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PEDIANEWS

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OUR MISSION

The Student Society of Pediatric Advocates (SSPA) is a student organization affiliated with the University of Georgia College of Pharmacy. We are a student group associated with the Pediatric Pharmacy Association (PPA). The Mission of the SSPA is to bring awareness to the proper use of medication therapy in pediatric populations through various service and education- based initiatives. Service activities center around lending our medication- based knowledge to pediatric patients and their parents in our community. Educational activities are directed toward student members in an effort to safely and effectively extend pharmacy practice to pediatric populations by building relationships with mentors and professionals in the health care community, as well as supplementing didactic coursework with lectures by specialists and our peers. Overall, SSPA advocates for the safety and happiness of young patients while learning and having fun along the way. The purpose of our newsletter is to educate pharmacy students about pediatric pharmacy and advocate for pediatric patients within the University of Georgia College of Pharmacy.

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INSIDE THIS ISSUE

Enflonsia In Focus: New Developments In RSV Prevention

Written by Karsin Bass, PharmD Candidate 2027

Respiratory syncytial virus, or RSV, is a common respiratory virus with rates peaking in the winter months. In adults, RSV usually causes mild cold-like symptoms such as runny nose, cough, sore throat, and congestion. In infants, however, this virus poses a much greater threat. Their immature immune system prevents them from mounting an effective response, and their developing respiratory systems have a higher baseline oxygen demand and a smaller anatomic size, making them more susceptible to and less tolerant of respiratory compromise.[1] Since RSV is the leading cause of bronchiolitis and pneumonia in children under the age of five, it is important to provide our most vulnerable patients with protection against severe RSV infection.[1] For infants, this protection is offered through a maternal vaccination given at 32 to 36 weeks gestation (Abrysvo®) or a monoclonal antibody therapy given directly to the infant upon entry to their first RSV season.[2] Historically, palivizumab (Synagis®) was the only monoclonal antibody therapy on the market for the prevention of severe RSV infection in infants. However, in 2023, a new agent was approved - nirsevimab (Beyfortus®). In comparison to palivizumab, nirsevimab provided a longer duration of protection (5 months), eliminating the need for monthly injections required by palivizumab.[3] More recently, in June of 2025, the newest RSV monoclonal antibody clesrovimab-cfor (Enflonsia®) was approved by the FDA, providing another option for protection.[2]

Similar to nirsevimab, clesrovimab is a human immunoglobulin G1 kappa monoclonal antibody that acts as an RSV F protein-directed fusion inhibitor. It provides passive protection for an estimated 5 months, thus providing sustained protection for the typical duration of RSV season with just a single administration.[4,5]

Results of clesrovimab's single phase 2b/3 randomized, double-blind, placebo-controlled trial, which was conducted in infants entering their first RSV season, demonstrated a 60% reduction in medically attended lower respiratory tract infections and an 84% reduction in RSV-associated hospitalizations. In addition, the safety profile was similar to those who received the placebo, with irritability and somnolence being the most prevalent.[2]

After FDA approval, the Advisory Committee on Immunization Practices (ACIP) and the American Academy of Pediatrics (AAP) both officially recommended clesrovimab as an additional long-acting monoclonal antibody alongside nirsevimab for the prevention of severe RSV infection in infants. Both agents are FDA approved and recommended for infants who are less than 8 months of age upon entering into RSV season and whose mother did not receive the RSV vaccine, received the RSV vaccine ≤14 days prior to birth since the mother will likely not have developed an adequate amount of antibodies yet, or whose RSV vaccination is unknown.[2] Nirsevimab, however, has also been studied in high-risk infants, such as those with chronic lung disease requiring medical support or who are severely immunocompromised, entering their second RSV season and carries that additional recommendation.[6] Compared

to nirsevimab, clesrovimab has the same mechanism of action, estimated length of protection, and route of administration. Both agents should be administered through an intramuscular injection preferably in the anterolateral aspect of the thigh. The gluteal muscle should be avoided as an injection site due to risk of sciatic nerve damage. Clesrovimab, though, is dosed at 105 mg regardless of patient size, whereas nirsevimab requires different dosing depending on the infant's weight.[4] Per the Center for Disease Control and Prevention (CDC), as of October 1, 2025, both Beyfortus® and Enflonsia® cost roughly $556 per pre-filled syringe.[7]

Overall, the approval of clesrovimab introduces another option for prevention of RSV infection in infants entering their first RSV season. Since there are no head-to-head trials comparing the two, it cannot be said if either clesrovimab or nirsevimab is superior. Therefore, the ACIP and AAP show no preference between the two agents, with both listed as first line options.[6] The addition of clesrovimab as an FDA approved RSV preventative therapy, though, helps ensure RSV prevention is more available to all infants in which such therapy is indicated.

References

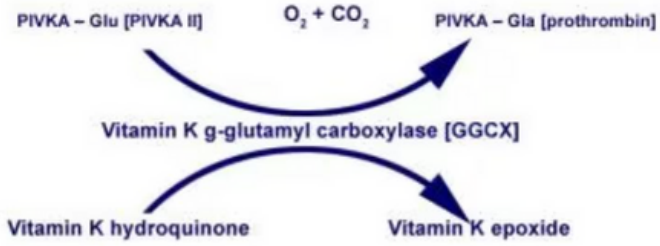
1. Centers for Disease Control and Prevention. (n.d.-b). *About RSV*. Centers for Disease Control and Prevention. https://www.cdc.gov/rsv/about/index.html
2. Moulia, D. L., Link-Gelles, R., Chu, H. Y., Jamieson, D., Brooks, O., Meyer, S., Weintraub, E. S., Shay, D. K., Prill, M. M., Thomas, E. S., Hutton, D., Ortega-Sanchez, I. R., MacNeil, A., McMorrow, M. L., & Jones, J. M. (2025). Use of clesrovimab for prevention of severe respiratory syncytial virus–associated lower respiratory tract infections in infants: Recommendations of the Advisory Committee on Immunization Practices — United States, 2025. *MMWR. Morbidity and Mortality Weekly Report*, *74*(32), 508–514. https://doi.org/10.15585/mmwr.mm7432a3
3. The beginning of a new era in RSV Control | Pediatrics | American Academy of Pediatrics. (n.d.-d). https://publications.aap.org/pediatrics/article/152/5/e2023063817/193904/The-Beginning-of-a-New-Era-in-RSV-Control
4. UpToDate Inc. (2025). Clesrovimab [Drug information]. Lexi-Drugs, UpToDate Lexidrug. Retrieved October 3, 2025, from http://online.lexi.com
5. UpToDate Inc. (2025). Nirsevimab [Drug information]. Lexi-Drugs, UpToDate Lexidrug. Retrieved October 3, 2025, from http://online.lexi.com
6. *RSV Immunization frequently asked questions*. Home. (n.d.-a). https://www.aap.org/en/patient-care/respiratory-syncytial-virus-rsv-prevention/rsv-frequently-asked-questions/?srsltid=AfmBOookS8Xl9uUzZ2KARSLGsixyldRHL1mm0CrSQ1Ea3wU5e-6Hsnhq
7. Centers for Disease Control and Prevention. (n.d.-c). *Current CDC vaccine price list*. Centers for Disease Control and Prevention. https://www.cdc.gov/vaccines-for-children/php/awardees/current-cdc-vaccine-price-list.html

Vitamin K Prophylaxis in Newborns

Written by Melina Kelley, PharmD Candidates 2027

Vitamin K plays a significant role in blood clotting. It is needed for the synthesis of a number of coagulation factors such as factors II, VII, IX, and X, and thus a deficiency in vitamin K may potentially result in severe bleeding.[1] Without a sufficient amount of vitamin K, even small cuts or bruises can bleed uncontrollably. Figure 1 displays a graphic on how the vitamin K cycle works. Vitamin K is converted to and from its active form to maintain normal coagulation. A lack of vitamin K can lead to ineffective prothrombin activation which impairs formation of blood clots.[2] Generally, vitamin K is absorbed from the gastrointestinal tract secondary to production by gastrointestinal bacteria or through consumption of foods rich in vitamin K, such as leafy greens, berries, cruciferous greens, and soybeans. Babies are born with little vitamin K in their system as it does not cross the placenta. Additionally, due to an underdeveloped liver, a sterile gastrointestinal environment, and the presence of only limited amounts in breastmilk, vitamin K levels remain low for several weeks after birth – until the baby establishes its own gastrointestinal microbiota. As such, in the neonatal period, babies are naturally vitamin K deficient, which can lead to hemorrhagic disease of the newborn (HDN), a complication characterized by bleeding into the brain.[3]

Figure 1. Vitamin K Cycle



Hemorrhagic disease of the newborn (HDN) can occur in three ways, the first being early HDN, which happens in the first 24 hours. If the mother is taking anticonvulsants or being treated with antituberculosis medications, the risk of early onset is increased. Although this can happen, prenatal vitamin K isn't recommended because of how these drugs affect the metabolism of vitamin K. Classic HDN presents within 2–7 days in infants who didn't receive vitamin K prophylaxis. Illness or delayed feeding can also be risk factors. Late onset HDN can arise between 7 days and 6 months in infants who also didn't get prophylaxis. Intracranial hemorrhages are seen in over half of these infants.[3] Studies show that a single IM injection of vitamin K shortly after birth can lower clinical bleeding in the first week of life. Additionally, while oral vitamin K trials have not specifically looked at the rate of clinical bleeding, they have evaluated other indicators of coagulation which were shown to be improved, suggesting that both formulations have clinical benefit in the setting of HDN prevention. Although there have been no specific trials comparing oral vitamin K to IM vitamin K, the two regimens can be evaluated through national epidemiological surveillance. There isn't much difference as long as oral therapy is completed.[1] Ultimately, it was decided by the American Academy of Pediatrics (AAP), that all newborn babies should receive a one-time IM dose of vitamin K within six hours of their birth. IM administration is preferred per the AAP as, compared to oral administration, it is more consistently absorbed, provides more reliable and sufficient amounts of vitamin K, and requires only one dose as opposed to multiple. Additionally, in the United States,

there is not an FDA approved oral vitamin K formulation available for neonates that provides the appropriate amount of vitamin K. When receiving one intramuscular injection, more supplementation is not generally needed, therefore making IM injections the recommended route.[4] For newborns weighing less than 1,500 grams, recommended dosing is 0.3–0.5 mg/kg IM once, and for newborns more than 1,500 grams, the dosing should be 1 mg IM. Both weight classes should be administered the injection within 6 hours of their birth.[5]

Parents have a say in making the decision on whether their baby receives vitamin K prophylaxis, so pharmacists should be prepared to help educate on this topic. Prophylaxis has been safely and effectively administered for decades and is the best chance at decreasing the risk of hemorrhagic disease of the newborn.[3] Adverse effects are minimal, with the most common being soreness around the injection site. To help ease the pain, recommendations include skin to skin contact, administration of glucose, or breastfeeding.[1] It is paramount that healthcare providers, including pharmacists, discuss with the new parents and encourage the use of prophylactic vitamin K in order to greatly reduce the risk of bleeding.

References

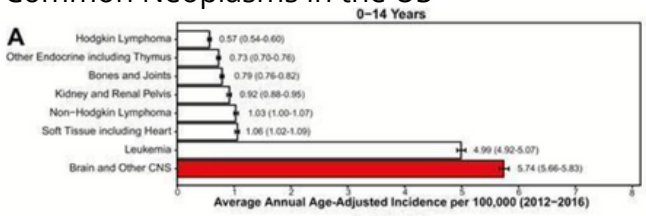
1. Jullien S. Vitamin K prophylaxis in newborns.
2. Nimavat M FAAP Dharmendra J. Vitamin K Deficiency Bleeding (VKDB) in Neonates and Infants: Background, Pathophysiology, Etiology. Medscape. Accessed October 27, 2025. https://emedicine.medscape.com/article/974489-overview?form=fpf
3. Vitamin K and newborn babies. Better Health Channel. Accessed April 6, 2025. https://www.betterhealth.vic.gov.au/health/healthyliving/vitamin-k-and-newborn-babies
4. CDC. Babies are born with very small amounts of vitamin K. Centers for Disease Control and Prevention. April 4, 2023. Accessed April 6, 2025. https://www.cdc.gov/breastfeeding/breastfeeding-special-circumstances/diet-and-micronutrients/vitamin-k.html
5. Hand I, Noble L, Abrams SA. Vitamin K and the newborn infant. Pediatrics. 2022;149(3). doi:10.1542/peds.2021-056036

FDA Approval of Dordaviprone for Diffuse Midline Glioma Treatment in Children

Written by Cassidy Terry, PharmD Candidate 2027

Central nervous system cancers account for some of the most devastating diagnoses in medicine, with children bearing an especially heavy burden from aggressive tumors. As indicated by Figure 1, brain and other central nervous system (CNS) cancers have a strikingly high incidence rate among pediatric patients 0-14 years of age.[1] One such CNS cancer is diffuse midline glioma, a type of malignant central nervous system (CNS) tumor that arises within the middle structures of the brain and accounts for approximately 75% of brain stem tumors in pediatric patients.[1] The prognosis is poor, with a median overall survival of less than 12 months and a 90% mortality rate within 2 years of diagnosis.[2] This excessive mortality risk is thought to be associated with the tumor's anatomic location and overall nature. While diffuse midline gliomas most commonly form in the thalamus, spinal cord, cerebellum, or pons of the brainstem, they spread quickly through cerebrospinal fluid to other areas of the central nervous system. The diffuse nature of these tumors, combined with the inadvertent protection from exposure to systemic therapies received from an intact blood brain barrier, poses significant challenges for treatment.[2] Surgical resection is not a reliable option due to the location of the tumors, and despite the use of radiation, prognosis continues to remain poor.

Figure 1. Average Age Adjusted Incidence of Common Neoplasms in the US[1]



Recent studies have discovered the presence of a specific mutation in the histone H3 gene, known as H3-K27M, which is present in approximately 80% of pediatric diffuse midline gliomas.[3] This mutation results in the substitution of lysine with methionine at position 27, a site crucial for epigenetic regulation of gene expression, and has been associated with significantly shorter overall survival compared to tumors lacking the mutation.[4] This hallmark mutation has therefore become an important treatment target and is a key focus of ongoing therapeutic development and targeted intervention approaches.

At this time, only one targeted therapy has been FDA approved for patients with progressive, H3-K27M associated diffuse midline glioma. Dordaviprone, marketed under the trade name Modeyso, is an orally administered small molecule that exerts anti-tumor effects through a variety of mechanisms.[5] Its small, lipophilic structure allows it to cross the blood brain barrier and accumulate in brain tissues, including brain tumors. It belongs to the imipridone class, a class of anti-cancer compounds that act as agonists to caseinolytic peptidase P, a mitochondrial protease.[5] Hyperactivation of caseinolytic peptidase P causes disruption in mitochondrial function, leading to mitochondrial stress and ultimately apoptosis of tumor cells. H3-K27M-mutant tumors are additionally characterized by epigenetic dysregulation and high levels of baseline oncogenic stress.[3] Dordaviprone amplifies this vulnerability by activating the Integrated Stress Response (ISR), a cellular pathway that responds to proteotoxic and metabolic stress

within cells by upregulating transcription factors, such as ATF4 and CHOP, that promote cell cycle arrest and tumor cell death.[5] Finally, dordaviprone selectively antagonizes dopamine D2 receptors, which are often overexpressed in H3-K27M mutated cells and promote cell proliferation – such antagonism reduces tumor cell expansion and overall proliferation. By disrupting mitochondrial function, inducing integrated stress responses, and antagonizing dopamine receptor D2 regulated cell proliferation, dordaviprone selectively disrupts several key survival pathways in K27M-mutant cells, making it an especially promising therapy for this aggressive tumor subtype.

In August 2025, the FDA granted accelerated approval for the use of dordaviprone, the first H3-K27M targeted therapy, in adults and pediatric patients aged 1 year old or greater with progressive H3-K27M-mutant diffuse midline glioma after prior therapy.[6] This decision was based on an analysis of five open-labeled, non-randomized clinical trials conducted in the United States that pooled a population of 50 adult and pediatric patients.[6] Baseline demographics included patients with an age range of 9-70 years old, with 6% of the population being younger than 17 years of age.[7] Patients included in this analysis had to meet the following criteria: 90 days post radiation therapy, conclusion of a washout period from prior anticancer therapies, and on stable or decreasing corticosteroid use.[6] Included patients also had to have a Karmofsky Performance Status/Lansky Performance Status (KPS/LPS) score of 60 or greater, meaning that they had to be at least partially independent and capable of performing most daily activities with minimal assistance from others.[7]

Participants received a single weekly dose of dordaviprone, with adult participants 18 and older receiving 625 mg weekly and pediatric patients given a body-weight based weekly dose using the criteria as followed: 10 kg to <12.5 kg receiving 125 mg weekly, 12.5 kg to <27.5 kg receiving 250 mg weekly, 27.5 kg to <42.5 kg receiving 375 mg weekly, 42.5 kg to <52.5 kg receiving 500 mg weekly, and 52.5 kg or greater receiving 625 mg weekly.[7] Overall response rate was measured at least 4 weeks after initial documentation, and in most of the clinical trials again at 6 to 8 weeks.[7] Results showed that of the 50 patients analyzed, 22% (n=11) had a measurable reduction in tumor size as assessed by MRI scans and RANO-HGG scoring criteria, a standardized scoring tool commonly used in the assessment of high-grade gliomas.[6] This is significant as any measurable radiographic response in diffuse midline glioma is rare, so even a response rate of 22% indicates a major improvement for this aggressive tumor type. Median duration of response was also measured and was found to be 10.3 months.[6] This means that, for patients who had a tumor shrinking response, the typical length of time that the tumor stayed controlled was 10 months. This is especially meaningful in a disease such as midline diffuse glioma where, with the use of historical treatment options, median overall survival is less than 12 months – introduction of a therapy that provides an additional 10 months of disease stability thus suggests clinical benefit and extended disease control. These findings highlight dordaviprone as a therapeutic advancement as it provides a systemic therapy option with short-term effective tumor control to a population of patients whose treatment options have historically been limited.

Diffuse midline glioma remains one of the most devastating and lethal pediatric brain

tumors, with its poor prognosis due in part to historically limited treatment options. The central location of these tumors combined with their diffuse nature pose challenges to the delivery and efficacy of systemic therapies.[3] Dordaviprone represents a promising step forward in the treatment of this aggressive tumor subtype. By selectively targeting key vulnerabilities in H3-K27M mutated cells through a variety of mechanisms, dordaviprone offers optimism to a population that has historically had limited systemic treatment options.

References

1. Ostrom QT, Cioffi G, Gittleman H, et al. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2012–2016. *Neuro-Oncology*. 2019;21(5):v1-v100. https://doi.org/10.1093/neuonc/noz150.
2. Bernstock JD, Hoffman SE, Kappel AD, et al. Immunotherapy approached for the treatment of diffuse midline gliomas. *OncoImmunology*. 2022;11(1). doi: 10.1080/2162402X.2022.2124058.
3. Feng J, Hao S, Pan C, et al. The H3.3 K27M mutation results in a poorer prognosis in brainstem gliomas than thalamic gliomas in adults. *Human Pathology*. 2015;46(11):1626-1632. https://doi.org/10.1080/2162402X.2022.2124058.
4. Saratsis AM, Knowles T, Petrovic A, Nazarian J. H3K27M mutant glioma: Disease definition and biological underpinnings. *Neuro Oncology*. 2024;26(2):S92-S100. doi: 10.1093/neuonc/noad164. PMID: 37818718; PMCID: PMC11066930.
5. Arrillaga-Romany I, Gardner SL, Odia Y, et al. ONC201 (Dordaviprone) in Recurrent H3 K27M-Mutant Diffuse Midline Glioma. *J Clinical Oncology*. 2024; 42(13):1542-1552. doi:10.1200/JCO.23.01134.
6. U.S. Food and Drug Administration. FDA grants accelerated approval to dordaviprone for diffuse midline glioma. *FDA*. 2025. https://www.fda.gov/drugs/resources-information-approved-drugs/fda-grants-accelerated-approval-dordaviprone-diffuse-midline-glioma.
7. NIH National Library of Medicine. Modeyso-dordavirpone capsule. 2025. https://dailymed.nlm.nih.gov/dailymed/lookup.cfm?setid=ad45b43e-fdef-47ad-9c34-055b41bdc576&utm.

Ajovy FDA Approval for Treatment of Episodic Migraine Prophylaxis in Children and Adolescents

Written by Madison Wiklund, PharmD Candidate 2027

Migraines are the most common recurrent headache complaint, with nearly 20% of patients with migraines experiencing their first attack before the age of five.[1] Recurrent migraines have the potential to cause significant discomfort in a pediatric patient's daily life, interfering with their participation in educational and social activities, both of which are essential for their growth and development. In general, the clinical presentation of migraines is complex, and can include three stages: a prodromal stage involving premonitory symptoms, a potential aura phase in which visual or auditory disturbances may be noted, and an acute headache phase involving the classic migraine symptoms.[2] Migraine presentation in children may differ from adults, but some similarities are seen. In children migraines may have a shorter duration, they are likely to be bilateral frontotemporal as opposed to unilateral, and while children can still experience aura symptoms, they may not be able to communicate this – changes in behavior may be the best indication of aura symptoms such as light and sound sensitivity.[1] The headache phase of a migraine is thought to be triggered by the release of inflammatory mediators into the cerebrospinal fluid. The inflammatory mediators activate trigeminovascular neurons and meningeal nociceptors, leading to central and peripheral sensitization that is expressed as a headache.[2] A key inflammatory molecule that plays a role in the pathogenesis of this disorder is calcitonin gene related peptide (CGRP).

Current first line treatment of acute migraines in children is the use of over the counter (OTC) medications such as acetaminophen, ibuprofen, and other age-appropriate nonsteroidal anti-inflammatory drugs (NSAIDs).[3] Triptans can be used second line for the acute treatment of migraines, although each triptan agent has its own age limitations. Sumatriptan, zolmitriptan, and almotriptan are FDA approved for use in children 12 years and older, while rizatriptan can be used in children as young as 6 years of age.[3] Because acute treatment options for pediatric patients with migraine are limited, and pharmacologic prophylaxis has shown significant efficacy in adults with migraine, there has been a recent interest in the use of these prophylactic migraine therapies in children. For a long time, topiramate was the first and only medication FDA approved for the prophylactic treatment of migraine in children, but is only approved for patients 12 years and older.[3] Off-label use of other prophylactic regimens is thus common and includes the use of medications such as propranolol, divalproex, and amitriptyline.[4] Off-label medication use, however, has the capacity to cause undue harm in patients secondary to unknown safety risks. The off-label use of these prophylactic therapies needs to be further described in pediatric patients with migraine to ensure their safe and appropriate use.

While traditional migraine therapies are still widely used in children and adults, anti-CGRP therapies have become more commonly used for acute and prophylactic migraine treatment in adults. The lack of prophylactic treatment options for pediatrics, and the success of anti-CGRP therapy in adults has led to strides in pediatric research for this class of medications. Anti-CGRP therapies are

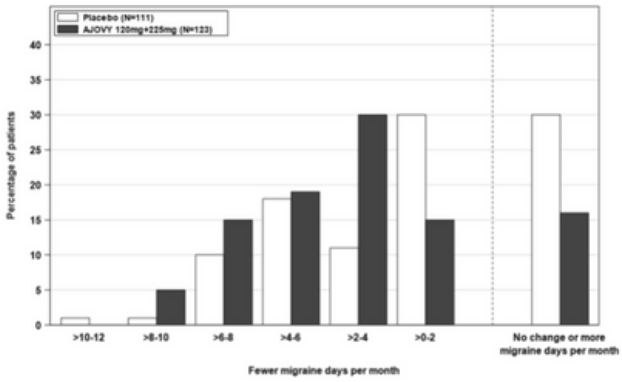
available in two varieties: small molecules and monoclonal antibodies. CGRP small molecule therapies include rimegepant (Nurtec ODT), ubrogepant (Ubrelvy), and atogepant (Qulipta). These medications are used in the acute treatment of headaches as well as their prevention. Monoclonal antibodies (mAbs) that target CGRP are used as prophylaxis only and include fremanzumab (Ajovy), erenumab (Aimovig), and galcanezumab (Emgality). While the use of anti-CGRP therapies is common in adults, until recently these medications have lacked approval in pediatric patients, although they have still been utilized off-label in practice.

A recent retrospective study investigated the efficacy and tolerability of anti CGRP therapies in 23 adolescents and young adults aged 12-21 with episodic migraines (EM), chronic migraines (CM), new daily persistent headaches (NDPH), or chronic post traumatic headaches (PTH).[5] The study included nine patients aged 12 to 15 years, 12 patients aged 16 to 18 years, and two patients who were older than 18 years.[5] Patients were included if they utilized mAb anti-CGRP medications or small molecule CGRP receptor antagonists specifically, fremanzumab (Ajovy), galcanezumab (Emgality), erenumab (Aimovig), eptinezumab (Vyepti), rimegepant (Nurtec ODT), ubrogepant (Ubrelvy), or atogepant (Qulipta).[5] The results were promising, showing that nearly 40% of participants had a greater than 50% reduction in the number of headache days per month after only one month of treatment with one of these therapies.[5] Patients who used anti-CGRP therapies also had less frequent use of rescue medications and greater response to them when they were used.[5] The small scale of this study along with results not being stratified by which medication was used, makes it difficult to draw conclusions on how these medications individually should be used in practice.

The lack of pediatric approval for these promising prophylactic agents all changed recently. As of August 2025, fremanzumab (Ajovy) became the only FDA approved preventative treatment for episodic migraine in children and adolescents.[6] Specifically, it is approved for patients aged 6-17 years who weigh at least 45 kilograms and experience less than 15 headache days per month.[6] The randomized controlled trial (RCT) cited in the package insert for Ajovy included 235 patients ages 6 to 17 years old with episodic migraine.[6] The primary endpoint was the mean change from baseline in the average monthly migraine days (MMD) during the three-month trial period.[6] Figure 1 displays the difference in the reduction of average MMD for patients who received fremanzumab (Ajovy) versus placebo. Secondary endpoints included the proportion of patients that reached at least a 50% reduction in MMD, the mean change from baseline in days where rescue headache medications were used, and the mean change from baseline in the average number of headache days that were at least of moderate severity.[6] Both primary and secondary efficacy endpoints showed improvements that were statistically significant in comparison to patients who received the placebo.[6] This study suggests that the most common adverse drug reactions are injection site related and hypersensitivity.[6] Of note, the trial included some patients who weighed under 45 kilograms and who received a 120 mg dose, however at this time fremanzumab (Ajovy) is only approved for patients weighing 45 kilograms or more and at a dose of 225 mg subcutaneously monthly.[6] Further research into this reduced dose in smaller populations

would aid in expanding the use of fremanzumab (Ajovy) in pediatric patients.

Figure 1. Change in Mean Monthly Migraine Days in Patients Age 6-17 Years Who Experience Episodic Migraine Receiving Fremanzumab (Ajovy) vs. Placebo[6]



While anti-CGRP mAbs, specifically fremanzumab (Ajovy), appear to be efficacious for the prevention of migraine in pediatric patients, they do not come without potential long-term safety concerns. There is some concern regarding the ability of anti-CGRP molecules to have an impact on central nervous system (CNS) development. Fremanzumab (Ajovy) is immunoglobulin G (IgG) based and thus not expected to cross the blood brain barrier (BBB), but worry arises due to the hypothesis that the decrease in peripheral CGRP could lead to redistribution of central CGRP. This, in theory, would lower levels of CGRP in the brain and potentially impact neurologic development.[7] As such, it is recommended that adolescent patients avoid the use of these therapies if they potentially have a compromised BBB, such as in the setting of stroke or meningitis.[7] Aside from its role in CNS development, CGRP is also associated with bone formation, glucose stimulated insulin release, vasodilation, and pro- and anti-inflammatory effects.[7] For these reasons it is recommended to also limit anti-CGRP use in patients with bone diseases, structural heart defects, or immunodeficiency.[7] These areas of concern are theoretical, making the long term effects of anti-CGRP therapy in these populations a relative unknown. Anti-CGRPs should be used judiciously in postpubescent adolescents who experience frequent migraine with moderate to severe disability.[7] Long term effects of anti-CGRP therapies in children is an area that would benefit from further research, but the current data is promising for the use of these therapies in pediatrics.

Migraines are a common and debilitating disorder that impact the quality of life of pediatric patients. The lack of prophylactic migraine treatment options in children highlights the need for further research into the safety and efficacy of currently FDA approved medications that are used in adults. Once monthly fremanzumab (Ajovy) is currently the only FDA approved option for select pediatric patients based on age and weight. While a once monthly injection could improve patient adherence, medication access and patient acceptability could be limiting factors for pediatric patients. Beyond administration, there are considerations to assess whether the benefits outweigh the potential long-term risks associated with the use of anti-CGRP mAbs in children. Further research into how the use of anti-CGRP molecules influences normal biological processes within pediatrics would be beneficial, but is of course not an easy topic to study directly. While fremanzumab's (Ajovy's) recent FDA approval is a step in the right direction when it comes to enhancing the breadth of medications available to the pediatric population, there is certainly more work to be done.

References

1. Youssef PE, Mack KJ. Episodic and chronic migraine in children. Dev Med Child Neurol. 2020;62(1):34-41. doi:10.1111/dmcn.14338
2. Abu-Arafeh I, Gelfand AA. The childhood migraine syndrome. Nat Rev Neurol. 2021;17(8):449-458. doi:10.1038/s41582-021-00497-6
3. Kohandel Gargari O, Aghajanian S, Togha M, et al. Preventive medications in pediatric migraine: a network meta-analysis. JAMA Netw Open. 2024;7(10):e2438666. doi:10.1001/jamanetworkopen.2024.38666
4. Association of Migraine Disorders. Migraine in children and adolescents. Association of Migraine Disorders website. https://www.migrainedisorders.org/migraine-disorders/migraine-in-children/.
5. Bandatmakur ASM, Dave P, Kerr M, Brunick C, Wen S, Hansen N. Effectiveness and tolerability of anti–calcitonin gene-related peptide therapy for migraine and other chronic headaches in adolescents and young adults: a retrospective study in the USA. Brain Sci. 2024;14(9):879. doi:10.3390/brainsci14090879
6. Teva Pharmaceuticals USA, Inc. AJOVY (fremanezumab-vfrm) injection, for subcutaneous use: prescribing information. Horsham, PA: Teva Pharmaceuticals USA, Inc.; 2025. https://www.ajovy.com/globalassets/ajovy-consumer/ajovy-pi.pdf
7. Szperka CL, VanderPluym J, Orr SL, et al. Recommendations on the use of anti-CGRP monoclonal antibodies in children and adolescents. Headache. 2018;58(10):1658-1669. doi:10.1111/head.13414

Indomethacin in Neonatology: Pharmacologic Closure of Patent Ductus Arteriosus

Written by Romina Valdes Daussa, PharmD Candidate 2027

In the neonatal intensive care unit, some of the greatest challenges arise not from new changes in a baby's condition, but from physiologic transitions that fail to occur. One example is a patent ductus arteriosus (PDA). The ductus arteriosus is a fetal vessel that diverts blood away from the fluid-filled lungs before birth. While this vessel serves an important purpose *in utero*, improving circulatory efficiency by allowing blood already oxygenated by the placenta to bypass the non-oxygen exposed fetal lungs, it can cause serious complications when it remains persistently open after delivery. After delivery, a rise in oxygen tension and a natural fall in circulating prostaglandins trigger the ductus arteriosus to constrict and close. When this expected closure does not occur, the persistent PDA can lead to excessive pulmonary blood flow, increased cardiac workload, and significant respiratory instability.

When a PDA remains hemodynamically significant, management options include surgical ligation or pharmacologic closure. Historically, indomethacin has been the medication of choice to help close this vessel when pharmacologic management is chosen. Indomethacin works by blocking prostaglandins which help keep the ductus arteriosus patent. Once prostaglandin levels fall, or are pharmacologically blocked, the ductus arteriosus constricts, leading to closure. High-certainty evidence shows that indomethacin reduces the risk of failed closure within one week by roughly 70 % compared to no treatment (relative risk ≈ 0.30) in preterm infants with symptomatic PDA.[1] Even so, approximately 20–30% of neonates fail to achieve closure after the first course of treatment, which highlights the need for additional pharmacologic options.[2] This incomplete efficacy is one reason why NICU teams increasingly rely on multiple agents and individualized decision-making rather than a single "gold standard."

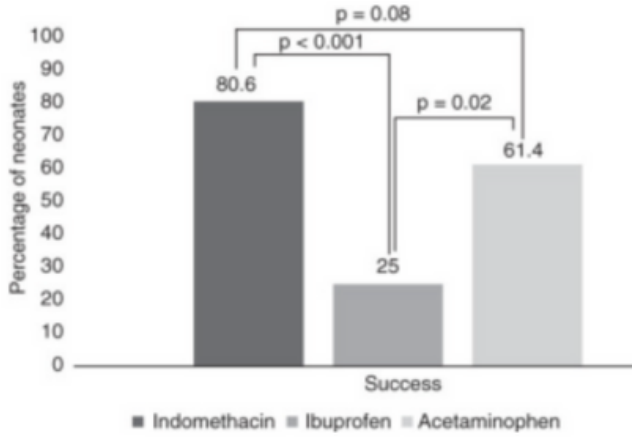
In addition to its limited success rate, indomethacin use does not come without risk; through its prostaglandin inhibitory activity, indomethacin can decrease blood flow to other organs, most notably the kidneys and the intestines. As such, indomethacin can impair renal function and increase the baby's risk of necrotizing enterocolitis (NEC).[3] Monitoring renal function in neonates is uniquely challenging. In the first days of life, serum creatinine often reflects maternal levels. Creatinine clearance equations are not validated in this population. Therefore, clinicians focus on trends in the infant's serum creatinine and urine output to assess for toxicity.

Alternative therapies have been explored. Ibuprofen, another nonsteroidal anti inflammatory drug (NSAID), inhibits prostaglandin production through the same cyclooxygenase pathway but may be associated with fewer renal side effects. Clinical studies suggest that ibuprofen has comparable efficacy to indomethacin for PDA closure.[4] Outside of the NSAID medication class, acetaminophen has been researched as another potential therapy, particularly in infants who cannot tolerate NSAIDs. Although the mechanism is not completely understood, acetaminophen is thought to work through inhibition of the peroxidase

component of prostaglandin H_2 synthase, thereby reducing prostaglandin production through a pathway distinct from traditional NSAIDs.[5] Its safety profile may also be advantageous, as acetaminophen does not typically affect renal or intestinal perfusion, though hepatic toxicity remains a consideration. These characteristics make acetaminophen an appealing alternative when NSAID-associated risks are high.

A recent meta-analysis compared first-course closure rates among indomethacin, ibuprofen, and acetaminophen. The study found that both indomethacin and acetaminophen achieved significantly higher closure rates than ibuprofen ($p < 0.001$ and $p = 0.02$, respectively). There was no statistically significant difference between indomethacin and acetaminophen ($p = 0.08$), indicating similar efficacy between these two agents. This distinction helps pharmacists and clinicians make informed decisions about which therapy to start and when to consider an alternative if the PDA remains open (Figure 1).[6]

Figure 1. Comparison of PDA treatment efficacy for first pharmacologic course using indomethacin, ibuprofen, or acetaminophen.[6]



In addition to the expansion of pharmacologic treatment options over time, the general treatment approach for closing neonatal PDAs has also evolved. Decades ago, the strategy was to close every PDA as soon as possible. Now, many physicians are more cautious, as not all PDAs are clinically significant, and aggressive early treatment has not always led to better long-term outcomes.[7] Current guidelines encourage an individualized approach, where the decision to treat depends on the infant's symptoms, overall stability, and the risk-benefit balance associated with pharmacologic and/or surgical closure. Despite the emergence of new alternatives and evolving perspectives, indomethacin remains a central component in neonatology. For many preterm infants, it provides a minimally invasive and well-studied option. Yet, its limitations and other available therapy options highlight the importance of a tailored, evidence-informed approach. Taken together, these therapies represent a valuable toolkit that allows clinicians to support even the most fragile patients as they navigate life-sustaining physiologic change.

References

1. Fowlie PW, Davis PG. *Indomethacin for symptomatic patent ductus arteriosus in preterm infants. Cochrane Database Syst Rev*. 2021;2021(8):CD000174. doi:10.1002/14651858.CD000174.pub3
2. Clyman RI, et al. *Indomethacin use for the management of patent ductus arteriosus: Outcomes, reopening, and strategies*. Pediatric Clin North Am. 2013;60(3):617-634.
3. Hamrick SE, Stevenson DK. Patent ductus arteriosus of the preterm infant. Pediatrics. 2020;146(5):e20201209. doi:10.1542/peds.2020-1209
4. Ohlsson A, Shah SS. *Ibuprofen for the treatment of patent ductus arteriosus in preterm or low birth weight infants*. Cochrane Database Syst Rev. 2020;2020(2):CD003481. doi:10.1002/14651858.CD003481.pub6
5. Oncel MY, Erdeve √ñ, Canpolat FE, et al. *Comparison of the efficacy and safety of indomethacin, ibuprofen and paracetamol in preterm infants with hemodynamically significant patent ductus arteriosus.* Pediatric Drugs. 2018;20(3):197-202. doi:10.1007/s40272-018-0294-0
6. Mitra S, Florez ID, Tamayo ME, et al. *Association of placebo, indomethacin, ibuprofen, and acetaminophen with closure of hemodynamically significant patent ductus arteriosus in preterm infants: a network meta-analysis*. JAMA Pediatric. 2018;172(3):e180298. doi:10.1001/jamapediatrics.2018.0298
7. Singer J, et al. *Active treatment vs expectant management of patent ductus arteriosus in preterm infants.* JAMA Pediatric. 2025;179(1):46-54. doi:10.1001/jamapediatrics.2024.3456

Crinecerfont in Pediatric Congenital Adrenal Hyperplasia

Written by Kathleen Gannon, PharmD Candidate 2027

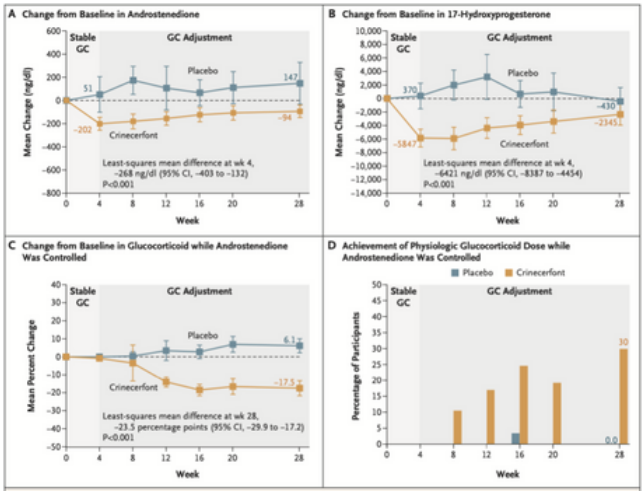
Classic congenital adrenal hyperplasia (CAH) is an autosomal recessive condition that disrupts the adrenal glands, which function in the production of mineralocorticoids, glucocorticoids, and sex steroids.[1] The most common form of CAH is a deficiency in the enzyme 21-hydroxylase, an enzyme responsible for cortisol synthesis. This enzyme deficiency results in an inhibition of cortisol production, which in turn signals to the brain that more needs to be made. Thus, adrenal stimulation is increased as a whole, resulting in the excessive production of other hormones produced by the adrenal glands, such as androgens.[2] Excess androgens in children can lead to precocious puberty, which is evidenced by stunted growth, variable effects on the size of male and female genitalia, and disruption of normal female ovarian function and the menses cycles.[2] CAH can be diagnosed in newborns with a genetic screening for 21-hydroxylase deficiency, which looks for elevations in a specific androgen hormone, 17-hydroxyprogesterone. If the test comes back positive, a repeat confirmatory test should be performed along with a serum electrolyte panel.[1] Currently hydrocortisone is the first-line treatment for CAH as recommended by The Endocrine Society. Hydrocortisone acts as a glucocorticoid replacement for cortisol, and aids in inhibiting excessive secretion of ACTH.[1] For CAH, hydrocortisone is dosed at supraphysiologic levels divided into 3 doses per day due to its short half-life. This supraphysiologic dosing, however, can lead to further complications as early as 5 to 6 years of age. Such complications include issues in bone formation due to the imbalance of osteoblasts and osteoclasts, weight gain, insulin resistance, and hypertension.[2]

In an effort to reduce the long- term effects of supraphysiologic hydrocortisone, attention has recently been given to finding additional, hydrocortisone sparing therapeutic options. There is a new drug that was recently approved by the FDA in 2024 called crinecerfont (Crenessity). Crinecerfont is an oral corticotropin-releasing factor type 1 antagonist. By antagonizing the corticotropin-releasing factor receptor in the pituitary gland androgen production is reduced, thus helping limit the amount of glucocorticoid treatment needed.[3]

The phase 3 trial that led to crinecerfont's FDA approval in pediatric patients consisted of a 28-week, randomized, double blind, placebo-controlled period followed by a 24-week, open-label period. Additionally, an optional open label extension period was offered and is still ongoing. The trial was conducted at 37 centers in the U.S., Canada, and Europe, and included patients 12 to 17 years of age with CAH who were receiving hydrocortisone and were stable for 1 month. Those receiving long-term hydrocortisone therapy for a condition other than CAH were excluded. There were a total of 103 participants with 69 participants randomized to the crinecerfont group.[2] Glucocorticoid doses were maintained from baseline through week 4, and then weeks 4-28 the dose of glucocorticoids were modified in one to four steps to a target of 8.0- 10.0 mg per square meter per day in hydrocortisone dose equivalents, contingent upon androstenedione remaining controlled.[2] The endpoints measured were the

androstenedione levels from baseline to week 4 (Figure 1, Panel A), the change in the serum 17- hydroxyprogesterone levels from baseline to week 4 (Figure 1, Panel B), percent daily change in glucocorticoid dose from baseline to week 28 while androstenedione was controlled (Figure 1, Panel C), and percentage of patients that were able to achieve physiologic glucocorticoid dosing while androstenedione was controlled (Figure 1, Panel D).[2]

Figure 1. Primary Efficacy Endpoints[2]



In panels A and B, the crinecerfont group had reductions in androstenedione and 17-hydroxyprogesterone levels by week 4 during the stable glucocorticoid period, and at week 28 after the adjustment glucocorticoid period, the levels still remained under baseline.[2] In panel C, while the androstenedione levels were controlled and maintained, the crinecerfont group glucocorticoid dose was decreased from baseline to week 28.[2] In panel D, 30% of patients in the crinecerfont were able to achieve a physiologic glucocorticoid dose at week 28 while androstenedione was controlled, and 0% in the placebo group achieved this.[2] For panels A- C, the p- value was <0.001, indicating that the results were statistically significant and in support of crinecerfont being a potential new option for CAH.[2] In the study, those being treated with crinecerfont were not noted to have experienced any adrenal crises or safety concerns related to vital signs, laboratory values, neuropsychiatric assessments, or electrocardiography.[2] Overall, the results showed that this new therapy reduced production of excess androgens and allowed glucocorticoid doses to be reduced to safer, more physiologic levels, leading to crinecerfont's FDA approval in pediatric patients in 2024.[3]

References

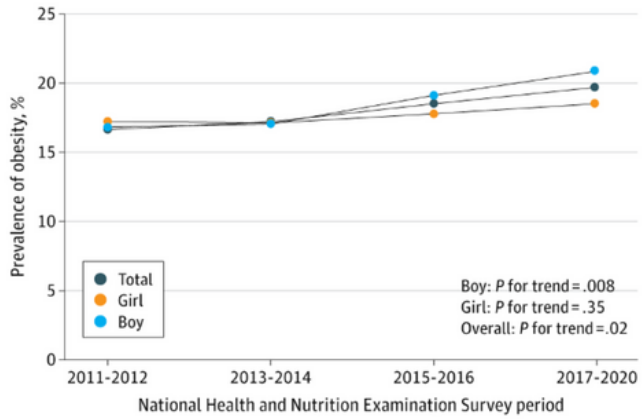
1. Sharma L. Congenital adrenal hyperplasia. StatPearls [Internet]. January 27, 2025. Accessed November 3, 2025. https://www.ncbi.nlm.nih.gov/books/NBK448098/.
2. Sarafoglou K, Kim MS, Lodish M, et al. Phase 3 trial of crinecerfont in pediatric congenital adrenal hyperplasia. N Engl J Med. 2024;391:493-503. Doi: 10.1056/NEJMoa2404655. Accessed November 3, 2025. https://pubmed.ncbi.nlm.nih.gov/38828945/.
3. Commissioner O of the. FDA approves new treatment for congenital adrenal hyperplasia. U.S. Food and Drug Administration. Accessed November 3, 2025. https://www.fda.gov/news-events/press-announcements/fda-approves-new-treatment-congenital-adrenal-hyperplasia.

