 2015.

Also in October the EMA gave its first scientific advice on a development plan for an Ebola vaccine, using a new ‘rolling review’ procedure for data assessment and sharing of outcomes with healthcare decision-makers in affected countries (8). At the time of writing, safety trials of vaccines were underway in the U.S., U.K., Mali and Switzerland, and about to begin
in Gabon, Germany and Kenya. The two Swiss trials are coordinated by WHO, with testing done on healthy volunteers, some of whom will be deployed in the fight against Ebola in West Africa (9).

At the meeting of the African Vaccine Regulatory Forum (AVAREF) in early November, delegates discussed collaborative mechanisms to fast-track clinical trial approvals and registration of Ebola treatments and vaccines in affected countries, and – importantly – reaffirmed the need to build stronger health systems (10).

Supportive care
Industry leaders and key partners have emphasized that community engagement remains key to fight Ebola and have called on local communities, national governments, NGOs and international organizations to scale up concerted activities urgently. (7). Meanwhile, a WHO-coordinated retrospective study has shown that supportive care, especially rehydration and correction of metabolic abnormalities, may contribute to patient survival (11).

Diagnostics
Quick and accurate diagnosis is key in fighting Ebola. WHO has launched two urgent initiatives to accelerate the delivery of rapid, sensitive, safe and simple Ebola diagnostic tests to West African countries. The first is a close collaboration of manufacturers, researchers, Médecins sans Frontières (MSF) staff, and the non-profit organization Foundation for Innovative New Diagnostics (FIND), and aims to support the development of suitable tests. The second is the establishment of an emergency rapid review mechanism for assessing a diagnostic’s quality, safety and performance. (12)

► (1) WHO Statement, 12 August 2014.
(2) WHO. Ebola situation assessment - 26 September 2014.
(3) WHO. Use of Convalescent Whole Blood or Plasma Collected from Patients Recovered from Ebola Virus Disease for Transfusion, as an Empirical Treatment during Outbreaks. Version 1.0, September 2014.
(4) WHO. Ebola situation assessment, 6 November 2014.
(5) EMA Press release, 26 September 2014.
(6) WHO. Experimental Ebola vaccines. 1 October 2014.
(7) WHO News release, 24 October 2014.
(8) EMA Press release, 29 October 2014.
(9) WHO News release, 6 November 2014.
(10) WHO Essential Medicines and Health Products. African regulators’ meeting looking to expedite approval of vaccines and therapies for Ebola [web page].

Clinical trials transparency

EMA adopts policy on publication of clinical reports
European Union – The EMA’s Management Board has unanimously adopted a new policy to publish the clinical trial reports that underpin the decision-making on medicines. The policy will enter into force on 1 January 2015 and will apply to clinical reports supporting all applications for centralized marketing authorizations submitted after that date.

According to the policy’s terms of use, the reports cannot be used for commercial purposes. In the limited instances
where they may contain commercially confidential information, this will be redacted in accordance with the principles outlined in the policy’s annexes.

The new policy will serve as a complementary tool ahead of the implementation of the new EU Clinical Trials Regulation that will come into force not before May 2016. Public access to clinical reports will enable academics and researchers to re-assess data sets, and will help to avoid duplication of clinical trial ► EMA Press release, 2 October 2014.

Pre-market assessment

EMA revises guidance on biosimilars
European Union – The EMA has published its revised guideline on biosimilars. The main change is that developers can now use a comparator product authorized outside the European Economic Area (EEA) in certain clinical studies and in non-clinical studies conducted in vivo. This new concept aims to avoid unnecessary repetition of clinical trials. The comparator must be authorized by a regulatory authority with similar rigorous scientific and regulatory standards to those of EMA, and the applicant must establish that the comparator is representative of the reference medicine authorized in the EEA.

A biosimilar is a biological medicine that is similar to an already authorized reference product (comparator). To obtain a marketing authorization the developer must demonstrate in studies that the biosimilar is as safe and effective as the reference medicine, and meets the EMA’s quality requirements.

