News from the EMA

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Launch of "EMA medical terms simplifier" for medical terms used by EMA

March 19, 2021

Medical writers at EMA have published an "EMA medical terms simplifier" (https://www.ema.europa.eu/en/documents/other/ema-medical-terms-simplifier_ en.pdf) on the "Glossaries" page of EMA's website (under "About us") to provide public-friendly descriptions of medical terms used for side effects of medicines and mechanisms of action. These descriptions are used daily to prepare EMA materials that are shared with the public.

The medical terms simplifier focuses on side effects and other terms used in medicines information and assessments of medicines. It does not cover rarely used terms, most disease states, very specialised areas, or the broader field of medical science.

The "EMA medical terms simplifier" has been assembled over many years by EMA medical writers who use these plain-language descriptions to prepare public-friendly communications. Having become increasingly aware that there was no single resource for describing common medical terms found in medicines information, the team worked to produce a public-domain version of this resource.

This resource may be of value to external stakeholders and partner organisations involved in communicating with the public. EMA medical writers will continue to maintain and further develop this resource over time.

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Success rate for marketing authorisation applications from SMEs doubles between 2016 and 2020

June 28, 2021

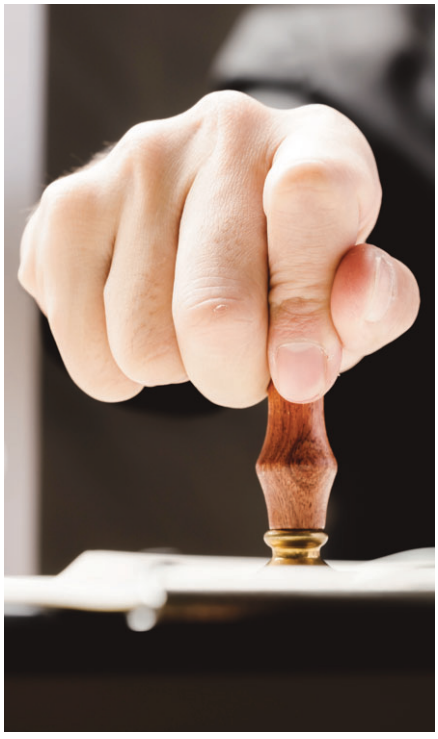
EMA has published a report highlighting the Agency's support for micro-, small-, and medium-sized enterprises (SMEs) which develop and market medicines for human or veterinary use in the European Union. The report covers the period from 2016 to 2020.

Since 2016, the success rate of marketing authorisation applications for human medicines submitted by SMEs has more than doubled. In 2016, 40% of medicines with an SME applicant received a positive opinion. In 2020, the number had increased to 89%. In 2020 alone, SMEs were behind 16 recommendations for approval of a new medicine, which accounted for almost 20% of all medicines for human use recommended for approval by EMA last year. Half of them targeted rare diseases.

In the veterinary area, 14 medicines received a positive opinion by the Agency in the last 5 years. Almost half of these had received scientific advice from the Agency. Six out of the 14 were veterinary medicines for minor use / minor species (MUMS).

The report features key facts and figures of companies that are registered as SMEs with EMA. SMEs are a major driver of innovation in the pharmaceutical industry and the Agency provides them with access to a number of incentives, including regulatory assistance from a dedicated SME Office and reduced fees for certain procedures.

The publication of the report marks the 15-year anniversary of the adoption of the SME Regulation that promotes innovation and the development of new medicines in Europe. Since the creation of the SME Office in 2005, more than 130 medicines developed by SMEs have been approved following an EMA recommendation and contribute to public and animal health.



New treatment for rare autoimmune disease of nerve cells

April 23, 2021

Photo: David Matos / Unsplash.com

EMA has recommended granting a marketing authorisation in the EU for Enspryng (satralizumab; from Roche) for the treatment of neuromyelitis optica spectrum disorders (NMOSD) in adults and adolescents from 12 years of age who are positive for anti-aquaporin-4 antibodies (AQP4-IgG).

