News from the EMA

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New treatment for adults with acute lymphoblastic leukaemia: Third CAR T-cell therapy for high-mortality cancer

May 23, 2025

EMA has recommended granting a conditional marketing authorisation in the European Union (EU) for Aucatzyl (obecabtagene autoleucel) to treat adults from 26 years of age with relapsed or refractory B-cell precursor acute lymphoblastic leukaemia (B ALL).

Acute lymphoblastic leukaemia (ALL) is a fast-growing and life-threatening cancer that affects the blood and bone marrow, specifically impacting white blood cells (lymphocytes). Relapsed ALL comes back after treatment, and refractory ALL does not respond to initial treatment. Despite multiple available therapeutic options, this condition is associated with significant mortality and a poor survival rate.

Aucatzyl is a genetically modified autologous chimeric antigen receptor (CAR) T-cell therapy, a type of personalised cancer immunotherapy that is based on collecting and modifying the patient's own immune cells to treat their cancer. The modified T cells attach to and kill the cancer cells, thereby helping to clear the cancer from the body.

The recommendation is based on the results of a single arm, open-label trial (FELIX study) in 113 patients. About 64% of patients had a durable response (a period without disease signs or symptoms after treatment) with a median duration of 14 months. Around 49% showed a complete response, meaning the signs of cancer disappeared.

The most common observed side effects include cytokine release syndrome (a potentially life-threatening condition that can cause high fever, vomiting, shortness of breath, pain, and low blood pressure), immune effector cell-associated neurotoxicity syndrome (a condition that includes problems with use of language, seizures, headache, hallucinations, and mental confusion), and infections. Monitoring and mitigation strategies for these side effects are described in the product information and in the risk management plan.

In its overall assessment of the available data, the Committee for Advanced Therapies (CAT), EMA's expert committee for cell- and gene-based medicines, found that the benefits of Aucatzyl outweighed the possible risks in patients with ALL. The Committee for Medicinal Products for Human Use (CHMP), EMA's human medicines committee, agreed with the CAT's assessment and positive opinion, and recommended approval of this medicine.

Aucatzyl was supported through EMA's PRIority MEdicines (PRIME) scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs.

Aucatzyl is recommended for a conditional marketing authorisation. This type of approval allows the Agency to recommend a medicine for marketing authorisation with less complete data than normally expected, if the benefit of a medicine's immediate availability to patients outweighs the risk inherent in the fact that not all the data are yet available. In order to confirm the safety and efficacy of Aucatzyl, the company has been requested to submit long-term follow-up results of the FELIX study, and to conduct a non-interventional study based on a patient registry.

The opinion adopted by the CHMP is an intermediary step on Aucatzyl'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.

Image: Freepik

New guideline on inclusion of pregnant and breastfeeding individuals in clinical trials

June 4, 2025

EMA has released for public consultation a new guideline[1] providing recommendations on how to include and/or retain pregnant and breastfeeding people in clinical trials. The goal is to ensure developers generate robust clinical data in those populations, so that these individuals and their healthcare providers can make informed, evidence-based decisions when using medicines.

This guideline, developed jointly by global regulators and medicines developers through the International Council for Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH), marks a change in paradigm in the development of medicines in pregnancy and breastfeeding. It highlights that in principle, including pregnant and breastfeeding people in clinical trials should be considered for all medicines intended for people who can potentially give birth to children. It lays out the principles and conditions that should be met to ensure the safety of clinical trial participants, as well as their foetuses and babies.

Currently, pregnant and breastfeeding people are often excluded from clinical trials and those who become pregnant while participating in a clinical trial are frequently discontinued from the clinical trial. Less than 0.4% of all clinical trials currently submitted in the EU include pregnant people, and this falls to 0,1% regarding lactating individuals, according to data from the Clinical Trials Information System (CTIS).

As a result, product leaflets usually lack details about the benefits and risks of a medicine specifically in pregnancy and breastfeeding, requiring patients and healthcare professionals to make treatment decisions without this essential information. This can lead to suboptimal treatment decisions and potential harm. Meanwhile, the vast majority of pregnant people take medications, for example because of chronic diseases, infections, or pregnancy complications. The situation is similar in breastfeeding populations.

The guideline outlines the scientific and regulatory principles, as well as ethical considerations, for the inclusion of pregnant and breastfeeding individuals in clinical trials, both pre- and post-authorisation. It encourages proactive planning and early consultation of medicine developers with regulatory authorities to ensure the safety and efficacy of treatments during pregnancy and breastfeeding.

The guideline was open for consultation until September 15, 2025.