While the revised guideline will come into force as of 30 April 2015, applicants can apply some or all of its provisions with immediate effect. Two related guidelines and procedural guidance are also being updated. ► EMA Press release, 29 October 2014.

EMA proposes harmonized clinical trials plan for vaccine in children
European Union – The EMA has proposed a single development plan for new tetanus-diphtheria-acellular pertussis vaccines that all pharmaceutical companies across the EU should follow. The proposal aims to avoid the duplication of similar clinical trials and the unnecessary exposure of children to clinical testing.

As the schedules of child vaccinations vary slightly between EU countries, a large number of fairly similar clinical trials are currently conducted in children when a new vaccine is being developed. The EMA collaborated with the European Centre for Disease Prevention and Control (ECDC) to define a single schedule for clinical trials. A panel of public health vaccinology experts have endorsed the proposal.

The proposed plan has been released for a three-month public consultation. ► EMA News, 23 September 2014.

EMA pilot to seek patient views on medicines risks and benefits
European Union – The European Medicines Agency (EMA) has launched a pilot project to involve patients in the assessment of the benefits and risks of medicines in its Committee for Medicinal Products for Human Use (CHMP). Patients will be invited to present their views on medicines for which there is an unmet medical need and where the Committee has doubts on its regulatory
decisions at any stage of the product life cycle. EMA has published a document outlining the principles of this approach.

The first active substance included in this pilot project has been afamelanotide, leading to the approval of a treatment for erythropoietic protoporphyria (EPP), a rare genetic blood disorder which causes an absolute intolerance to light (see also page 466).

The pilot project stems from a wider EMA strategy to involve patients in the Agency’s activities. It will run for at least one year, leading up to a proposal for full implementation.

► EMA Press release, 26 September 2014.

**Australia to recognize EU conformity assessment for medical devices**

**Australia** – New regulations will allow Australian manufacturers to obtain market approval for most medical devices based on conformity assessment certification from European notified bodies, the accredited organizations that carry out product assessments in the EU.

The highest risk devices such as those containing medicines or tissues of animal, biological or microbial origin, or Class 4 in vitro diagnostics (IVDs) including HIV tests, will still need TGA conformity assessment. The respective regulatory amendments are expected to be in place later this year.

► Australian Assistant Minister for Health, Media release, 15 October 2014.

Editor’s note: As the above media release mentions, regulators commonly adapt the level of control for IVDs to the level of risk that product deficiencies would pose for public health. IVDs (including products like tuberculosis or malaria IVDs, which are considered ‘low-risk’ in industrialized countries) are crucial in guiding treatment decisions for priority diseases. On the other hand, regulation of IVDs is still very limited or absent in many countries. Read more in WHO Drug Information Vol. 28, No. 3, 2014 on what WHO is doing to bring quality-assured IVDs to its Member States.

**Pharmacovigilance**

**Canada passes Vanessa’s Law**

**Canada** – The Government of Canada has passed modernized laws for drugs and medical devices. The Protecting Canadians from Unsafe Drugs Act, known as “Vanessa’s Law”, will enable the Government to recall unsafe medicines, impose tough penalties, compel pharmaceutical companies to make changes to products or do further testing, require mandatory adverse events reporting by health care institutions, and require transparency on regulatory decisions.

The Act introduces the most profound and important changes to the Food and Drugs Act in its fifty years of existence. It is named after an Australian Member of Parliament’s daughter who died of a heart attack while on a prescription drug that was later deemed unsafe and removed from the market.


**EU project on using smartphones for drug safety information**

**European Union** – The MHRA is leading a consortium of regulators, academics and the pharmaceutical industry in a three-year project, known as WEB-RADR, to develop new ways of gathering information on suspected adverse drug reactions (ADRs) using smartphones and social media. WEB-RADR will help to
develop recommendations on how these new tools should be used ethically and scientifically alongside existing drug safety monitoring systems.

