

News from the EMA

SECTION EDITOR



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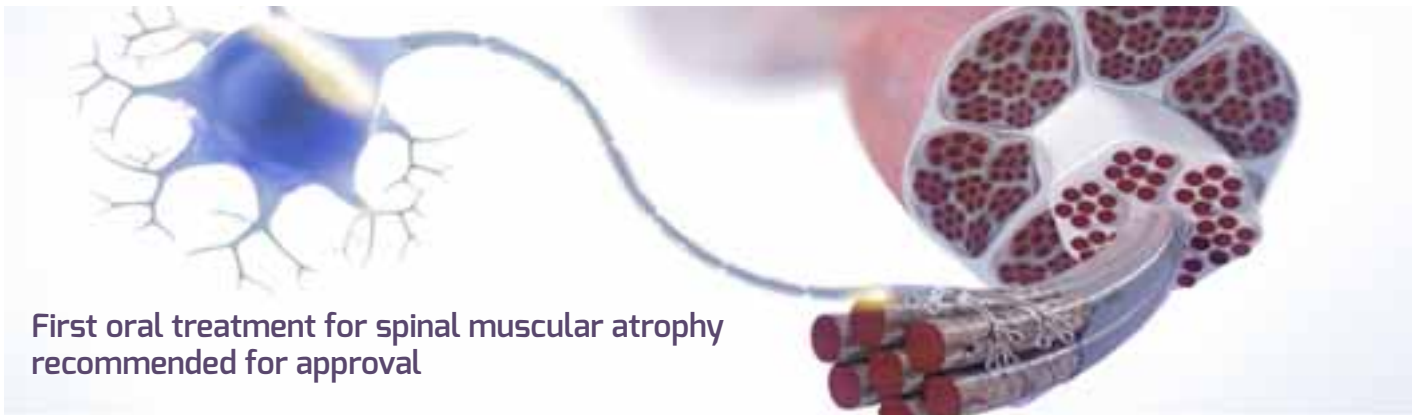


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First oral treatment for spinal muscular atrophy recommended for approval

February 26, 2021 – EMA has recommended granting a marketing authorisation in the European Union (EU) for the first treatment that can be given orally to patients with certain types of spinal muscular atrophy (SMA), a rare and often fatal genetic disease that causes muscle weakness and progressive loss of movement.

Spinal muscular atrophy is an inherited disease usually diagnosed in the first year of life that affects the motor neurons (neurons from the brain and spinal cord that control muscle movements). Patients with the disease lack a protein called 'survival motor neuron' (SMN), which causes the motor neurons to deteriorate and eventually die. This is a long-term debilitating and life-threatening disease because it causes breathing problems and muscle wasting that worsens over time.

The SMN protein can be made by two genes, SMN1 and SMN2. Patients with SMA lack a working SMN1 gene but have at least one copy of the SMN2 gene, which mostly produces a short SMN protein that does not work as well as a full-length protein.

Risdiplam, the active substance of Evrysdi, has shown that it can enable the SMN2 gene to produce a full-length SMN protein, which is able to work normally. This is expected to increase survival of motor neurons and reduce symptoms of the disease. Evrysdi is indicated for the treatment of 5q SMA in patients 2 months of age and older, with a clinical diagnosis of Type 1, Type 2 or Type 3 SMA or with one to four SMN2 copies.

Although a number of treatment options have

become available over recent years, they all require frequent clinic visits or invasive procedures. During the COVID-19 pandemic these treatments have become more difficult to access due to measures to promote physical distancing and changes in hospital priorities that have postponed elective procedures. New therapies with easier routes of administration are needed to help patients with this life-long chronic disease to adhere to their treatment and get the full benefit from it.

Evrysdi has been developed as a non-invasive oral treatment that can be used at home. It was accepted into PRIME, a support scheme EMA developed for promising new medicines that address an unmet medical need. Representatives of patient organisations were also consulted during the assessment of benefits and risks of Evrysdi to bring their unique real-life perspective and ensure that patients' needs are taken into account in the regulatory decision-making process. EMA's human medicines committee (CHMP) reviewed the application for marketing authorisation under an accelerated timetable to enable faster patient access to this medicine.