NMOSD is a rare and life-threatening condition that most commonly affects the optic nerves and spinal cord. This disorder can lead to reduction or loss of vision, loss of sensation, loss of bowel and bladder control, weakness and paralysis of the arms and legs. NMOSD is thought to be caused by an abnormal reaction of the immune system that causes damage to healthy nerve cells. It is characterised by relapsing attacks, with symptoms coming back periodically. It is estimated that NMOSD affects approximately 1-2 in 100,000 people in the EU.

Enspryng works by reducing and preventing the attacks caused by NMOSD. Satralizumab, the active substance contained in Enspryng, is an antibody designed to block the inflammatory effects of interleukin-6 receptor (IL-6), which is involved in the pathogenesis of the NMOSD.

Enspryng will be available as a pre-filled syringe and will be administered as a solution through an injection under the patient's skin (subcutaneously). The first three injections are given 2 weeks apart followed by one injection every 4 weeks. It can be used on its own or in combination with medicines that reduce the activity of the immune system (immunosuppressive therapy).

The opinion of EMA's human medicines committee (CHMP) is mainly based on two randomised clinical studies which involved a total of 184 patients. The clinical studies showed that the chance of a relapse happening in 119 patients who were AQP4+ and received Enspryng alone or in combination with immunosuppressive therapy was a quarter of that in the control group receiving placebo alone or in combination with other immunosuppressive therapy. The most common side effects observed in clinical trials were headache, joint pain, white blood cells count decreased, and reactions at the site of injection.

The opinion adopted by the CHMP is an intermediary step on Enspryng's path to patient access. The opinion will now be sent to the European Commission for the adoption of a decision on an EU-wide marketing authorisation. Once a marketing authorisation has been granted, decisions about price and reimbursement will take place at the level of each Member State, taking into account the potential role or use of this medicine in the context of the national health system of that country.

First gene therapy to treat children with rare inherited neurological disease

May 21, 2021

EMA has recommended granting a marketing authorisation in the EU for the gene therapy Skysona (elivaldogene autotemcel; from bluebird bio, Netherlands) for the treatment of children with cerebral adrenoleukodystrophy (CALD), a severe form of a rare inherited neurological disease. his disease, seen almost exclusively in males, affects the brain and leads to an irreversible loss of neurological functions.

CALD is the most common form of adrenoleukodystrophy (ALD), a rare disease affecting approximately 1 in 21,000 newborn males. This condition is caused by abnormalities in a gene called ABCD1 which is responsible for the production of a protein called ALDP (adrenoleukodystrophy protein). Patients with the disease lack ALDP which is needed to break down fatty substances in the body called very long chain fatty acids (VLCFA). As patients with CALD cannot break down these fatty substances, they gradually build up in cells in the brain. The build-up of VLCFA leads to inflammation and destruction of the protective sheath (myelin) that insulates and improves the way the nerves function.

Forty percent of boys diagnosed with ALD develop CALD, typically during childhood. If untreated, nearly half of patients with CALD die within 5 years of symptom onset. Currently, there is no medicine approved for the treatment of this disease. The only therapeutic intervention available to CALD patients is transplantation of stem cells (cells that can develop into different types of blood cells) from a donor. This procedure presents several potential complications and risks which are reduced for those patients who have a matching sibling donor. However, these represent less than 30% of patients with CALD. Therefore, there is an unmet medical need for these patients.

Skysona is made up of immature bone marrow cells that are taken from the patient. The cells are then modified by a virus – a so-called "lentivirus" that has been changed in order not to cause disease in humans – that contains a functional copy of the gene ABCD1 for the ALDP protein, so that this gene is carried into the cells. When these modified cells are given back into the patient by a drip (infusion) into a vein, they are expected to spread through the body and develop into different types of healthy cells, including brain cells, that produce the ALDP protein that patients with CALD lack. As a result, patients should be able to break down the accumulated VLCFA and this will help to reduce the symptoms of the disease.