The project is funded though the Innovative Medicines Initiative, a public-private partnership between the European Commission and the European Federation of Pharmaceutical Industries and Associations (EFPIA).


**EMA expands public web access to reports on suspected side effects**

European Union – The EMA has added to its website information on suspected adverse drug reactions for an additional 1 700 active substances contained in medicines approved in the European Union (EU) by national authorities. The information comes directly from the EudraVigilance database. The web site was launched in 2012 and initially only contained adverse events information for centrally authorized medicines. Over the next few years it will be expanded to cover all medicines available in the EU.

Since July 2012 European pharmacovigilance legislation provides the possibility for patients to report side effects directly to the authorities in all EU Member States. Increasing numbers of patient reports are being received in the EudraVigilance database.

► EMA Press release, 6 October 2014.

**Australia, Switzerland create web portals to report adverse reactions**

Australia - The TGA has launched a new web-based service for consumers to report adverse events associated with medicines and vaccines.


In 2013 only about 3% of adverse events reports received by the TGA came from consumers. The new web site is part of TGA’s activities taken in line with an international trend for regulators to encourage reporting by consumers. The TGA has also published a brochure outlining what and how to report, and is undertaking awareness activities and consumer research. (1)

Switzerland – With immediate effect, healthcare professionals and pharmaceutical companies can report suspected adverse drug reactions directly on the Internet through Swissmedic’s “EIViS” (Electronic Vigilance System) online reporting portal. Use of the portal is subject to registration on the EIViS website, and companies are also required to attend a Swissmedic training course. Data protection and security satisfy the most stringent requirements.

Swissmedic hopes that EIViS will result in more and better reports being received nearer to the event, helping to improve drug and patient safety in Switzerland. (2)

► (1) TGA News, 24 September 2014.

(2) Swissmedic Announcement, 6 October 2014.

**New MHRA guidance on reporting adverse drug reactions in children**

United Kingdom – The MHRA has announced new simplified guidance on how healthcare professionals should report suspected adverse drug reactions (ADRs) in children to its Yellow Card Scheme (mhra.gov.uk/yellowcard).

Recognizing that it is impractical to report all suspected ADRs in children, the new guidance asks that healthcare professionals report those reactions that are serious, medically significant or result...
in harm, and those that are associated with newer drugs and vaccines, identified by a black triangle symbol in the Yellow Card Scheme. The guidance also places greater importance on the reporting of medication errors in children resulting in suspected ADRs, and explains the many reasons why monitoring of ADRs in children is particularly important.


Organizations

Australia and New Zealand to keep separate regulatory authorities

The Australian and New Zealand Governments have agreed to cease efforts to establish a joint therapeutic products regulator, the Australia New Zealand Therapeutic Products Agency (ANZTPA). The decision was taken after a review of progress and an assessment of the costs and benefits involved. The two countries will continue to co-operate on the regulation of therapeutic products. (1)

The New Zealand authority has announced that work will now be undertaken to strengthen the national regulatory scheme for therapeutic products. (2)

► (2) Medsafe Media release, 20 November 2014.

Veterinary medicines

EU proposes veterinary medicines legislation revisions

European Union – The EMA has welcomed a major revision of the legal framework for veterinary medicines in the EU proposed by the European Commission. The revision includes measures to fight the development of antimicrobial resistance, notably by restricting the veterinary use of certain antimicrobials that are reserved for the treatment of infections in people. It also proposes streamlined marketing authorization procedures, simpler pharmacovigilance rules, better incentives for innovation, and clearer rules for internet retailing of veterinary medicines.

Other EU institutions will now consider the Commission’s proposals and will adopt their positions.

► EMA News, 10 September 2014.

Sales of veterinary antibiotics in Europe decrease

European Union – Sales of veterinary antibiotics have decreased by 15% according to the Fourth European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report. Increased awareness of the threat of antimicrobial resistance as well as national programmes, campaigns and restrictions have been cited among the reasons for the decrease.