EMA's recommendation is based on two clinical studies, one investigating the effects of Evrysdi on patients with infantile-onset SMA and the other on later-onset SMA. The results from the trials show beneficial effects in very young patients in terms of their motor development and survival at 12 months, compared to data on the natural course of the disease in these patients. The positive effect in later-onset SMA (Type 2

and 3) has been demonstrated in a double-blind placebo-controlled trial, including patients between 2 and 25 years of age. The main adverse reactions observed in trials were headaches, mouth ulcerations and aphthous ulcers, urinary tract infections including cystitis, arthralgia, nausea, pyrexia, and dizziness/vertigo.

As part of its recommendation for marketing authorisation, the CHMP requested that the company performs a post-authorisation efficacy study (PAES): a long-term prospective, observational study to further evaluate disease progression in SMA patients (both pre-symptomatic and symptomatic) with 1 to 4 SMN2 copies treated with risdiplam, in comparison to natural history data in untreated patients.

As for all medicines, a risk management plan (RMP) will ensure rigorous safety monitoring of the medicine once authorised across the EU. Further efficacy and safety data will be collected through ongoing studies and post-marketing reports and will be regularly reviewed by the CHMP and EMA's safety committee (PRAC).

The opinion adopted by the CHMP is an intermediary step on Evrysdi'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/use of this medicine in the context of the national health system of that country.

EMA advises against use of ivermectin for the prevention or treatment of COVID-19 outside randomised clinical trials

March 22, 2021 – EMA has reviewed the latest evidence on the use of ivermectin for the prevention and treatment of COVID-19 and concluded that the available data do not support its use for COVID-19 outside well-designed clinical trials.

In the EU, ivermectin tablets are approved for treating some parasitic worm infestations while ivermectin skin preparations are approved for treating skin conditions such as rosacea. Ivermectin is also authorised for veterinary use for a wide range of animal species for internal and external parasites.

Following recent media reports and publications on the use of ivermectin, EMA reviewed the latest published evidence from laboratory studies, observational studies, clinical trials, and meta-analyses. Laboratory studies found that ivermectin could block replication of SARS-CoV-2 (the virus that causes COVID-19), but at much higher ivermectin concentrations than those achieved with the currently authorised doses.

Results from clinical studies were varied, with some studies showing no benefit and others reporting a potential benefit. Most studies EMA reviewed were small and had additional limitations, including different dosing regimens and use of concomitant medications. EMA therefore concluded that the currently available evidence is not sufficient to support the use of ivermectin in COVID-19 outside clinical trials.

Although ivermectin is generally well tolerated at doses authorised for other indications, side effects could increase with the much higher doses that would be needed to obtain concentrations of ivermectin in the lungs that are

effective against the virus. Toxicity when ivermectin is used at higher than approved doses therefore cannot be excluded.

EMA therefore concluded that use of ivermectin for prevention or treatment of COVID-19 cannot currently be recommended outside controlled clinical trials. Further well-designed, randomised studies are needed to draw conclusions as to whether the product is effective and safe in the prevention and treatment of COVID-19. This EMA public health statement has been endorsed by the COVID-19 EMA pandemic Task Force (COVID-ETF), in light of the ongoing discussions on the use of ivermectin in the prevention and treatment of COVID-19.



The March 2022 edition

Sustainability is a key focus area across all economic sectors, including the pharmaceutical and healthcare industry.

This issue will focus on where and how scientific and medical writing can contribute to current debates on scientific and environmental problems and their impact on human health. The issue will also cover emerging career opportunities for medical writers in this area.

**Guest Editors:
Surayya Taranum
and Elisa Sala**

Don't miss!

Sustainable Communications

EMA reviewing data on use of monoclonal antibodies for treating COVID-19: casirivimab, imdevimab, bamlanivimab, etesevimab, and regdanvimab

March 5, 11 and 26, 2021 – EMA’s human medicines committee (CHMP) has completed its review of data on the use of the monoclonal antibody to treat patients with COVID-19, namely, regdanvimab (also known as CT-P59) being developed by Celltrion Healthcare, REGN-COV2 monoclonal antibody combination of casirivimab and imdevimab; combination of bamlanivimab and etesevimab which are being developed by Eli Lilly to be used in combination. The reviews were undertaken to provide a harmonised scientific opinion at EU level to support national decision-making on the possible use of these antibodies prior to marketing authorisation.

