

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

NDA 21-894

PROPRIETARY NAME REVIEW(S)



**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

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Subject: Final Name Review for Xenazine

Drug Name(s): Tetrabenazine tablets

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Xenazine, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, DMEDP has no objections to the use of the proprietary name, Xenazine.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEDP rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

Xenazine is the proprietary name for the proposed product, Tetrabenazine tablets, to be submitted for DMEDP review. DMEDP has reviewed the proposed name, Xenazine, three times previously with no objections to the name.

DMEDP completed a first review of the proposed name, Xenazine, in OSE Review #05-0120, dated 9/22/2005, in which DMEDP had no objections to the use of the proprietary name. Additionally, label and labeling changes were recommended in this review.

DMEDP completed a second review of the proposed name, Xenazine, in OSE Review #05-0120-1, dated 3/10/2006, in which DMEDP had no objections to the use of the proprietary name. Label and labeling changes were also recommended in this review.

DMEDP completed a third review of the proposed name, Xenazine, in OSE Review #2007-2216, dated 12/18/2007, in which DMEDP had no objections to the use of the proprietary name. Label and labeling changes were recommended in a separate review, OSE Review #2008-162, dated 3/6/2008.

Xenazine was first approved in the U.K. in 1971 for the treatment of chorea and other movement disorders; it is currently approved in several European countries for the same indication under the proprietary name Xenazine. In the U.S., there are no currently approved drugs to treat chorea associated with Huntington's Disease, although some anti-psychotic drugs are used off-label.

1.1 INTRODUCTION

This review was written in response to a request from the Division of Neurology Products (DNP) to re-evaluate the product a final time for its potential to contribute to medication errors. The proposed proprietary name, Xenazine, is evaluated to determine if the name could be potentially confused with other proprietary or established drug names.

1.2 PRODUCT INFORMATION

Tetrabenazine is a monoamine depletory agent for oral administration. It is proposed to be indicated in the treatment of chorea associated with Huntington's Disease. It is initially dosed twice a day and titrated upward to 'best dose', defined as the dose that provides efficacy and is tolerated by the patient. The starting daily dose is 25 mg (12.5 mg in the morning and 12.5 mg in the evening). One week later, the daily dose should be increased to 37.5 mg (12.5 mg in the morning, at noon, and at night). The dose should then be increased by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects occur or until a maximum daily dose of 100 mg is reached. The maximum dose given at any time should not exceed 37.5 mg. Daily doses should be given in divided doses, generally three times a day. It is supplied in bottles of 112 tablets.

2 METHODS AND MATERIALS

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Xenazine, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Xenazine, the medication error staff of DMEDP searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.¹ FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently lead to medication errors in the clinical setting. DMEDP 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.² DMEDP uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEDP considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

² National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/about/MedErrors.html>. Last accessed 10/11/2007.

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

2.1 PROPRIETARY NAME RISK ASSESSMENT

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'X' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.⁴⁵

To identify drug names that may look similar to Xenazine, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (capital letter 'X'), downstrokes (lowercase cursive 'z'), cross-strokes (none), and dotted letters ('i'). Additionally, several letters in Xenazine may be vulnerable to ambiguity when scripted, including the letter 'X' may appear as 'Y'; lower case 'x' appear as a lower case 'y' or 'x'; and cursive 'z' may appear as cursive letters 'g' or 'y'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Xenazine.

When searching to identify potential names that may look or sound similar to Xenazine, the Medication Error Staff search for names with similar number of syllables (3), stresses (zen-AH-zine or zen-IH-zine), and placement of vowel and consonant sounds. DMEDP notes that there is no way of testing all variance in phonetic pronunciation that occurs from person to person when the name is spoken (i.e., regional phonetic accents). Additionally, the Sponsor's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Xenazine) the established name (tetrabenazine), proposed indication (treatment of chorea associated with Huntington's Disease), strength (12.5 mg and 25 mg), dose (first week: 25 mg [12.5 mg in the morning and 12.5 mg in the evening] second week: 37.5 mg [12.5 mg in the morning, at noon, and at night], third week and beyond: dose increased by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects or until a maximum daily dose of 100 mg is reached), frequency of administration (generally two to three times a day), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than look and sound-alike name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. Artificial Intelligence in Medicine (2005)

comments related to the safety of the proposed name or product based on their professional experience with medication errors.

2.1.2 Database and Information Sources

The proposed proprietary name, Xenazine, was provided to the medication error staff of DMEDP to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Xenazine using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.3 CDER Expert Panel Discussion

An Expert Panel Discussion was held by DMEDP to gather CDER professional opinions on the safety of the product and the proprietary name, Xenazine. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMEDP Medication Errors Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.2 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMEDP seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Xenazine convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Xenazine to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMEDP will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMEDP identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug another drug product.

In the event that DMEDP objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMEDP will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to use the name, while DMEDP will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMEDP will not object to the use of the proprietary name. If any of these conditions are met, then DMEDP will object to the use of the proprietary name. The threshold

set for objection to the proposed proprietary name may seem low to the Sponsor; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, all who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMEDP contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Sponsor, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEDP believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMEDP objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMEDP is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEDP to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so DMEDP may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

Searches identified twenty three names as having some similarity to the name Xenazine.

Twelve of the twenty three names were thought to look like Xenazine, which include: Xenical, Kinerase, Kinevac, Venofer, Xenon XE, Emadine, Thorazine, Aurazine Sol, Xeneisol, Fentanyl, Xenaderm, and Zenapax. Six of the twenty three names were thought to sound like Xenazine, which include: Sonazine, Xanthine, Cenestin, Phenazine, and Xanadine. The remaining five names were thought to look and sound similar to Xenazine and include: Zenaxin, Xenadrine, Senexon, Marezine, and Sinequan.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEDP staff (see section 3.1 above), and noted no additional names.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.2.1 Safety Evaluator Risk Assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look or sound similar to Xenazine and represent a potential source of drug name confusion.

Twelve of the twenty three names (Xenadrine product line, Sonazine, Thorazine, Xenaderm, Emadene, Phenazine, Xenazine (foreign), Xenical, Zenapax, Senexon, and Xanthine) were identified in DMEDP's previous reviews on the proposed proprietary name, Xenazine (OSE # 05-0120, dated 9/22/05; OSE # 05-0120-1, dated 3/10/2006; and OSE #2007-2216, dated 12/18/2007). These names were determined not to pose a risk of confusion and error with Xenazine.

