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5.85.019

Section:	Prescription Drugs	**Effective Date:**	April 1, 2025
Subsection:	Hematological Agents	**Original Policy Date:**	October 24, 2014
Subject:	Zavesca Yargesa	**Page:**	1 of 6

Last Review Date: March 7, 2025

Zavesca Yargesa

Description

Zavesca (miglustat)

Yargesa (miglustat)

Background
Gaucher disease is an inherited lysosomal storage disorder in humans that results in the inability to produce glucocerebrosidase, an enzyme necessary for fat metabolism. The enzyme deficiency causes fat materials (lipids) to collect and build up over time, causing problems in the spleen, liver, and bone marrow. Accumulation of lipids in these areas results in the enlargement of the liver and spleen, anemia, thrombocytopenia, lung disease and bone abnormalities (1).

Zavesca and Yargesa are oral medications for the long-term treatment of adult patients with the type 1 form of Gaucher disease. The drug reduces the harmful buildup of the fatty materials by reducing the amount of glucosylceramide- based glycosphingolipids the body produces (1-2).

Regulatory Status
FDA-approved indication: Zavesca and Yargesa are glucosylceramide synthase inhibitors indicated as monotherapy for treatment of adult patients with mild/moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option (1-2).

Zavesca and Yargesa are also used in combination with Miplyffa (arimoclomol) for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC) in adult and pediatric patients 2 years of age and older (3).

People with type 1 Gaucher disease also may have lowered levels of hemoglobin (a substance in red blood cells) and platelets (blood-clotting cells) that may cause anemia (low red blood cell count) (1).

Clinically significant adverse reactions may occur with Zavesca and Yargesa therapy including peripheral neuropathy, tremor, reduction in platelet count, diarrhea, and weight loss. Based on the severity of the adverse reaction, Zavesca and Yargesa therapy should have a dose reduction or discontinued. Patients with mild to moderate renal insufficiency should have a dose reduction. Use of Zavesca and Yargesa in patients with severe renal impairment (creatinine clearance < 30mL/min/1.73 m^2) is not recommended. Therapy should be directed by physicians knowledgeable in the management of patients with Gaucher disease (1-2).

Safety and effectiveness of Zavesca and Yargesa in pediatric patients with Gaucher disease have not been established. Safety and effectiveness of Zavesca and Yargesa in pediatric patients less than 2 years of age with NPC have not been established (1-3).

Related policies

Cerdelga, Cerezyme, Elelyso, VPRIV

Policy

This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.

Zavesca and Yargesa may be considered **medically necessary** if the conditions indicated below are met.

Zavesca and Yargesa may be considered **investigational** for all other indications.

Prior-Approval Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Mild-to-moderate type 1 Gaucher disease
    a. 18 years of age or older

b. Enzyme replacement therapy (such as Cerezyme, Elelyso, VPRIV) is not a therapeutic option (e.g., due to constraints such as allergy, hypersensitivity, or poor venous access)
c. **NO** dual therapy with another medication for Type 1 Gaucher disease (see Appendix 1)

2. Niemann-Pick disease type C (NPC)
    a. 2 years of age or older
    b. NPC diagnosis confirmed by genetic testing identifying disease causing variants in the NPC1 or NPC2 genes
    c. Used for the neurological manifestations of NPC
    d. Used in combination with Miplyffa (arimoclomol)

Prior–Approval *Renewal* Requirements

Diagnoses

Patient must have **ONE** of the following:

1. Type 1 Gaucher disease
    a. 18 years of age or older
    b. **NO** dual therapy with another medication for Type 1 Gaucher disease (see Appendix 1)

2. Niemann-Pick disease type C (NPC)
    a. 2 years of age or older
    b. Neurological manifestations have improved or stabilized
    c. Used in combination with Miplyffa (arimoclomol)

Policy Guidelines

Pre - PA Allowance

None

Prior - Approval Limits

Duration 2 years

Prior–Approval *Renewal* Limits

Same as above

Rationale

Summary
Zavesca and Yargesa are oral medications for the long-term monotherapy treatment of adult patients with mild/moderate type 1 Gaucher disease for whom enzyme replacement therapy is not a therapeutic option due to constraints such as allergy, hypersensitivity, or poor venous access. Zavesca and Yargesa are also used for the treatment of neurological manifestations of Niemann-Pick disease type C (NPC). Safety and effectiveness of Zavesca and Yargesa in pediatric patients with Gaucher disease have not been established. Safety and effectiveness of Zavesca and Yargesa in pediatric patients less than 2 years of age with NPC have not been established (1-3).

Prior approval is required to ensure the safe, clinically appropriate, and cost-effective use of Zavesca and Yargesa while maintaining optimal therapeutic outcomes.

References
1. Zavesca [package insert]. San Francisco, CA: Actelion Pharmaceuticals US Inc.; August 2022.
2. Yargesa [package insert]. Parsippany, NJ: Edenbridge Pharmaceuticals, LLC.; October 2023.
3. Miplyffa [package insert]. Celebration, FL: Zevra Therapeutics, Inc.; September 2024.

Policy History

Date	Action
November 2014	Addition to PA
December 2014	Annual editorial review and reference update
December 2015	Annual review
December 2016	Annual review and reference update Policy number change from 5.10.19 to 5.85.19
September 2017	Annual editorial review and reference update Removal of Ceredase which is no long marketed
September 2018	Annual review and reference update
September 2019	Annual editorial review. Changed approval duration from lifetime to 2 years
September 2020	Annual review

December 2021	Annual review and reference update
December 2022	Annual review and reference update. Changed policy number to 5.85.019
June 2023	Annual review
June 2024	Annual review
October 2024	Addition of Yargesa to policy. Added indication of Niemann-Pick disease type C (NPC)
March 2025	Annual review

Keywords

This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 7, 2025 and is effective on April 1, 2025.

Appendix 1 - List of Medications for Type 1 Gaucher Disease

Generic Name	Brand Name
eliglustat	Cerdelga
imiglucerase	Cerezyme
miglustat	Zavesca/Yargesa
taliglucerase alfa	Elelyso
velaglucerase alfa	VPRIV