The ESVAC report is issued every year to inform antimicrobial policy and the responsible use of antimicrobials in EU Member States.

► EMA Press release, 15 October 2014.
Netupitant and palonosetron for chemotherapy-induced nausea

Product name: Akynzeo®

Class: Netupitant and palonosetron fixed-dose combination; ATC code: A04AA55

Approval: FDA

Use: Treatment of nausea and vomiting in patients undergoing cancer chemotherapy.

Benefits: Added effectiveness in preventing vomiting episodes in the acute, delayed and overall phases after the start of cancer chemotherapy, compared with oral palonosetron alone.

► FDA News release, 10 October 2014.

Naloxegol for opioid-induced constipation

Product name: Movantik®

Class: Peripherally acting opioid receptor antagonist; ATC code: A06AH03

Approval: FDA, EMA

Use: Oral treatment for opioid-induced constipation in adults with chronic non-cancer pain.

Benefits: Additional supportive care option to decrease the constipating side effects of opioids.

Safety information: The FDA is requiring a postmarketing study to further evaluate the potential risk of cardiovascular adverse events.

► FDA News, 16 September 2014.

► EMA /CHMP Summary of opinion, 25 September 2014.

Dulaglutide for type 2 diabetes

Product name: Trulicity®

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

Approval: FDA; EMA

Use: Once-weekly subcutaneous injection to improve glycaemic control in adults with type 2 diabetes.

Benefits: New treatment option for patients with type 2 diabetes who cannot be managed with first-line regimens. Can be used alone or added to existing treatment regimens.

Safety information: Dulaglutide should not be used in patients with diabetic ketoacidosis or those with severe stomach or intestinal problems. As thyroid C-cell tumours have been observed in rodent studies, dulaglutide should not be used in patients with a personal or family history of medullary thyroid carcinoma (MTC), or in patients with multiple endocrine neoplasia syndrome type 2 (which predisposes them to MTC).

► FDA News release, 18 September 2014.

► EMA /CHMP Summary of opinion, 25 September 2014.

Antihaemophilic factor (recombinant), porcine sequence in acquired haemophilia A

Product name: Obizur®

Class: Porcine coagulation factor VIII

Approval: FDA (orphan drug designation)

Use: Treatment of bleeding episodes in adults with acquired hemophilia A (acquired factor VIII deficiency).

Benefits: Porcine Factor VIII is similar enough to human Factor VIII to be effective in blood clotting, but is less likely to be affected by the antibodies against human Factor VIII that are present in people with acquired haemophilia A.

► FDA News release, 24 October 2014.

Nonacog gamma in haemophilia B

Product name: Rixubis®

Class: Antihaemorrhagic, blood coagulation factor IX; ATC code: B02BD04

Approval: EMA

Use: Treatment and prophylaxis of bleeding in patients with haemophilia B (congenital factor IX deficiency) in patients of all age groups.
Benefits: Ability to prevent and treat bleeds in patients with haemophilia B including during surgery.
► EMA/CHMP Summary of opinion, 23 October 2014.

Afamelanotide for erythropoietic protoporphyria

Product name: Scenesse®
Class: Protective against UV radiation for systemic use; ATC code: D02BB02
Approval: EMA (orphan designation)
Use: Prevention of phototoxicity in adults with erythropoietic protoporphyria (EPP), a rare genetic disease causing intolerance to light.
Benefits: Afamelanotide stimulates the production of eumelanin, which naturally protects the skin against phototoxic reactions caused by sunlight, thereby significantly improving patients' quality of life.
Safety information: The company will implement a risk management plan and establish a registry of patients to collect safety and efficacy data.
Note: The approval was granted under exceptional circumstances, despite a lack of robust efficacy data due to the difficulties to recruit patients for placebo-controlled trials. Assessment was supported by data from the use of the medicine in compassionate use programmes globally. In addition, the EMA Committee heard feedback from patients and healthcare professionals involved in an expert group. This was the first time that patients were involved in EMA discussions on the benefits and risks of a medicine (see also page 461).
► EMA Press release, 24 October 2014.