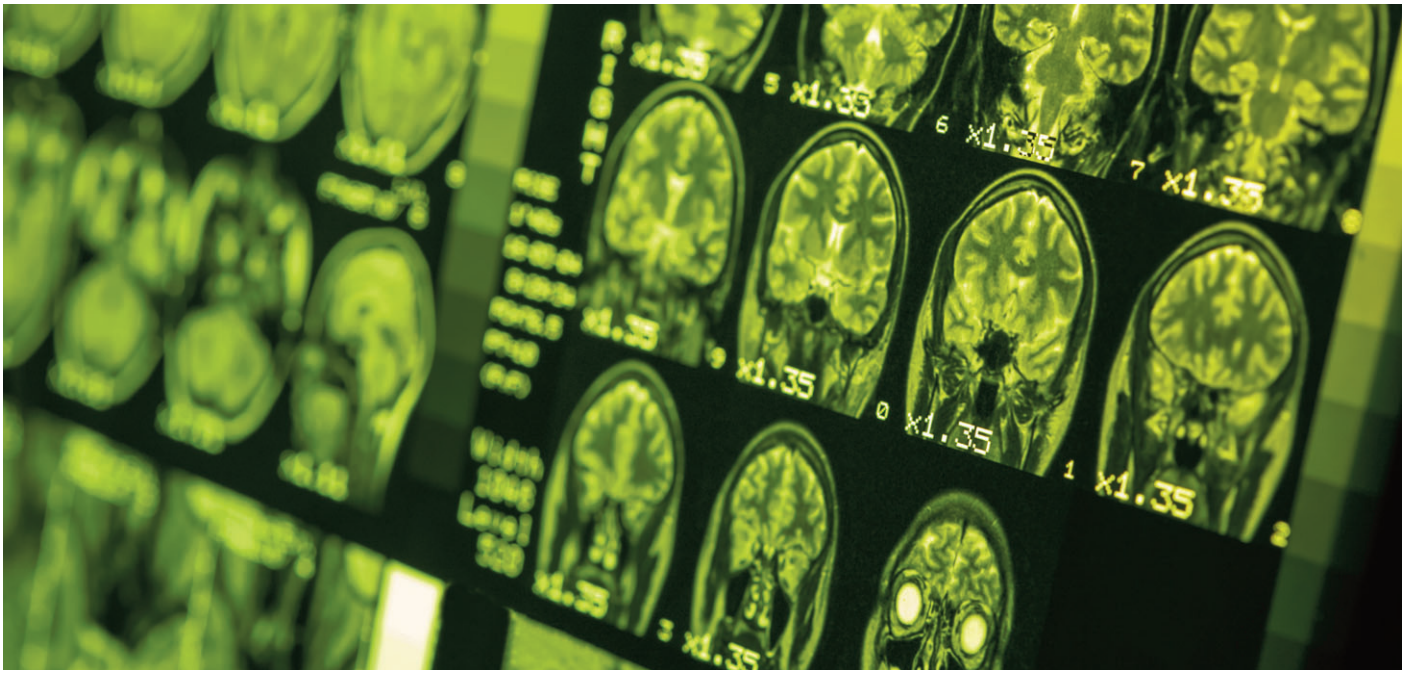
Skysona is a one-time treatment which can only be given in a specialised hospital by doctors who are experienced in treating patients with CALD, transplanting bone marrow, and using gene therapy medicines.

EMA's recommendation for a marketing authorisation is based on evidence from a single-arm clinical trial that enrolled 32 male patients with CALD aged 17 years or younger. The results from this study were compared to those from a study in which 59 patients had a stem cell transplantation (either from a matched sibling donor or a matched non-sibling donor). All the patients in the main clinical trial were enrolled in a long-term follow-up study.

An analysis conducted after 24 months from the infusion on 30 subjects enrolled in the study concluded that for 27 of them (90%) treatment with Skysona preserved motor function and communication ability and improved survival when compared to untreated patients at an early stage of cerebral disease. The most serious adverse reaction in the clinical trials for Skysona was low levels of all types of blood cells (pancytopenia).

Adding a new gene into the stem cells could theoretically cause blood cancers. This was not seen during the clinical trial but after the treatment, patients will be monitored with blood tests to check for any signs of cancer of the blood. Additional long-term efficacy and safety data are being collected through one ongoing study and a long-term registry. All results must be included in post-marketing safety reports, which are continuously reviewed by EMA.

