Drug & Poison Information Center Bulletin
Faculty of Pharmacy - Tanta University

SEPTEMBER, 2025 | Volume 12, Issue 3

Inside this issue:

FDA expands treatment options for hereditary angioedema

Hereditary angioedema (HAE) is an autosomal dominant disease caused by low levels of the plasma protein C1 inhibitor (C1-INH). A deficiency in C1-INH allow unchecked activation of the classic complement pathway and other biochemical systems, including the bradykinin system. Patients may present with any combination of painless, nonpruritic, nonpitting swelling of the skin (cutaneous angioedema), severe abdominal pain, or acute airway obstruction.

In June and July 2025, the U.S. Food and Drug Administration (FDA) approved two medications for hereditary angioedema. **Andembry** (active ingredient: garadacimab-gxii), developed by CSL Behring GmbH, was approved for the prevention of hereditary angioedema attacks. **Ekterly** (active ingredient: sebetralstat), produced by KalVista Pharmaceuticals, received approval for the treatment of acute hereditary angioedema attacks.

1-Andembry

It is an activated Factor XII (FXIIa) inhibitor (monoclonal antibody). It is a fully human recombinant monoclonal antibody (IgG4/λ-light chain) produced in Chinese hamster ovary (CHO) cells.

Mechanism of action: It binds to the catalytic domain of activated Factor XII (FXIIa and βFXIIa) and inhibits its catalytic activity. FXII is the first factor activated in the contact activation pathway and initiates the inflammatory bradykinin-producing kallikrein-kinin system.

The inhibition of FXIIa decreases the activation of prekallikrein to kallikrein and the generation of bradykinin, which is associated with inflammation and swelling in HAE attacks.

Dosage form: Andembry is formulated as an injection in a prefilled autoinjector or prefilled syringe for subcutaneous use.

Indicated use: It is indicated for preventing HAE attacks (prophylaxis) in adult and pediatric patients aged 12 years and older.

Recommended dose: The recommended dosage of Andembry is an initial loading dose of 400 mg (two injections of 200 mg) administered subcutaneously on the first day of treatment, followed by a maintenance dosage of 200 mg administered subcutaneously once monthly.

Reported adverse effects : Andembry's most common adverse reactions (incidence ≥7%) are nasopharyngitis and abdominal pain.

2-Ekterly

Ekterly is a competitive and reversible inhibitor of plasma kallikrein, a serine protease that cleaves high molecular weight kininogen (HK) to release bradykinin. Bradykinin increases vascular permeability by activating its receptors, leading to edema.

Mechanism of action: It blocks the cleavage of HK, lowering bradykinin levels and relieving acute HAE symptoms. Sebetralstat also disrupts the kallikrein-kinin system's positive feedback, reducing the production of F XIIa and plasma kallikrein.

Dosage form: It is supplied as 300 mg film-coated tablets for oral administration.

Indicated use: Ekterly is indicated for the treatment of acute attacks of HAE in adult and pediatric patients aged 12 years and older.

Recommended dose:

- One dose of 600 mg (two tablets) orally at the earliest recognition of an acute HAE attack.
- A second dose of 600 mg (two tablets) may be taken at least 3 hours after the first dose if the response is inadequate, or if symptoms worsen or recur.
- The maximum recommended dosage is 1,200 mg (four tablets) in any 24 hours.

Reported adverse effects: Ekterly's most common adverse reaction is headache (incidence ≥ 2%).

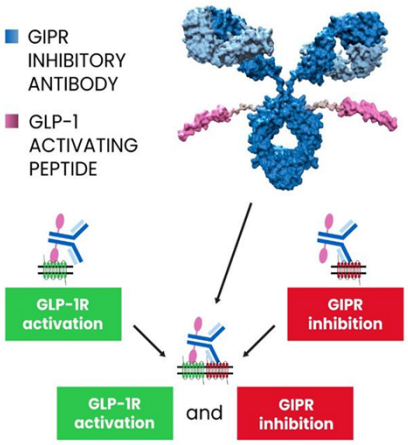
References:

- FDA 2025 Novel Drug Approvals. Available at: https://www.fda.gov/drugs/novel-drug-approvals-fda/novel-drug-approvals-2025. Accessed in July, 2025.
- Hereditary Angioedema Medscape Monograph. Available at: https://emedicine.medscape.com/article/135604-overview#a1. Accessed in July, 2025.
- Andembry FDA Label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/761367s000lbl.pdf. Accessed in July, 2025.
- Ekterly FDA Label. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2025/219301s000lbl.pdf. Accessed in July, 2025.