Ledipasvir & sofosbuvir for hepatitis C infection

Product name: Harvoni®
Class: Fixed-dose combination of two direct-acting antivirals. Sofosbuvir is an NS5B inhibitor; ledipasvir – a new drug – is an NS5A inhibitor. ATC Code (temporary classification): J05AX65
Approval: EMA (accelerated assessment), FDA (priority review, breakthrough therapy designation)
Use: Treatment of chronic hepatitis C virus infection in adults.
Benefits: High cure rates in patients with chronic HCV infection without the need for treatments involving interferons. The latter are associated with poor tolerability and potentially serious side effects that rule out such treatment in a considerable proportion of HCV patients.
► EMA News, 26 September 2014.
FDA News release, 10 October 2014.

Dasabuvir for hepatitis C infection

Product name: Exviera®
Class: Antiviral agent, NS5B inhibitor. ATC code (temporary classification): J05AX16
Approval: EMA (accelerated assessment)
Use: Treatment of chronic hepatitis C in adults, in combination with other medicinal products.

Darunavir & cobicistat for HIV infection

Product name: Rezolsta®
Approval: EMA

Class: Antiretroviral fixed-dose combination; ATC code: J05AR14
Use: Treatment of human immunodeficiency virus (HIV) in antiretroviral therapy (ART)-naïve adults and ART-experienced adults with no darunavir (DRV) resistance associated mutations.
Benefits: Ability to provide sustainable virological suppression if given in combination with other antiretroviral medicinal products for treatment of HIV-1 infection.
► EMA/CHMP Summary of opinion, 25 September 2014.
**Benefits**: Ability to inhibit viral replication in infected host cells which can lead to the eradication of the virus, correlating to a cure of chronic hepatitis C virus (HCV) infection, in both non-cirrhotic and compensated cirrhotic patients with genotype 1a/1b HCV infection.

[EMA/CHMP opinion, 20 November 2014.](#)

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**Ombitasvir & paritaprevir & ritonavir for hepatitis C infection**

**Product name**: Viekirax®

**Class**: Fixed-dose combination of two antiviral agents, inhibitors of NS5A (ombitasvir) and NS3/4A (paritaprevir), with ritonavir as a pharmacokinetic enhancer. ATC code (temporary classification): J05AX67

**Approval**: EMA (accelerated assessment)

**Use**: Treatment of chronic hepatitis C in adults, in combination with other medicinal products.

**Benefits**: Ability to inhibit viral replication in infected host cells which can lead to the eradication of the virus, correlating to a cure of chronic hepatitis C virus (HCV) infection, in both non-cirrhotic and compensated cirrhotic patients with genotype 1a/1b and 4 HCV infection.

[EMA/CHMP opinion, 20 November 2014.](#)

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**Meningococcus B vaccine**

**Product name**: Trumenba®

**Class**: Meningococcal Group B vaccine; ATC code: J07AH09

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

**Use**: Prevention of invasive meningococcal disease caused by *Neisseria meningitidis* serogroup B in individuals 10–25 years of age.

**Benefits**: First licenced meningococcal group B vaccine in the U.S.; in addition to licenced vaccines for serogroups A, C, Y and W.

[FDA News release, 29 October 2014.](#)

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**Pembrolizumab for advanced melanoma**

**Product name**: Keytruda®

**Class**: Antineoplastic; PD-1 pathway blocker (first in class). ATC code (temporary classification): L01XC18

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

**Use**: Treatment of advanced or unresectable melanoma no longer responding to other drugs (ipilimumab, or ipilimumab and a BRAF inhibitor in patients whose tumors express a BRAF V600 mutation)

**Benefits**: Substantial improvement over existing therapies; shrinking tumours in approximately 24 percent of patients. Improvement on survival remains to be established.

