Epysqli®
(eculizumab-aagh)
Injection • 300mg/30mL

PNH

BILLING AND CODING INFORMATION FOR EPYSQLI® (eculizumab-aagh)

In paroxysmal nocturnal hemoglobinuria (PNH)

INDICATIONS

EPYSQLI is indicated for the treatment of patients with paroxysmal nocturnal hemoglobinuria (PNH) to reduce hemolysis.

EPYSQLI is indicated for the treatment of patients with atypical hemolytic uremic syndrome (aHUS) to inhibit complement-mediated thrombotic microangiopathy.

Limitation of Use

EPYSQLI is not indicated for the treatment of patients with Shiga toxin E. coli related hemolytic uremic syndrome (STEC-HUS).

EPYSQLI is indicated for the treatment of generalized myasthenia gravis (gMG) in adult patients who are anti-acetylcholine receptor (AchR) antibody positive.

IMPORTANT SAFETY INFORMATION

WARNING: SERIOUS MENINGOCOCCAL INFECTIONS

Eculizumab products, complement inhibitors, increase the risk of serious infections caused by *Neisseria meningitidis*. Life-threatening and fatal meningococcal infections have occurred in patients treated with complement inhibitors. These infections may become rapidly life-threatening or fatal if not recognized and treated early.

- **Complete or update vaccination for meningococcal bacteria (for serogroups A, C, W, Y, and B) at least 2 weeks prior to the first dose of EPYSQLI, unless the risks of delaying therapy with EPYSQLI outweigh the risk of developing a serious infection. Comply with the most current Advisory Committee on Immunization Practices (ACIP) recommendations for vaccinations against meningococcal bacteria in patients receiving a complement inhibitor. Initiate prophylactic antibacterial drug therapy. Vaccinate as soon as possible.**
- **Patients receiving eculizumab products are at increased risk for invasive disease caused by *Neisseria meningitidis*, even if they develop antibodies following vaccination. Monitor patients for early signs and symptoms of serious meningococcal infections and evaluate immediately if infection is suspected.**

Because of the risk of serious meningococcal infections, EPYSQLI is available only through a restricted program under a Risk Evaluation and Mitigation Strategy (REMS) called EPYSQLI REMS.

Please see additional Important Safety Information on pages 7-9 and click here for full Prescribing Information for EPYSQLI, including BOXED WARNINGS.

teva

Coding for EPYSQLI® (eculizumab-aagh) in PNH

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Use of this billing and coding guide

This guide is intended for informational purposes only, and not intended to take the place of the healthcare provider's diagnosis and treatment decisions. Healthcare providers are responsible for the accuracy, legitimacy, and completeness of any claims, invoices, and other documentation supplied to payers. The healthcare provider should contact the payer for answers to specific questions about payment or coverage. Specific direction from the payer supersedes the codes included here. Using the codes listed in this guide does not guarantee reimbursement.

Diagnosis coding

The ICD-10-CM diagnosis code below should be used to report the patient-specific diagnosis of PNH.

ICD-10-CM diagnosis code[1]	Code descriptor
D59.5	Paroxysmal nocturnal hemoglobinuria

ICD-10-CM, International Classification of Diseases, 10th Revision, Clinical Modification.

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Coding for EPYSQLI® (eculizumab-aagh) in PNH (cont)

Drug coding

The designated HCPCS billing code (Level II) for this specific drug can be used on medical claim forms for reimbursement from payers. As of March 31, 2025, the billing units for all eculizumab products changed from 10 mg units to 2 mg units.[2]

HCPCS code[2]	Code descriptor
Q5151	Injection, eculizumab-aagh (epysqli), biosimilar, 2 mg

The following HCPCS modifiers may be required for EPYSQLI.

Modifier[3,4]	Description	Commercial requirement	Medicare requirement
JZ	Zero drug amount discarded/not administered to any patient	Varies by payer	Y
JG	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes	N	Y
JW	Drug amount discarded/not administered to any patient	Varies by payer	Y
RE	Furnished in full compliance with FDA-mandated risk evaluation and mitigation strategy (REMS)	Y	Y
TB	Drug or biological acquired with 340B drug pricing program discount, reported for informational purposes for select entities	N	Y

Some payers, including Medicaid, require the NDC on medical claims for billing. Payers typically require healthcare providers to use the 11-digit NDC format, often without the use of hyphens or any punctuation.[5]

11-digit NDC[6]	Code descriptor	Strength
51759-0208-13	Single-dose vial per carton	300 mg/30 mL (10 mg/mL)

FDA, US Food and Drug Administration; HCPCS, Healthcare Common Procedure Coding System; NDC, National Drug Code.