Reference

1. ICH E21 Guideline on inclusion of pregnant and breastfeeding individuals in clinical trials – Scientific guideline. Available from: https://www.ema.europa.eu/en/ich-e21-guideline-inclusion-pregnant-breastfeeding-individuals-clinical-trials-scientific-guideline

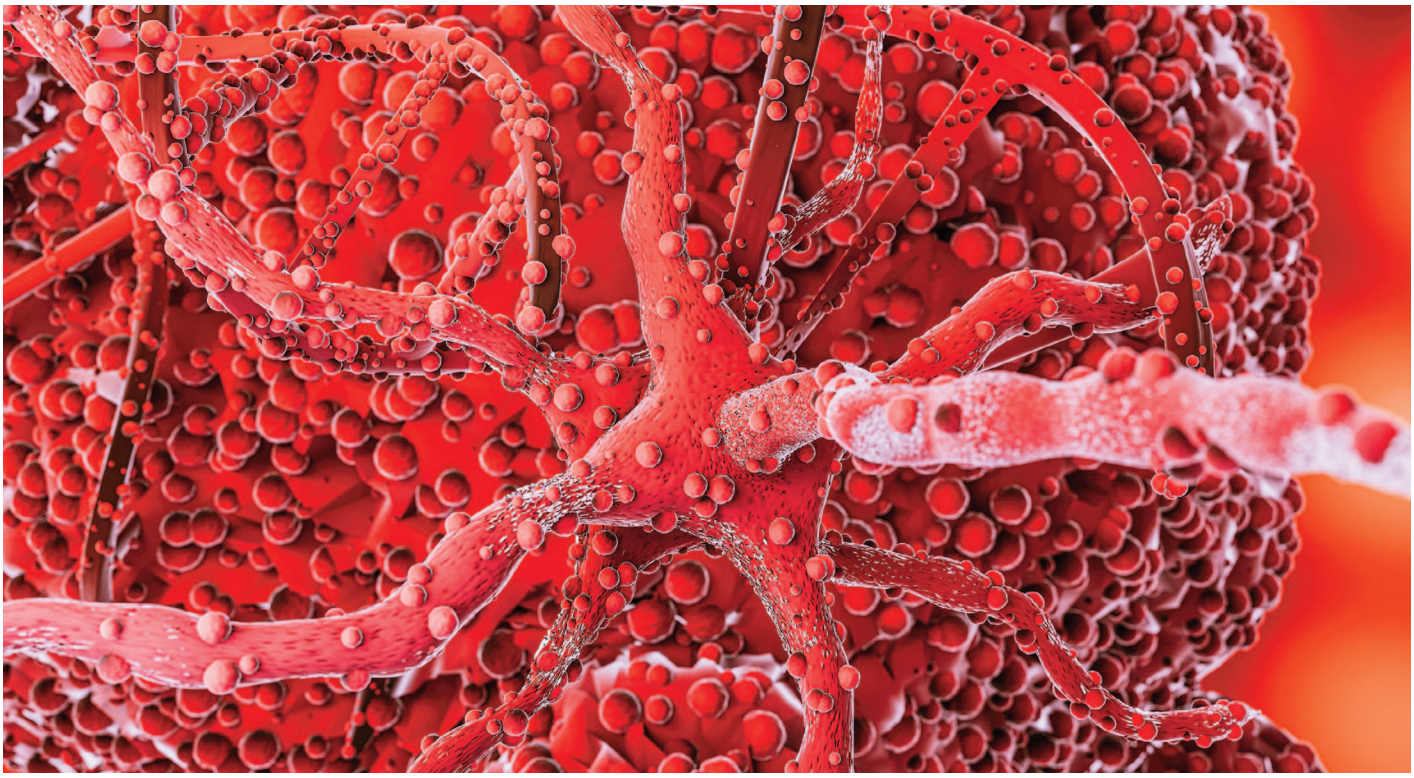

Image: Freepik

New stem cell therapy to treat patients with blood cancers

June 20, 2025

EMA has recommended granting a conditional marketing authorisation in the EU for Zemcelpro (dorocubicel/unexpanded umbilical cord cells) to treat adults with haematological malignancies (blood cell cancers). Zemcelpro can be used in patients requiring an allogeneic haematopoietic stem cell transplantation (allo-HSCT, transplantation of stems cell from a donor) following myeloablative conditioning (chemotherapy and/or radiotherapy) for whom no other type of suitable donor cells is available.

Haematological malignancies categorised depending on where they are first detected and include leukaemias (blood), lymphomas (lymph nodes), myelodysplastic syndrome and myelomas (bone marrow). They are frequently diagnosed cancers, and the only potential curative treatment option for several of these cancers is allo-HSCT. This type of transplant involves using donated stem cells to replace the recipient's bone marrow cells to form new bone marrow that produces healthy blood cells.