Skysona was designated as an orphan medicinal product on June 6, 2012. Skysona is indicated for the treatment of early cerebral adrenoleukodystrophy in patients less than 18 years of age, with an ABCD1 genetic mutation, and for whom a human leukocyte antigen (HLA) matched sibling haematopoietic stem cell (HSC) donor is not available.



First treatment for rare liver disease

May 21, 2021

EMA has recommended granting a marketing authorisation in the European Union for Bylvay (odevixibat; from Albireo) for the treatment of Progressive Familial Intrahepatic Cholestasis (PFIC) in patients aged 6 months or older. PFIC is a rare, life-threatening liver disease. Patients have liver cells that are less able to secrete bile (a fluid produced in the liver that helps to break down fats). The build-up of bile in liver cells causes liver disease. The symptoms typically develop in infancy, usually in the first months of life. Approximately only half of the children affected by the disease survive beyond the age of 10 years.

Severe itching (pruritus) is common in children diagnosed with PFIC. This can lead to sometimes serious scratching injuries, loss of sleep, irritability, and poor attention. There is a high unmet need for these patients whose treatment options are limited to surgical intervention and off-label symptomatic medical therapies. If untreated, many PFIC patients progress to end-stage liver disease and require liver transplantation.

The active substance of Bylvay is odevixibat, a reversible, potent, selective inhibitor of the ileal bile acid transporter (IBAT) that acts locally in the distal ileum (the last part of the small intestine), reducing the reuptake of bile acids and increasing the clearance of bile acids through the colon.

The main study on which the recommendation by EMA's CHMP is based was a double-blind, randomised, placebo-controlled phase 3 study, which investigated the efficacy and safety of Bylvay in children with PFIC. The results showed a significant reduction in serum bile acids accompanied by a significant reduction in pruritus in patients treated with odevixibat. These results were maintained in an ongoing, long-term open-label follow-up study. Hepatic parameters and fibrosis scores were improving or were stable for the duration of the study (max. 72 weeks). However, more data are needed to determine if odevixibat can delay disease progression and the need for liver transplantation. The CHMP therefore requested a registry-based efficacy study as a follow-up.

The most common side effects are diarrhoea, abdominal pain, haemorrhagic diarrhoea, soft faeces, and hepatomegaly (enlarged liver). No clinically significant differences in the pharmacokinetic, safety and tolerability profile of odevixibat were observed based on age, sex or race.

As PFIC is a very rare disease, the CHMP agreed that it is not possible to provide comprehensive data on the efficacy under normal conditions of use. Therefore, the Committee recommended granting a marketing authorisation under exceptional circumstances and requested the applicant to complete a registry-based study to further characterise the efficacy of Bylvay in patients aged 6 years or older.

A marketing authorisation under exceptional circumstances allows patients access to medicines that cannot be approved using a standard authorisation route as comprehensive data cannot be obtained, either because there are only very few patients with the disease, the collection of complete information on the efficacy and safety of the medicine would be unethical, or there are gaps in the scientific knowledge. These medicines are subject to specific post-authorisation obligations and monitoring.

Bylvay, was designated as an orphan medicinal product on July 17, 2012, for the treatment of Progressive Familial Intrahepatic Cholestasis. On October 13, 2017, the medicine was accepted in EMA's PRIority MEdicines (PRIME) scheme that offers extra support to developers of medicines that have the potential to address patients' unmet medical needs. The CHMP reviewed the application for Bylvay under its accelerated assessment procedure, which allows the speeding up of patients' access to medicines.

First cell-based gene therapy to treat adult patients with multiple myeloma

June 26, 2021

EMA has recommended granting a conditional marketing authorisation in the EU for Abecma (idecabtagene vicleucel; from Celgene Europe BV) for the treatment of adult patients with relapsed and refractory multiple myeloma who have received at least three previous therapies, including an immunomodulatory agent, a proteasome inhibitor, and an anti-CD38 antibody, and whose cancer has worsened since receiving the last treatment.

