

<p><b>Policy Name</b></p> <p>Treosulfan (Grafapex)</p>	<p><b>Policy Number</b></p> <p>MP-RX-FP-174-25</p>	<p><b>Scope</b></p> <p><input checked="" type="checkbox"/> MMM MA      <input checked="" type="checkbox"/> MMM Multihealth</p>								
<p><b>Service Category</b></p> <table border="0"> <tr> <td><input type="checkbox"/> Anesthesia</td> <td><input type="checkbox"/> Medicine Services and Procedures</td> </tr> <tr> <td><input type="checkbox"/> Surgery</td> <td><input type="checkbox"/> Evaluation and Management Services</td> </tr> <tr> <td><input type="checkbox"/> Radiology Procedures</td> <td><input type="checkbox"/> DME/Prosthetics or Supplies</td> </tr> <tr> <td><input type="checkbox"/> Pathology and Laboratory Procedures</td> <td><input checked="" type="checkbox"/> Part B Drugs</td> </tr> </table>			<input type="checkbox"/> Anesthesia	<input type="checkbox"/> Medicine Services and Procedures	<input type="checkbox"/> Surgery	<input type="checkbox"/> Evaluation and Management Services	<input type="checkbox"/> Radiology Procedures	<input type="checkbox"/> DME/Prosthetics or Supplies	<input type="checkbox"/> Pathology and Laboratory Procedures	<input checked="" type="checkbox"/> Part B Drugs
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<p><b>Service Description</b></p> <p>This document addresses the use of <b>Treosulfan (Grafapex)</b>, 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.</p> <p><b>Background Information</b></p> <p>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&lt;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.</p> <p><b>Definitions and Measures</b></p> <p>Hematopoietic stem cells: Primitive cells capable of replication and formation into mature blood cells to repopulate the bone marrow.</p>										

# Medical Policy

Healthcare Services Department

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## Applicable Codes

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.

HCPCS	Description
C9175	Injection, treosulfan, 50 mg [Grafapex]
J9999	Not otherwise classified, antineoplastic drugs [when specified as Grafapex (treosulfan)]

ICD-10	Description
Z94.81	Bone marrow transplant status
Z94.84	Stem cells transplant status

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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.

*Provider must submit documentation (such as office chart notes, lab results or other clinical information) supporting that member has met all approval criteria.*

### Treosulfan (Grafapex)

#### A. Criteria For Initial Approval

- 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 **Treosulfan (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

- a. Initial Approval Duration: Per allogeneic hematopoietic stem cell transplantation (alloHSCT).
- b. 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. 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	10 g/m <sup>2</sup> 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).

## 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. 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

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## Policy History

Revision Type	Summary of Changes	P&T Approval Date	MPCC Approval Date
Policy Inception 6/26/2025	Elevance Health adopted medical policy.	7/21/2025	8/8/2025