Stem cells used for transplantation are preferentially sourced from a matched donor, including a matched sibling or a matched unrelated donor. Umbilical cord blood cells can be used in patients who lack access to any type of suitable donor. However, the number of stem cells in umbilical cord blood is often low and can delay engraftment, the successful establishment and proliferation of the donor stem cells in the recipient's bone marrow.

Zemcelpro is a cell therapy containing stem cells from a donor's umbilical cord blood, some of which have been grown and multiplied (dorocubicel). By increasing the number of cells, Zemcelpro makes the stem cells from a small cord blood unit more effective.

The recommendation is largely based on a pooled analysis of two single arm, open-label studies which included 25 patients. In total, 21/25 (84%) patients achieved neutrophil engraftment (when donor stem cells successfully establish themselves in the recipient's bone marrow and produce neutrophils, a type of white blood cell) within a median time of 20 days, and 17 (68%) patients achieved platelet engraftment within a median time of 40 days.

The most common side effects observed in a wider pool of 116 patients treated with Zemcelpro include low levels of various types of blood cells and of antibodies that help fight infections, high blood pressure, infections, and engraftment syndrome, an inflammatory condition that can occur after HSCT. Acute graft-versus-host disease (GvHD), when donor/transplanted cells attack the body shortly after a transplant) up to 100 days after transplantation was reported in 60% of patients, and chronic GvHD appearing up to one year after transplantation was reported in 13% of patients. Monitoring and mitigation strategies for these side effects are described in the product information and in the risk management plan.

In its overall assessment of the available data, the CAT, EMA's expert committee for cell- and gene-based medicines, found that the benefits of Zemcelpro outweighed the possible risks in patients with haematological malignancies requiring allo-HSCT for whom no matched donor cells are available. The CHMP, EMA's human medicines committee, agreed with the CAT's assessment and positive opinion, and recommended approval of this medicine.

Zemcelpro was supported through EMA's PRIME scheme, which provides early and enhanced scientific and regulatory support to medicines that have a particular potential to address patients' unmet medical needs. Zemcelpro is recommended for a conditional marketing authorisation. In order to confirm the safety and efficacy of Zemcelpro, the company has been requested to submit long-term follow-up results of the single arm studies, conduct a randomised controlled study and a study based on a patient registry.

