Drug Coverage Policy

Effective Date.....05/15/2025
Coverage Policy Number.....IP0727
Policy Title.....Grafapex

Transplantation – Grafapex

- Grafapex™ (treosulfan intravenous infusion – Medexus)

INSTRUCTIONS FOR USE
The following Coverage Policy applies to health benefit plans administered by Cigna Companies. Certain Cigna Companies and/or lines of business only provide utilization review services to clients and do not make coverage determinations. References to standard benefit plan language and coverage determinations do not apply to those clients. Coverage Policies are intended to provide guidance in interpreting certain standard benefit plans administered by Cigna Companies. Please note, the terms of a customer's particular benefit plan document [Group Service Agreement, Evidence of Coverage, Certificate of Coverage, Summary Plan Description (SPD) or similar plan document] may differ significantly from the standard benefit plans upon which these Coverage Policies are based. For example, a customer's benefit plan document may contain a specific exclusion related to a topic addressed in a Coverage Policy. In the event of a conflict, a customer's benefit plan document always supersedes the information in the Coverage Policies. In the absence of a controlling federal or state coverage mandate, benefits are ultimately determined by the terms of the applicable benefit plan document. Coverage determinations in each specific instance require consideration of 1) the terms of the applicable benefit plan document in effect on the date of service; 2) any applicable laws/regulations; 3) any relevant collateral source materials including Coverage Policies and; 4) the specific facts of the particular situation. Each coverage request should be reviewed on its own merits. Medical directors are expected to exercise clinical judgment where appropriate and have discretion in making individual coverage determinations. Where coverage for care or services does not depend on specific circumstances, reimbursement will only be provided if a requested service(s) is submitted in accordance with the relevant criteria outlined in the applicable Coverage Policy, including covered diagnosis and/or procedure code(s). Reimbursement is not allowed for services when billed for conditions or diagnoses that are not covered under this Coverage Policy (see "Coding Information" below). When billing, providers must use the most appropriate codes as of the effective date of the submission. Claims submitted for services that are not accompanied by covered code(s) under the applicable Coverage Policy will be denied as not covered. Coverage Policies relate exclusively to the administration of health benefit plans. Coverage Policies are not recommendations for treatment and should never be used as treatment guidelines. In certain markets, delegated vendor guidelines may be used to support medical necessity and other coverage determinations.

Overview

Grafapex, an alkylating drug, is indicated for use in combination with fludarabine as a preparatory regimen for allogeneic hematopoietic stem cell transplantation (HSCT) in adult and pediatric patients ≥ 1 year of age for acute myeloid leukemia (AML) and myelodysplastic syndrome (MDS).

Disease Overview
Allogeneic HSCT has a vital role in the management of patients with various hematologic malignancies.[2] In patients undergoing allogeneic HSCT, conditioning regimens are given to eradicate malignant cells in the bone marrow (if utilizing a myeloablative regimen) and to immunosuppress the recipient to promote engraftment of healthy donor cells. It is estimated that over 8,000 allogeneic transplants were performed in the US in 2021. Common malignancies treated in this manner include AML and MDS. Allogeneic HSCT is done to replace the malignant hematopoietic cells with those derived from a healthy donor.

Dosing Information
The recommended dose of Grafapex is 10 g/m^2 of body surface area per day as a 2-hour intravenous (IV) infusion which is administered on 3 consecutive days (Day -4, -3, -2) in combination with fludarabine before hematopoietic stem cell fusion (Day 0).[1]

Guidelines
The National Comprehensive Cancer Network (NCCN) guidelines for hematopoietic cell transplantation (version 2.024 – August 30, 2024) have not addressed Grafapex.[2] The NCCN guidelines recommended various conditioning regimens utilized in patients undergoing allogeneic HSCT, including busulfan and fludarabine. These agents have been used together, along with other agents (e.g., cyclophosphamide, thiotepa, clofarabine).

Safety
Grafapex has a Boxed Warning regarding myelosuppression.[1]

Coverage Policy

POLICY STATEMENT
Prior Authorization is required for medical benefit coverage of Grafapex. Approval is recommended for those who meet the **Criteria** and **Dosing** for the listed indication. Requests for doses outside of the established dosing documented in this policy will be considered on a case-by-case basis by a clinician (i.e., Medical Director or Pharmacist). All approvals are provided for 30 days to allow for an adequate time frame to administer the doses. Because of the specialized skills required for evaluation and diagnosis of patients treated with Grafapex as well as the monitoring required for adverse events and long-term efficacy, approval requires Grafapex to be prescribed by or in consultation with a physician who specializes in the condition being treated.

Grafapex is considered medically necessary when ONE of the following is met (1 or 2):

FDA-Approved Indications

1. **Acute Myeloid Leukemia.** Approve for 30 days if the patient meets ALL of the following (A, B, C, and D):
   - **A)** Patient is ≥ 1 year of age; AND
   - **B)** Patient is using Grafapex in combination with fludarabine; AND
   - **C)** Patient is undergoing allogeneic hematopoietic stem cell transplantation; AND
   - **D)** The medication is prescribed by or in consultation with a hematologist, oncologist, transplant specialist physician, or a physician associated with a transplant center.

Dosing. Approve a dose of up to 10 mg/m^2 body surface area per day given by intravenous infusion for up to 3 consecutive days.

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2. **Myelodysplastic Syndrome.** Approve for 30 days if the patient meets ALL of the following (A, B, C, and D):
   A) Patient is ≥ 1 year of age; AND
   B) Patient is using Grafapex in combination with fludarabine; AND
   C) Patient is undergoing allogeneic hematopoietic stem cell transplantation; AND
   D) The medication is prescribed by or in consultation with a hematologist, oncologist, transplant specialist physician, or a physician associated with a transplant center.

   Dosing. Approve a dose of up to 10 mg/m^2 body surface area per day given by intravenous infusion for up to 3 consecutive days.

Grafapex for any other use is considered not medically necessary. Criteria will be updated as new published data are available.

Coding Information

1) This list of codes may not be all-inclusive.
2) Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

HCPCS Codes	Description
J9999	Not otherwise classified, antineoplastic drugs

References

1. Grafapex™ intravenous infusion [prescribing information]. Chicago, IL: Medexus; January 2025.
2. The NCCN Hematopoietic Cell Transplantation (HCT) Guidelines in Oncology (version 2.2024 – August 30, 2024). © 2024 National Comprehensive Cancer Network. Available at: http://www.nccn.org. Accessed on February 22, 2025.

Revision Details

Type of Revision	Summary of Changes	Date
New	New policy	05/15/2025

The policy effective date is in force until updated or retired.