Medical Drug Clinical Criteria

Subject:	Grafapex (treosulfan)		
Document #:	CC-0280	**Publish Date:**	03/18/2025
Status:	New	**Last Review Date:**	02/21/2025

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Overview

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 <5% in bone marrow) or myelodysplastic syndrome (blast counts <20% in bone marrow). Individuals had Karnofsky index of 60% or higher and were indicated for allogeneic HSCT but considered increased mortality risk for standard myeloablative preparative regimens based on age ≥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.

Grafapex has a black box warning pertaining to severe and prolonged myelosuppression. Hematopoietic stem cell transplantation is required to prevent potentially fatal complications of the prolonged myelosuppression. Monitoring hematologic laboratory parameters is recommended.

Definitions and Measures

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

Clinical Criteria

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.

Grafapex (treosulfan)

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.

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

Coding

The following codes for treatments and procedures applicable to this document are included below for informational purposes. Inclusion or exclusion of a procedure, diagnosis or device code(s) does not constitute or imply member coverage or provider reimbursement policy. Please refer to the member's contract benefits in effect at the time of service to determine coverage or non-coverage of these services as it applies to an individual member.

HCPCS

C9399	Unclassified drugs or biologicals [when specified as Grafapex (treosulfan)]
J9999	Not otherwise classified, antineoplastic drugs [when specified as Grafapex (treosulfan)]

ICD-10 Diagnosis

	All diagnosis pend

Document History

New: 02/21/2025
Document History:

- 02/21/2025 – Annual Review: New clinical criteria for Grafapex. Coding Reviewed: Added HCPCS NOC C9399, J9999, and all diagnosis pend for Grafapex.

References

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.

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.