These five monoclonal antibodies have shown activity against SARS-CoV-2, the virus that causes COVID-19. The antibodies have been designed to attach to the spike protein of SARS-CoV-2, and thereby reduce the ability of the virus to enter the body’s cells. Casirivimab and imdevimab attach to the spike protein of SARS-CoV-2 at two different sites. Similarly, bamlanivimab and etesevimab antibodies also attach to different parts of the spike protein. Using the antibody combinations, REGN-COV2 (casirivimab + imdevimab) or bamlanivimab + etesevimab is

expected to have a greater effect than using a single antibody.

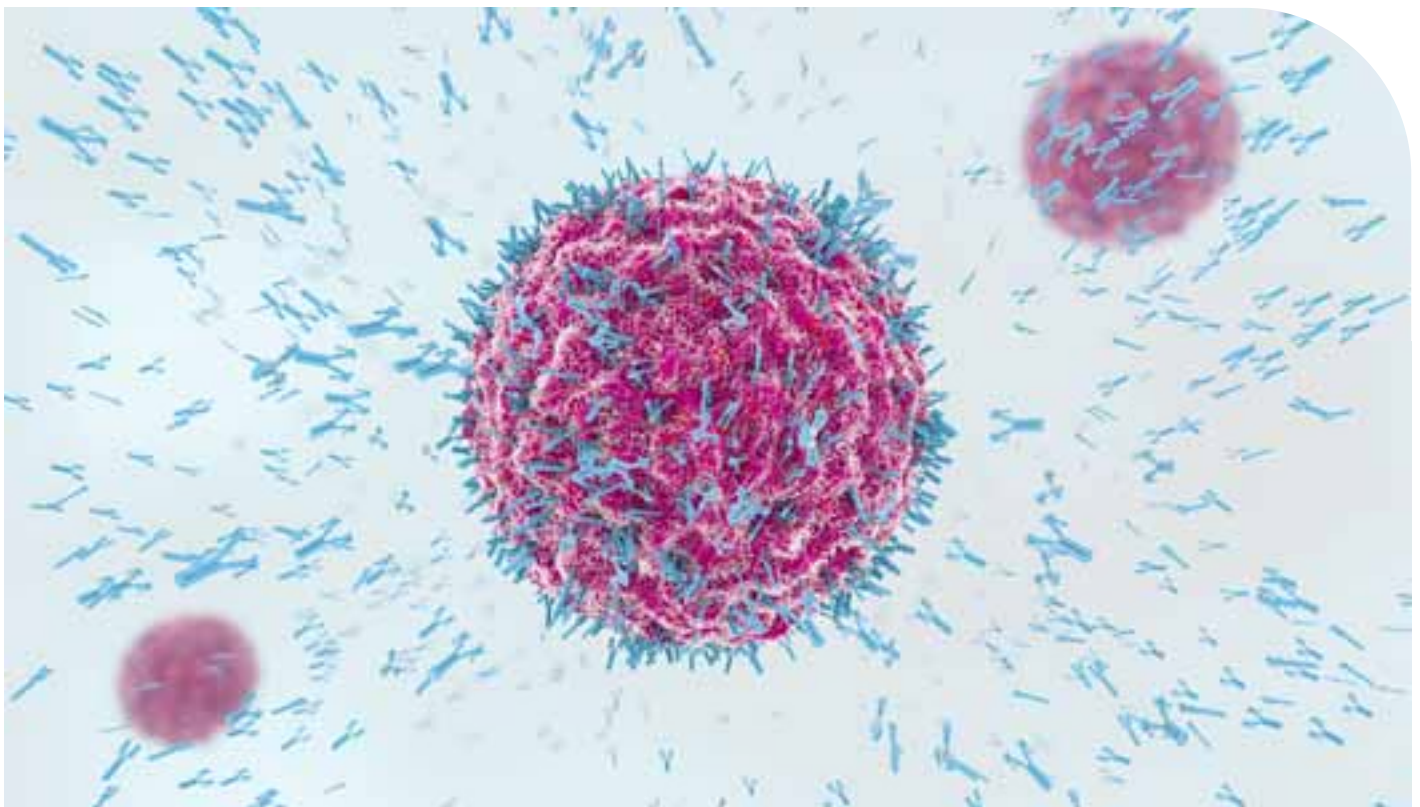
The Agency concluded that the combinations REGN-COV2 and bamlanivimab + etesevimab can be used for the treatment of confirmed COVID-19 in patients who do not require supplemental oxygen and who are at high risk of progressing to severe COVID-19. Preliminary results indicate that the REGN-COV2 combination reduced the viral load (amount of virus in the back of the nose and throat) more than placebo (a dummy treatment) and led to fewer COVID-19-related medical visits. In terms of safety, most side effects reported were mild or moderate, however reactions related to the infusion (including allergic reactions) have been seen and should be monitored for. In case of bamlanivimab + etesevimab EMA has not yet evaluated the full dataset and it is too early to draw any conclusions regarding the benefit-risk balance of the medicines. The Agency also looked at the use of bamlanivimab alone and concluded that, despite uncertainties around the benefits of monotherapy, it can be considered a treatment option.