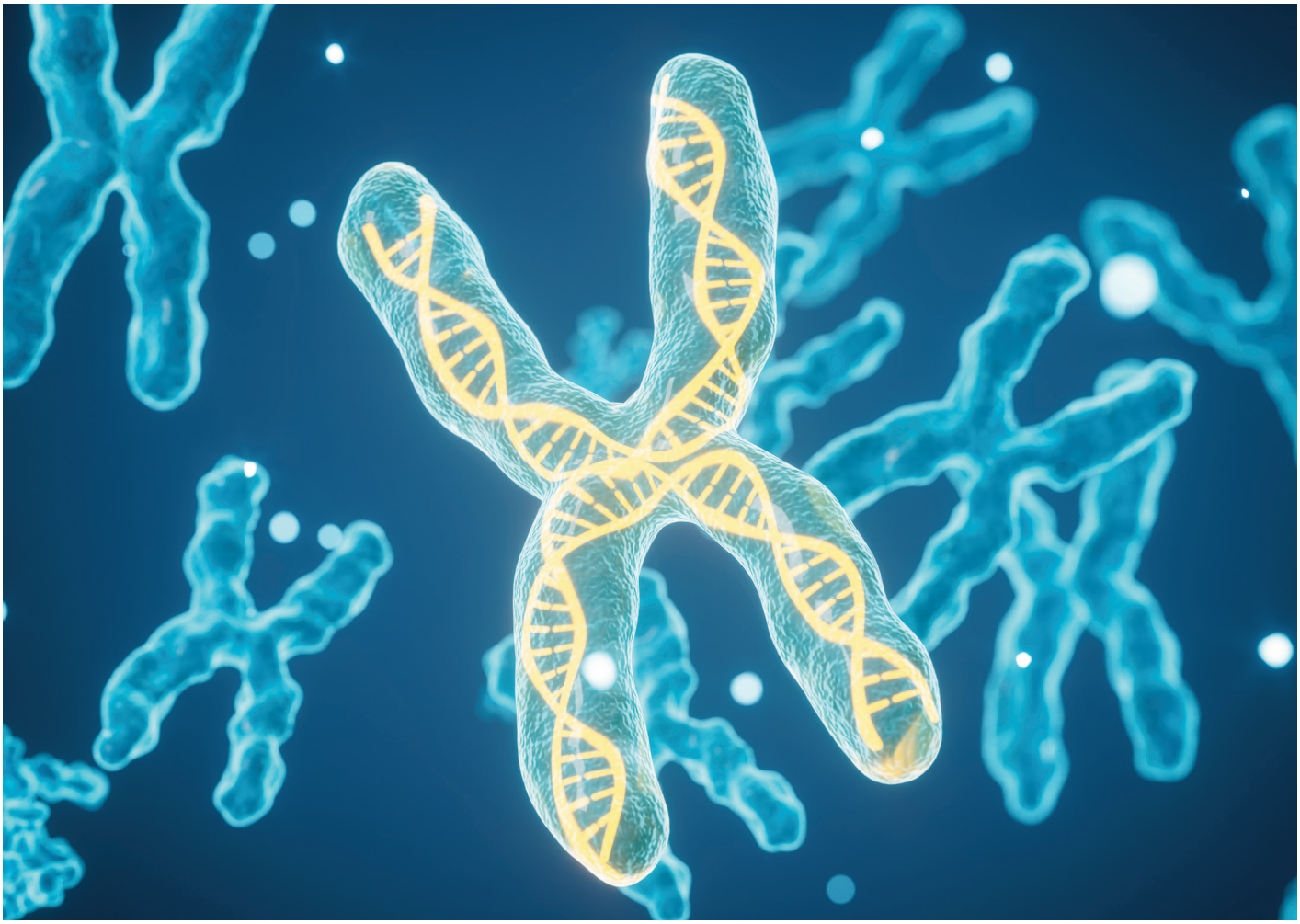

Image: Freepik

Strengthening supply chain of anti-D immunoglobulins

July 4, 2025

FMA and the Heads of Medicines Agencies (HMA), through the Executive Steering Group on Shortages and Safety of Medicinal Products (MSSG), have issued recommendations to address vulnerabilities in the supply chain of anti-D immunoglobulins.

These medicines are currently the only available treatment for the prevention of RhD immunisation during pregnancy. RhD immunisation happens when a pregnant person with RhD-negative blood type is exposed to RhD-positive blood from their foetus. This can lead to an immune reaction that can seriously impact the health of the foetus, and later of the newborn, and have potentially fatal outcomes.

Plasma, the liquid part of blood, collected from donors and containing the anti-D immunoglobulin is currently the only source for manufacturing these medicines. The numbers of donors are declining, and anti-D immunoglobulins are only produced in a limited number of countries, all located outside the EU. For this reason, the MSSG has been monitoring the supply chain of these medicines and has issued these recommendations to national regulators, the European Commission, as well as to the plasma industry and relevant research organisations, to support actions to strengthen their availability and prevent serious shortages.

EU Member States are recommended to create plans to secure the supply of anti-D immunoglobulins in the EU, guided by relevant safety, legal, ethical and regulatory aspects. These plans should also focus on reducing unnecessary use, for example through non-invasive pre-natal screening. Countries should support development and validation of alternatives to these medicines through research and funding and create prioritisation guidelines to manage shortages. In addition, they should implement communication campaigns to increase awareness of plasma collection for the development of plasma-derived medicinal products, such as anti-D immunoglobulins.

The European Commission is encouraged to identify measures to ensure supply continuity of these medicines and support and coordinate Member States' activities. Policy measures set out in the proposed Critical Medicines Act could be leveraged, such as joint procurement of manufacturing services to establish or increase supply of these medicines to the EU.

Finally, industry should ensure the adequate supply of anti-D immunoglobulins in Europe, including through investments in optimising manufacturing capacity and developing alternatives to plasma-derived anti-D immunoglobulins.

Anti-D immunoglobulins are included in the Union list of critical medicines; therefore, a stable supply of these medicines is considered vital for the functioning of EU health systems and the wellbeing of its citizens. While the recommendations address the anti-D immunoglobulin supply chain, the principles are also applicable to address vulnerabilities in the supply chain of other plasma-derived medicines.

Image: Freepik

New injection for easier prevention of HIV infection in the EU and worldwide

July 25, 2025

EMA has recommended granting a marketing authorisation in the EU for Yeytuo (lenacapavir) for pre-exposure prophylaxis (PrEP) in combination with safer sex practices to reduce the risk of sexually acquired human immunodeficiency virus type 1 (HIV-1) infection in adults and adolescents at high risk of becoming infected. PrEP is a cornerstone of HIV-control efforts in Europe and worldwide and is very effective at preventing infections if taken as prescribed. However, uptake and adherence are often suboptimal because access to some medicines is limited, and other available medicines require strict daily intake. Yeytuo will facilitate PrEP uptake and compliance because it only has to be administered twice a year via a subcutaneous injection. Of note, two tablets of Yeytuo on the first two days are required when starting the treatment, after which the medicine is given by injection every six months.

