CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022462Orig1s000

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

Date:	November 9, 2010
Application Type/Number:	NDA 022462
Through:	Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Kristina A. Toliver, PharmD, Team Leader Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Gablofen (Baclofen Intrathecal Injection) 50 mcg/mL, 500 mcg/mL, and 2000 mcg/mL
Applicant/Sponsor:	CNS Therapeutics, Inc.
OSE RCM #:	2010-1273

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2 METHODS AND RESULTS 3
3 CONCLUSIONS AND RECOMMENDATIONS 3
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1 INTRODUCTION

This re-assessment of the proprietary name is written in response to the anticipated approval of this NDA within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Gablofen, acceptable in OSE Reviews #2009-2141, dated January 28, 2010, #2010-867, dated April 21, 2010, and #2010-1273, dated July 7, 2010. The Division of Neurology Products did not have any concerns with the proposed name, Gablofen, and the Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on November 19, 2009.

2 METHODS AND RESULTS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We use the same search criteria previously used in the above stated reviews. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern.

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA based the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focused on the avoidance of medication errors.

The searches of the databases did not yield any additional names thought to look or sound similar to Gablofen and represent a potential source of drug name confusion. DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Gablofen, as of October 20, 2010.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Gablofen, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Gablofen, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

We are willing to meet with the Division for further discussion, if needed. If you have further questions or need clarifications, please contact Laurie Kelley, OSE Regulatory Project Manager, at 301-796-5068.

4 REFERENCES

1. OSE Review 2010-1273, dated July 7, 2010. DMEPA Proprietary Name Review, Gablofen. Loretta Holmes, BSN, PharmD, Safety Evaluator.
2. OSE Review 2009-2141, dated January 28, 2010. DMEPA Proprietary Name Review, Gablofen. Loretta Holmes, BSN, PharmD, Safety Evaluator.
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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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

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USAN Stems List contains all the recognized USAN stems.

4. *CDER Proposed Names List*

Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis (DMEPA) for review. The list is updated weekly and maintained by DMEPA.

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/s/

KRISTINA C ARNWINE
11/09/2010

DENISE P TOYER
11/10/2010

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:	July 7, 2010
To:	Russell Katz, MD, Director Division of Neurology Products
Through:	Kristina A. Toliver, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
Drug Name(s):	Gablofen (Baclofen Intrathecal Injection) 50 mcg/mL, 500 mcg/mL, and 2000 mcg/mL
Application Type/Number:	NDA 022462
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For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see section 4) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the previous proprietary name review. We use the same search criteria previously used in the above stated reviews.

(b) (4)

Additionally, DMEPA searched the United States Adopted Names (USAN) stem list to determine if the name contains any USAN stems as of the last USAN update. DMEPA based the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focused on the avoidance of medication errors.

DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Gablofen, as of June 23, 2010.

The searches of the databases did not yield any additional names thought to look or sound similar to Gablofen and represent a potential source of drug name confusion. DMEPA's evaluation did not identify any vulnerability with the Applicant's decision to market the 50 mcg/mL, 500 mcg/mL, and 2000 mcg/mL concentrations (b) (4).

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Gablofen, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Gablofen, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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NDA-22462	ORIG-1	CNS THERAPEUTICS INC	BACLOFEN INTRATHECAL INJ 0.05 MG/ML/0.5

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/s/

LORETTA HOLMES
07/07/2010

KRISTINA C ARNWINE
07/07/2010

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07/07/2010

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:	May 3, 2010
To:	Russell Katz, MD, Director Division of Neurology Products
Through:	Kristina A. Toliver, PharmD, Team Leader Kellie A. Taylor, PharmD, MPH, Associate Director Carol A. Holquist, RPh, Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Label and Labeling Review
Drug Name:	Gablofen (Baclofen Intrathecal Injection) 50 mcg/mL, 500 mcg/mL, 2000 mcg/mL, (b) (4)
Application Type/Number:	NDA 022462
Applicant:	CNS Therapeutics, Inc.
OSE RCM #:	2009-2164

1 INTRODUCTION

This review responds to the Division of Neurology Products' request for DMEPA assessment of the container labels, carton and insert labeling for Gablofen (Baclofen Intrathecal Injection), NDA 022462 which is a 505(b)(2) application. The Reference Listed Drug (RLD) is Lioresal (Baclofen Injection), NDA 020075.

2 METHODS AND MATERIALS

DMEPA uses Failure Mode and Effects Analysis (FMEA) to evaluate the container labels, carton, and insert labeling. This review summarizes our medication error evaluation of the labels and labeling of Gablofen submitted by the Applicant on December 18, 2009 (insert labeling) and February 16, 2010 (container labels and carton labeling), see Appendices B through D.

