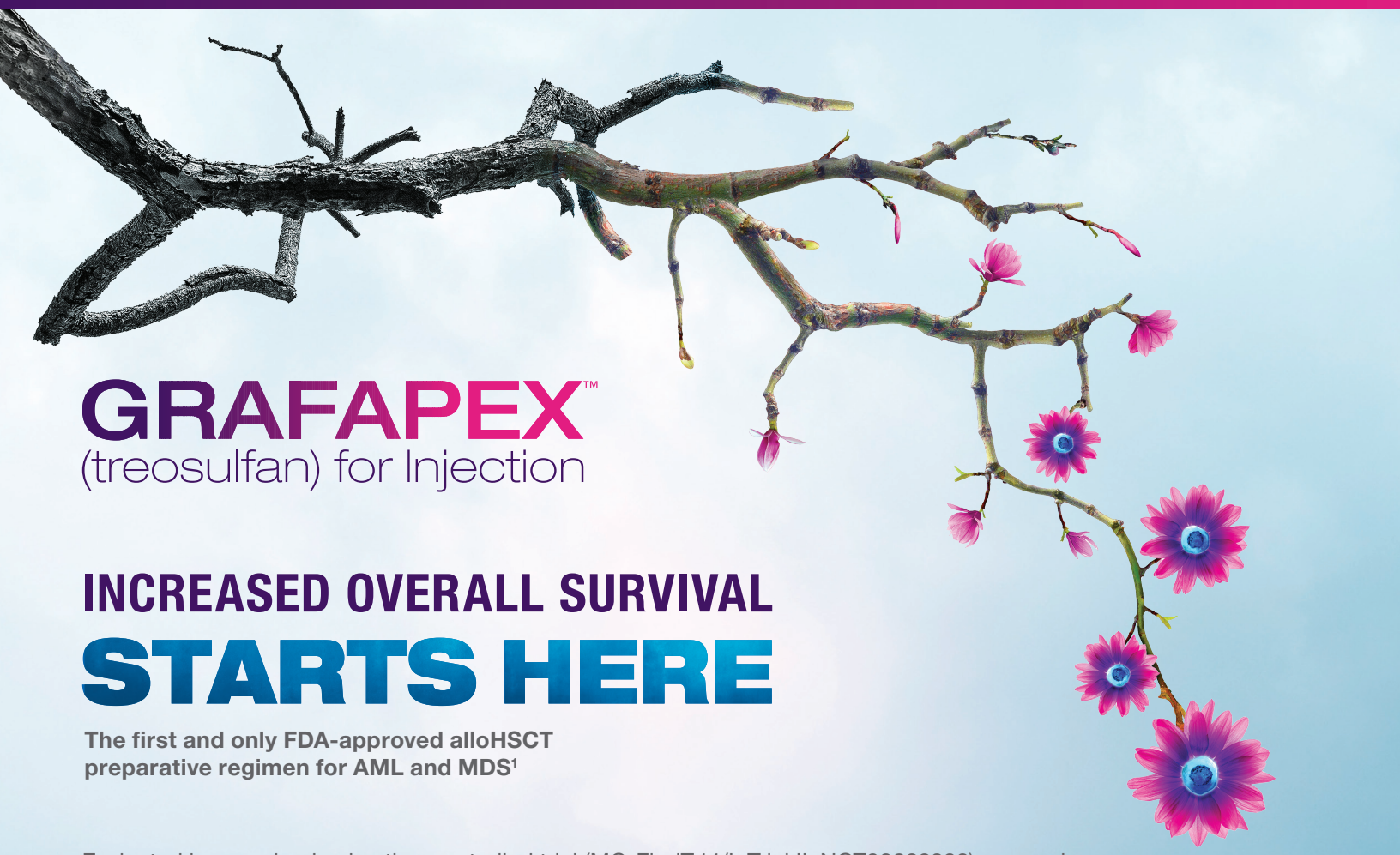

GRAFAPEX™
(treosulfan) for Injection

INCREASED OVERALL SURVIVAL
STARTS HERE

The first and only FDA-approved alloHSCT preparative regimen for AML and MDS[1]

Evaluated in a randomized active-controlled trial (MC-FludT.14/L Trial II; NCT00822393) comparing GRAFAPEX to busulfan in combination with fludarabine as a preparative regimen for allogeneic transplantation.

Overall survival since time of randomization MC-FLudT.14/L Trial II HR 0.67 (95% CI: 0.51, 0.90).[1]

alloHSCT, allogeneic hematopoietic stem cell transplantation; AML, acute myeloid leukemia; CI, confidence interval; HR, hazard ratio; MDS, myelodysplastic syndrome.

Indications, Important Safety Information, Including Boxed Warning, for GRAFAPEX™ (treosulfan) for Injection

Indications and Usage

Acute Myeloid Leukemia: GRAFAPEX is an alkylating drug indicated in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients >1 year old with acute myeloid leukemia.