Multiple myeloma is a rare cancer of a type of white blood cell called plasma cells. Normal plasma cells are found in the bone marrow and are an important part of the immune system. Plasma cells make the antibodies that enable the body to recognise and attack germs such as viruses or bacteria. In multiple myeloma, the proliferation of plasma cells is out of control, resulting in abnormal, immature plasma cells multiplying and filling up the bone marrow. When plasma cells become cancerous, they no longer protect the body from infections and produce abnormal proteins that can cause problems affecting the kidneys, bones, or blood.

Despite the development and approval of a range of new medicines for the treatment of multiple myeloma over the past few years, there are limited therapeutic options for patients who have already received three major classes of drugs (immunomodulatory agents, proteasome inhibitors, and monoclonal antibodies) and no longer respond to these medicines. Therefore, new medicines are needed for patients whose disease returns after treatment.

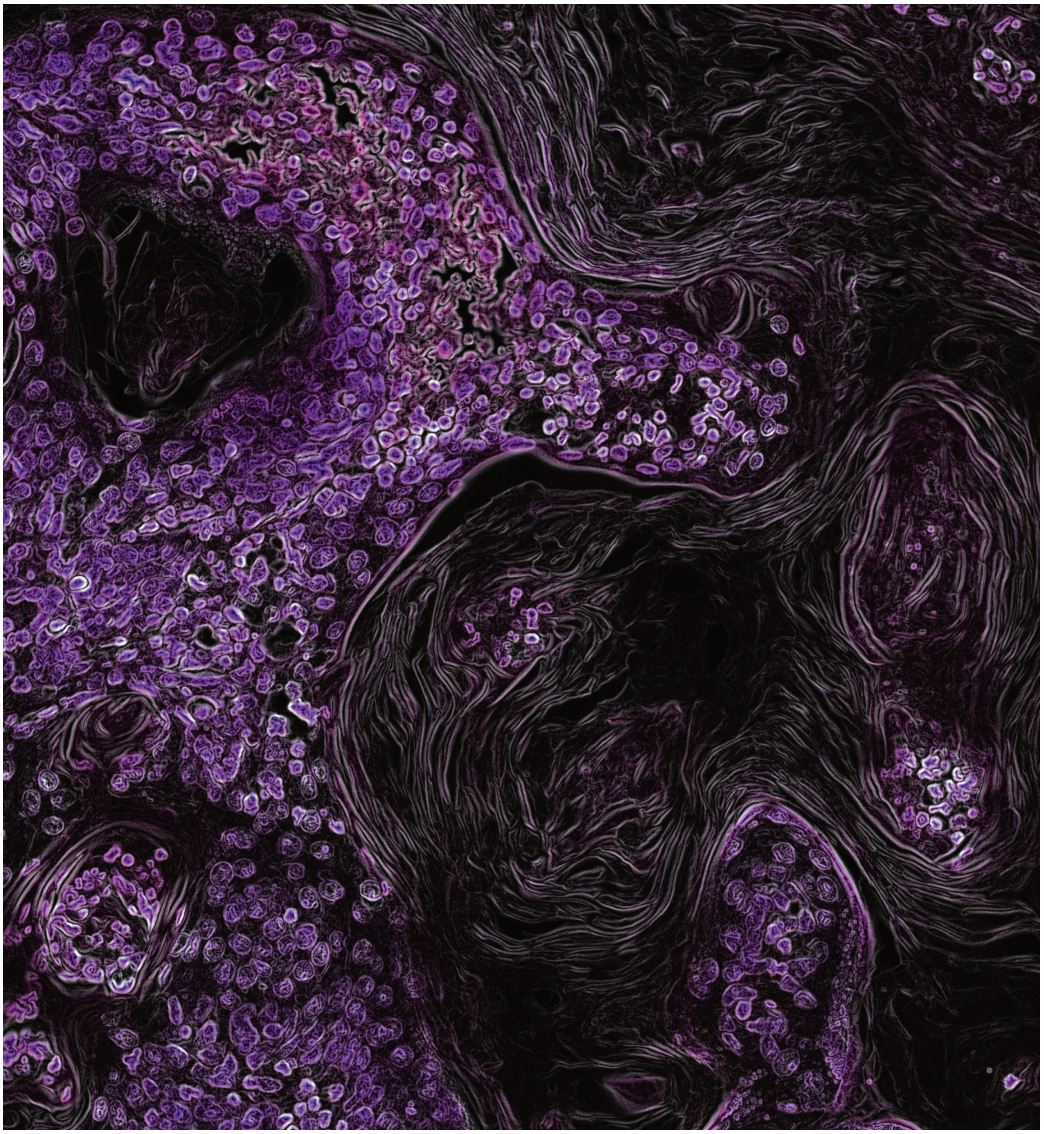


Photo: Eric Snyder / Unsplash.com

Abecma is a genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy and the first cell-based gene therapy to treat adult patients with multiple myeloma. Each dose of Abecma is created by collecting a patient's own T-cells (i.e. white blood cells that help the body fight infections) and genetically modifying them so that they include a new gene that helps the body target and kill the myeloma cells. These modified immune cells are then infused back into the patient's blood.

The main study on which the recommendation for a conditional marketing authorisation is based was a Phase 2, multicentre, open label, single-arm clinical trial. The study investigated the efficacy and safety of Abecma in 140 adult patients with relapsed or refractory multiple myeloma who had received at least three prior therapies, including an immunomodulatory agent, a proteasome inhibitor and an anti-CD38 antibody, and who didn't respond to the last treatment regimen. About 67% of patients enrolled in the study responded to the treatment and maintained remission (a period without disease signs or symptoms after treatment) for about 11 months on average. Of those studied, 30% showed complete response (i.e. disappearance of signs of cancer).

The main safety concerns related to the administration of Abecma are cytokine release syndrome (CRS) (i.e. a condition causing fever, vomiting, shortness of breath, headache, and low blood pressure), neurological toxicity, cytopenias (i.e. low number of cells in the blood) and infections, which can be life-threatening.