**Safety information**: Potential for severe immune-mediated side effects that can involve healthy organs, including the lung, colon, hormone-producing glands and liver. In safety studies, such effects occurred uncommonly.

[FDA News release, 4 September 2014.](#)

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**Ramucirumab for gastric cancer**

**Product name**: Cyramza®

**Class**: Human receptor-targeted antibody that specifically binds VEGF Receptor 2 and blocks angiogenesis by binding of VEGF-A, VEGF-C, and VEGF-D.

**Approval**: EMA (orphan designation)

**Use**: Treatment of adult patients with advanced gastric cancer or gastro-oesophageal junction adenocarcinoma with disease progression after prior platinum and fluoropyrimidine chemotherapy. Ramucirumab can be used in combination with paclitaxel, or as monotherapy in patients for whom treatment in combination with paclitaxel is not appropriate.

**Benefits**: Ability to improve the survival in patients compared to chemotherapy alone (when used in combination with...
chemotherapy) and compared to placebo (when used alone).

► EMA/CHMP Summary of opinion, 25 September 2014.

Secukinumab for plaque psoriasis
Product name: Cosentyx®
Class: Immunosuppressant; ATC code: L04AC10
Approval: EMA
Use: Treatment of moderate to severe plaque psoriasis in adults who are candidates for systemic therapy
Benefits: More efficacious than placebo with respect to two co-primary endpoints in clinical studies.
► EMA/CHMP opinion, 20 November 2014.

Pirfenidone for idiopathic pulmonary fibrosis
Product name: Esbriet®
Class: Immunosuppressant; ATC code: L04AX05
Approval: FDA (fast track, priority review, orphan product, and breakthrough designations).
Use: Treatment of idiopathic pulmonary fibrosis
Benefits: Additional treatment option for patients with idiopathic pulmonary fibrosis, a serious, chronic condition. Current treatments include oxygen therapy, pulmonary rehabilitation, and lung transplant.
Notes: The FDA also approved nintedanib for the same use, see below.
Pirfenidone was approved by EMA in 2011 under orphan designation.
Safety information: Not recommended for patients with moderate to severe liver problems. Can cause birth defects or death to an unborn baby; women who are able to get pregnant should use adequate contraception during and for at least three months after the last dose of treatment.
► EMA/CHMP Summary of opinion, 25 September 2014.
FDA News release, 15 October 2014.

Nintedanib for non-small cell lung cancer / idiopathic pulmonary fibrosis
Product name: EU: Vargatef®, Ofev®; U.S.: Ofev®
Class: Tyrosine kinase inhibitor anti-neoplastic agent, angiogenesis inhibitor.
ATC code (temporary classification): L01XE31
Approval: EMA (orphan designation for Ofev®), FDA (fast track, priority review, orphan product, and breakthrough designations)
Use: Vargatef®: In combination with docetaxel, treatment of locally advanced, metastatic or locally recurrent non-small cell lung cancer of adenocarcinoma tumour histology after first-line chemotherapy. Ofev®: Treatment of idiopathic pulmonary fibrosis.
Benefits: Vargatef®: Improvement in progression-free survival and overall survival compared to docetaxel plus placebo.
Ofev®: Additional treatment option for patients with idiopathic pulmonary fibrosis.
Safety information: Not recommended for patients with moderate to severe liver problems. Can cause birth defects or death to an unborn baby; women who are able to get pregnant should use adequate contraception during and for at least three months after the last dose of treatment.
► EMA/CHMP Summary of opinion, 25 September 2014.
FDA News release, 15 October 2014.

Olaparib for a subtype of ovarian cancer
Product name: Lynparza®
Class: Poly ADP ribose polymerase (PARP) inhibitor (first-in-class)
Approval: EMA (orphan designation)
Use: Monotherapy for the maintenance treatment of adult patients with relapsed, platinum-sensitive epithelial ovarian,
Fallopian tube or primary peritoneal cancer carrying a BRCA gene mutation, and who have responded to platinum-based chemotherapy.