Container Labels and Carton Labeling

- 50 mcg/mL syringe, 1 mL syringe
- 500 mcg/mL, 20 mL vial
- 2000 mcg/mL, 20 mL vial

(b) (4)

Tray Labeling

- 50 mcg/mL syringe, 1 mL syringe

Insert Labeling (no image)

2.1 AERS SELECTION OF MEDICATION ERROR CASES

Since Baclofen Injection is a currently marketed product under the proprietary name, Lioresal, in the U.S., DMEPA searched the FDA Adverse Event Reporting System (AERS) for medication errors associated with Baclofen. The root cause of errors associated with Baclofen may also indicate risks that are present in the proposed labels and labeling of Gablofen. DMEPA searched AERS using the High Level Group Term "Medication Errors" and the High Level Terms "Product Label Issues" and "Product Packaging Issues" and the tradename "Lioresal". The search was conducted on November 18, 2009 and the FDA Received Dates were limited to January 1, 2006 through November 18, 2009. These dates cover the year 2006 (and forward) in which we identified a signal case involving look-alike Lioresal Intrathecal Kit labels.

3 RESULTS AND DISCUSSION

Overall, the search retrieved 357 reports which were manually reviewed to identify risks specific to Baclofen that could also present with the proposed product, Gablofen. Eleven relevant cases were identified, most of which describe errors in which a wrong volume of Lioresal was dispensed or a wrong strength error where either the 500 mcg/mL or 2000 mcg/mL strength was intended but the other strength was used. Three of the 11 cases reported similar labels or labeling as the contributory factor (see Appendix A for a sampling of these case narratives). However, look-alike labels and labeling cannot be ruled out as a contributing factor in most of the other eight cases. Lioresal is available in three strengths (50 mcg/mL, 500 mcg/mL, and 2000 mcg/mL) and a variety of packaging configurations for the refill kits. The 50 mcg/mL strength is available in a one mL volume and is typically used to administer the test dose which may be a reason why the errors occurred between the 500 mcg/mL (available in a 10 mg/20 mL size) and 2000 mcg/mL (available in 10 mg/5 mL and 40 mg/20 mL sizes) concentrations.

Gablofen will be marketed in a one mL (50 mcg/mL) syringe and a 20 mL vial for the remaining strengths (500 mcg/mL, 2000 mcg/mL, (b) (4)). Although this will minimize the potential to dispense the wrong volume of the desired concentration, we are concerned that there is the risk of dispensing the wrong concentration. In order to help minimize the potential to confuse the concentrations and prevent errors with Gablofen, the statement of concentration will have to be clearly presented and the labels and labeling well differentiated from each other.

Most of the remaining 346 cases describe overdoses or underdoses but none of these cases appear to be related to the product labeling. Some of these cases can be directly attributed to issues concerning the functioning of the intrathecal pump system (e.g., the catheter and pump) while the others can be attributed to healthcare provider performance deficit upon manipulation of the intrathecal pump system. Due to the cumbersome nature of the pump and human interaction with it, we anticipate these types of issues will be encountered with the use of Gablofen since the Medtronic pump will also be used to administer this product. However, we do not see any improvements that can be made to the Gablofen labels and labeling to help minimize these errors. Further evaluation of the Lioresal cases will be provided in more detail in the forthcoming OSE Review #2006-883.

4 RECOMMENDATIONS

Our evaluation noted areas where information on the container labels and carton labeling can be improved to minimize the potential for medication errors. We provide comments on the established name in Section 4.1 *Comments to the Division*. Section 4.2 *Comments to the Applicant* contains our recommendations for the container labels and carton labeling. We request the recommendations in Section 4.2 be communicated to the Applicant prior to approval.

We would be willing to meet with the Division for further discussion, if needed. Please copy the Division of Medication Error Prevention and Analysis on any communication to the Applicant with regard to this review. If you have further questions or need clarifications, please contact OSE Regulatory Project Manager, Laurie Kelley, at 301-796-5068.

4.1 COMMENTS TO THE DIVISION

We note the established name for the intrathecal formulation of Lioresal, the Reference Listed Drug, is “baclofen injection” which differs from the proposed established name for Gablofen which is “baclofen intrathecal injection”. We recommend the established names match but will defer to CMC on which representation is more appropriate for the established name of this NDA.

4.2 COMMENTS TO THE APPLICANT

A. General Comments

1. Color is used on the principal display panel to differentiate the strengths. However, the colors are similar shades of blue or green and the strengths are represented in a black box with white lettering. The blue and green shades may be difficult to distinguish from one another and all strengths are presented in the same color which minimizes this differentiation. Use colors that provide more differentiation from each other.
2. Increase the overall size of the proprietary and established names.
3. Change the route of administration statement from (b) (4) to “For intrathecal use only” and increase the size and prominence of this statement.

4. Add the statement “Discard unused portion” and place it in conjunction with the statement “Single Use Syringe” or “Single Use Vial”, as appropriate on the respective container labels and carton labeling (e.g., “Single Use Syringe—Discard Unused Portion” or “Single Use Vial—Discard Unused Portion”). If unable to fit properly on one line, place the latter portion of the statement on the next line below.

5. We note the total drug content statement is stated in “mg/mL” and the drug content per mL is stated in “mcg/mL”. The use of two different dosage units may be confusing. We recommend the same units be used for the total drug content and drug content per mL. The units used should correspond with the units used in the insert labeling to specify the dosage.

B. Container Labels (50 mcg/mL syringe; 500 mcg/mL, 2000 mcg/mL, (b) (4)

1. The black print on colored background is difficult to read. Use colors that provide sufficient contrast to allow for easy readability of the black print.

C. Tray Labeling

1. The company name “CNS Therapeutics, Inc.” is too prominent on the labeling. Relocate the name to a less prominent area on the labeling and decrease the font size.

2. Add an “Rx only” statement.

D. Carton Labeling (50 mcg/mL syringe; 500 mcg/mL, 2000 mcg/mL, (b) (4)

1. The cartons have a narrow band of color at the top of the principal display and back panels and this band is used to provide color differentiation between the strengths. Due to the narrowness of the band and the similarity of the band colors between the strengths (shades of blue or green), the cartons are not well differentiated. Consider using color on a larger portion of the carton labeling in order to provide better color visibility. For example, using a colored background for the statement of strength rather than the currently used black background will provide a larger portion of color on the labeling and may also serve as a better means to differentiate the strengths.

2. Add a net quantity statement to the principal display panel of the 50 mcg/mL carton.

5 REFERENCES

AERS Case Series SE11514729-APR-2010.TXT.

APPENDICES

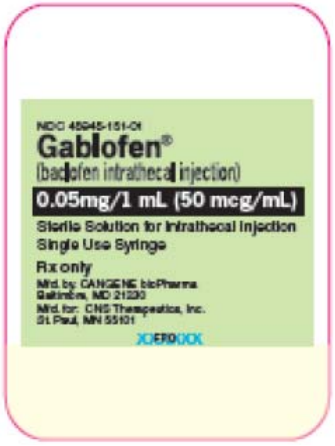
Appendix A. AERS Search Results

ISR Number	Date Rec'd	Strength, concentration, or volume desired	Dispensed or administered	Cause	Outcome
5081512-7	08/16/06	500 mcg/mL	2000 mcg/mL	Similar kit boxes	The pump was filled with the incorrect strength product which was later withdrawn from the pump. The pump was then filled with the correct strength. The patient experienced a minor delay in therapy.
5141341-2	10/30/06	2 mg/mL	1 mg/mL	Pump uses unsafe abbreviations such as the "mμ" symbol for mcg and also uses many trailing zeros after decimal points. The clinical reference guide also has the same issue.	The new concentration for refill was 2 mg/mL (previously 1 mg/mL) but the previous rate in mL/hr was set in the pump and not changed based on the new concentration
5458558-X	08/13/07	2000 mcg/mL	2000 mg/mL	Not stated	Following implant, the pump was incorrectly programmed initially as 2000 *mg/mL* instead of 2000 *mcg/mL*

ISR Number	Date Rec'd	Strength, concentration, or volume desired	Dispensed or administered	Cause	Outcome
5863270-9	08/18/08	2000 mcg/mL	500 mcg/mL	Not stated	At refill, the concentration of Baclofen was changed from 500 mcg/mL to 2000 mcg/mL. The pump was programmed with the 500 mcg/mL rate. A bridge bolus was performed and the patient recovered without sequelae.
5879180-7	08/18/08	500 mcg/mL	2000 mcg/mL	Not stated	Unspecified overdose symptoms; final outcome not stated.
6120381-0	03/16/09	Refill kit; 40 mg/20 mL (2000 mcg/mL)	Refill kit; 10 mg/5 mL (2000 mcg/mL)	Look-alike labels/labeling	Not stated
6219119-8	06/05/09	The reporter made a general comment that the Refill kits; 40 mg/20 mL x 1 vial and the 40 mg/20 mL x 2 vials kits look alike and the wrong kit was filled.		Look-alike labels/labeling	The pharmacist caught the error before the product was dispensed.
6274750-9	07/17/09	2000 mcg/mL	500 mcg/mL	Not stated	At pump refill, the old concentration, 500 mcg/mL was programmed. The pump was not reprogrammed to reflect the new concentration of 2000 mcg/mL. The patient was admitted to the intensive care unit. The patient required ventilation support but eventually recovered to baseline.
6331270-0	08/17/09	500 mcg/mL	2000 mcg/mL	Not stated	The pump was refilled with the higher strength but was still programmed with the settings for the 500 mcg/mL strength. Patient experienced unspecified overdose symptoms. The pump rate was later reduced to compensate for the concentration difference.

