fitusiran (Qfitlia™)

Medicare Advantage Medical Policy #MA-137
Original Effective Date: 11/01/2025
Current Effective Date: 11/01/2025

Applies to all products administered or underwritten by the Health Plan, unless otherwise provided in the applicable contract. Medical technology is constantly evolving, and we reserve the right to review and update Medical Policy periodically.

When Services May Be Eligible for Coverage

Coverage for eligible medical treatments or procedures, drugs, devices or biological products may be provided only if:

- *Benefits are available in the member's contract/certificate, and*
- *Medical necessity criteria and guidelines are met.*

Based on review of available data, the Health Plan may consider fitusiran (Qfitlia™)‡ for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in patients with hemophilia A or hemophilia B to be **eligible for coverage.****

Patient Selection Criteria
Coverage eligibility for fitusiran (Qfitlia) will be considered when the following criteria are met:
Initial

- Patient is 12 years of age or older; AND
- Patient has a diagnosis of severe hemophilia A (as defined by a plasma factor VIII level ≤ 1% of normal [< 1 IU/dL]) or moderately severe to severe hemophilia B (as defined by a baseline plasma factor IX level ≤ 2 % [≤ 2 IU/dL]); AND
- According to the prescriber, Qfitlia will not be used in combination with ANY of the following:
    - Prophylactic factor VIII or factor IX products beyond the first 7 days of therapy. Note that the use of factor products for the treatment of breakthrough bleeding is permitted; OR
    - emicizumab (Hemlibra®)‡; OR
    - marstacimab-hncq (Hympavzi™)‡; OR
    - concizumab-mtci (Alhemo®)‡; OR
    - Bypassing agents (e.g., FEIBA®, NovoSeven®)‡ beyond the first 7 days of therapy. Note that the use of bypassing agents for the treatment of breakthrough bleeding is permitted; AND
- Patient does NOT have antithrombin activity (AT) less than 60%; AND
- Dose will not exceed 50 mg once monthly.

Continuation

- Patient has received an initial authorization for Qfitlia from the plan OR has provided documentation of authorization from previous Medicare Advantage plan; AND
- Provider attests that the patient has responded to Qfitlia as evidenced by a decrease in bleeding episodes or bleeding time as well as a decrease in antithrombin activity (AT); AND
- According to the prescriber, Qfitlia will not be used in combination with ANY of the following:

  - Prophylactic factor VIII or factor IX products. Note that the use of factor products for the treatment of breakthrough bleeding is permitted; OR
  - emicizumab (Hemlibra); OR
  - marstacimab-hncq (Hympavzi); OR
  - concizumab-mtci (Alhemo); OR
  - Bypassing agents (e.g., FEIBA, NovoSeven). Note that the use of bypassing agents for the treatment of breakthrough bleeding is permitted; AND
- Dose will not exceed 50 mg once monthly.

When Services Are Considered Not Medically Necessary

Based on review of available data, the Health Plan considers the use of fitusiran (Qfitlia) when the patient's hemophilia is not severe or moderately severe to be **not medically necessary.****

Based on review of available data, the Health Plan considers the continued use of fitusiran (Qfitlia) when the patient has not responded to the treatment as evidenced by a decrease in bleeding episodes or bleeding time and a decrease in antithrombin activity be **not medically necessary.****

When Services Are Considered Investigational

Coverage is not available for investigational medical treatments or procedures, drugs, devices or biological products.

Based on review of available data, the Health Plan considers the use of fitusiran (Qfitlia) when the patient selection criteria are not met (except those denoted above as **not medically necessary****) to be **investigational.***

Background/Overview

Qfitlia is an antithrombin (AT)-directed siRNA indicated for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A or B with or without factor VIII or factor IX inhibitors. It is administered subcutaneously once monthly or once every other month depending on the patient's AT levels with a target of 15-35% AT activity. Qfitlia has black box warnings regarding thrombotic events as well as acute and recurrent gallbladder disease. It has a significant advantage over other products for the prevention of bleeds in that it is administered much less frequently and via subcutaneous injection. It can also be used in patients with and without inhibitors to factor products.

Hemophilia is a bleeding disorder that is caused by a deficiency or dysfunction in one of the clotting factors that enables blood to clot. Hemophilia A is caused by a deficiency in factor VIII (FVIII) and hemophilia B is caused by a deficiency in factor IX (FIX). Because the disorder is transmitted on the X-chromosome, it primarily affects males. The incidence of hemophilia is one in every 5,000 males born in the United States, approximately 80% of whom have hemophilia A. The condition is characterized by bleeding in joints, either spontaneously or in a provoked joint. Bleeding can occur

in many different body areas (e.g., muscles, central nervous system, gastrointestinal). The bleeding manifestations can lead to substantial morbidity, as well as mortality, if not properly treated.