Additional efficacy and safety data are being collected through the submission of follow-up data from the main clinical trial and through an ongoing study that will compare the efficacy and safety of the medicine with standard triplet regimens in patients with relapsed and refractory multiple myeloma.

Abecma was designated as an orphan medicinal product on April 20, 2017. Following this positive CHMP opinion, the Committee for Orphan Medicinal Products (COMP) will assess whether the orphan designation should be maintained.

Use of antibiotics in animals is decreasing

June 30, 2021

Use of antibiotics has decreased and is now lower in food-producing animals than in humans, says the latest report published by the European Food Safety Authority (EFSA), the EMA, and the European Centre for Disease Prevention and Control (ECDC).

Making a One Health approach, the report from the three EU agencies presents data on antibiotic consumption and development of antimicrobial resistance (AMR) in Europe for 2016–2018. AMR is a significant global public health problem that represents a serious economic burden.

The significant fall in antibiotic use in food-producing animals suggests that the measures taken at country level to reduce use are proving to be effective. Use of a class of antibiotics called polymyxins, which includes colistin, nearly halved between 2016 and 2018 in food-producing animals. This is a positive development, as polymyxins are also used in hospitals to treat patients infected with multidrug-resistant bacteria.

The picture in the EU is diverse – the situation varies significantly by country and by antibiotic class. For example, aminopenicillins, 3rd- and 4th-generation cephalosporins and quinolones (fluoroquinolones and other quinolones) are used more in humans than in food-producing animals, while polymyxins (colistin) and tetracyclines are used more in food-producing animals than in humans.

The report shows that the use of carbapenems, 3rd- and 4th-generation cephalosporins and quinolones in humans is associated with resistance to these antibiotics in Escherichia coli infections in humans. Similar associations were found for food-producing animals.

The report also identifies links between antimicrobial consumption in animals and AMR in bacteria from food-producing animals, which in turn is associated with AMR in bacteria from humans. An example of this is Campylobacter spp. bacteria, which are found in food producing animals and cause foodborne infections in humans. Experts found an association between resistance in these bacteria in animals and resistance in the same bacteria in humans. The results presented in this report call for continued efforts to tackle AMR at national, EU, and global level across the healthcare sectors.

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