Ph. Amr M. Nowier. B.Sc.

A new GLP-1 agonist is coming
MariTide: Revolutionizing obesity treatment

MariTide, known chemically as maridebart cafraglutide, represents a novel and promising approach in the pharmacological treatment of obesity and metabolic disorders. This investigational drug is unique in its dual mechanism, exhibiting both glucagon-like peptide-1 (GLP-1) receptor agonism and glucose-dependent insulinotropic polypeptide receptor (GIPR) antagonism, which distinguishes it markedly from traditional GLP-1 receptor agonists (GLP-1RAs), or dual GLP-1 and GIP agonists (Tirzepatide)



Mechanism of Action and Pharmacology

Maridebart cafraglutide functions by simultaneously activating the GLP-1 receptor and blocking the GIP receptor. GLP-1 is an incretin hormone that, physiologically, is secreted from enteroendocrine L cells in the distal intestine, exerting multifaceted effects including stimulation of glucose-dependent insulin secretion, inhibition of glucagon release, slowing of gastric emptying, and reduction of appetite and food intake. The traditional GLP-1 receptor agonists replicate these effects, improving glycemic control and inducing weight loss in patients with type 2 diabetes or obesity. Maridebart cafraglutide enhances this mechanism by incorporating antagonism of the GIP receptor, which is normally activated by GIP, another incretin promoting insulin secretion and fat storage. By blocking GIP receptors, maridebart simultaneously reduces the adipogenic effects associated with GIP signaling. This dual action GLP-1 receptor activation coupled with GIP receptor blockade results in synergistic benefits for weight reduction and metabolic regulation that surpass what is achievable by GLP-1 receptor agonism alone.

Pharmacologically, maridebart is a bispecific molecule, engineered by conjugating a fully human monoclonal antibody against human GIPR to two GLP-1 agonist peptides, creating a long-acting peptide–antibody conjugate. This structure enables sustained receptor activity and prolonged therapeutic effects, suitable for once-monthly administration.

Comparison with tirzepatide (Mounjaro):

Tirzepatide works by activating both GIP and GLP-1 hormone receptors. While maridebart cafraglutide primarily activates GLP-1 and blocks GIP activity. Clinical trials for maridebart cafraglutide have shown significant weight loss and improvements in blood sugar levels, with the potential for less frequent dosing compared to tirzepatide.

Comparison with previous GLP-1 receptor agonists: Benefits and advantages

Conventional GLP-1 receptor agonists, such as liraglutide, exenatide, and semaglutide, mimic the natural GLP-1 hormone's effects, enhancing glucose-dependent insulin secretion, suppressing glucagon, and reducing appetite. However, their pharmacokinetic profiles involve frequent dosing schedules ranging from daily to weekly injections due to their shorter half-lives compared to antibody conjugates like maridebart.

While traditional GLP-1RAs improve blood sugar and cause moderate weight loss, maridebart shows superior efficacy, achieving up to 20% weight loss in a year surpassing semaglutide's 15%. This effect is sustained without plateau, highlighting long-term benefit. Its dual action GLP-1 agonism with GIP antagonism enhances insulin sensitivity, reduces fat accumulation signals, and improves metabolic profiles. This mechanism also contributes to better tolerability and greater efficacy than GLP-1 monotherapy.

Maridebart offers a major convenience advantage with its once-monthly dosing, reducing patient burden and potentially improving adherence in chronic conditions like obesity and type 2 diabetes. Unlike traditional GLP-1 analogues that require frequent injections and titration, Maridebart simplifies treatment without sacrificing efficacy. Preliminary data also indicate a favorable safety profile with possible enhancement of cardiovascular and metabolic benefits.