Failure mode and effects analysis was then applied to determine if the proposed name, Xenazine, could be potentially confused with any of the remaining eleven names and lead to medication error. This analysis determined that the name similarity between Xenazine and the identified names was unlikely to result in medication error for any of the eleven names for the following reasons: Three names are no longer marketed in the United States and no generic version is available (See Appendix B). One name is marketed outside the United States (See Appendix C). Seven names have minimal orthographic and/or phonetic similarity to Xenazine (Appendix D).

4 DISCUSSION

The results of the Proprietary Name Risk Assessment found that the proposed name, Xenazine, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise once the product is commercially marketed. However, DMEDP believes that these limitations are sufficiently minimized by the use of an Expert Panel.

Our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics, future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, DMEDP recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Sponsor to provide the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Xenazine, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, DMEDP does not object to the use of the proprietary name, Xenazine, for this product.

6 RECOMMENDATIONS

- A. If **any** of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEDP rescinds this Risk Assessment finding, and recommends that the proposed name be resubmitted for review.
- B. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. *Micromedex Integrated Index (<http://weblern/>)*

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. *Phonetic and Orthographic Computer Analysis (POCA)*

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for DMEDP, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)*

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

5. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

6. Division of Medication Errors and Technical Support proprietary name consultation requests

This is a list of proposed and pending names that is generated by DMEDP from the Access database/tracking system.

7. Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)

Drugs@FDA contains most of the drug products approved 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 and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

8. Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. WWW location <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

10. Clinical Pharmacology Online (<http://weblern/>)

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. Natural Medicines Comprehensive Databases (<http://weblern/>)

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

13. Stat!Ref (<http://weblern/>)

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

14. USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

16. Lexi-Comp (www.pharmacist.com)

A web-based searchable version of the Drug Information Handbook.

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

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APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEDP also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMEDP will consider the Sponsor’s intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, DMEDP also considers a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Products no longer on the market and no generic equivalent is available

Proprietary Name	Similarity to Xenazine
Xeneisol	Look
Marezine	Look and Sound
Aurazine	Look

Appendix C: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Xenazine
Zenaxin (albendazole in Mexico)	Look and Sound

Appendix D: Names lacking convincing look-alike and/or sound-alike similarities with Xenazine

Proprietary Name	Similarity to Xenazine
Kinerase	Look
Kinevac	Look
Venofer	Look
Xenon XE	Look
Fentanyl	Look
Cenestin	Sound
Sinequan	Look and Sound

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**Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology**

Date: December 19, 2007

To: Russell Katz, M.D., Director
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Through: Kellie Taylor, Pharm.D., M.P.H., Team Leader
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From: Laura Pincock, R.Ph., Pharm.D., Safety Evaluator

Subject: Final Name Review for Xenazine

Drug Name(s): Tetrabenazine tablets

Submission Number: NDA #: 21-894

Application Type/Number:

Applicant/sponsor: Prestwick Pharmaceuticals, Inc.

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Xenazine, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. Thus, DMETS has no objections to the use of the proprietary name, Xenazine.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. Additionally, if the product approval is delayed beyond 90 days from the signature date of this review, the proposed name must be resubmitted for evaluation.

1 BACKGROUND

Xenazine is the proprietary name for the proposed product, Tetrabenazine tablets, to be submitted for DMETS review. DMETS has reviewed the proposed name, Xenazine, two times previously with no objections to the name.

DMETS completed a first review of the proposed name, Xenazine, in OSE Review #05-0120, dated 9/22/2005, in which DMETS had no objections to the use of the proprietary name. Additionally, label and labeling changes were recommended in this review.

DMETS completed a second review of the proposed name, Xenazine, in OSE Review #05-0120-1, dated 3/10/2006, in which DMETS had no objections to the use of the proprietary name. Label and labeling changes were also recommended in this review.

Xenazine was first approved in the U.K. in 1971 for the treatment of chorea and other movement disorders; it is currently approved in several European countries for the same indication under the proprietary name Xenazine. In the U.S., there are no currently approved drugs to treat chorea associated with Huntington's Disease, although some anti-psychotic drugs are used off-label.

Tetrabenazine was discussed at a FDA Advisory Committee Meeting on December 6, 2007. The Advisory Panel voted unanimously to recommend the approval of tetrabenazine

1.1 INTRODUCTION

This review was written in response to a request from the Division of Neurology Products (DNP) to re-evaluate the product for its potential to contribute to medication errors. The proposed proprietary name, Xenazine, is evaluated to determine if the name could be potentially confused with other proprietary or established drug names.

1.2 PRODUCT INFORMATION

Tetrabenazine is a monoamine depletory agent for oral administration. It is proposed to be indicated in the treatment of chorea associated with Huntington's Disease. It is initially dosed twice a day and titrated upward to 'best dose', defined as the dose that provides efficacy and is tolerated by the patient. The starting daily dose is 25 mg (12.5 mg in the morning and 12.5 mg in the evening). One week later, the daily dose should be increased to 37.5 mg (12.5 mg in the morning, at noon, and at night). The dose should then be increased by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects occur or until a maximum daily dose of 100 mg is reached. The maximum dose given at any time should not exceed 37.5 mg. Daily doses should be given in divided doses, generally three times a day. It is supplied in bottles of 112 tablets.

Prestwick Pharmaceuticals, the Sponsor, submitted a new drug application (NDA 21-894) to the FDA on September 23, 2005 for Xenazine (tetrabenazine) 12.5 mg and 25 mg tablets. The proposed indication is

the treatment of chorea associated with Huntington's Disease. On March 26, 2006, the Sponsor received an approvable letter from the FDA specifying the issues requiring a response from the Sponsor before the NDA is approved. The Sponsor has submitted a Risk Minimization Action Plan as part of the response to the issues in the Approvable Letter. The Sponsor indicates the RiskMAP is to address the risks of depression and to promote appropriate titration and dosing.

2 METHODS AND MATERIALS

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name, Xenazine, and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, and ANDA products currently under review by the Agency.

For the proprietary name, Xenazine, the medication error staff of DMETS searched a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2).

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name (see detail 2.1.4). The overall risk assessment is based on the findings of a Failure Modes and Effects Analysis (FMEA) of the proprietary name, and is focused on the avoidance of medication errors. FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.¹ FMEA is used to analyze whether the drug names identified with look- or sound-alike similarity to the proposed name could cause confusion that subsequently lead to medication errors in the clinical setting. DMETS 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.² DMETS uses the clinical expertise of the medication error staff to anticipate the conditions of the clinical setting that the product is likely to be used in based on the characteristics of the proposed product.

In addition, the product characteristics provide the context for the verbal and written communication of the drug names and can interact with the orthographic and phonetic attributes of the names to increase the risk of confusion when there is overlap, or, in some instances, decrease the risk of confusion by helping to differentiate the products through dissimilarity. As such, the Staff considers the product characteristics associated with the proposed drug throughout the risk assessment, since the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed drug name include, but are not limited to established name of the proposed product, the proposed indication, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMETS considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.³

¹ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

² National Coordinating Council for Medication Error Reporting and Prevention.
<http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

³ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

2.1 PROPRIETARY NAME RISK ASSESSMENT

2.1.1 Search Criteria

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted as outlined in Appendix A.

For this review, particular consideration was given to drug names beginning with the letter 'X' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.⁴⁵

To identify drug names that may look similar to Xenazine, the Staff also consider the other orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (capital letter 'X'), downstrokes (lowercase cursive 'z'), cross-strokes (none), and dotted letters ('i'). Additionally, several letters in Xenazine may be vulnerable to ambiguity when scripted, including the letter 'X' may appear as 'Y'; lower case 'x' appear as a lower case 'y' or 'x'; and cursive 'z' may appear as cursive letters 'g' or 'y'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Xenazine.

When searching to identify potential names that may look or sound similar to Xenazine, the Medication Error Staff search for names with similar number of syllables (3), stresses (zen-AH-zine or zen-IH-zine), and placement of vowel and consonant sounds. DMETS notes that there is no way of testing all variance in phonetic pronunciation that occurs from person to person when the name is spoken (i.e., regional phonetic accents). Additionally, the Sponsor's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Xenazine) the established name (tetraabenazine), proposed indication (treatment of chorea associated with Huntington's Disease), strength (12.5 mg and 25 mg), dose (first week: 25 mg [12.5 mg in the morning and 12.5 mg in the evening] second week: 37.5 mg [12.5 mg in the morning, at noon, and at night], third week and beyond: dose increased by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects or until a maximum daily dose of 100 mg is reached), frequency of administration (generally two to three times a day), route (oral) and dosage form of the product (tablet). Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff general take into consideration.

Lastly, the Medication Error Staff also consider the potential for the proposed name to inadvertently function as a source of error for reasons other than look and sound-alike name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. As such, these broader safety implications of the name are considered and evaluated throughout this assessment and the Medication Error Staff provide additional comments related to the safety of the proposed name or product based on their professional experience with medication errors.

⁴ Institute for Safe Medication Practices. Confused Drug name List (1996-2006). Available at <http://www.ismp.org/Tools/confuseddrugnames.pdf>

⁵ Kondrack, G and Dorr, B. Automatic Identification of Confusable Drug Names. *Artificial Intelligence in Medicine* (2005)

2.1.2 Data base and information sources

The proposed proprietary name, Xenazine, was provided to the medication error staff of DMETS to conduct a search of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to Xenazine using the criteria outlined in 2.1.1. A standard description of the databases used in the searches is provided in Section 7. To complement the process, the Medication Error Staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the Medication Error Staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The findings of the individual Safety Evaluators were then pooled and presented to the Expert Panel.

2.1.3 CDER Expert Panel Discussion

An Expert Panel Discussion was held by DMETS to gather CDER professional opinions on the safety of the product and the proprietary name, Xenazine. Potential concerns regarding drug marketing and promotion related to the proposed names were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC).

The pooled results of the medication error staff were presented to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend the addition of names, additional searches by the Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

2.2 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

Based on the criteria set forth in Section 2.1.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, DMETS seeks to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

In order to perform an FMEA of the proposed name, the Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is not yet marketed, the Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Appendix A. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, expert panel evaluation, and studies, and identifies potential failure modes by asking: "Is the name Xenazine convincingly similar to another drug name,

⁶ Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

which may cause practitioners to become confused at any point in the usual practice setting?" An affirmative answer indicates a failure mode and represents a potential for Xenazine to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not convinced that the names possess similarity that would cause confusion at any point in the medication use system, and the name is eliminated from further review.

In the second stage of the Risk Assessment, all potential failure modes are evaluated to determine the likely *effect* of the drug name confusion, by asking "Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?" The answer to this question is a central component of the Safety Evaluator's overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would ultimately not be a source of medication errors in the usual practice setting, the name is eliminated from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend that an alternate proprietary name be used. In rare instances, the FMEA findings may provide other risk-reduction strategies, such as product reformulation to avoid an overlap in strength or an alternate modifier designation may be recommended as a means of reducing the risk of medication errors resulting from drug name confusion.

DMETS will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator's Risk Assessment:

1. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the review Division concurs with DDMAC's findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a trade name or otherwise. [21 U.S.C 321(n); see also 21 U.S.C. 352(a) & (n)].
2. DMETS identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
3. FMEA identifies potential for confusion between the proposed proprietary name and other proprietary or established drug names, and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
4. The proposed proprietary name contains an USAN stem, particularly in a manner that is contradictory to the USAN Council's definition.
5. Medication Error Staff identify a potential source of medication error within the proposed proprietary name. The proprietary name may be misleading, or inadvertently introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug another drug product.

In the event that DMETS objects to the use of the proposed proprietary name, based upon the potential for confusion with another proposed (but not yet approved) proprietary name, DMETS will provide a contingency objection based on the date of approval: whichever product is awarded approval first has the right to the use the name, while DMETS will recommend that the second product to reach approval seek an alternative name.

If none of these conditions are met, then DMETS will not object to the use of the proprietary name. If any of these conditions are met, then DMETS will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the IOM, WHO, JCAHO, and ISMP, all who have examined medication

errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

Furthermore, DMETS contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and preventable source of medication error that, in many instances, can be identified and remedied prior to approval to avoid patient harm.

Additionally, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to remedy post-approval. Educational efforts and so on are low-leverage strategies that have proven to have limited effectiveness at alleviating the medication errors involving drug name confusion. Higher-leverage strategies, such as drug name changes, have been undertaken in the past; but at great financial cost to the Sponsor, and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for the approving the error-prone proprietary name. Moreover, even after Sponsor's have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioner's vocabulary, and as such, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMETS believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval (see limitations of the process).

If DMETS objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the FMEA process is used to identify strategies to reduce the risk of medication errors. DMETS is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMETS to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name, and so DMETS may be able to provide the Sponsor with recommendations that reduce or eliminate the potential for error would render the proposed name acceptable.

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

DMETS conducted a search of the internet, several standard published databases and information sources (see Section 7 References) for existing drug names which sound-alike or look-alike to Xenazine to a degree where potential confusion between drug names could occur and result in medication errors in the usual clinical practice settings. In total, 13 names were identified as having some similarity to the name Xenazine.

Four of the thirteen names were thought to look like Xenazine, which include: Xenical, Genzine (Gen-Xene), Zenapax, and Xenaderm. Two of the thirteen names were thought to sound like Xenazine, which include: Senexon and Cenestin. The remaining seven names were thought to look and sound similar to Xenazine and include: Phenazine, Xenon XE 133, Xenazine, Pentazine, Kenazine, Xenazyme, and Xanthine.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMETS staff (see section 3.1 above), and noted one additional name, Gen-Xene, thought to have both orthographic and phonetic similarity to Xenazine. The name Genzine was determined to be a misspelling of the name Gen-Xene.

DDMAC had no concerns regarding the proposed name from a promotional perspective, and did not offer any additional comments relating to the proposed name.

3.2.1 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator identified no additional names thought to look or sound similar to Xenazine and represent a potential source of drug name confusion.

Six of the thirteen names (Xenaderm, Cenestin, Phenazine, Xenon, Xenazine, and Pentazine) were identified in DMETS' previous reviews on the proposed proprietary name, Xenazine (OSE # 05-0120, dated 9/22/05, and OSE # 05-0120-1, dated 3/10/2006). These names were determined not to pose a risk of confusion and error with Xenazine.

Further analysis determined that the name similarity between Xenazine and three of the remaining seven identified names was unlikely to result in medication errors. One name (Xenazyme) was found in the U.S. Patent and Trademark Office database however, the patent status was "abandoned." One name (Kenazine) was identified as a brand of Chlorpromazine but no further product or dosing information is available in major drug information resources such as Micromedex, Clinical Pharmacology, Facts and Comparisons, or Saegis. The third name, Xanthine, is an abbreviated name for a drug class (e.g., Xanthine derivatives such as theophylline) and is not an actual drug name for which prescriptions will be ordered.

As such, a total of four names (Gen-Xene, Xenical, Zenapax, and Senexon) were analyzed to determine if the similar appearance and/or sound of the drug name could lead to confusion with Xenazine and if the drug name confusion would likely result in a medication error. For the four names identified, it was determined that medication errors were unlikely because the products do not overlap in strength or dosage with Xenazine and have limited orthographic and/or visual similarity to Xenazine (Appendix C). Therefore, no names underwent further evaluation in the FMEA process.

4 DISCUSSION

The results of the Proprietary Name Risk Assessment found that the proposed name, Xenazine, has some similarity to other proprietary and established drug names, but the findings of the FMEA process indicate that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors.

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise once the product is commercially marketed. However, DMETS believes that these limitations are sufficiently minimized by the use of an Expert Panel.

Our risk assessment also faces limitations beyond the control of the Agency. First, our risk assessment is based on current health care practices and drug product characteristics; future changes to either could increase the vulnerability of the proposed name to confusion. Since these changes cannot be predicted for or accounted by the current Proprietary Name Risk Assessment process, such changes limit our findings. To help counterbalance this impact, DMETS recommends that the proprietary name be re-submitted for review if approval of the product is delayed beyond 90 days.

Overall, our Risk Assessment is limited by our current understanding of medication errors and causality. The successful application of Failure Modes and Effect Analysis depends upon the learning gained for a spontaneous reporting program. It is quite possible that our understanding of medication error causality would benefit from unreported medication errors; and, that this understanding could have enabled the Staff to identify vulnerability in the proposed name, packaging, and labeling that was not identified in this assessment. To help minimize this limitation in future assessments, we encourage the Sponsor to provide

the Agency with medication error reports involving their marketed drug products regardless of adverse event severity.

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Xenazine, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, DMETS does not object to the use of the proprietary name, Xenazine, for this product. However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the name be resubmitted for review. If the event that our Risk Assessment finding is rescinded, the evaluation of the name on resubmission is independent of the previous Risk Assessment, and as such, the conclusions on re-review of the name are subject to change. Additionally, if the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

6 RECOMMENDATIONS

- A. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMETS rescinds this Risk Assessment finding, and recommends that the proposed name be resubmitted for review.
- B. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.

7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

AERS is a database application in CDER FDA that contains adverse event reports for approved drugs and therapeutic biologics. These reports are submitted to the FDA mostly from the manufactures that have approved products in the U.S. The main utility of a spontaneous reporting system that captures reports from health care professionals and consumers, such as AERS, is to identify potential postmarketing safety issues. There are inherent limitations to the voluntary or spontaneous reporting system, such as underreporting and duplicate reporting; for any given report, there is no certainty that the reported suspect product(s) caused the reported adverse event(s); and raw counts from AERS cannot be used to calculate incidence rates or estimates of drug risk for a particular product or used for comparing risk between products.

2. *Micromedex Integrated Index (<http://weblern/>)*

Contains a variety of databases covering pharmacology, therapeutics, toxicology and diagnostics.

3. *Phonetic and Orthographic Computer Analysis (POCA)*

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists which operates in a similar fashion. This is a database which was created for DMETS, FDA.

4. *Drug Facts and Comparisons, online version, St. Louis, MO (<http://weblern/>)*

Drug Facts and Comparisons is a compendium organized by therapeutic Course; contains monographs on prescription and OTC drugs, with charts comparing similar products.

5. *AMF Decision Support System [DSS]*

DSS is a government database used to track individual submissions and assignments in review divisions.