**Benefits:** Targeted treatment of a subtype of ovarian cancer for which limited treatment options are available.

► EMA Press release, 24 October 2014.

**Blinatumomab for a rare form of acute lymphoblastic leukaemia**

**Product name:** Blincyto®

**Class:** Immunotherapeutic monoclonal antibody, T-cell engager

**Approval:** FDA (breakthrough therapy designation, priority review and orphan product designation)

**Use:** Treatment of relapsed or refractory Philadelphia chromosome-negative precursor B-cell acute lymphoblastic leukaemia.

**Benefits:** Potential for substantial improvement over available therapies. The manufacturer is required to conduct a study to verify that the drug improves survival.

**Safety information:** Boxed warning about the risks of low blood pressure and difficulty breathing (cytokine release syndrome) at the start of the first treatment, difficulty with thinking (encephalopathy) and other nervous system side effects. The medicine was approved with a Risk Evaluation and Mitigation Strategy, which consists of a communication plan to inform health care providers about the serious risks and the potential for preparation and administration errors.

► FDA News release, 3 December 2014.

**Abuse-deterrent hydrocodone single-entity, extended release product**

**Product name:** Hysingla ER®

**Class:** Opioid analgesic

**Approval:** FDA (in line with guidance on abuse-deterrent properties)

**Use:** To treat pain severe enough to require daily, around-the-clock, long-term opioid treatment and for which alternative treatment options are inadequate.

**Benefits:** The formulation is expected to reduce abuse by ingestion, snorting or injection.

**Safety information:** The product can still be abused or misused, and can then cause an overdose that may result in death. Additional postmarketing studies will be conducted to assess the effects of the abuse-deterrent features on the risk for abuse, and the consequences of that abuse in the community.

**Note:** This is the fourth extended-release opioid analgesic to be approved by the FDA with labelling consistent with the FDA’s 2013 draft guidance on evaluation and labelling of abuse-deterrent opioids (after OxyContin®, Targiniq® and Embeda®).


**Labelling changes approved**

**Ketoconazole for Cushing’s syndrome**

**Product name:** Ketoconazole HRA®

**Class:** Antimycotic for systemic use; ATC code: J02AB02

**Approval:** EMA (orphan designation; accelerated approval of new indication)

**Use:** Treatment of Cushing’s syndrome

**Benefits:** Additional treatment option when surgery or other medicines fail or cannot be administered.

**Note:** Ketoconazole has been used “off-label” for more than 30 years to treat this rare and potentially life-threatening condition, although it has never been authorized for this indication in the EU.

**Safety information:** In July 2013, EMA recommended to suspend the marketing
authorizations of oral ketoconazole medicines to treat fungal infections due to the risk of liver injury. In the treatment of Cushing’s syndrome however, the benefits are greater than the risks, which can be managed by close monitoring of the patients’ liver function. The product is to be prescribed only by specialists as the posology needs to be individualized for each patient. Relevant information will be sent to healthcare professionals in the EU.

EMA Press release, 26 September 2014.

Ulipristal emergency contraceptive without prescription

Product name: ellaOne®
Class: Emergency contraceptive; ATC code: G03AD02
Approval: EMA/CHMP recommendation, to be sent to the European Commission for a legally binding decision.
Use: To prevent unintended pregnancy. Must be taken within 120 hours (five days) of unprotected intercourse or contraceptive failure; works best if taken within 24 hours.
Benefits: Making the medicine available without prescription in the EU should speed up women’s access to the medicine and therefore increase its effectiveness.
Safety information: The safety profile of ulipristal is comparable to that of levonorgestrel-containing emergency contraceptives, which are already available without prescription in most EU countries and are registered for use up to 72 hours after unprotected intercourse or contraceptive failure.
Notes: If granted by the European Commission, the re-classification to non-prescription status would in principle need to be implemented by all EU Member States. Any exception regarding the non-prescription status of this medicine would fall within the responsibilities of the Member States.