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Coding for EPYSQLI® (eculizumab-aagh) in PNH (cont)

Drug administration

Report the administration of EPYSQLI in inpatient settings with the following ICD-10-PCS procedure codes.

ICD-10-PCS code[7]	Code descriptor
3E033GR	Introduction of other therapeutic monoclonal antibody into peripheral vein, percutaneous approach
3E043GR	Introduction of other therapeutic monoclonal antibody into central vein, percutaneous approach

Report administration of EPYSQLI in physician offices and hospital outpatient facilities with the following CPT® codes.

CPT code[8,9]	Code descriptor
96365	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); initial, up to one hour
96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug); each additional hour (code separately in addition to primary procedure code 96365)
96413[a]	Chemotherapy administration, intravenous infusion technique, up to one hour, single or initial substance/drug
96415[a]	Chemotherapy administration, intravenous infusion technique; each additional hour (code separately in addition to primary procedure code 96413)

[a]Billing highly complex administration codes (96413 and 96415) requires the provider in the medical record to document the complexity beyond what is required for therapeutic infusions (96365 and 96366).[9]

CPT, Current Procedural Terminology; ICD-10-PCS, International Classification of Diseases, 10th Revision, Procedure Coding System.

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Coding for meningococcal vaccination

Diagnosis coding

Assign the diagnosis code for the prophylactic vaccination with the diagnosis code for PNH, along with any other conditions the patient may have.

ICD-10-CM diagnosis code[1]	Code descriptor
Z23	Encounter for immunization

Vaccine coding

Prescribers should consult respective payer billing guidelines, as coverage of meningococcal vaccines may vary by payer.

CPT code[8,10]	Code descriptor
90619	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, tetanus toxoid carrier (MenACWY-TT), for intramuscular use
90620	Meningococcal recombinant protein and outer membrane vesicle vaccine, serogroup B (MenB-4C), 2 dose schedule, for intramuscular use
90621	Meningococcal recombinant lipoprotein vaccine, serogroup B (MenB-FHbp), 2 or 3 dose schedule, for intramuscular use
90733	Meningococcal polysaccharide vaccine, serogroups A, C, Y, W-135, quadrivalent (MPSV4), for subcutaneous use
90734	Meningococcal conjugate vaccine, serogroups A, C, W, Y, quadrivalent, diphtheria toxoid carrier (MenACWY-D) or CRM197 carrier (MenACWY-CRM), for intramuscular use
90749	Unlisted vaccine/toxoid

Coding for meningococcal vaccination (cont)

Vaccine administration coding

Report administration of meningococcal vaccines in outpatient settings with the following CPT codes.

CPT code[8,11]	Code descriptor
90471	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); 1 vaccine (single or combination vaccine/toxoid)
90472	Immunization administration (includes percutaneous, intradermal, subcutaneous, or intramuscular injections); each additional vaccine (single or combination vaccine/toxoid) (code separately in addition to primary procedure code 90471)

IMPORTANT SAFETY INFORMATION (cont)

CONTRAINDICATIONS

EPYSQLI is contraindicated for initiation in patients with unresolved serious *Neisseria meningitidis* infection.

WARNINGS AND PRECAUTIONS

Serious Meningococcal Infections

Eculizumab products, complement inhibitors, increase a patient's susceptibility to serious, life-threatening, or fatal infections caused by meningococcal bacteria (septicemia and/or meningitis) in any serogroup, including non-groupable strains. Life-threatening and fatal meningococcal infections have occurred in both vaccinated and unvaccinated patients treated with complement inhibitors.

Complete or update meningococcal vaccination (for serogroups A, C, W, Y, and B) at least 2 weeks prior to administration of the first dose of EPYSQLI, according to current ACIP recommendations for patients receiving a complement inhibitor. Revaccinate patients in accordance with ACIP recommendations, considering the duration of therapy with EPYSQLI. Note that ACIP recommends an administration schedule in patients receiving complement inhibitors that differs from the administration schedule in the vaccine prescribing information. If urgent EPYSQLI therapy is indicated in a patient who is not up to date with meningococcal vaccines according to ACIP recommendations, provide the patient with antibacterial drug prophylaxis and administer meningococcal vaccines as soon as possible. Various durations and regimens of antibacterial drug prophylaxis have been considered, but the optimal durations and drug regimens for prophylaxis and their efficacy have not been studied in unvaccinated or vaccinated patients receiving complement inhibitors, including eculizumab products. The benefits and risks of treatment with EPYSQLI, as well as the benefits and risks of antibacterial drug prophylaxis in unvaccinated or vaccinated patients, must be considered against the known risks for serious infections caused by *Neisseria meningitidis*.