Disease severity is usually defined by plasma levels of factor VIII or IX (depending on hemophilia type) and has been classified as follows:

- Severe: levels less than 1% of normal
- Moderate: levels 1-5% of normal
- Mild: levels > 5 to 40% of normal

The main treatment strategy for both types of hemophilia is factor replacement therapy in which administration of the deficient clotting factor is given to achieve adequate hemostasis. Depending on individual patient characteristics such as disease severity and number of bleeds, patients may receive prophylactic factor replacement therapy or only receive treatment in response to a bleed ("on demand therapy"). Many different factor VIII and IX replacement therapies are FDA approved. There are now some alternatives to factor replacement products. For patients with hemophilia A, emicizumab (Hemlibra) is a bispecific factor IXa and factor X-directed antibody that is administered subcutaneously and mimics the function of factor VIII. Additionally, marstacimab-hncq (Hympavzi) and concizumab-mtci (Alhemo) are anti-tissue factor pathway inhibitors approved for use in patients with hemophilia A or B. Currently, Hympavzi is approved in patients without inhibitors and Alhemo is approved in patients with inhibitors to factor.

After administration of factor replacement therapies, some patients may develop an immune response known as a factor inhibitor. These inhibitors are antibodies directed against the deficient factor and are more common among patients with more severe disease. Inhibitors occur in approximately 30% of patients with hemophilia A, usually after the first 20 to 30 days of exposure to factor replacement. The inhibitor interferes with the efficacy of the replacement products and can lead to bleeding, morbidity, decreased quality of life, and mortality. An inhibitor should be suspected if a bleeding event is not efficiently controlled by usual doses of factor replacement therapy or if breakthrough bleeding increases while receiving routine prophylaxis. Inhibitors are generally classified as high-titer (> 5 Bethesda units) or low titer (< 5 Bethesda units). Low-titer inhibitors can usually be overcome by using supratherapeutic doses of factor replacement therapy and are usually transient. High-titer inhibitors can be permanent if not eradicated. Bleeding episodes in patients with high-titer inhibitors are often managed with bypassing agents (such as FEIBA and NovoSeven) which generate thrombin by bypassing the specific missing coagulation factor. Immune tolerance therapy may also be used to eradicate inhibitors via frequent and regular exposure to high doses of factor concentrates over several months to years. Successful immune tolerance therapy allows the patient to resume the use of standard factor therapies for prophylaxis and management of bleeding.

FDA or Other Governmental Regulatory Approval

U.S. Food and Drug Administration (FDA)
Qfitlia was approved in March 2025 for routine prophylaxis to prevent or reduce the frequency of bleeding episodes in adult and pediatric patients 12 years of age and older with hemophilia A or hemophilia B, with or without factor VIII or IX inhibitors.

Rationale/Source

This medical policy was developed through consideration of peer-reviewed medical literature generally recognized by the relevant medical community, U.S. Food and Drug Administration approval status, nationally accepted standards of medical practice and accepted standards of medical practice in this community, technology evaluation centers, reference to regulations, other plan medical policies, and accredited national guidelines.

The efficacy and safety of Qfitlia in adult and pediatric patients aged 12 years and older with hemophilia A or B with or without inhibitors were established in two clinical studies:

- Hemophilia A or B with Inhibitory Antibodies: ATLAS-INH
- Hemophilia A or B without Inhibitory Antibodies: ATLAS-A/B

Patients in the above parent studies rolled over into the long-term extension study ATLAS-OLE.

The clinical studies ATLAS-INH and ATLAS-A/B tested an 80 mg monthly fixed dose of Qfitlia. Because of thrombotic events with this dose, the Qfitlia AT-DR targeting AT activity of 15–35% was implemented in ATLAS-OLE. The AT-DR was initiated when studies ATLAS-INH and ATLAS-A/B were nearly completed, therefore, the efficacy of Qfitlia AT-DR treatment was assessed by comparing the Qfitlia AT-DR treatment data from the long-term extension study ATLAS-OLE to the control data from studies ATLAS-INH and ATLAS-A/B. The efficacy analyses were conducted according to the intent to treat (ITT) principle preserving the randomization in the parent studies.

ATLAS-INH

ATLAS-INH was a randomized, multicenter, open-label clinical study in 57 adult and pediatric males (aged ≥ 12 years) with hemophilia A or B with inhibitory antibodies to factor VIII (FVIII) or factor IX (FIX), who previously received on-demand (episodic) treatment with bypassing agents (BPAs) for bleeding. Eligible patients were randomized in a 2:1 ratio to receive Qfitlia prophylaxis at a fixed dose of 80 mg subcutaneous (SC) monthly (N = 38) or BPA on-demand for treatment of breakthrough bleeding episodes (N = 19) for 9 months.

