Novartis receives third FDA approval for oral Fabhalta® (iptacopan) - the first and only treatment approved in C3 glomerulopathy (C3G)

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- *Phase III study showed sustained proteinuria reduction at one year with favorable safety*[1]
- *Fabhalta is the only oral alternative complement pathway inhibitor thought to target the underlying cause of C3G*[1-3]
- *C3G is an ultra-rare kidney disease typically diagnosed in young adults and often progresses to kidney failure*[2-4]
- *Novartis continues to advance multiple kidney disease treatments with high unmet need, compounding capabilities and strengthening unique leadership presence*

EAST HANOVER, N.J., March 20, 2025 -- Novartis today announced that oral Fabhalta® (iptacopan) has received U.S. Food and Drug Administration (FDA) approval for the treatment of adults with C3 glomerulopathy (C3G), to reduce proteinuria, making it the first and only treatment approved for this condition[1-4].

"C3G is a debilitating disease often affecting young people, impacting many aspects of their physical and emotional health, and our previous treatment options came with significant challenges," said Carla Nester, M.D., M.S.A., F.A.S.N., Professor of Pediatrics-Nephrology at the University of Iowa and Fabhalta APPEAR-C3G Study Co-Investigator. "This approval of Fabhalta is historic for the entire C3G community as now, for the first time, we have a therapy that is believed to treat the underlying cause of the disease, providing the potential for a new standard of care for patients."

Fabhalta is the only oral inhibitor of the alternative complement pathway to selectively target what is thought to be the underlying cause of the disease[1-3]. Before the approval of Fabhalta, patients had to rely on supportive care, broad immunosuppression, and symptom management[5-6].

"As someone whose family has suffered from C3G across multiple generations, it is difficult to fully express the physical and emotional challenges of living with this unrelenting disease," said Lindsey Fuller, C3G patient and Co-Leader of C3G Warriors. "To finally have an approved treatment – and one that can be taken orally – is something people with C3G have been waiting for. Today's approval brings new hope for me, my family, and so many others."

C3G is a progressive and ultra-rare kidney disease that, until now, has had no approved treatments[2-5]. The average age of diagnosis is around 23 years old[2]. Prognosis is poor, with approximately half of people living with C3G progressing to kidney failure within 10 years of diagnosis, requiring lifelong dialysis and/or kidney transplantation[2,7]. People living with C3G may experience high levels of fatigue, mobility issues affecting everyday life activities, and mental health symptoms, including depression and anxiety[8,9].

Data supporting approval

The pivotal Phase III APPEAR-C3G study evaluated the efficacy and safety of twice-daily oral Fabhalta in adult patients with C3G[1,10]. The study was comprised of a 6-month randomized, double-blind treatment period with Fabhalta compared to placebo in addition to supportive care, followed by an additional 6-month open-label treatment period where all participants received Fabhalta[1,10].

Treatment with Fabhalta resulted in clinically meaningful proteinuria reduction, which was seen as early as 14 days and sustained at 12 months[1,10]. Similarly, in the open-label period, proteinuria reduction was seen in participants who switched to Fabhalta[1,10].

Fabhalta demonstrated a favorable safety profile, with no new safety signals[1]. In patients with C3G, the most common adverse reactions (≥10%) with Fabhalta were nasopharyngitis and viral infections[1]. Fabhalta may cause serious infections caused by encapsulated bacteria and is available only through a Risk Evaluation and Mitigation Strategy (REMS) that requires specific vaccinations[1].

Last month, Fabhalta received a positive CHMP Opinion in C3G by the European Medicines Agency (EMA)[11]. Regulatory reviews for this indication are ongoing in China and Japan.

Transforming care in kidney disease

"We extend our deepest gratitude to the patients and investigators who participated in our clinical trials, without whom this first FDA approval in C3G wouldn't have been possible," said Victor Bultó, President US, Novartis. "With this additional approval for Fabhalta – the second in kidney disease – we will leverage our established capabilities and expertise to bring this innovative treatment to patients in need as we work to help transform care for people living with kidney diseases."

This is the third US approval for Fabhalta and its second within the Novartis kidney disease portfolio since August 2024, when Fabhalta was granted accelerated approval by the FDA for the reduction of proteinuria in adults with primary immunoglobulin A nephropathy (IgAN) at risk of rapid disease progression. Continued approval for this indication is contingent upon confirmatory evidence[1]. Fabhalta received its first FDA approval in December 2023 for the treatment of adults with paroxysmal nocturnal hemoglobinuria (PNH)[1]. Discovered by Novartis, Fabhalta is also being studied in a broad range of other rare kidney diseases, including atypical hemolytic uremic syndrome (aHUS), immune complex membranoproliferative glomerulonephritis (IC-MPGN) and lupus nephritis (LN). Studies are ongoing to evaluate the safety and efficacy profiles in these investigational indications.

In addition to Fabhalta, Novartis is advancing the late-stage development of two additional IgAN therapies with highly differentiated mechanisms of action: atrasentan, an investigational oral endothelin A receptor antagonist that received FDA filing acceptance in Q2 2024 with a decision anticipated in H1 2025, and zigakibart, an investigational subcutaneously administered anti-APRIL monoclonal antibody that is currently in Phase III development.

About APPEAR-C3G

APPEAR-C3G (NCT04817618) is a Phase III multicenter, randomized, double-blind, parallel group, placebo-controlled study to evaluate the efficacy and safety of twice-daily oral Fabhalta (200 mg) in patients with native kidney C3G[1,12]. The study comprises a 6-month double-blind period in which adult patients were randomized 1:1 to receive Fabhalta or placebo on top of supportive care, followed by a 6-month open-label period in which all patients receive Fabhalta (including those who were previously on placebo)[1,12]. The primary endpoint for the double-blind period was proteinuria reduction from baseline at 6 months for Fabhalta compared to placebo as measured by 24-hour urine protein-creatinine ratio (UPCR)[1,12]. In addition to the results from adult patients with C3G, enrollment is ongoing in a separate cohort of adolescent patients with C3G[12].