6. *Division of Medication Errors and Technical Support proprietary name consultation requests*

This is a list of proposed and pending names that is generated by DMETS from the Access database/tracking system.

7. *Drugs@FDA (<http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm>)*

Drugs@FDA contains most of the drug products approved 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 and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologicals, discontinued drugs and "Chemical Type 6" approvals.

8. *Electronic online version of the FDA Orange Book (<http://www.fda.gov/cder/ob/default.htm>)*

Provides a compilation of approved drug products with therapeutic equivalence evaluations.

9. *WWW location <http://www.uspto.gov>.*

Provides information regarding patent and trademarks.

10. *Clinical Pharmacology Online (<http://weblern/>)*

Contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. Provides a keyword search engine.

11. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com*

The Pharma In-Use Search database contains over 400,000 unique pharmaceutical trademarks and tradenames that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

12. *Natural Medicines Comprehensive Databases (<http://weblern/>)*

Contains up-to-date clinical data on the natural medicines, herbal medicines, and dietary supplements used in the western world.

13. *Stat!Ref (<http://weblern/>)*

Contains full-text information from approximately 30 texts. Includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology and Dictionary of Medical Acronyms Abbreviations.

14. *USAN Stems (<http://www.ama-assn.org/ama/pub/category/4782.html>)*

List contains all the recognized USAN stems.

15. *Red Book Pharmacy's Fundamental Reference*

Contains prices and product information for prescription, over-the-counter drugs, medical devices, and accessories.

16. *Lexi-Comp (www.pharmacist.com)*

A web-based searchable version of the Drug Information Handbook.

17. *Medical Abbreviations Book*

Contains commonly used medical abbreviations and their definitions.

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APPENDICES

Appendix A:

The Medication Error Staff consider the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMETS also compare the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. The Medication Error Staff also examine the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly *and* dissimilarly spelled drug name pairs to appear very similar to one another and the similar appearance of drug names when scripted has lead to medication errors. The Medication Error Staff apply their expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (i.e. “T” may look like “F,” lower case ‘a’ looks like a lower case ‘u,’ etc), along with other orthographic attributes that determine the overall appearance of the drug name when scripted (see detail in Table 1 below). Additionally, since verbal communication of medication names is common in clinical settings, the Medication Error Staff compare the pronunciation of the proposed proprietary name with the pronunciation of other drug names. If provided, DMETS will consider the Sponsor’s intended pronunciation of the proprietary name. However, because the Sponsor has little control over how the name will be spoken in practice, DMETS also considers a variety of pronunciations that could occur in the English language.

Table 1. Criteria used to identify drug names that look- or sound-similar to a proposed proprietary name

Type of similarity	Considerations when searching the databases		
	Potential causes of drug name similarity	Attributes examined to identify similar drug names	Potential Effects
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication Names may look similar when scripted and lead to drug name confusion in written communication
	Orthographic similarity	Similar spelling Length of the name Upstrokes Downstrokes Cross-strokes Dotted letters	<ul style="list-style-type: none"> Names may look similar when scripted, and lead to drug name confusion in written communication

		Ambiguity introduced by scripting letters Overlapping product characteristics	
Sound-alike	Phonetic similarity	Identical prefix Identical infix Identical suffix Number of syllables Stresses Placement of vowel sounds Placement of consonant sounds Overlapping product characteristics	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Appendix B: Proprietary names used only in Foreign Countries

Proprietary Name	Similarity to Xenazine	Country
Xenazine	Look and Sound	Europe (same product already marketed in Europe)

Appendix C: Products with no numerical overlap in strength and dose.

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
Xenazine (tetra benazine)		12.5 mg, 25 mg	25 mg orally (12.5 mg tablet in the morning and 12.5 mg in the evening). Weekly dosage increases by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects or until a maximum daily dose of 100 mg is reached. Daily doses should be given in divided doses, generally three times a day.
Gen-Xene	Sound and Look	3.75 mg, 7.5 mg, 15 mg	7.5-15 mg tablet orally 2-4 times/day
Xenical	Look	120 mg	120 mg capsule orally 3 times day with each main meal containing fat (during or up to 1 hour after the meal); omit dose if meal is occasionally missed or contains no fat.
Zenapax	Look	5 mg/mL (5 mL)	1 mg/kg infused over 15 minutes within 24 hours before transplantation (day 0), then every 14 days for 4 additional doses.
Senexon (OTC)	Sound	8.8 mg/5 mL (240 mL) 8.6 mg	10—15 ml (436—654 mg standardized senna extract) orally two times per day. 1—2 tablets (187—374 mg standardized senna concentrate, or 8.6—17.2 mg sennosides) orally twice daily.

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Laura Pincock
12/18/2007 11:42:50 AM
DRUG SAFETY OFFICE REVIEWER

Kellie Taylor
12/18/2007 11:45:06 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
12/18/2007 03:59:18 PM
DRUG SAFETY OFFICE REVIEWER

MEMORANDUM

**Division of Medication Errors and Technical Support
Office of Drug Safety
HFD-420; WO22, Rm. 4447
Center for Drug Evaluation and Research**

To: Russell Katz, MD
Director, Division of Neurology Products, HFD-120

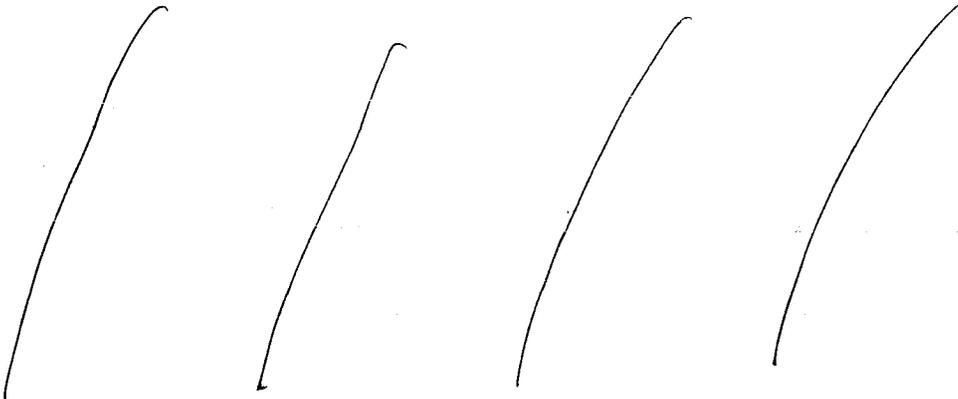
From: Tina M. Tezky, PharmD, Safety Evaluator
Division of Medication Errors and Technical Support, HFD-420