Of the 57 enrolled patients all had inhibitors; 45 patients had Hemophilia A and 12 had Hemophilia B. All patients in the study were male. Generally, the demographic and patient characteristics at baseline were comparable between the patients with hemophilia A and B.

ATLAS A/B
ATLAS A/B was a randomized, multicenter, open-label clinical study in 120 adult and pediatric males (aged ≥ 12 years) with hemophilia A or B without inhibitory antibodies to FVIII or FIX, who previously received on-demand (episodic) treatment with clotting factor concentrates (CFC) for bleeding. Eligible patients were randomized in a 2:1 ratio to receive Qfitlia prophylaxis at a fixed dose of 80 mg SC monthly (N=80) or CFCs on-demand to treat breakthrough bleeding episodes (N=40) for 9 months.

Of the 120 enrolled patients none had inhibitors; 93 patients had Hemophilia A and 27 had Hemophilia B. All patients in the study were male. Generally, the demographic and patient characteristics at baseline were comparable between the patients with hemophilia A and B.

ATLAS-OLE
A total of 227 patients rolled over from two clinical studies (ATLAS-INH and ATLAS-A/B) and ATLAS-PPX, a crossover study in patients previously on CFC or BPA prophylaxis, and were treated with Qfitlia in ATLAS-OLE. This multicenter open-label extension study evaluated the long-term safety and efficacy of Qfitlia in adult and pediatric males aged ≥ 12 years with hemophilia A or B, with or without inhibitory antibodies to FVIII or FIX. Eligible patients initially received Qfitlia 80 mg SC once monthly. The study was amended to evaluate the efficacy and safety of the AT-DR. A total of 213 patients were subsequently transitioned to AT-DR targeting AT activity of 15–35%.

In the AT-DR, the Qfitlia starting dose was 50 mg every two months, and dosing was individually adjusted based on AT activity level using the INNOVANCE Antithrombin assay. The dose could be increased to 50 mg every month or 80 mg every month or decreased to 20 mg every two months or 20 mg every month. Qfitlia was discontinued if AT activity was < 15% at the lowest dose. No patients required escalation to 80 mg every month to achieve the target AT range. The dose required to maintain AT activity 15–35% in patients who initiated dosing on 50 mg every two months was: 50 mg every two months (35.8% of patients), 50 mg every month (15.7% of patients), 20 mg every two months (30.9% of patients), or 20 mg every month (2.9% of patients). A total of 14.7% of patients discontinued Qfitlia due to more than one AT activity < 15%.

Patients with known co-existing coagulation disorders other than hemophilia A or B, increased risk of thrombosis as assessed by history of arterial or venous thromboembolism, significant valvular disease or atrial fibrillation, or co-existing thrombophilic disorder (e.g., Factor V Leiden mutation), AT activity < 60% at screening, platelet count ≤ 100,000/μL, eGFR ≤ 45 mL/min (using the MDRD), or clinically significant liver disease were not eligible for enrollment.

The efficacy of Qfitlia AT-DR in ATLAS-OLE was evaluated for a duration of 7 months (primary efficacy period) following a 6-month dose adjustment period. The median observed annualized bleeding rate (IQR) for treated bleeds was 3.7 (0.0; 7.5) overall, 1.9 (0.0; 5.6) in inhibitor patients and 3.8 (0.0; 11.2) in non-inhibitor patients.

Qfitlia Prophylaxis Compared to On-Demand BPA or CFC

The efficacy results of Qfitlia prophylaxis using AT-DR in ATLAS-OLE compared to on-demand BPA or CFC control data from studies ATLAS-INH and ATLAS-A/B with respect to rate of treated bleeds are as follows. In patients with inhibitors (ATLAS-INH), those in the Qfitlia group experienced an annual bleed rate (ABR) of 5.1 (95% CI 2.8, 9.5) compared to a rate of 19.1 (95% CI: 11.8, 31.0) in those receiving on-demand BPA. This corresponds to a 73% reduction in bleeds ($p = 0.0006$). In patients without inhibitors (ATLAS-A/B), those in the Qfitlia group experienced an ABR of 9.0 (95% CI 5.6, 14.5) compared to a rate of 31.4 (95% CI: 20.5, 48.2) in those receiving on-demand CFC. This corresponds to a 71% reduction in bleeds ($p < 0.0001$).

References

1. Qfitlia [package insert]. Genzyme Corporation. Cambridge, MA. Updated March 2025.
2. Qfitlia (fitusiran) New Drug Review. IPD Analytics. Updated April 2025.

