Medical Policy

Utilization Management and Clinical Medical Policy

Policy Name:	Policy Number:	Scope:	Origination Date:	Effective Date:
Treosulfan (Grafapex®)	**MP-RX-FP-174-25**	☒ **MMM MA** ☒ **MMM MultiHealth**	**8/8/2025** **Last Review Date:** **7/1/2026**	**7/1/2026** **Frequently Revision:** **Annual**

Service Category:

☐ Anesthesia
☐ Surgery
☐ Radiology Procedures
☐ Pathology and Laboratory Procedures
☐ Medicine Services and Procedures
☐ Evaluation and Management Services
☐ DME/Prosthetics or Supplies
☒ Other: Part B Drugs

Service Description:

This document addresses the use of Treosulfan (Grafapex) , a drug approved by the Food and Drug Administration (FDA) as a preparative regimen for allogeneic hematopoietic stem cell transplantation (HSCT) used in combination with fludarabine.

Background Information:

This document addresses the use of Grafapex (treosulfan). Grafapex is an alkylating agent, used in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation (HSCT). Efficacy was evaluated in MC-FludT.14/L Trial II (NCT00822393). This trial was an open-label, randomized, non-inferiority, phase 3 trial that compared treosulfan to reduced intensity conditioning busulfan with fludarabine as a preparative regimen for allogeneic transplantation. Eligible patients were 18-70 years old, had acute myeloid leukemia in first or consecutive complete hematological remission (blast counts 50 years of age, an HSCT-specific comorbidity index of more than 2, or both. 2- year event-free survival was 64% (95% CI 56·0–70·9) in the treosulfan group and 50·4% (42·8–57·5) in the busulfan group (HR 0·65 [95% CI 0·47–0·90]; p<0.0001 for non-inferiority, p=0.0051 for superiority). Treosulfan was non-inferior to busulfan when used in combination with fludarabine as a conditioning regimen for allogeneic HSCT for older or comorbid patients with acute myeloid leukemia or myelodysplastic syndrome.

Definitions and Measures

- Hematopoietic stem cells: Primitive cells capable of replication and formation into mature blood cells to repopulate the bone marrow.

Approved Indications

A. Use in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation (alloHSCT) in adult and pediatric patients 1 year of age and older with acute myeloid leukemia (AML).
B. Use in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients 1 year of age and older with myelodysplastic syndrome (MDS).

Other Uses

A. None.

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Medical Necessity Guidelines:

When a drug is being reviewed for coverage under a member's medical benefit plan or is otherwise subject to clinical review (including prior authorization), the following criteria will be used to determine whether the drug meets any applicable medical necessity requirements for the intended/prescribed purpose.

Treosulfan (Grafapex®)

A. Criteria For Initial Approval (*Provider must submit documentation [such as office chart notes, lab results, pathology reports, imaging studies, and any other pertinent clinical information] supporting the patient's diagnosis for the drug and confirming that the patient has met **all** approval criteria.)*

Requests for Grafapex (treosulfan) may be approved if the following criteria are met:

i. Individual has a diagnosis of acute myeloid leukemia (AML) or myelodysplastic syndrome (MDS); **AND**
ii. Individual is using as preparative regimen for allogeneic hematopoietic stem cell transplantation (alloHSCT); **AND**
iii. Individual is using in combination with fludarabine.

B. Criteria For Continuation of Therapy

i. MMM considers continuation of T*reosulfan (Grafapex)* therapy medically necessary in members requesting reauthorization for an indication listed in Section A above (Criteria for Initial Approval) when there is no evidence of an unacceptable toxicity while on the current regimen.

C. Authorization Duration

i. Initial Approval Duration: Per allogeneic hematopoietic stem cell transplantation (alloHSCT).
ii. Reauthorization Approval Duration: Per allogeneic hematopoietic stem cell transplantation (alloHSCT).

D. Conditions Not Covered

Any other use is considered experimental, investigational, or unproven, including the following (this list may not be all inclusive):

i. Requests for Grafapex (treosulfan) may not be approved when the above criteria in section A are not met and for all other indications.

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Limits or Restrictions:

A. Therapeutic Alternatives

The list below includes preferred alternative therapies recommended in the approval criteria and may be subject to prior authorization.

i. N/A

B. Quantity Limitations

Approvals may be subject to dosing limits in accordance with FDA-approved labeling, accepted compendia, and/or evidence-based practice guidelines. The chart below includes dosing recommendations as per the FDA-approved prescribing information.

Drug	Dose
GRAFAPEX (treosulfan)- for injection, for intravenous use 1g vial 5g vial	• 10 g/m² body surface area (BSA) per day as a two-hour intravenous infusion, given on three consecutive days (day -4, -3, -2) in conjunction with fludarabine before hematopoietic stem cell infusion (day 0).

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Codes Information:

The following list(s) of procedure and/or diagnosis codes is provided for reference purposes only and may not be all inclusive. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Benefit coverage for health services is determined by the member specific benefit plan document and applicable laws that may require coverage for a specific service. The inclusion of a code does not imply any right to reimbursement or guarantee claim payment. Other Policies and Guidelines may apply.

ICD-10 Diagnostic Codes:

Codes	Description
C92.00	Acute myeloblastic leukemia, not having achieved remission
D46.9	Myelodysplastic syndrome, unspecified
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

HCPCS Codes:

Codes	Description
J0614	Injection, treosulfan 50 mg [Grafapex]

Reference Information:

1. DailyMed. Package inserts. U.S. National Library of Medicine, National Institutes of Health website. http://dailymed.nlm.nih.gov/dailymed/about.cfm. Updated periodically.
2. DrugPoints® System [electronic version]. Truven Health Analytics, Greenwood Village, CO. Updated periodically.
3. Lexi-Comp ONLINE™ with AHFS™, Hudson, Ohio: Lexi-Comp, Inc. Updated periodically.
4. NCCN Clinical Practice Guidelines in Oncology™. © 2026 National Comprehensive Cancer Network, Inc. For additional information visit the NCCN website: http://www.nccn.org/index.asp. Accessed on January 8, 2026.
    a. Hematopoietic Cell Transplantation. V3.2025. Revised September 24, 2025.
5. Beelen, Dietrich Wilhelm et al. "Treosulfan or busulfan plus fludarabine as conditioning treatment before allogeneic haemopoietic stem cell transplantation for older patients with acute myeloid leukaemia or myelodysplastic syndrome (MC-FludT.14/L): a randomised, non-inferiority, phase 3 trial." The Lancet. Haematology vol. 7,1 (2020): e28-e39. doi:10.1016/S2352-3026(19)30157-7

Federal and state laws or requirements, contract language, and Plan utilization management programs or polices may take precedence over the application of this clinical criteria.

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Policy History:

Type of Review	Summary of Changes	P&T Approval Date	UM/CMPC Approval Date
Annual Review	Added FDA approved indications and available dosage forms. Coding Update: Removed HCPCS C9175 and J9999 and added J0614. Added ICD-10-CM C92.00 and D46.9. Updated reference list and incorporated new policy template.	6/19/2026	7/1/2026
Policy Inception	Elevance Health adopted medical policy.	7/21/2025	8/8/2025