Through: Denise Toyer, PharmD, Deputy Director
Carol Holquist, RPh, Director
Division of Medication Errors and Technical Support, HFD-420

Date: February 28, 2005

Re: ODS Consult #05-0120-1; Xenazine (tetrabenazine) tablets; NDA 21-894

This memorandum is in response to the February 3, 2006 request from your Division for a re-review of the proprietary name, Xenazine. The proposed proprietary name was previously found acceptable by the Division of Medication Errors and Technical Support (DMETS) on September 22, 2005 (ODS consult 05-0120). Since we conducted our previous review, DMETS has identified one additional proprietary name, _____ which has the potential for confusion with Xenazine.

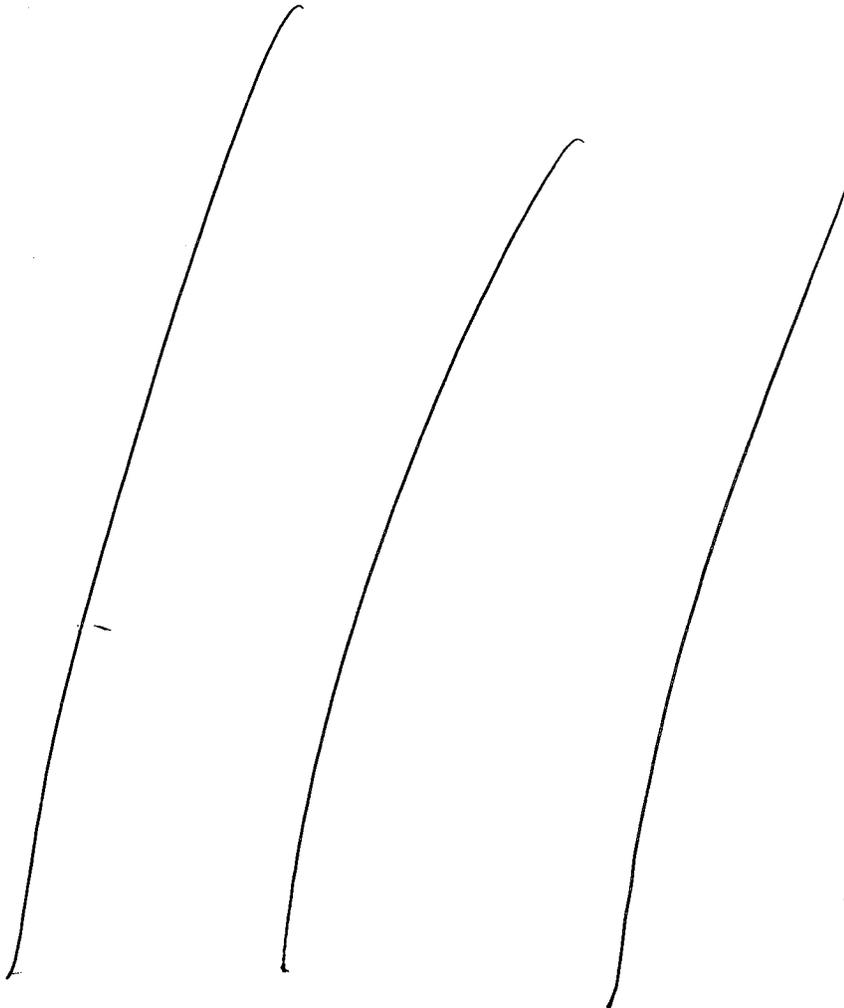


Thus, the phonetic and orthographic differences, in addition to the product characteristics of each drug such as the product strength and instructions for use will help decrease the potential for confusion between the two names.

Xenazine

Additionally, DMETS reviewed the container labels, carton and insert labeling of Xenazine from a safety perspective. DMETS has identified the following areas of possible improvement, which might minimize potential user error.

A. GENERAL COMMENTS



In summary, DMETS does not have any objections to the use of the proprietary name Xenazine. Additionally, DDMAC finds the proprietary name Xenazine acceptable from a promotional perspective. DMETS recommends implementation of the label and labeling revisions outlined above. DMETS considers this a final review. However, if the approval of the NDA is delayed beyond 90 days from the date of this review, the name must be re-evaluated. A re-review of the name before NDA approval will rule out any objections based upon approvals of other proprietary/established names from this date forward. If you have any questions or need clarification, please contact Diane Smith at 301-796-3242.

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/s/

Tina Tezky
3/10/2006 11:09:54 AM
DRUG SAFETY OFFICE REVIEWER

Denise Toyer
3/10/2006 11:36:24 AM
DRUG SAFETY OFFICE REVIEWER

Carol Holquist
3/10/2006 12:47:47 PM
DRUG SAFETY OFFICE REVIEWER

CONSULTATION RESPONSE
DIVISION OF MEDICATION ERRORS AND TECHNICAL SUPPORT
OFFICE OF DRUG SAFETY
(DMETS; HFD-420)

DATE RECEIVED: May 17, 2005	DESIRED COMPLETION DATE: September 23, 2005 PDUFA DATE: February 25, 2006	ODS CONSULT #: 05-0120
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TO: Russell Katz, MD
Director, Division of Neuropharmacological Drug Products
HFD-120

THROUGH: Theresa Wheelous
Project Manager
HFD-120

PRODUCT NAME:

Xenazine
(Tetrabenazine Tablets)
12.5 mg and 25 mg

IND SPONSOR: Prestwick Pharmaceuticals, Inc.

IND#: 63,909 (NDA# 21-894)

SAFETY EVALUATOR: Linda M. Wisniewski, RN

RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name, Xenazine. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated upon submission of the NDA and approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.

- B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.

- C. DDMAC finds the proprietary name, Xenazine, acceptable from a promotional perspective.