Myelodysplastic Syndrome: GRAFAPEX is an alkylating drug indicated in combination with fludarabine as a preparative regimen for allogeneic hematopoietic stem cell transplantation in adult and pediatric patients >1 year old with myelodysplastic syndrome.

This product includes the following Boxed Warning:

WARNING: MYELOSUPPRESSION

- **GRAFAPEX causes severe and prolonged myelosuppression at the recommended dosage.**
- **Hematopoietic stem cell transplantation is required to prevent potentially fatal complications of the prolonged myelosuppression. Monitor hematologic laboratory parameters.**

Please see enclosed Prescribing Information, including Boxed Warning for GRAFAPEX.

GRAFAPEX™ (treosulfan) for Injection ORDERING AND DOSING SCHEDULE

How supplied[1]

- GRAFAPEX is a white, sterile, lyophilized powder for reconstitution
- GRAFAPEX is supplied as single-dose vials:
  - 1 g NDC 59137-335-01
  - 5 g NDC 59137-365-01

How to order

- Cencora dba ASD Healthcare
  - service@asdhealthcare.com
  - 1-800-746-6273

Table 1: GRAFAPEX Billing Information

ICD-10-PCS Codes	Description
XW04388	Introduction of treosulfan into central vein, percutaneous approach, new technology group 8
XW03388	Introduction of treosulfan into peripheral vein, percutaneous approach, new technology group 8
HCPCS Codes	**Description**
J3490	Unclassified drugs
C9399	Unclassified drug or biological

Recommended dosage[1]

The recommended dosage of GRAFAPEX is 10 g/m² by intravenous infusion given daily for three days, beginning on Day –4 prior to transplantation in combination with fludarabine as outlined in Table 2.

Table 2: Dosage Regimen for GRAFAPEX-Based Allogeneic HSCT[1]

Treatment	Day –6	Day –5	Day –4	Day –3	Day –2	Day –1	Day 0
GRAFAPEX 10 g/m²/day intravenously			X	X	X		
Fludarabine 30 mg/m²/day intravenously	X	X	X	X	X		
Allogeneic hematopoietic stem cell infusion							X

HCPCS, Healthcare Common Procedure Coding System; ICD, International Classification of Diseases.

Important Safety Information *(continued)*

Warnings and Precautions

Myelosuppression: Profound myelosuppression with pancytopenia is the desired therapeutic effect of a GRAFAPEX-based preparative regimen, occurring in all patients. Do not begin the preparative regimen if the stem cell donor is not available. Monitor blood cell counts at least daily until hematopoietic recovery. Provide standard supportive care for infections, anemia, and thrombocytopenia until there is adequate hematopoietic recovery.

Seizures: Monitor patients for signs of neurological adverse reactions, including seizure. Clonazepam prophylaxis may be considered for patients at higher risk for seizures, including infants.

Skin Disorders: An increase in skin disorders (eg, rash, dermatitis) was observed when patients received sodium bicarbonate–containing hydration in the course of treosulfan infusion. Keep skin clean and dry on days of GRAFAPEX infusion. Diaper dermatitis may occur because of excretion of treosulfan in the urine. Change diapers frequently during the 12 hours after each infusion of GRAFAPEX. Dermatitis may occur under occlusive dressings; change occlusive dressings after each infusion of GRAFAPEX.

HOW TO PREPARE GRAFAPEX

Preparation and Administration Instructions[1]

Reconstitute GRAFAPEX prior to intravenous infusion.

GRAFAPEX is a hazardous drug. Follow applicable special handling and disposal procedures.

1. **Use aseptic technique** to prepare GRAFAPEX.
2. **Calculate the dose,** the total volume of reconstituted GRAFAPEX solution required, and the number of GRAFAPEX vials needed.
3. **Reconstitute each vial** with 0.45% Sodium Chloride Injection, 0.9% Sodium Chloride Injection, 5% Dextrose Injection, or Sterile Water for Injection, in its original glass container using volumes described in Table 3 to obtain a final concentration of approximately 0.05 g/mL of GRAFAPEX. Reconstitution with Sterile Water for Injection alone is not recommended in children less than or equal to 12 years of age due to the resulting hypo-osmolarity of the final solution.
4. **Shake the vial(s)** to dissolve.
5. **Inspect the reconstituted solution** for discoloration and particulate matter. The reconstituted solution appears as a clear colorless solution. Solutions showing any sign of precipitation should not be used. In case that solubility issues occur, prolonged standing time or slight warming of the reconstituted solution (hand warm) may be useful.
6. **Determine the volume** of 0.05 g/mL reconstituted solution needed based on the required dose. Reconstituted solutions of GRAFAPEX may be combined into a larger glass vial, ethylene-vinyl acetate (EVA) bag, or polyolefin (PO) bag. Discard any unused portion left in the vial(s).

Table 3: Reconstruction Solution Volume[1]

Strength	Volume
1 g/vial	20 mL
5 g/vial	100 mL

If not used immediately, store reconstituted GRAFAPEX solution at room temperature 20°C to 25°C (68°F to 77°F) for up to 24 hours. Do not use if the solution contains a precipitate. **Do not refrigerate.**[1]

Infuse GRAFAPEX intravenously over 2 hours. Confirm patency of the intravenous line prior to infusion. Monitor for extravasation; if extravasation occurs, stop the infusion.[1]

Important Safety Information *(continued)*

Warnings and Precautions (*continued*)

Injection Site Reactions and Tissue Necrosis: Treosulfan may cause local tissue necrosis and injection site reactions, including erythema, pain, and swelling, in cases of extravasation. Assure venous access patency prior to starting GRAFAPEX infusion, and monitor the intravenous infusion site for redness, swelling, pain, infection, and necrosis during and after administration of GRAFAPEX. If extravasation occurs, stop the infusion immediately and manage medically as required. Do not administer by intramuscular or subcutaneous routes.

Please see enclosed Prescribing Information, including Boxed Warning for GRAFAPEX.

GRAFAPEX™
(treosulfan) for Injection

Important Safety Information *(continued)*

Warnings and Precautions (*continued*)

Secondary Malignancies: There is an increased risk of a secondary malignancy with the use of GRAFAPEX. Treosulfan is carcinogenic and genotoxic.

The risk of secondary malignancy is increased in patients with Fanconi anemia and other DNA breakage disorders. The safety of GRAFAPEX has not been established for patients with these disorders.

Increased Early Morbidity and Mortality at Dosages Higher Than Recommended: A higher incidence of early fatal and/or serious adverse reactions has been observed in patients receiving treosulfan at dosages of 14 g/m^2 (1.4 times the recommended dose). Avoid exceeding the recommended GRAFAPEX dosage of 10 g/m^2 daily for three consecutive days.

Embryo-Fetal Toxicity: GRAFAPEX can cause fetal harm. Advise patients of reproductive potential of the potential risk to a fetus and to use effective contraception.

Adverse Reactions

The most common adverse reactions (≥20%) in patients treated with GRAFAPEX were musculoskeletal pain, stomatitis, pyrexia, nausea, edema, infection, and vomiting. Select Grade 3 or 4 nonhematological laboratory abnormalities were increased GGT, increased bilirubin, increased ALT, increased AST, and increased creatinine.

Drug Interactions

Effect of GRAFAPEX on Other Drugs (Certain CYP2C19 and CYP3A Substrates): Concomitant use of GRAFAPEX is predicted to increase the exposure of CYP2C19 and CYP3A4 substrates based on a mechanistic understanding of treosulfan metabolism, which may increase the risk of adverse reactions.

Use in Specific Populations

- **Pregnancy:** GRAFAPEX can cause fetal harm. There are no available human clinical data on the use of treosulfan in pregnant women to support an estimation of a drug-associated risk. Specific embryo-fetal developmental toxicity studies with treosulfan in animals were not conducted.
- **Lactation:** There is no data on the presence of treosulfan or its metabolites in human milk, its effects on milk production, or the effects of treosulfan on the breastfed child. Because of the potential for serious adverse reactions in breastfed children, advise women not to breastfeed during treatment with GRAFAPEX and for at least 1 week after the last dose.
- **Patients With Renal Impairment:** No dosage adjustment is recommended for patients with mild renal impairment (creatinine clearance [CLcr] 60–89 mL/min). The effect of moderate or severe renal impairment and age >65 years on GRAFAPEX pharmacokinetics is unknown.
- **Pediatric Use:** The safety profile in children 1 year of age and older is comparable to that seen in adult patients, except that the incidence of hepatic and gastrointestinal toxicities was higher in pediatric patients than in adults.
- **Geriatric Use:** No significant differences in safety or effectiveness were observed between elderly subjects and younger subjects.
- **Hepatic Impairment:** No dosage adjustment is recommended for patients with mild hepatic impairment (total bilirubin less than or equal to upper limit of normal [ULN] with aspartate aminotransferase [AST] greater than ULN or total bilirubin greater than 1 to 1.5 times ULN with any AST). The effect of moderate or severe hepatic impairment and age >65 years on GRAFAPEX pharmacokinetics is unknown.

For adverse events, medical inquiries, and GRAFAPEX product-related concerns, please call 1-855-336-3322.

Please see enclosed Prescribing Information, including Boxed Warning for GRAFAPEX.

Reference: 1 GRAFAPEX (treosulfan) for Injection Prescribing Information. Medexus Pharma, Inc. 2025.

CORE CONNECTIONS

Get support every step of the way with CORE Connections

Obtain more information on reimbursement support, medical affairs, customer services, and medical information requests.

1-84-GRAFAPEX (844-723-2739)

9:00 AM to 6:00 PM EST Monday through Friday (excluding holidays)

coreconnectionscare@pharmacord.com

MEDEXUS PHARMA

MP-TREO-0048 January 2025

GRAFAPEX™ (treosulfan) for Injection