Vaccination does not eliminate the risk of serious meningococcal infections, despite development of antibodies following vaccination.

Closely monitor patients for early signs and symptoms of meningococcal infection and evaluate patients immediately if infection is suspected. Inform patients of these signs and symptoms and instruct patients to seek immediate medical care if these signs and symptoms occur. Promptly treat known infections. Meningococcal infection may become rapidly life-threatening or fatal if not recognized and treated early. Consider interruption of EPYSQLI in patients who are undergoing treatment for serious meningococcal infection, depending on the risks of interrupting treatment in the disease being treated.

EPYSQLI REMS

EPYSQLI is available only through a restricted program under a REMS called EPYSQLI REMS, because of the risk of serious meningococcal infections.

Notable requirements of the EPYSQLI REMS include the following:

- Prescribers must enroll in the REMS.
- Prescribers must counsel patients about the risk of serious meningococcal infection.
- Prescribers must provide the patients with the REMS educational materials.
- Prescribers must assess patient vaccination status for meningococcal vaccines (against serogroups A, C, W, Y and B) and vaccinate if needed according to current ACIP recommendations two weeks prior to the first dose of EPYSQLI.
- Prescribers must provide a prescription for antibacterial drug prophylaxis if treatment must be started urgently and the patient is not up to date with meningococcal vaccines according to current ACIP recommendations at least two weeks prior to the first dose of EPYSQLI.

Please see additional Important Safety Information on pages 7-9 and click here for full Prescribing Information for EPYSQLI, including BOXED WARNINGS.

IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

EPYSQLI REMS (cont)

- Healthcare settings and pharmacies that dispense EPYSQLI must be certified in the REMS and must verify prescribers are certified.
- Patients must receive counseling from the prescriber about the need to receive meningococcal vaccines per ACIP recommendations, the need to take antibiotics as directed by the prescriber, and the signs and symptoms of meningococcal infection.
- Patients must be instructed to carry the Patient Safety Card with them at all times during and for 3 months following treatment with EPYSQLI.

Further information is available at www.EPYSQLIREMS.com or 1-866-318-0342.

Other Infections

Serious infections with *Neisseria* species (other than *Neisseria meningitidis*), including disseminated gonococcal infections, have been reported.

Eculizumab products block terminal complement activation; therefore, patients may have increased susceptibility to infections, especially with encapsulated bacteria, such as infections with *Neisseria meningitidis* but also *Streptococcus pneumoniae, Haemophilus influenzae*, and to a lesser extent, *Neisseria gonorrhoeae*. Additionally, *Aspergillus* infections have occurred in immunocompromised and neutropenic patients. Children treated with eculizumab products may be at increased risk of developing serious infections due to *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib). Administer vaccinations for the prevention of *Streptococcus pneumoniae* and *Haemophilus influenzae* type b (Hib) infections according to ACIP recommendations. Patients receiving eculizumab products are at increased risk for infections due to these organisms, even if they develop antibodies following vaccination.

Monitoring Disease Manifestations after EPYSQLI Discontinuation

Treatment Discontinuation for PNH

Monitor patients after discontinuing EPYSQLI for at least 8 weeks to detect hemolysis.

Treatment Discontinuation for aHUS

After discontinuing EPYSQLI, monitor patients with aHUS for signs and symptoms of thrombotic microangiopathy (TMA) complications for at least 12 weeks. In aHUS clinical trials, 18 patients (5 in the prospective studies) discontinued eculizumab treatment. TMA complications occurred following a missed dose in 5 patients, and eculizumab was reinitiated in 4 of these 5 patients.

Clinical signs and symptoms of TMA include changes in mental status, seizures, angina, dyspnea, or thrombosis. In addition, the following changes in laboratory parameters may identify a TMA complication: occurrence of two, or repeated measurement of any one of the following: a decrease in platelet count by 25% or more compared to baseline or the peak platelet count during EPYSQLI treatment; an increase in serum creatinine by 25% or more compared to baseline or nadir during EPYSQLI treatment; or, an increase in serum LDH by 25% or more over baseline or nadir during EPYSQLI treatment.

If TMA complications occur after EPYSQLI discontinuation, consider reinstitution of EPYSQLI treatment, plasma therapy [plasmapheresis, plasma exchange, or fresh frozen plasma infusion (PE/PI)], or appropriate organ-specific supportive measures.