Denise Toyer, PharmD.
Deputy Director
Division of Medication Errors and Technical Support
Office of Drug Safety
Phone: (301) 827-3242 Fax: (301) 443-9664

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**APPEARS THIS WAY
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**Division of Medication Errors and Technical Support (DMETS)
Office of Drug Safety
HFD-420; PKLN Rm. 6-34
Center for Drug Evaluation and Research**

PROPRIETARY NAME REVIEW

DATE OF REVIEW: May 25, 2005
IND#: IND# 63,909 (NDA# 21-894)
NAME OF DRUG: Xenazine
IND HOLDER: Prestwick Pharmaceuticals, Inc.

I. INTRODUCTION:

This consult was written in response to a request from the Division of Neuropharmacological Drug Products (HFD-120), for assessment of the proprietary name, "Xenazine", regarding potential name confusion with other proprietary or established drug names. DMETS notes that on June 14, 2005, the sponsor withdrew the NDA for Xenazine. However, the sponsor plans to resubmit the NDA at a later time and therefore still plans to use the name, Xenazine. Container labels and insert labeling were submitted for review and comment.

PRODUCT INFORMATION

Xenazine is a monoamine depletor for oral administration. It is indicated in the treatment of chorea associated with Huntington's disease. It is dosed twice a day and titrated upward to 'best dose', defined as the dose that provides efficacy and is tolerable. The starting dose should be 25 mg per day (12.5 mg in the morning and 12.5 mg in the evening). One week later, the dose should be increased to 37.5 mg per day (12.5 mg in the morning, 12.5 mg at noon, and 12.5 mg in the evening). The dose should then be increased by 12.5 mg increments until satisfactory control of chorea is achieved or until side effects occur or until a maximal dose of 100 mg per day is reached. Daily doses should be given in divided doses, generally t.i.d. It is supplied in bottles of 112 tablets.

II. RISK ASSESSMENT:

The medication error staff of DMETS conducted a search of several standard published drug product reference texts^{1,2} as well as several FDA databases³ for existing drug names which sound-alike or look-alike to Xenazine to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted⁴. The Saegis⁵ Pharma-In-Use database was searched for drug names with potential for confusion. An expert panel discussion was conducted to review all findings from the searches. In addition, DMETS conducted three prescription analysis studies consisting of two written prescription studies (inpatient and outpatient) and one verbal prescription study, involving health care practitioners within FDA. This exercise was conducted to simulate the prescription ordering process in order to evaluate potential errors in handwriting and verbal communication of the name.

A. EXPERT PANEL DISCUSSION (EPD)

An Expert Panel discussion was held by DMETS to gather professional opinions on the safety of the proprietary name Xenazine. Potential concerns regarding drug marketing and promotion related to the proposed name were also discussed. This group is composed of DMETS Medication Errors Prevention Staff and representation from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

1. DDMAC finds the proprietary name, Xenazine, acceptable from a promotional perspective.
2. The Expert Panel identified three proprietary names that were thought to have the potential for confusion with Xenazine. These products are listed in Table 1 (see page 4), along with the dosage forms available and usual dosage.

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¹ MICROMEDEX Integrated Index, 2005, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes all products/databases within ChemKnowledge, DrugKnowledge, and RegsKnowledge Systems.

² Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

³ AMF Decision Support System [DSS], Drugs@FDA, the Division of Medication Errors and Technical Support [DMETS] database of Proprietary name consultation requests, and the electronic online version of the FDA Orange Book.

⁴ WWW location <http://www.uspto.gov/tmdb/index.html>.

⁵ Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at www.thomson-thomson.com

Table 1: Potential Sound-Alike/Look-Alike Names Identified by DMETS Expert Panel

Product Name	Dosage forms/Established name	Usual adult dose	Other
Xenazine	Tetrabenazine Tablets 25 mg and 250 mg	25 mg to 100 mg daily in two to three divided doses	NA
Xenadrine EFX	Over-the-Counter: Dietary Supplement	Two capsules twice daily.	LA
Xenadrine NRG 8-Hour		Two to four tablets daily.	
Xenazine 40+		Two capsules before breakfast and two capsules in mid-afternoon with 8 ounces of water.	
Sonazine	Chlorpromazine Hydrochloride Oral concentrate: 30 mg/mL, 100 mg/mL Oral Syrup: 10 mg/mL	25 mg to 2000 mg daily in divided doses (two or three times a day). Adjust to lowest dose that provides desired effect.	LA/SA
Xtrozine & Xtrozine LA	Phendimetrazine Tartrate Capsules: 35 mg XR Capsules: 105 mg	Tablets: 35 mg two or three times daily, one hour before meals. Capsules: 105 mg once daily in am 30-60 minutes before breakfast.	

*Frequently used, not all-inclusive.
**L/A (look-alike), S/A (sound-alike)

B. PHONETIC and ORTHOGRAPHIC COMPUTER ANALYSIS (POCA)

As part of the name similarity assessment, proposed names are evaluated via a phonetic/orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. The phonetic search module returns a numeric score to the search engine based on the phonetic similarity to the input text. Likewise, an orthographic algorithm exists which operates in a similar fashion. All names considered to have significant phonetic or orthographic similarities to Xenazine were discussed by the Expert Panel.

C. PRESCRIPTION ANALYSIS STUDIES

1. Methodology:

Three separate studies were conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Xenazine with marketed U.S. drug names (proprietary and established) due to similarity in visual appearance with handwritten prescriptions or verbal pronunciation of the drug name. These studies employed a total of 122 health care professionals (pharmacists, physicians, and nurses). This exercise was conducted in an attempt to simulate the prescription ordering process. An inpatient order and outpatient prescriptions were written, each consisting of a combination of marketed and unapproved drug products and a prescription for Xenazine (see page 5). These prescriptions were optically scanned and one prescription was delivered to a random sample of the participating health professionals via e-mail. In addition, the outpatient orders were recorded on voice mail. The voice mail messages were then sent to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants sent their interpretations of the orders via e-mail to the medication error staff.

HANDWRITTEN PRESCRIPTION	VERBAL PRESCRIPTION
Outpatient RX: <i>Xenazine</i> <i>12.5 mg TID</i> <i>#</i>	Xenazine 12.5 mg TID
Inpatient RX: <i>Xenazine 12.5 mg TID</i>	

2. Results:

None of the interpretations of the proposed name overlap, sound similar, or look similar to any currently marketed U.S. product. See Appendix A for the complete listing of interpretations from the verbal and written studies.