An Overview of the Pharmacological Management of Childhood Obesity

Written by Paige Miller, PharmD Candidate 2027

Obesity, especially pediatric obesity, has become an exponentially growing global public health concern. In the United States, the prevalence of obesity among children aged 2-19 years old has significantly increased over the last couple decades (Figure 1). As the prevalence of childhood obesity has increased, many weight-related and metabolic comorbidities, such as type 2 diabetes mellitus, nonalcoholic fatty liver disease, cardiovascular disease, and obstructive sleep apnea, have concurrently become more prevalent among pediatric patients, underlying the importance of weight management in this population.[1] Although increasing daily physical activity and optimizing one's diet is a fundamental component of managing obesity, the adjunctive use of medications can play a key role in greatly improving the overall management of childhood obesity. Currently, medications such as orlisat, phentermine, and glucagon-like peptide 1 (GLP-1) receptor agonists are used to help manage obesity in children.[2]

Figure 1. Prevalence of Obesity in US Youth Aged 2 to19 Years Old Stratified by Sex From 2011 to 2020 [3]



Orlisat is currently FDA approved for the long-term management of obesity in children who are at least 12 years old. Orlistat is classified as a lipase inhibitor and thus works by blocking lipase enzymes in the intestines, preventing the absorption of dietary fat. The recommended dosing for orilsat is 120 mg three to four times daily with meals. Some common side effects include oily stools, abdominal pain, flatulence, fecal urgency and incontinence which is caused because of undigested fat reaching the large intestines.[2]

Phentermine is currently FDA approved for the short-term management (up to 12 weeks duration) of obesity in adolescents 17 years or older. Phentermine is a central nervous system stimulant and works by blocking the reuptake of norepinephrine in the brain and stimulates pro-opiomelancortin neurons to cause improved control of appetite. The recommended dosing consists of 37.5 mg daily before the first meal of the day or 1 to 2 hours after said meal. Common side effects of phentermine are caused due to its effect on the central and peripheral nervous system and can cause symptoms that include insomnia, dry mouth, heart rate and blood pressure elevation as well as mood alteration.[1]

Of the many GLP-1 receptor agonist medications currently available in the United States, the only 2 that are approved for the management of obesity in pediatric patients are liraglutide and semaglutide. As a class, GLP-1 receptor agonists act as exogenous incretin hormones, stimulating

insulin secretion and decreasing gastric emptying time. Both semaglutide and liraglutide are FDA approved to be used in adolescents 12 years or older. Semaglutide is a once weekly subcutaneous injection whose dose is slowly increased over the course of 17 weeks. Conversely, liraglutide is a daily subcutaneous injection whose dose is increased weekly over the course of 5 weeks. Its labeling also mentions that, after the patient has been on their highest tolerated dose for 12 weeks, a change in 4 to 5 percent of baseline body weight loss should be evaluated. Alternative treatment should be explored if there has not been a change.[6] Common side effects of both semaglutide and liraglutide include nausea, vomiting, diarrhea and a feeling fullness since they both mimic the GLP-1 hormone which causes delayed gastric emptying.

Childhood obesity is a chronic disease that can put a patient at an increased risk the development of comorbidities usually later in life, as well as an increased risk for mortality.[2] There are many medications that are currently approved by the FDA for the treatment of obesity in adults, however there is a large gap in research involving the use of these medications in pediatric patients. With the rising rates of childhood obesity, the emergence of safe and effective pharmacologic treatment to assist with controlling obesity in the pediatric patient population is a crucial step forward to eliminate this treatment gap.

References

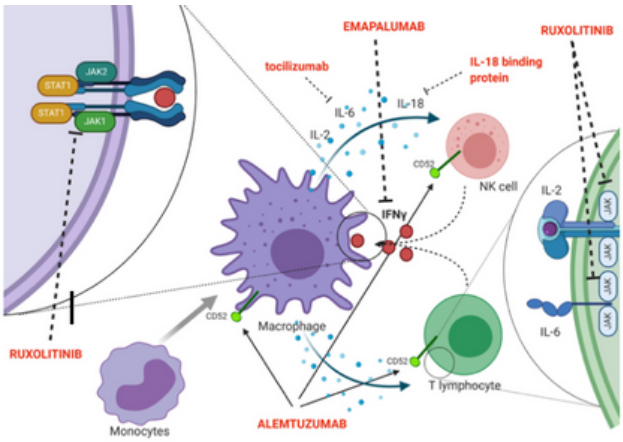
1. Singhal V, Sella AC, Malhotra S. Pharmacotherapy in pediatric obesity: current evidence and landscape. Curr Opin Endocrinol Diabetes Obes. 2021;28(1):55-63. doi:10.1097/MED.0000000000000587
2. Smith JD, Fu E, Kobayashi MA. Prevention and Management of Childhood Obesity and Its Psychological and Health Comorbidities. Annu Rev Clin Psychol. 2020;16:351-378. doi:10.1146/annurev-clinpsy-100219-060201
3. Hu K, Staiano AE. Trends in Obesity Prevalence Among Children and Adolescents Aged 2 to 19 Years in the US From 2011 to 2020. JAMA Pediatr. 2022;176(10):1037-1039. doi:10.1001/jamapediatrics.2022.2052
4. Norgren S, Danielsson P, Jurold R, Lötborn M, Marcus C. Orlistat treatment in obese prepubertal children: a pilot study. Acta Paediatr. 2003;92(6):666-670. doi:10.1080/08035250310002353
5. Weghuber D, Barrett T, Barrientos-Pérez M, et al. Once-Weekly Semaglutide in Adolescents with Obesity. N Engl J Med. 2022;387(24):2245-2257. doi:10.1056/NEJMoa2208601
6. Fox CK, Barrientos-Pérez M, Bomberg EM, et al. Liraglutide for Children 6 to <12 Years of Age with Obesity - A Randomized Trial. N Engl J Med. 2025;392(6):555-565. doi:10.1056/NEJMoa2407379

Emapalumab efficacy for pediatric patients with HLH

Written by Jane Aloi, PharmD Candidate 2029

Hemophagocytic lymphohistiocytosis (HLH) refers to a collective grouping of life-threatening hyperinflammatory disorders that cause mass dysregulation of the immune system. Clinically, if left untreated, HLH can progress to multiorgan failure and death. The pathophysiology of HLH involves the excessive production of inflammatory cytokines, such as interferon gamma (INFγ), tumor necrosis factor-alpha (TNF-α), and interleukin-6 (IL-6), which ultimately leads to overstimulation of macrophages. These macrophages go on to engulf healthy blood cells, causing pancytopenia.[1] The two subtypes of HLH include primary and secondary. Primary HLH is caused by genetic factors and manifests itself in young children under 18 months of age, whereas secondary HLH is triggered by neoplasms, certain infections, and autoimmune disorders later in life. While not caused by a specific single mutation, those predisposed to primary HLH often have genetic abnormalities related to dysfunctional cytotoxic T-cell and NK cells, leading to a defective cytokine signaling response.[2] Primary HLH is inevitably fatal without treatment, and the only curative treatment available is allogenic hematopoietic stem cell transplantation.[2] For patients experiencing an episode of HLH, a regimen known as HLH-94 can be used to bridge the patient until they are able to be transplanted. The HLH-94 regimen, which consists of dexamethasone and etoposide with or without intrathecal methotrexate, is not 100% effective, though, leaving a need for additional therapeutic options.[1]

Figure 1. INFγ pathophysiology and impact on HLH progression[3]