About C3 glomerulopathy (C3G)

Each year, approximately 1-2 people per million worldwide are newly diagnosed with C3G, a form of membranoproliferative glomerulonephritis (MPGN)[3].

In C3G, overactivation of the alternative complement pathway – part of the immune system – causes deposits of C3 protein to build up in kidney glomeruli, which are a network of blood vessels that filter waste and remove extra fluids from the blood[4,13]. This triggers inflammation and glomerular damage that results in proteinuria (protein in urine), hematuria (blood in urine) and reduced kidney function[4,14].

Indication
FABHALTA is a prescription medicine used to treat adults with a kidney disease called complement 3 glomerulopathy (C3G), to reduce protein in the urine (proteinuria).

It is not known if FABHALTA is safe and effective in children with C3G.

Important Safety Information
FABHALTA is a medicine that affects part of the immune system and may lower one's ability to fight infections. FABHALTA increases the chance of getting serious infections caused by encapsulated bacteria, including Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae type b. These serious infections may quickly become life-threatening or fatal if not recognized and treated early. Patients must complete or update vaccinations against Streptococcus pneumoniae and Neisseria meningitidis at least 2 weeks before the first dose of FABHALTA. If patients have not completed vaccinations and FABHALTA must be started right away, they should receive the required vaccinations as soon as possible. If patients have not been vaccinated and FABHALTA must be started right away, they should also receive antibiotics to take for as long as their health care provider tells them. If patients have been vaccinated against these bacteria in the past, they might need additional vaccinations before starting FABHALTA. Their health care provider will decide if they need additional vaccinations. Vaccines do not prevent all infections caused by encapsulated bacteria. Patients should call their health care provider or get emergency medical care right away if they have any of these signs and symptoms of a serious infection: fever with or without shivers or chills; fever with chest pain and cough; fever with high heart rate; headache and fever; confusion; clammy skin; fever and rash; fever with breathlessness or fast breathing; headache with nausea or vomiting; headache with stiff neck or stiff back; body aches with flu-like symptoms; or eyes sensitive to light. Health care providers will give their patients a Patient Safety Card about the risk of serious infections. Patients must carry it with them at all times during treatment and for 2 weeks after the last dose of FABHALTA. The risk of serious infections may continue for a few weeks after their last dose of FABHALTA. It is important for patients to show this card to any health care provider who treats them. This will help health care providers diagnose and treat patients quickly.

FABHALTA is only available through a program called the FABHALTA Risk Evaluation and Mitigation Strategy (REMS). Before patients can take FABHALTA, their health care provider must enroll in the FABHALTA REMS program, counsel their patients about the risk of serious infections caused by certain bacteria, give their patients information about the symptoms of serious infections, make sure that their patients are vaccinated against serious infections caused by encapsulated bacteria and that they receive antibiotics if they need to start FABHALTA right away and are not up-to-date on vaccinations, as well as give patients a Patient Safety Card about the risk of serious infections.

Patients should not take FABHALTA if they are allergic to FABHALTA or any of the ingredients in FABHALTA. Patients should not take FABHALTA if they have a serious infection caused by encapsulated bacteria, including Streptococcus pneumoniae, Neisseria meningitidis, or Haemophilus influenzae type b, when starting FABHALTA.

Before taking FABHALTA, patients should tell their health care provider about all their medical conditions, including if they have an infection or fever, have liver problems, are pregnant or plan to become pregnant (it is not known if FABHALTA will harm an unborn baby), or are breastfeeding or plan to breastfeed as it is not known if FABHALTA passes into breast milk. Patients should not breastfeed during treatment and for 5 days after the final

dose of FABHALTA.

Patients should tell their health care provider about all the medicines they take, including prescription and over-the-counter medicines, vitamins, and herbal supplements. Taking FABHALTA with certain other medicines may affect the way FABHALTA works and may cause side effects. Patients should know the medicines they take and the vaccines they receive. Patients should keep a list of them to show their health care provider and pharmacist when they get a new medicine.

FABHALTA may cause serious side effects, including those mentioned above as well as increased cholesterol and triglyceride (lipid) levels in the blood. Health care providers will do blood tests to check patients' cholesterol and triglycerides during treatment with FABHALTA. Health care providers may start patients on medicine to lower cholesterol if needed.

The most common side effects of FABHALTA in adults include: headache; nasal congestion, runny nose, cough, sneezing, and sore throat (nasopharyngitis); diarrhea; pain in the stomach (abdomen); infections (bacterial and viral); nausea; and rash.

Please see full Prescribing Information, including Boxed WARNING and Medication Guide.

Novartis in kidney disease
Building on a 40-year legacy that began in transplant, Novartis is on a mission to empower breakthroughs and transform care in kidney health, starting with kidney conditions that have significant unmet need. Historically these conditions have had considerably less funding and research, leading to a treatment landscape largely focused on reactive or end-stage disease management, often with significant physical, emotional, and financial burdens. Our pipeline targets the underlying causes of disease, with an aim to protect kidney health and delay or prevent dialysis and/or transplantation. Our goal is to help patients get back to living life on their terms—whether at work, in school, or with loved ones, and by partnering with patients, advocates, clinicians, and policymakers we aim to raise awareness, accelerate diagnosis and get patients the right care, sooner.

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About Novartis

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