D. SAFETY EVALUATOR RISK ASSESSMENT

In reviewing the proprietary name Xenazine, the primary concerns related to look-alike and sound-alike confusion with Xenadrine, Sonazine, and Xtrozine.

Upon further review of the names gathered from EPD, the name Xenadrine will not be reviewed further due to a lack of look-alike similarities with Xenazine as a result of the use of multiple modifiers within the Xenadrine product line (e.g. 40+, NRG 8-Hour Power, and EFX).

DMETS also conducted prescription studies to simulate the prescription ordering process. In this case, there was no confirmation that the proposed name could be confused with any of the aforementioned names. However, negative findings are not predicative as to what may occur once the drug is widely prescribed, as these studies have limitations primarily due to a small sample size. The majority of misinterpretations were misspelled/phonetic variations of the proposed name, Xenazine.

1. Sonazine may look and sound similar to Xenazine when written or spoken. Sonazine is indicated in the treatment of a variety of psychotic disorders and intractable hiccoughs. The first syllable, 'So' and 'Xe', may sound similar. If the first letter of a word is 'x', it can be pronounced phonetically like a 'z', such as in the word Xerox, and in turn, the 'z' sound may sound similar to an 's' sound. This phonetic similarity, coupled with the fact that both names share the same last six letters (nazine), creates phonetic similarities between these two names. Orthographically, both names contain eight letters, the last six of which are the same (nazine). Although the second letter of each name is different (e vs. o), they may look similar when scripted, particularly if the 'e' is scripted with a wide loop. However, the first letter of each name is orthographically different (X vs. S). Additionally, there are some other differentiating product characteristics that may help to differentiate these two products, such as dosage form (tablets vs. oral concentrate and oral syrup), and strength (12.5 mg and 25 mg vs. 10 mg/mL, 30 mg/mL, and 100 mg/mL). Although both products overlap at doses of 25 mg to 100 mg and dosing frequency of twice daily, the dosage forms are distinctly different. Because Sonazine is supplied in two types of oral liquid, oral concentrate and oral syrup, it is likely

to be ordered in units of mL's (e.g. 5 mL) and the specific dosage form would need to be included in an order. Whereas, Xenazine would need to include the strength and number of tablets to be administered. This additional information will help to differentiate orders for these two products when written. Although there are phonetic similarities in addition to orthographic similarities, the dosage forms and additional prescribing information required for Sonazine, will help to differentiate these two products and decrease confusion.

Sonazine
Xenazine

2. Xenazine may look similar to the root name of the Xtrozine product line. The Xtrozine product line includes Xtrozine LA and Xtrozine. Xtrozine is indicated in the treatment of obesity. Both names begin with the letter 'X' and end in letters that may look similar when scripted (azine vs. ozine). However, the second letter of each name is scripted differently (t vs. e). The 't' of Xtrozine requires an upstroke and a cross-bar, whereas, Xenazine requires no upstrokes. However, this difference may not be obvious if the 't' is not clearly written or if the cross bar of the 't' is not clearly distinguishable. Although both products may be administered twice a day, there are some product characteristics that may also help to differentiate these two products, such as dose and strength (12.5 mg and 25 mg vs. 35 mg and 105 mg). Due to the availability of multiple strengths with both products, a strength will be indicated on a prescription in addition to the specific dosing regimen which may help to decrease confusion between the two products. Despite some orthographic similarities between Xenazine and Xtrozine, different product characteristics such as the strength and dosing regimen will help to minimize the potential for confusion between the name pair.

Xtrozine
Xenazine

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III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES:

In the review of the container labels and insert labeling of Xenazine, DMETS has attempted to focus on safety issues relating to possible medication errors. However, we note that the labels and labeling were submitted in black and white and may not represent the true color of the labels and labeling. Therefore, DMETS cannot assess if there are any safety concerns due to the colors utilized on the labels and labeling. However, upon review of the draft labels and labeling, DMETS has identified the following areas of possible improvement, which might minimize potential user error.



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IV. RECOMMENDATIONS:

- A. DMETS has no objections to the use of the proprietary name, Xenazine. This is considered a tentative decision and the firm should be notified that this name with its associated labels and labeling must be re-evaluated upon submission of the NDA and approximately 90 days prior to the expected approval of the NDA. A re-review of the name prior to NDA approval will rule out any objections based upon approvals of other proprietary or established names from the signature date of this document.
- B. DMETS recommends implementation of the label and labeling revisions outlined in section III of this review that might lead to safer use of the product. We would be willing to revisit these issues if the Division receives another draft of the labeling from the manufacturer.
- C. DDMAC finds the proprietary name Xenazine acceptable from a promotional perspective.

DMETS would appreciate feedback of the final outcome of this consult. We would be willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Diane Smith, project manager, at 301-827-1998.

Linda M. Wisniewski, RN
Safety Evaluator
Division of Medication Errors and Technical Support
Office of Drug Safety

Linda Kim-Jung, PharmD.
Team Leader
Division of Medication Errors and Technical Support
Office of Drug Safety

Appendix A:

Inpatient Written	Outpatient Written	Verbal
Xenazine	Xenazine	Genicene
Frenayinc	Xenazine	Xenazine
Venayirc	Xenazine	Xenicine
Xenayine	Xenazine	Xenosine
Xenaying	Xenazine	Xenosyn
Xeneyiac	Xenazine	Ximayine
Xianyinc	Xenazine	Zenacin
Xicnayinc	Xenazine	Zenacin
Xinayiac	Xenazine	Zenafem
Xrnayiac	Xenazine	Zenafine
Yangiax	Xenazine	Zenasien
Yenargine	Xenazine	Zenasine
Yenaznc	Xenazine	Zenathen
yerayiac	Xenazine	zenazine
Yimazine	Xenazine	Zencyne
Yinayinc	Xenazine	Zenecen
Yinayinr	Xenazine	Zenecene
Yinazinc	Xenazine	Zenefin
	Xenazine	Zenephene
	Xenazine	Zenocine
	Xenazine	Zenophene
	Xenazine	Zenosine
	Xenazine	Zenosine
	Xenazine	Zenosine
	Xenazine	Zinafin
		Zinothine

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