Policy History

Original Effective Date: 11/01/2025
Current Effective Date: 11/01/2025
08/19/2025 UM Committee review and approval. New policy.
Next Scheduled Review Date: 08/2026

Coding

The five character codes included in the Health Plan Medical Policy Coverage Guidelines are obtained from Current Procedural Terminology (CPT®)‡, copyright 2024 by the American Medical Association (AMA). CPT is developed by the AMA as a listing of descriptive terms and five character identifying codes and modifiers for reporting medical services and procedures performed by physicians.

The responsibility for the content of the Health Plan Medical Policy Coverage Guidelines is with the Health Plan and no endorsement by the AMA is intended or should be implied. The AMA disclaims responsibility for any consequences or liability attributable or related to any use, nonuse or interpretation of information contained in the Health Plan Medical Policy Coverage Guidelines. Fee schedules, relative value units, conversion factors and/or related components are not assigned by the AMA, are not part of CPT, and the AMA is not recommending their use. The AMA does not directly or indirectly practice medicine or dispense medical services. The AMA assumes no liability for data contained or not contained herein. Any use of CPT outside of the Health Plan Medical Policy Coverage Guidelines should refer to the most current Current Procedural Terminology which contains the complete and most current listing of CPT codes and descriptive terms. Applicable FARS/DFARS apply.

Codes used to identify services associated with this policy may include (but may not be limited to) the following:

Code Type	Code
CPT	No code
HCPCS	C9399, J3490
ICD-10 Diagnosis	All Related Diagnoses

*Investigational – A medical treatment, procedure, drug, device, or biological product is Investigational if the effectiveness has not been clearly tested and it has not been incorporated into standard medical practice. Any determination we make that a medical treatment, procedure, drug, device, or biological product is Investigational will be based on a consideration of the following:

A. Whether the medical treatment, procedure, drug, device, or biological product can be lawfully marketed without approval of the U.S. Food and Drug Administration (FDA) and whether such approval has been granted at the time the medical treatment, procedure, drug, device, or biological product is sought to be furnished; or
B. Whether the medical treatment, procedure, drug, device, or biological product requires further studies or clinical trials to determine its maximum tolerated dose, toxicity, safety, effectiveness, or effectiveness as compared with the standard means of treatment or diagnosis, must improve health outcomes, according to the consensus of opinion among experts as shown by reliable evidence, including:
    1. Consultation with technology evaluation center(s);
    2. Credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community; or
    3. Reference to federal regulations.

**Medically Necessary (or "Medical Necessity") - Health care services, treatment, procedures, equipment, drugs, devices, items or supplies that a Provider, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury, disease or its symptoms, and that are:

A. In accordance with nationally accepted standards of medical practice;
B. Clinically appropriate, in terms of type, frequency, extent, level of care, site and duration, and considered effective for the patient's illness, injury or disease; and
C. Not primarily for the personal comfort or convenience of the patient, physician or other health care provider, and not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.

For these purposes, "nationally accepted standards of medical practice" means standards that are based on credible scientific evidence published in peer-reviewed medical literature generally recognized by the relevant medical community, Physician Specialty Society recommendations and the views of Physicians practicing in relevant clinical areas and any other relevant factors.

‡ Indicated trademarks are the registered trademarks of their respective owners.

NOTICE: If the Patient's health insurance contract contains language that differs from the Health Plan Medical Policy definition noted above, the definition in the health insurance contract will be relied upon for specific coverage determinations.

NOTICE: Medical Policies are scientific based opinions, provided solely for coverage and informational purposes. Medical Policies should not be construed to suggest that the Health Plan recommends, advocates, requires, encourages, or discourages any particular treatment, procedure, or service, or any particular course of treatment, procedure, or service.

NOTICE: Federal and State law, as well as contract language, including definitions and specific contract provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage.

Medicare Advantage Members

Established coverage criteria for Medicare Advantage members can be found in Medicare coverage guidelines in statutes, regulations, National Coverage Determinations (NCD)s, and Local Coverage Determinations (LCD)s. To determine if a National or Local Coverage Determination addresses coverage for a specific service, refer to the Medicare Coverage Database at the following link: https://www.cms.gov/medicare-coverage-database/search.aspx. You may wish to review the Guide to the MCD Search here: https://www.cms.gov/medicare-coverage-database/help/mcd-bene-help.aspx.

When coverage criteria are not fully established in applicable Medicare statutes, regulations, NCDs or LCDs, internal coverage criteria may be developed. This policy is to serve as the summary of evidence, a list of resources and an explanation of the rationale that supports the adoption of this internal coverage criteria.