HIV-1 infection is of major public health significance. According to the WHO, in 2024 an estimated 1.3 million people became newly infected with HIV globally, including 160,000 new HIV infections in the European region and 650,000 in Africa, the region most affected by HIV.

HIV-1 impacts the body's immune system, particularly white blood cells that are important in helping to fight infections. If left untreated, HIV-1 infection can progress to acquired immune deficiency syndrome (AIDS), where the immune system is severely damaged, making the body vulnerable to opportunistic infections and some cancer types. Sexual intercourse is the most common mode of transmission of HIV-1.

Yeytuo contains lenacapavir, a first-in-class substance that binds to the proteins that make up the outer layer of HIV-1 (the capsid). By binding to these proteins, lenacapavir interferes with multiple steps in the HIV-1 lifecycle, thereby inhibiting viral replication, ultimately preventing HIV-1 infection.

CHMP's recommendation is based on the results of two randomised, double-blind, active-controlled, multinational trials. In the PURPOSE 1 trial, cisgender women, including pregnant and lactating women, between the age of 16 and 24 who have sex with cisgender males, were randomised in a 2:1 ratio to receive Yeytuo (n=2134) or Truvada (n=1068). At the time of the primary analysis, no new HIV-1 infections were observed in the Yeytuo group compared to 16 in the Truvada group.

In the PURPOSE 2 trial, men and gender-diverse persons from 16 years old who have sex with male partners, were randomised in a 2:1 ratio to receive Yeytuo (n=2179) or Truvada (n=1086). At the time of the primary analysis, two new HIV-1 infections were observed in the Yeytuo group compared to nine in the Truvada group. In both studies, participants who received Yeytuo showed higher adherence to their treatment than participants who received Truvada.

The most common side effects observed were injection site reactions, including pain and hard lumps (injection site nodules) that can persist for a long time or not disappear.

Yeytuo was evaluated by the CHMP, EMA's human medicine committee, under an accelerated timetable because it is considered to be of major public health interest in the EU and the rest of the world. The CHMP simultaneously reviewed the medicine for the EU market, under the centralised procedure, and for non-EU countries, under the 'EU-Medicines for all' (EU-M4all) programme in collaboration with the WHO and the target countries. The CHMP scientific opinion under the EU-M4all procedure supports global regulatory capacity building and contributes to the protection and promotion of public health beyond the EU.

Image: Freepik

First reformulation of an inhaled medicine with environmentally friendly gas propellant

Jul 25, 2025

EMA has recommended a change in the composition of Trixeo Aerosphere and its duplicate product Riltrava Aerosphere to replace the existing gas propellant with a low global warming potential (GWP) gas alternative. The new low GWP alternative propellant has a 1000-fold reduction in global warming potential and similar physical properties compared to the current propellant.

Trixeo Aerosphere and Riltrava Aerosphere are the first inhaled medicines in the EU that have a gas propellant with low GWP. They are used for maintenance treatment in a subset of adults with moderate-to-severe chronic obstructive pulmonary disease (COPD) and are administered as two inhalations twice daily using a metered dose inhaler (MDI).

A critical component of the formulation of an MDI is the propellant (liquified compressed gas) that generates an aerosol cloud containing the small particles of active pharmaceutical ingredients that are then inhaled by the patient.

High GWP gases, including hydrofluorocarbon gases such as the propellants used in pressurised MDIs treating respiratory diseases, are being phased out for environmental reasons in line with the current EU Regulation on fluorinated greenhouse gases (EU Regulation 2024/573), and applicable legislation in other regulatory constituencies. The marketing authorisation holder for Trixeo/Riltrava Aerosphere investigated replacement options for the current propellant, with a focus on a lower GWP propellant that could maintain the same performance properties for the medicinal product.

The reformulated Trixeo/Riltrava Aerosphere with the same active ingredients and dose has been characterised in line with the principles outlined in the draft Guideline on the requirements for demonstrating therapeutic equivalence between orally inhaled products for asthma and COPD and is therapeutically equivalent (i.e., works the same way and gives the same results in the lungs and the body) to the product currently on the market. Studies have confirmed that the safety and efficacy of the reformulated medicine are equivalent to those of the currently approved product.

The opinion will now be sent to the European Commission for the adoption of a decision on the variation to the marketing authorisation.