Monoclonal antibodies have been an emerging therapeutic in the last decade that continue to grow. Emapalumab (Gamifant) is a human monoclonal antibody that specifically targets and inhibits INFγ, which is suggested to be strongly implicated in the pathophysiology of HLH.[2] Emapalumab can block both bound and free INFγ.[2] As such, emapalumab is FDA approved for the treatment of refractory or recurrent primary HLH in all ages.[2] A significant trial of emapalumab (NI-0501-04) looked at patients 0-18 years of age meeting diagnostic criteria for primary HLH and who had active disease at enrollment.[3] Initially 34 patients were enrolled in the study, 27 of which did not respond adequately to traditional treatments and 7 of which had not received any prior treatment.[2] The median age of enrollment was 0.85 years.[2] Responses to emapalumab were categorized by complete remission (no fever, no abnormalities of spleen size, no low white or red blood cell counts, no increased ferritin levels, no clotting impairment, and no CNS involvement) while partial remission was designated by three or more abnormal

laboratory values but still meeting the criteria for complete remission.[2] Improvement in prior HLH lab values was also included as a response value.[2] Follow-up after 8 weeks of treatment with emapalumab showed 63% (n=27) of patients who had received previous treatment and 65% (n=34) of all patients treated responsed to the medication.[3] Of the patients who received traditional treatment prior to receiving emapalumab, 70% (n=19) were able to survive to HSCT. 65% of all patients treated (n=22) were able to move onto HSCT. Of those treated before, 74% (n=20) of patients at last check-in were alive, and of the entire group 71% (n=24) survived.[3] 12 months after HSCT transplantation, probability of survival of prior treated patients was 89.5% (95% CI, 64.1 to 97.3), and 90.2% (95% CI 66.2 to 97.5) for all treated patients.[3]

All patients had some degree of adverse events while receiving emapalumab, the majority of which were deemed to be unrelated to emapalumab. Overall, ten patients died however none of these deaths were determined to be related to emapalumab.[3] 13 patients developed infections during the trial, of which 2 cases of infection were deemed directly attributable to emapalumab.[3] Neither patient who developed infections associated with emapalumab usage experienced mortality from their infection.[3] Notably, there was no negative changes in laboratory values, vital signs, or organ function that were directly caused by emapalumab usage, and adverse effects from treatment were no different in comparison to patients receiving additional therapies for their HLH.[3]

Emapalumab is not only a novel treatment for those recently diagnosed with primary HLH, but also those in which first-line treatment options have not had the desired effect. This is essential for not only providing treatment for patients in which traditional protocols are ineffective, but also in its importance to allow patients to survive and stabilize until they can undergo conditioning and receive hemopoietic stem cell transplantation.[3] HLH patients are often critically ill. Many patients during the study developed infections during treatment, however only two of these infections were directly related to emapalumab.[3] Emapalumab did not worsen HLH progression in any patient, and severe adverse effects were rare. Not only is this a promising therapy for patients not responsive to typical treatment, but it provides future direction to focus on inhibition of INFγ and its effects on treatment of HLH.

References

1. Kwak, A, Jung, N, Shim, YJ, Heung, SK, Lim, HJ, Lee, JM, Heo, MH, & Young, A retrospective analysis of etiology and outcomes of hemophagocytic lymphohistiocytosis in children and adults. *Yeungnam Univ J Med*. 2021;38(3), 208-218. DOI: https://doi.org/10.12701/yujm.2020.00591.
2. Merli, P, Algeri, M, Gaspari, S, & Locatelli, F. Novel Therapeutic Approaches to Familial HLH (Emapalumanb in FHL). *Front. Immunol*. 2020;11. DOI: https://doi.org/10.3389/fimmu.2020.608492
3. Locatelli, F, Jordan, MB, Allen, C., et al. Emapalumab in Children with Primary Hemophagocytic Lymphohistiocytosis. *NEJM.* 2020; 382(19):1811-1822. DOI: 10.1056/NEJMoa1911326

Guselkumab for the treatment of chronic plaque psoriasis in pediatric patients

Written by Rachel Hill, PharmD Candidate 2026

Psoriasis is a chronic immune-mediated inflammatory skin disease that affects nearly 20,000 children under the age of 10, representing a significant treatment gap for this vulnerable population. As of September 29, 2025, guselkumab (Tremfya, Johnson & Johnson) is the first IL-23 inhibitor approved for pediatric patients ≥ 6 years of age and ≥ 40 kg living with moderate-to-severe plaque psoriasis or active psoriatic arthritis. Beyond the physical symptoms of erythema, scaly plaques, and pruritus, pediatric psoriasis can profoundly affect self-esteem, quality of life, and psychosocial development. Plaque psoriasis and psoriatic arthritis are driven by dysregulated immune activation, particularly overexpression of the IL-23 / Th17 inflammatory pathway, which promotes keratinocyte proliferation and chronic skin and joint inflammation**.** While medications that modulate these complex processes at any level are suspected to provide some degree of clinical improvement, recent research has noted that biologics that target inflammatory cytokines such as IL-12, IL-17, and IL-23 generally achieve higher rates of disease control than historic biologics that target tumor necrosis factor (TNF), such as etanercept.[2] By inhibiting IL-23 signaling, guselkumab helps normalize excessive immune activity without broadly suppressing immune function.

In pediatric patients, guselkumab's safety and efficacy was supported by the phase 3 PROTOSTAR trial, which demonstrated that, at week 16, 66% of guselkumab-treated children achieved an Investigator Global Assessment (IGA) score of clear or almost clear skin, compared to just 16% receiving placebo.[2] By week 52, response rates were even more profound, with 86% of pediatric patients achieving an IGA score of clear or almost clear skin. There were no major adverse events noted during the study period, including no development of serious infections – infections observed included only mild infections such as the common cold.

Aside from offering patients potential improved disease control, guselkumab additionally offers the opportunity of reduced medication burden. Guselkumab is administered as a subcutaneous injection every eight weeks after two initial loading doses, reducing treatment burden compared to agents requiring biweekly administration. For pediatric patients who may have increased anxiety surrounding medication, a reduction in this burden has the potential for monumental impacts.

The pediatric approval of guselkumab underscores the importance of bridging adult and pediatric research in chronic autoimmune diseases. As more biologics are studied in younger populations, clinicians will gain a deeper understanding of how early targeted intervention may alter long-term disease progression. For families, this approval represents hope for better disease control, fewer hospital visits, and improved psychosocial well-being during critical stages of childhood and adolescence. Continued post-marketing surveillance and registry data will further define guselkumab's role in optimizing pediatric psoriasis management and may pave the way for expanded indications across other inflammatory conditions, including inflammatory bowel disease.

References

1. Janssen labels. HIGHLIGHTS OF PRESCRIBING INFORMATION. TREMFYA® Prescribing Information. September 30, 2025. Accessed November 14, 2025. https://www.jnjlabels.com/package-insert/product-monograph/prescribing information/TREMFYA-pi.pdf.
2. Janssen Research & Development L. A Study to Evaluate the Efficacy, Safety, and Pharmacokinetics of Subcutaneously Administered Guselkumab for the Treatment of Chronic Plaque Psoriasis in Pediatric Participants (PROTOSTAR). Clinicaltrials.gov. July 19, 2023. Accessed November 14, 2025. https://clinicaltrials.gov/study/NCT03451851.
3. Prajapati VH, Seyger MM, Wilsmann-Theis D, et al. Guselkumab for the treatment of moderate-to-severe plaque psoriasis in paediatric patients: Results of the phase III randomized placebo-controlled PROTOSTAR study. *British Journal of Dermatology*. 2024;192(4):618-628. doi:10.1093/bjd/ljae502