EMA reviewed data from an ongoing study looking into the effects of regdanvimab in adult

outpatients with COVID-19 symptoms described as mild to moderate who do not need supplemental oxygen. Results from the first part of the study indicate that regdanvimab may lower the rate of hospitalisation. However, the results were not robust enough to reach a firm conclusion on the medicine’s benefits at this time. In terms of safety, most side effects were mild or moderate. The Agency concluded that regdanvimab can be used for the treatment of confirmed COVID-19 in adult patients who do not require supplemental oxygen therapy and who are at high risk of progressing to severe COVID-19.

The Agency has started rolling reviews on these monoclonal antibodies based on the preliminary results.

EMA will evaluate all data on these medicines, including evidence from clinical trials as they become available. The rolling reviews will continue until enough evidence is available to support formal marketing authorisation applications. EMA will assess the medicine’s compliance with the usual standards for effectiveness, safety, and quality. While the overall review timeline cannot be forecast yet, the process should be quicker than a regular evaluation due to the time gained during the rolling review.



AstraZeneca's COVID-19 vaccine: EMA finds possible link to very rare cases of unusual blood clots with low blood platelets; and confirms that overall benefit-risk remains positive

April 07, 2021 – EMA's Pharmacovigilance Risk Assessment Committee (PRAC) has concluded today that unusual blood clots with low blood platelets should be listed as very rare side effects of Vaxzevria (formerly COVID-19 Vaccine AstraZeneca). In reaching its conclusion, the committee took into consideration all currently available evidence, including the advice from an ad hoc expert group.

EMA is reminding healthcare professionals and people receiving the vaccine to remain aware of the possibility of very rare cases of blood clots combined with low levels of blood platelets occurring within 2 weeks of vaccination. So far, most of the cases reported have occurred in women under 60 years of age within 2 weeks of vaccination. Based on the currently available evidence, specific risk factors have not been confirmed.

The PRAC noted that the blood clots occurred in veins in the brain (cerebral venous sinus thrombosis, CVST) and the abdomen (splanchnic vein thrombosis) and in arteries, together with low levels of blood platelets and sometimes bleeding. The Committee carried out an in-depth review of 62 cases of cerebral venous sinus thrombosis and 24 cases of splanchnic



vein thrombosis reported in the EU drug safety database (EudraVigilance) as of March 22, 2021, 18 of which were fatal. The cases came mainly from spontaneous reporting systems of the European Economic Area (EEA) and the UK, where around 25 million people had received the vaccine. As of April 4, 2021, a total of 169 cases of CVST and 53 cases of splanchnic vein thrombosis were reported to EudraVigilance. Around 34 million people had been vaccinated in the EEA and UK by this date.

At present the review has not identified any specific risk factors, such as age, gender or a pre-

vious medical history of clotting disorders, for these very rare events. One plausible explanation for the combination of blood clots and low blood platelets is an immune response, leading to a condition similar to that sometimes seen in patients treated with heparin (heparin induced thrombocytopenia, HIT). The PRAC has requested new studies and amendments to ongoing ones to provide more information and will take any further actions necessary.

The PRAC stresses the importance of prompt specialist medical treatment. By recognising the signs of blood clots and low blood platelets and treating them early, healthcare professionals can help those affected in their recovery and avoid complications.

EMA's scientific assessment underpins the safe and effective use of COVID-19 vaccines. COVID-19 is associated with a risk of hospitalisation and death. The reported combination of blood clots and low blood platelets is very rare, and the overall benefits of the vaccine in preventing COVID-19 outweigh the risks of side effects.