Thrombosis Prevention and Management

The effect of withdrawal of anticoagulant therapy during eculizumab products treatment has not been established. Therefore, treatment with eculizumab products should not alter anticoagulant management.

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IMPORTANT SAFETY INFORMATION (cont)

WARNINGS AND PRECAUTIONS (cont)

Infusion-Related Reactions

Administration of eculizumab products may result in infusion-related reactions, including anaphylaxis or other hypersensitivity reactions. In clinical trials, no patients experienced an infusion-related reaction which required discontinuation of eculizumab. Interrupt EPYSQLI infusion and institute appropriate supportive measures if signs of cardiovascular instability or respiratory compromise occur.

ADVERSE REACTIONS

The most frequently reported adverse reactions in the PNH randomized trial (≥10% overall and greater than placebo) are: headache, nasopharyngitis, back pain, and nausea.

The most frequently reported adverse reactions in aHUS single arm prospective trials (≥20%) are: headache, diarrhea, hypertension, upper respiratory infection, abdominal pain, vomiting, nasopharyngitis, anemia, cough, peripheral edema, nausea, urinary tract infections, pyrexia.

The most frequently reported adverse reaction in the gMG placebo-controlled clinical trial (≥10%) is: musculoskeletal pain.

DRUG INTERACTIONS

Plasmapheresis, Plasma Exchange, or Fresh Frozen Plasma Infusion

Concomitant use of eculizumab products with plasma exchange (PE), plasmapheresis (PP) or fresh frozen plasma infusion (PE/PI) treatment can reduce serum eculizumab product concentrations and requires a supplemental dose of EPYSQLI.

Neonatal Fc Receptor Blockers

Concomitant use of eculizumab products with neonatal Fc receptor (FcRn) blockers may lower systemic exposures and reduce effectiveness of eculizumab products. Closely monitor for reduced effectiveness of EPYSQLI.

To report SUSPECTED ADVERSE REACTIONS, contact Teva Pharmaceuticals at 1-888-483-8279 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please click here for full Prescribing Information for EPYSQLI, including BOXED WARNINGS.

References: 1. ICD-10-CM tabular list of diseases and injuries. Centers for Disease Control and Prevention. January 2025. Accessed March 13, 2025. https://ftp.cdc.gov/pub/Health_Statistics/NCHS/Publications/ICD10CM/2025-Update/ **2.** HCPCS quarterly update. Centers for Medicare and Medicaid Services. Updated February 28, 2025. Accessed March 13, 2025. https://www.cms.gov/medicare/coding-billing/healthcare-common-procedure-system/quarterly-update **3.** Medicare-FFS program billing 340B modifiers under the Hospital Outpatient Prospective Payment System (OPPS) frequently asked questions. Centers for Medicare and Medicaid Services. March 3, 2023. Accessed February 25, 2025. https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitaloutpatientpps/downloads/billing-340b-modifiers-under-hospital-opps.pdf **4.** HCPCS modifier RE. Palmetto GBA. July 16, 2020. Accessed February 25, 2025. https://www.palmettogba.com/palmetto/jmb.nsf/DIDC/8EELCK4315~Claims~Modifier Lookup **5.** US Food and Drug Administration. Future format of the National Drug Code; public hearing; request for comments. *Fed Regist.* 2018;83(152):38666-38669. Accessed March 6, 2025. https://www.federalregister.gov/documents/2018/08/07/2018-16807/future-format-of-the-national-drug-code-public-hearing-request-for-comments **6.** EPYSQLI® (eculizumab-aagh) injection. Prescribing information. Samsung Bioepis Co, Ltd; 2024. **7.** 2025 ICD-10-PCS codes. ICD10Data.com. Accessed February 18, 2025. https://www.icd10data.com/ICD10PCS/Codes **8.** CPT® codes lookup. Codify by AAPC. Accessed February 18, 2025. https://www.aapc.com/codes/cpt-codes-range/ **9.** Billing and coding: approved drugs and biologicals; includes cancer chemotherapeutic agents (A53049). Centers for Medicare and Medicaid Services. Updated November 2, 2023. Accessed March 6, 2025. https://www.cms.gov/medicare-coverage-database/view/article.aspx?articleId=53049 **10.** CPT codes mapped to CVX codes. Immunization Information Systems, Centers for Disease Control and Prevention. Accessed March 13, 2025. https://www2a.cdc.gov/vaccines/iis/iisstandards/vaccines.asp?rpt=cpt **11.** CPT code 90471. Value Set Authority Center, National Library of Medicine. Accessed March 13, 2025. https://vsac.nlm.nih.gov/context/cs/codesystem/CPT/version/2020/code/90471/info