References:

- Jastreboff AM, Ryan DH, Bays HE, et al. Once-monthly maridebart cafraglutide for the treatment of obesity - A Phase 2 Trial. N Engl J Med. 2025. doi:10.1056/NEJMoa2504214.
- Véniant MM, Lu SC, Atangan L, et al. A GIPR antagonist conjugated to GLP-1 analogues promotes weight loss with improved metabolic parameters in preclinical and phase 1 settings. Nat Metab. 2024;6(2):290-303. doi:10.1038/s42255-023-00966-w
- Maridebart cafraglutide - Amgen. Available at: https://adis.springer.com/drugs/800059636. Accessed in July, 2025.

Refresh your knowledge..

Creatine supplement in adolescent: Innocent or guilty?

Creatine is a naturally occurring compound synthesized in the liver, kidneys, and pancreas and stored predominantly in skeletal muscle as phosphocreatine, where it supports rapid ATP regeneration during high-intensity activities. It is also present in dietary sources such as red meat and seafood. Creatine supplementation is popular among athletes for its performance-enhancing potential, but its use in adolescents remains controversial due to limited long-term safety data.

Potential benefits :

1. Increased muscle mass and strength: Supplementation increases intramuscular creatine and phosphocreatine stores, enhancing muscle mass and strength gains, especially when combined with resistance training. Studies in youth athletes (mainly soccer players and swimmers) have reported improvements in lean body mass and power output.
2. Improved exercise performance: Creatine has been shown to improve anaerobic capacity, sprint performance, and repeated high-intensity effort in sports requiring short bursts of maximal exertion.
3. Potential therapeutic applications: Beyond sports, creatine is being studied for possible roles in rehabilitation, certain neuromuscular disorders, and neuroprotection, although these applications are experimental and not standard for adolescent athletes.
4. Emerging cognitive and health effects: Novel studies suggest creatine may benefit cognitive function under stress conditions such as sleep deprivation, and possibly support bone health, mood regulation, and healthy aging. However, evidence in adolescents is minimal, and more research is needed to establish these potential effects.

Recommendations:

- Consult Healthcare Professionals: Adolescents and guardians should seek medical advice before starting creatine supplementation.
- Prioritize Healthy Lifestyle: A balanced diet, structured training, adequate rest, and hydration remain the foundations of performance and health.
- Evaluate Risks vs. Benefits: Any potential ergogenic benefits must be weighed against uncertainties regarding long-term effects.

Conclusion:

Creatine supplementation in adolescents is a nuanced issue. Evidence supports potential benefits in muscle performance and recovery, but limited adolescent-specific safety data means caution is warranted. Current expert consensus leans toward reserving creatine use for older teens engaged in competitive sports, under professional supervision, and only after optimizing diet and training. A cautious, individualized approach that prioritizes healthy lifestyle habits is generally recommended over routine supplementation.

References:

- Kreider RB, Jagim AR, Antonio J, et al. Creatine supplementation is safe, beneficial throughout the lifespan, and should not be restricted. Front Nutr. 2025;12:1578564.
- Metzger GA, Minneci PM, Gehred A, Day A, Klingele KE. Creatine supplements and the youth athlete a literature review. J Orthop. 2023;38:73-78.
- Kreider RB, Kalman DS, Antonio J, et al. International Society of Sports Nutrition position stand: safety and efficacy of creatine supplementation in exercise, sport, and medicine. J Int Soc Sports Nutr. 2017;14:18.
- Rae C, Digney AL, McEwan SR, Bates TC. Oral creatine monohydrate supplementation improves brain performance: a double–blind, placebo-controlled, cross-over trial. Proc R Soc Lond B Biol Sci. 2003;270(1529):2147-2150.
- Forbes SC, Candow DG, Ostojic SM, Roberts MD, Chilibeck PD. Meta-analysis examining the importance of creatine ingestion strategies on muscle mass and strength in older adults. Nutrients. 2021;13(6):1912.

Bassant M. Mahboub, M.Sc., PhD. Cand. and Ph. Nahla Eldeep. B.Sc.

Contact us

Facebook: Drug and Poison Information Center-Faculty of Pharmacy-Tanta University

Hotline: 090071020

Phone: 040/3331577-3336007

Email: Tanta_DPIC@pharm.tanta.edu.eg

We are on the web

https://pha.tanta.edu.eg/units/Drug%20Information/Default.aspx

Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

Editorial board members: