CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

214759Orig1s000

PROPRIETARY NAME REVIEW(S)

PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis 2 (DMEPA 2)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

*** This document contains proprietary information that cannot be released to the public***

Date of This Review:	July 25, 2024
Application Type and Number:	NDA 214759
Product Name, Dosage Form, and Strength:	Grafapex (treosulfan) for Injection, 1 g/vial and 5 g/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	medac Gesellschaft für klinische Spezialpräparate mbH (medac)
PNR ID #:	2024-1044725759
DMEPA 2 Safety Evaluator:	Jody Kundreskas, PharmD
DMEPA 2 Team Leader:	Nicole Iverson, PharmD, BCPS
DMEPA 2 Associate Director for Nomenclature and Labeling:	Hina Mehta, PharmD

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Grafapex, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the Reference section and Appendix A, respectively. medac submitted an external name study, conducted by [redacted] (b) (4), for this proposed proprietary name. The submitted external name study was previously reviewed under NDA 214759 (see Section 1.1 below). We note that the external name study POCA search results were updated with this submission, and no new names were identified.

1.1 REGULATORY HISTORY

medac previously submitted the proposed proprietary name, [redacted] (b) (4)*** under IND 054552 on June 5, 2020 and under NDA 214759 on October 20, 2020. However, on November 20, 2020, we found the name, [redacted] (b) (4)*** unacceptable due to similarity in pronunciation, orthographic and phonetic similarities, and overlapping product characteristics with the proprietary name [redacted] (b) (4), and orthographic similarities and overlapping product characteristics with the proprietary name, [redacted] (b) (4)[b]

Thus, medac submitted the proposed proprietary name, Grafapex, for review on February 5, 2021 under NDA 214759 and we found the name conditionally acceptable on April 21, 2021.[c] However, the Application received a Complete Response letter on July 30, 2021 due to clinical and statistical issues. The Applicant resubmitted NDA 214759 on April 21, 2022 which was considered an incomplete response which was communicated on May 16, 2022. The Applicant resubmitted NDA 214759 on August 10, 2022 which was considered an incomplete response which was communicated on September 15, 2022. The Applicant resubmitted NDA 214759 on April 30, 2024.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission and the Prescribing Information received on April 30, 2024[d,e].

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[a] Request for Proprietary Name Review for Grafapex (NDA 214759). [redacted] (b) (4); 2024 FEB. Available from: \\CDSESUB1\EVSPROD\nda214759\0027\m1\us\118-prop-names\request-proprietary-name-review.pdf.

[b] Iverson, N. Proprietary Name Review for [redacted] (b) (4)*** (IND 054552 and NDA 214759). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 20. PNR ID No. 2020-40485434 and 2020-43531303.

[c] DeGraw, S. Proprietary Name Review for Grafapex (NDA 214759). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2021 APR 21. PNR ID No. 2021-1044723800.

[d] Request for Proprietary Name Review for Grafapex (NDA 214759). Wedel (Germany): medac Gesellschaft für klinische Spezialpräparate mbH; 2024 APR 30. Available from: \\CDSESUB1\EVSPROD\nda214759\0070\m1\us\118-prop-names\request-proprietary-name-review.pdf.

[e] Proposed prescribing information for Grafapex (NDA 214759). Wedel (Germany): medac Gesellschaft für klinische Spezialpräparate mbH; 2024 APR 30. Available from: \\CDSESUB1\EVSPROD\nda214759\0070\m1\us\114-labeling\114a-draft-label\draft-label-text.pdf.

Table 1. Relevant Product Information for Grafapex	
Intended pronunciation:	graf-uh-PECKS
Active ingredient:	treosulfan
Indication:	• Acute Myeloid Leukemia 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 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.
Dosage Form:	for Injection
Strength:	1 g/vial and 5 g/vial
Route of administration:	Intravenous infusion
Dose and frequency:	10 g/m^2 body surface area (BSA) per day as a two-hour intravenous infusion, given on three consecutive days (day -4, -3, -2) before hematopoietic stem cell infusion (day 0).
How Supplied:	GRAFAPEX is a white, sterile, lyophilized powder for reconstitution supplied as 1 g or 5 g single-dose vials. GRAFAPEX is distributed as unit cartons of one vial treosulfan 1 g NDC xxxxx-xxx-xx and one vial treosulfan 5 g NDC xxxxx-xxx-xx.
Storage:	(b) (4) This product should be stored at room temperature (25°C / 77°F). GRAFAPEX is a hazardous drug. Follow applicable special handling and disposal procedures.

2 DISCUSSION

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Grafapex.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Grafapex would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis 2 (DMEPA 2) concurred with the findings of OPDP's assessment for Grafapex. The Division of Hematologic Malignancies 1 (DHM 1) concurred with the findings of OPDP's assessment for Grafapex.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Grafapex.

2.2.1 UNITED STATES ADOPTED NAMES (USAN) SEARCH

There is no USAN stem present in the proposed proprietary name.[f]

2.2.2 COMPONENTS OF THE PROPOSED PROPRIETARY NAME

medac did not provide a derivation or intended meaning for the proposed proprietary name, Grafapex, in their submission. This proprietary name is comprised of a single word that contains the letter strings "AF", "EX", and "PE", which are medical abbreviations for "augmented formula", "atrial fibrillation", or "atrial flutter", the medical abbreviation for "extra strength", and the medical abbreviation for "phenylephrine", respectively. Although we typically discourage the inclusion of medical abbreviations in proprietary names, we note the letter strings "AF" and "PE" are located in the infix of the proposed name and are unlikely to be separated from the surrounding letters or to be misunderstood within the context of a prescription and lead to confusion.

As the letter string "EX" is located at the end of the name, we evaluated the potential risk of misinterpreting the proposed proprietary name as "[drug name similar to Grafep] EX" with EX being interpreted as a modifier, and we did not identify any concerns.[g] We note that the terminal letter string "EX" is common in existing drug literature (e.g., Arimidex, Casodex, Ciprodex, Clobex, Darzalex, Efudex, Imitrex, Precedex, Valtrex, Xiaflex) and we are unaware of post-marketing reports of medication errors associated with this specific abbreviation through our routine surveillance. Therefore, in this case, we do not object to the proposed proprietary name based on the inclusion of these medical abbreviations.

Beyond these abbreviations, Grafepex does not contain any other components (i.e., route of administration, frequency, etc.) that can contribute to medication error.

2.2.3 COMMENTS FROM OTHER REVIEW DISCIPLINES AT INITIAL REVIEW

On May 16, 2024, the Division of Hematologic Malignancies 1 (DHM 1) did not forward any comments or concerns relating to Grafapex at the initial phase of the review.

2.2.4 FDA PRESCRIPTION SIMULATION STUDIES

One hundred and six practitioners participated in DMEPA's prescription simulation studies for Grafapex.

One inpatient study participant misinterpreted the proposed proprietary name as "Mafapex", which is a close variation of the products "Mirapex" and "Mifeprex". We had previously evaluated these name pairs in our April 2021 proprietary name review. We reevaluated these

[f] USAN stem search conducted on June 6, 2024.

[g] POCA search conducted on June 6, 2024 in version 5.9.

name pairs and agree with the findings from our previous review for the names and did not alter our previous conclusion.

2.2.5 PHONETIC AND ORTHOGRAPHIC COMPUTER ANALYSIS (POCA) SEARCH RESULTS

Our POCA search[h] identified 105 names with a combined score of ≥55% or an individual orthographic or phonetic score of ≥70%. We had identified and evaluated some of the names in our previous proprietary name review. We re-evaluated the previously identified names of concern considering any lessons learned from recent post-marketing experience, which may have altered our previous conclusion regarding the acceptability of the name. We note that none of the product characteristics have changed, and we agree with the findings from our previous review for the names evaluated previously. Therefore, we identified three names not previously analyzed. These names are included in Table 2 below.

2.2.6 NAMES RETRIEVED FOR REVIEW ORGANIZED BY NAME PAIR SIMILARITY

Table 2 provides the number of names retrieved from our POCA search. These name pairs are organized as highly similar, moderately similar, or low similarity for further evaluation.

Table 2. Names Retrieved for Review Organized by Name Pair Similarity	
Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	0
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	3
Low similarity name pair: combined match percentage score ≤54%	0

2.2.7 SAFETY ANALYSIS OF NAMES WITH POTENTIAL ORTHOGRAPHIC, SPELLING, AND PHONETIC SIMILARITIES

Our analysis of the three names contained in Table 2 determined none of the names will pose a risk for confusion with Grafapex as described in Appendices C through H.

2.2.8 COMMUNICATION OF DMEPA'S DETERMINATION

On July 25, 2024, DMEPA 2 communicated our determination to the Division of Hematologic Malignancies 1 (DHM 1).

3 CONCLUSION

The proposed proprietary name, Grafapex, is conditionally acceptable.

[h] POCA search conducted on June 6, 2024 in version 5.9.

3.1 COMMENTS TO MEDAC GESELLSCHAFT FÜR KLINISCHE SPEZIALPRÄPARATE MBH

We have completed our review of the proposed proprietary name, Grafapex, and have concluded that this proprietary name is conditionally acceptable.

If any of the proposed product characteristics as stated in your submission, received on April 30, 2024, are altered prior to approval of the marketing application, the proprietary name must be resubmitted for review.

4 REFERENCES

1. United States Adopted Names (USAN) Stems

USAN Stems List contains all the recognized USAN stems, available at https://www.ama-assn.org/about/united-states-adopted-names/united-states-adopted-names-approved-stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved brand name and generic drugs; therapeutic biological products, prescription and over-the-counter human drugs; and discontinued drugs (see Drugs@FDA Glossary of Terms, available at https://www.fda.gov/drugs/drug-approvals-and-databases/drugsfda-glossary-terms).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Purple Book

The Purple Book is an online database that contains information about biological products, including biosimilar and interchangeable biological products, licensed (approved) by the FDA under the Public Health Service (PHS) Act. See Purple Book: Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations, available at https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or.

Division of Medication Errors Prevention and Analysis pending proprietary name requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis.

5 APPENDICES

APPENDIX A. FDA'S PROPRIETARY NAME RISK ASSESSMENT EVALUATES PROPOSED PROPRIETARY NAMES FOR MISBRANDING AND SAFETY CONCERNS

1. Misbranding Assessment: For prescription drug products, the Office of Prescription Drug Promotion (OPDP) assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by the Office of Non-Prescription Drugs (ONPD). OPDP or ONPD evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or ONPD provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

2. Safety Assessment: The safety assessment is conducted by DMEPA, and includes the following:

    a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 3*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.[i]

*Table 3. Prescreening Checklist for Proposed Proprietary Name Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.	
Y/N	Is the proposed name obviously similar in spelling and pronunciation to other names?
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	Are there inert or inactive ingredients referenced in the proprietary name?
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	Does the proprietary name include combinations of active ingredients?
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	Is there a United States Adopted Name (USAN) stem in the proprietary name?
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.

[i] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors. Last accessed 10/05/2020.

*Table 3. Prescreening Checklist for Proposed Proprietary Name Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.	
Y/N	Is this proprietary name used for another product that does not share at least one common active ingredient?
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	Is this a proprietary name of a discontinued product?
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@FDA, Cerner RxNorm, Purple Book, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 4-6) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 4).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in

the confusion of drug names[j]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.

- Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 5).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 6) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA also conducts prescription simulation studies using FDA health care professionals.

   Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

   In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND), Office of Generic Drugs (OGD), and/or Office of Pharmaceutical Quality (OPQ) for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-

[j] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the Safety Evaluator's assessment.

The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name.

Additionally, other review disciplines opinions such as OPQ may be considered depending on the proposed proprietary name.

When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary Safety Evaluator assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name.

Table 4. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.

Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	Y/N	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	Y/N	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

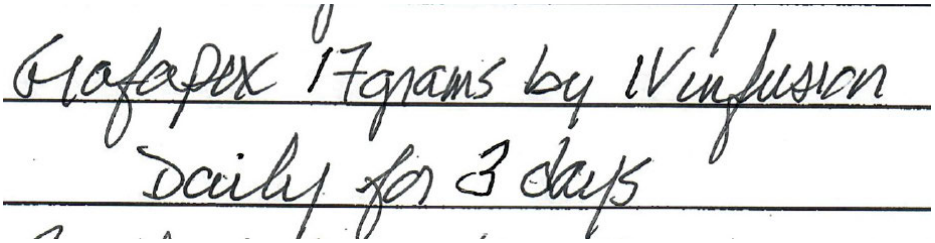
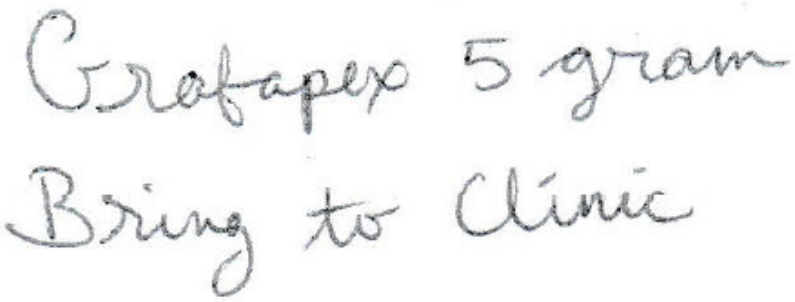
<table>
<tr><th colspan="3">Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).</th></tr>
<tr><td>Step 1</td><td colspan="2">Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation.
For single strength products, also consider circumstances where the strength may not be expressed.
For any i.e., drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components.
To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:
• Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa.
• Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.
• Similar sounding doses: 15 mg is similar in sound to 50 mg</td></tr>
<tr><td>Step 2</td><td colspan="2">Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names with overlapping or similar strengths or doses.</td></tr>
<tr><td></td><td>Orthographic Checklist (Y/N to each question)
• Do the names begin with different first letters?
• Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.
• Are the lengths of the names dissimilar* when scripted?
• *FDA considers the length of names different if the names differ by two or more letters.
• Considering variations in scripting of some letters (such as z and f), is there a different number or</td><td>Phonetic Checklist (Y/N to each question)
• Do the names have different number of syllables?
• Do the names have different syllabic stresses?
• Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
• Across a range of dialects, are the names consistently pronounced differently?</td></tr>
</table>

Table 5: Moderately Similar Name Pair Checklist (i.e., combined score is **≥55%** to **≤69%).**		
	placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	

Table 6. Low Similarity Name Pair Checklist (i.e., combined score is **≤54%).**
Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

APPENDIX B. PRESCRIPTION SIMULATION SAMPLES AND RESULTS

Figure 1. Grafapex Study (Conducted on 5/10/2024)

Handwritten Medication Order Prescription	Verbal Prescription
Medication Order:  	Grafapex 5 grams Bring to clinic Dispense 12 vials
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Grafapex	

FDA Prescription Simulation Responses (Aggregate Report)					
Study Name: Grafapex People Received Study: 198 People Responded: 106					
Total	22	27	26	31	106
INTERPRETATION	INPATIENT	OUTPATIENT	VOICE	CPOE	TOTAL
FIAFAPEX	1	0	0	0	1
GIAFAPEX	3	0	0	0	3
GLAFAPEX	4	0	0	0	4
GLOFAPEX	2	0	0	0	2
GRAFAOEX	0	1	0	0	1
GRAFAPAX	0	0	2	0	2

GRAFAPEX	8	23	6	31	68
GRAFAPHIX	0	0	1	0	1
GRAGAPEX	0	1	0	0	1
GRAPHAPEX	0	0	7	0	7
GRAPHIPEX	0	0	1	0	1
GRFPEX	1	0	0	0	1
GROFAPEX	1	2	0	0	3
GRPHIPEX	0	0	1	0	1
HAFAPEX	1	0	0	0	1
MAFAPEX	1	0	0	0	1
RAFAPEX	0	0	6	0	6
RAPAPAX	0	0	1	0	1
RAPPAPEX	0	0	1	0	1

APPENDIX C. HIGHLY SIMILAR NAMES (e.g., combined POCA score is **≥70%)**

No.	Proposed name: Grafapex Pronunciation: graf-uh-PECKS Established name: treosulfan Dosage form: for Injection Strength(s): 1 g/vial and 5 g/vial Dosage: 10 g/m^2 BSA per day as an intravenous infusion given on 3 consecutive days before hematopoietic stem cell infusion	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion Other prevention of failure mode expected to minimize the risk of confusion between these two names.
1.	N/A		

APPENDIX D. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	N/A	

APPENDIX E. MODERATELY SIMILAR NAMES (e.g., combined POCA score is **≥55%** to **≤69%)** with overlap or numerical similarity in Strength and/or Dose

No.	Proposed name: Grafapex Pronunciation: graf-uh-PECKS Established name: treosulfan Dosage form: for Injection Strength(s): 1 g/vial and 5 g/vial Dosage: 10 g/m^2 BSA per day as an intravenous infusion given on 3 consecutive days before hematopoietic stem cell infusion	POCA Score (%)	Prevention of Failure Mode In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names
1.	N/A		

APPENDIX F: LOW SIMILARITY NAMES (e.g., combined POCA score is **≤54%)**

No.	Name	POCA Score (%)
1.	N/A	

APPENDIX G. Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions (b) (4)
1.	Graspa***	58	
2.	Guaidex	56	International product marketed in Hong Kong.

APPENDIX H. Names not likely to be confused due to absence of attributes that are known to cause name confusion[k].

No.	Name	POCA Score (%)
1.	Proflexa	60

[k] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

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/s/

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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	April 21, 2021
Application Type and Number:	NDA 214759
Product Name and Strength:	Grafapex (treosulfan) for injection, 1 g/vial and 5 g/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Medac GmbH (Medac)
PNR ID #:	2021-1044723800
DMEPA Safety Evaluator:	Stephanie DeGraw, PharmD
DMEPA Team Leader:	Hina Mehta, PharmD

Contents

1 INTRODUCTION

This review evaluates the proposed proprietary name, Grafapex, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed proprietary name are outlined in the reference section and Appendix A respectively. Medac submitted an external name study, conducted by (b) (4), for this proposed proprietary name.

1.1 REGULATORY HISTORY

Medac previously submitted the proposed proprietary name, (b) (4) *** on June 5, 2020 under IND 054552 and on October 20, 2020 under NDA 214759. However, we found the name, (b) (4) *** unacceptable due to similarity in pronunciation, orthographic similarities, as well as overlapping product characteristics with the proprietary name, (b) (4) and orthographic similarities and overlapping product characteristics with the proprietary name, (b) (4) on November 20, 2020.[a]

Thus, Medac submitted the name, Grafapex, for review on February 5, 2021.

1.2 PRODUCT INFORMATION

The following product information is provided in the proprietary name submission received on February 5, 2021.

- Intended Pronunciation: graf-uh-PECKS
- Active Ingredient: treosulfan
- Indication of Use: As a part of conditioning treatment prior to allogenic hematopoietic stem cell transplantation (alloHSCT) in adult patients with acute myeloid leukemia (AML) and myelodysplastic syndromes (MDS).
- Route of Administration: intravenous infusion
- Dosage Form: for injection
- Strength: 1 g/vial and 5 g/vial
- Dose and Frequency: 10 g/m² BSA per day as a two-hour intravenous infusion, given on three consecutive days (day -4, -3, -2) before hematopoietic stem cell infusion (day 0)
- How Supplied: white, sterile, lyophilized powder for injection in single-dose glass vials containing 1 gm or 5 gm of treosulfan
- Storage: Unopened vials should be stored at room temperature (25°C/77°F).

[a] Iverson, N. Proprietary Name Review for (b) (4) *** (IND 054552 and NDA 214759). Silver Spring (MD): FDA, CDER, OSE, DMEPA (US); 2020 NOV 20. Panorama No. 2020-40485434 and 2020-43531303.

2 RESULTS

The following sections provide information obtained and considered in the overall evaluation of the proposed proprietary name, Grafapex.

2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that Grafapex would not misbrand the proposed product. The Division of Medication Error Prevention and Analysis (DMEPA) and the Division of Hematologic Malignancies 1 (DHM 1) concurred with the findings of OPDP's assessment for Grafapex.

2.2 SAFETY ASSESSMENT

The following aspects were considered in the safety evaluation of the proposed proprietary name, Grafapex.

2.2.1 United States Adopted Names (USAN) Search

There is no USAN stem present in the proposed proprietary name[b].

2.2.2 Components of the Proposed Proprietary Name

Medac did not provide a derivation or intended meaning for the proposed proprietary name, Grafapex, in their submission. This proprietary name is comprised of a single word that does not contain any components (i.e. a modifier, route of administration, dosage form, etc.) that are misleading or can contribute to medication error.

2.2.3 Comments from Other Review Disciplines at Initial Review

On February 19, 2021, the Division of Hematologic Malignancies 1 (DHM 1) did not forward any comments or concerns relating to Grafapex at the initial phase of the review.

2.2.4 FDA Name Simulation Studies

Seventy-nine practitioners participated in DMEPA's prescription studies for Grafapex. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Appendix B contains the results from the prescription simulation studies.

2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results

Our POCA search[c] identified 104 names with a combined phonetic and orthographic score of ≥55% or an individual phonetic or orthographic score ≥70%. These names are included in Table 1 below.

[b] USAN stem search conducted on March 2, 2021.

[c] POCA search conducted on March 2, 2021 in version 4.4.

2.2.6 *Names Retrieved for Review Organized by Name Pair Similarity*

Table 1 lists the number of names retrieved from our POCA search and the (b) (4) (b) (4) external study. These name pairs are organized as highly similar, moderately similar or low similarity for further evaluation.

Table 1. Names Retrieved for Review Organized by Name Pair Similarity

Similarity Category	Number of Names
Highly similar name pair: combined match percentage score ≥70%	1
Moderately similar name pair: combined match percentage score ≥55% to ≤ 69%	101
Low similarity name pair: combined match percentage score ≤54%	2

2.2.7 *Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities*

Our analysis of the 104 names contained in Table 1 determined none of the names will pose a risk for confusion with Grafapex as described in Appendices C through H.

2.2.8 *Communication of DMEPA's Analysis at Midpoint of Review*

DMEPA communicated our findings to the Division of Hematologic Malignancies 1 (DHM 1). At that time, we also requested additional information or concerns that could inform our review. On April 21, 2021, the Division of Hematologic Malignancies 1 (DHM 1) stated no additional concerns with the proposed proprietary name, Grafapex.

3 CONCLUSION

The proposed proprietary name, Grafapex, is acceptable.

If you have any questions or need clarifications, please contact Neil Vora, OSE project manager, at 240-402-4845.

3.1 COMMENTS TO MEDAC GMBH

We have completed our review of the proposed proprietary name, Grafapex, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your submission, received on February 5, 2021, are altered prior to approval of the marketing application, the name must be resubmitted for review.

4 REFERENCES

1. USAN Stems (https://www.ama-assn.org/about/united-states-adopted-names-approved-stems)

USAN Stems List contains all the recognized USAN stems.

2. Phonetic and Orthographic Computer Analysis (POCA)

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

Drugs@FDA

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological).

RxNorm

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (http://www.nlm.nih.gov/research/umls/rxnorm/overview.html).

Division of Medication Errors Prevention and Analysis proprietary name consultation requests

This is a list of proposed and pending names that is generated by the Division of Medication Error Prevention and Analysis from the Access database/tracking system.

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment**: For prescription drug products, OPDP assesses the name for misbranding concerns. For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNDP. OPDP or DNDP evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNDP provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment**: The safety assessment is conducted by DMEPA, and includes the following:
    a. Preliminary Assessment: We consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.) See prescreening checklist below in Table 2*. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [d]

[d] National Coordinating Council for Medication Error Reporting and Prevention. https://www.nccmerp.org/about-medication-errors Last accessed 10/05/2020.

***Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
Y/N	**Is the proposed name obviously similar in spelling and pronunciation to other names?**
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
Y/N	**Are there inert or inactive ingredients referenced in the proprietary name?**
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
Y/N	**Does the proprietary name include combinations of active ingredients?**
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
Y/N	**Is there a United States Adopted Name (USAN) stem in the proprietary name?**
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
Y/N	**Is this proprietary name used for another product that does not share at least one common active ingredient?**
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
Y/N	**Is this a proprietary name of a discontinued product?**
	Proprietary names should not use the proprietary name of a discontinued product if that discontinued drug product does not contain the same active ingredients.

b. Phonetic and Orthographic Computer Analysis (POCA): Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 55% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score ≥70%.
- Moderately similar pair: combined match percentage score ≥55% to ≤ 69%.
- Low similarity: combined match percentage score ≤54%.

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and

predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of ≥ 70 percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names are further evaluated to identify the presence of attributes that are known to cause name confusion.
    - Name attributes: We note that the beginning of the drug name plays a significant role in contributing to confusion. Additionally, drug name pairs that start with the same first letter and contain a shared letter string of at least 3 letters in both names are major contributing factor in the confusion of drug names[e]. We evaluate all moderately similar names retrieved from POCA to identify the above attributes. These names are further evaluated to identify overlapping or similar strengths or doses.
    - Product attributes: Moderately similar names of products that have overlapping or similar strengths or doses represent an area for concern for FDA. The dose and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and the information can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form) may be limited when the strength or dose overlaps. DMEPA reviews such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).

- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

[e] Shah, M, Merchant, L, Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

Four separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of the proposed proprietary name with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions, verbal pronunciation of the drug name or during computerized provider order entry. The studies employ healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The primary Safety Evaluator uses the results to identify vulnerability of the proposed name to be misinterpreted by healthcare practitioners during written, verbal, or electronic prescribing.

In order to evaluate the potential for misinterpretation of the proposed proprietary name during written, verbal, or electronic prescribing of the name, written inpatient medication orders, written outpatient prescriptions, verbal orders, and electronic orders are simulated, each consisting of a combination of marketed and unapproved drug products, including the proposed name.

d. Comments from Other Review Disciplines: DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with OPDP's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

   The OND/OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to provide any further information that might inform DMEPA's final decision on the proposed name.

   Additionally, other review disciplines opinions such as ONDQA or OBP may be considered depending on the proposed proprietary name.

   When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings and provides an overall risk assessment of the proposed proprietary name.

Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is ≥ 70%).

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair does not share a common strength or dose.			
Orthographic Checklist		Phonetic Checklist	
Y/N	Do the names begin with different first letters? *Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.*	**Y/N**	Do the names have different number of syllables?
Y/N	Are the lengths of the names dissimilar* when scripted? **FDA considers the length of names different if the names differ by two or more letters.*	**Y/N**	Do the names have different syllabic stresses?
Y/N	Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names?	**Y/N**	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	**Y/N**	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is ≥55% to ≤69%).

Step 1	Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation. For single strength products, also consider circumstances where the strength may not be expressed. For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components. To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion: • Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa. • Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity. • Similar sounding doses: 15 mg is similar in sound to 50 mg
Step 2	Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names **with** overlapping or similar strengths or doses.

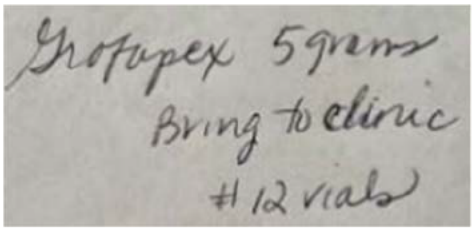
	Orthographic Checklist (Y/N to each question) • Do the names begin with different first letters? Note that even when names begin with different first letters, certain letters may be confused with each other when scripted. • Are the lengths of the names dissimilar* when scripted? *FDA considers the length of names different if the names differ by two or more letters. • Considering variations in scripting of some letters (such as *z* and *f*), is there a different number or placement of upstroke/downstroke letters present in the names? • Is there different number or placement of cross-stroke or dotted letters present in the names? • Do the infixes of the name appear dissimilar when scripted? • Do the suffixes of the names appear dissimilar when scripted?	Phonetic Checklist (Y/N to each question) • Do the names have different number of syllables? • Do the names have different syllabic stresses? • Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion? • Across a range of dialects, are the names consistently pronounced differently?

Table 5: Low Similarity Name Pair Checklist (i.e., combined score is ≤54%).

Names with low similarity are generally acceptable unless there are data to suggest that the name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

Appendix B: Prescription Simulation Samples and Results

Figure 1. Grafapex Study (Conducted on March 5, 2021)

Handwritten Medication Order/Prescription	Verbal Prescription
Medication Order: Grafapex 17g IV infusion over 2hrs x 3 days	Grafapex 5 grams Bring to clinic Dispense 12 vials
Outpatient Prescription:  	
CPOE Study Sample (displayed as sans-serif, 12-point, bold font)	
Grafapex	

FDA Prescription Simulation Responses (Aggregate Report)

209 People Received Study
79 People Responded

Study Name: Grafapex

Total	15	21	13	30	
INTERPRETATION	**OUTPATIENT**	**CPOE**	**VOICE**	**INPATIENT**	**TOTAL**
GRAFAPAX	0	0	1	0	1
GRAFAPEX	0	21	1	29	51
GRAFAPEX 17 G	0	0	0	1	1
GRAFIPEX	0	0	3	0	3
GRAPHAPAX	0	0	2	0	2
GRAPHAPEX	0	0	3	0	3
GRAPHIPAX	0	0	1	0	1
GRAPHIPEX	0	0	2	0	2
GROFAPEX	13	0	0	0	13
GROFOPEX	1	0	0	0	1
GROTAPEX	1	0	0	0	1

Appendix C: Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	**Proposed name:** Grafapex **Established name:** treosulfan **Dosage form:** for injection **Strength(s):** 1 g/vial and 5 g/vial **Usual Dose:** 10 g/m² per day as a 2-hour intravenous infusion, given on three consecutive days	POCA Score (%)	**Orthographic and/or phonetic differences in the names sufficient to prevent confusion** **Other prevention of failure mode expected to minimize the risk of confusion between these two names.**
1.	Grafapex***	100	Subject of this review

Appendix D: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Name	POCA Score (%)
1.	Grastek	66
2.	Paraflex	66
3.	Granix	64
4.	Regranex	64
5.	Gris-Peg	60
6.	Capex	58
7.	Mirapex Er	57
8.	Trilipix	55

Appendix E: Moderately Similar Names (e.g., combined POCA score is ≥55% to ≤69%) with overlap or numerical similarity in Strength and/or Dose

No.	**Proposed name:** Grafapex **Established name:** treosulfan **Dosage form:** for injection **Strength(s):** 1 g/vial and 5 g/vial **Usual Dose:** 10 g/m² per day as a 2-hour intravenous infusion, given on three consecutive days	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
1.	Gammaplex	68	This name pair has sufficient orthographic and phonetic differences.
2.	Mirapex	64	This name pair has sufficient orthographic and phonetic differences.
3.	Precedex	64	This name pair has sufficient orthographic and phonetic differences.

No.	**Proposed name:** Grafapex **Established name:** treosulfan **Dosage form:** for injection **Strength(s):** 1 g/vial and 5 g/vial **Usual Dose:** 10 g/m² per day as a 2-hour intravenous infusion, given on three consecutive days	POCA Score (%)	**Prevention of Failure Mode** **In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names**
4.	Trimpex	60	This name pair has sufficient orthographic and phonetic differences.
5.	Guaifenex G	58	This name pair has sufficient orthographic and phonetic differences.
6.	Carafate	57	This name pair has sufficient orthographic and phonetic differences.
7.	Gattex	57	This name pair has sufficient orthographic and phonetic differences.
8.	Gamunex	56	This name pair has sufficient orthographic and phonetic differences.
9.	Grazoprevir	56	This name pair has sufficient orthographic and phonetic differences.
10.	Guai-Dex	56	This name pair has sufficient orthographic and phonetic differences.
11.	Guaifenex Gp	55	This name pair has sufficient orthographic and phonetic differences.

Appendix F: Low Similarity Names (e.g., combined POCA score is ≤54%)

No.	Name	POCA Score (%)
1.	Trisenox	54
2.	Gengraf	42

Appendix G: Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Granulex	65	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
2.	Crantex	64	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.

No.	Name	POCA Score (%)	Failure preventions
3.	Genapax	64	Brand discontinued with no generic equivalents available. ANDA 085017 withdrawn FR effective 01/1/1992.
4.	Grape Seed	64	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
5.	Grape Extract	62	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
6.	Grapiprant	62	Veterinary product.
7.	Kraftpleg	62	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
8.	Laraflex	61	International product formerly marketed in the UK.
9.	Dexampex	60	Brand discontinued with no generic equivalents available. ANDA 083735 and ANDA 085355 withdrawn FR effective 03/23/1993.
10.	Guaipax	60	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
11.	Propanix	60	International product formerly marketed in the UK.
12.	Trimpex 200	60	Brand discontinued with no generic equivalents available. NDA 017952 withdrawn FR effective 06/04/2004.
13.	(b) (4)***	58	(b) (4)
14.	Dothapax	58	International product formerly marketed in the UK.
15.	Guaitex	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
16.	Guiatex	58	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
17.	Placidex	58	International product formerly marketed in the UK.
18.	Previcox	58	Veterinary product.
19.	(b) (4)***	57	Proposed proprietary name for IND 114843 found unacceptable by DMEPA (OSE# 2019-30776796 dated 10/09/2019). Subsequently, the proposed proprietary name Risvan*** was found conditionally acceptable for IND 114843 (OSE# 2020-39501394 dated 10/22/2020).
20.	Tobraflex	57	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.
21.	Veraflox	57	Veterinary product

No.	Name	POCA Score (%)	Failure preventions
22.	Guiadex	56	Name identified in RxNorm database. Product is deactivated and no generic equivalents are available.
23.	Methampex	56	Brand discontinued with no generic equivalents available. ANDA 083889 withdrawn FR effective 03/23/1993
24.	Clavamox	55	Veterinary product.
25.	Gastrinex	55	Name identified in RxNorm database. Unable to find product characteristics in commonly used drug databases.

Appendix H: Names not likely to be confused due to absence of attributes that are known to cause name confusion[f].

No.	Name	POCA Score (%)
1.	Derma-Pax	65
2.	Triatex	63
3.	Dermafix	62
4.	Dermaplex	62
5.	Proferdex	62
6.	Respa-Gf	62
7.	Keratex	61
8.	Mifeprex	61
9.	Terfinax	61
10.	Bisa-Plex	60
11.	Dermaflex	60
12.	Egrifta Sv	60
13.	Rapiflux	60
14.	Robadex	60
15.	Proflex	59
16.	Trianex	59
17.	Borofax	58
18.	Broflex	58
19.	Bromfenex	58
20.	Darzalex	58
21.	Diaprex	58
22.	Dosaflex	58
23.	Duradex	58

[f] Shah, M, Merchant, L, Chan, I, and Taylor, K. Characteristics That May Help in the Identification of Potentially Confusing Proprietary Drug Names. Therapeutic Innovation & Regulatory Science, September 2016

No.	Name	POCA Score (%)
24.	Migralex	58
25.	Peranex	58
26.	Plasma-Plex	58
27.	Preservex	58
28.	Prevail-Fx	58
29.	Relifex	58
30.	Relpax	58
31.	Transvax***	58
32.	Acarexx	57
33.	Alphatrex	57
34.	Anaplex	57
35.	Posatex	57
36.	Rapi-Ject	57
37.	Repronex	57
38.	Versacaps	57
39.	Aciphex	56
40.	Betatrex	56
41.	Britlofex	56
42.	Bromphenex	56
43.	Clearplex	56
44.	Cleviprex	56
45.	Coagadex	56
46.	Crantex Er	56
47.	Deramaxx	56
48.	Divaproex	56
49.	Fanatrex	56
50.	Parasitexx	56
51.	Pradaxa	56
52.	Repan Cf	56
53.	Vesagex	56
54.	Casodex	55
55.	Regimex	55
56.	Tripleflex	55
57.	Zenapax	55

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HINA S MEHTA
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PROPRIETARY NAME REVIEW

Division of Medication Error Prevention and Analysis (DMEPA)
Office of Medication Error Prevention and Risk Management (OMEPRM)
Office of Surveillance and Epidemiology (OSE)
Center for Drug Evaluation and Research (CDER)

***** This document contains proprietary information that cannot be released to the public*****

Date of This Review:	November 20, 2020
Application Type and Number:	IND 054552 and NDA 214759
Product Name and Strength:	(b) (4) (treosulfan) for Injection, 1,000 mg/vial and 5,000 mg/vial
Product Type:	Single Ingredient Product
Rx or OTC:	Prescription (Rx)
Applicant/Sponsor Name:	Medac GmbH (Medac)
Panorama #:	2020-40485434 and 2020-43531303
DMEPA Safety Evaluator:	Nicole Iverson, PharmD, BCPS
DMEPA Team Leader:	Hina Mehta, PharmD
DMEPA Associate Director of Nomenclature and Labeling:	Chi-Ming (Alice) Tu, PharmD, BCPS

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