ISR Number	Date Rec'd	Strength, concentration, or volume desired	Dispensed or administered	Cause	Outcome
6360421-7	08/17/09	500 mcg/mL	2000 mcg/mL	Not stated	Patient experienced overdose symptoms. The pump was later emptied and refilled with the correct concentration.
6401822-8	20/14/09	Refill kit: 500 mcg/mL	Refill kit: 2000 mcg/mL	Not stated	Patient experienced overdose symptoms, was admitted to the intensive care unit. The drug was removed from the pump and the pump was refilled with the correct concentration. Patient was later discharged home.

Appendix B. Container Labels



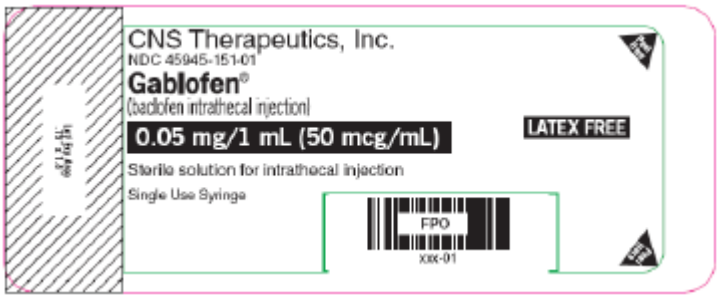
Syringe Label (50 mcg/mL)

Vial Label (500 mcg/mL)

Vial Label (2000 mcg/mL)

(b) (4)

Appendix C. Tray Labeling

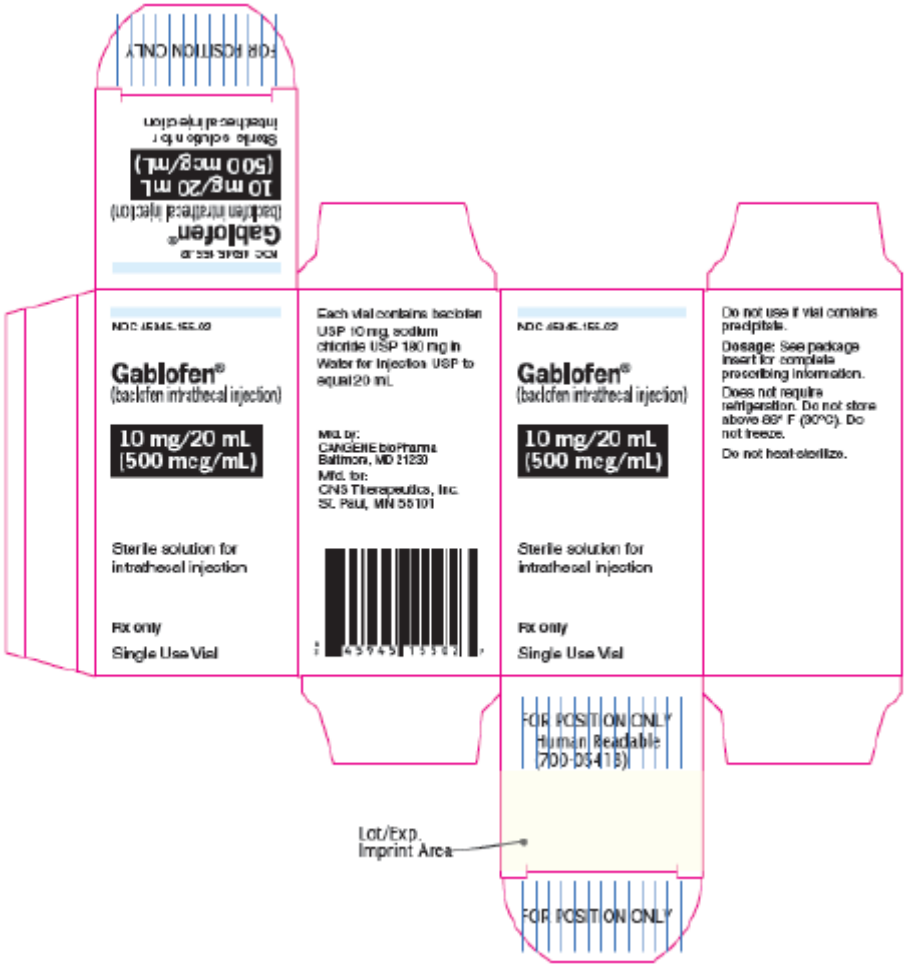


Syringe Tray

Appendix D. Carton Labeling

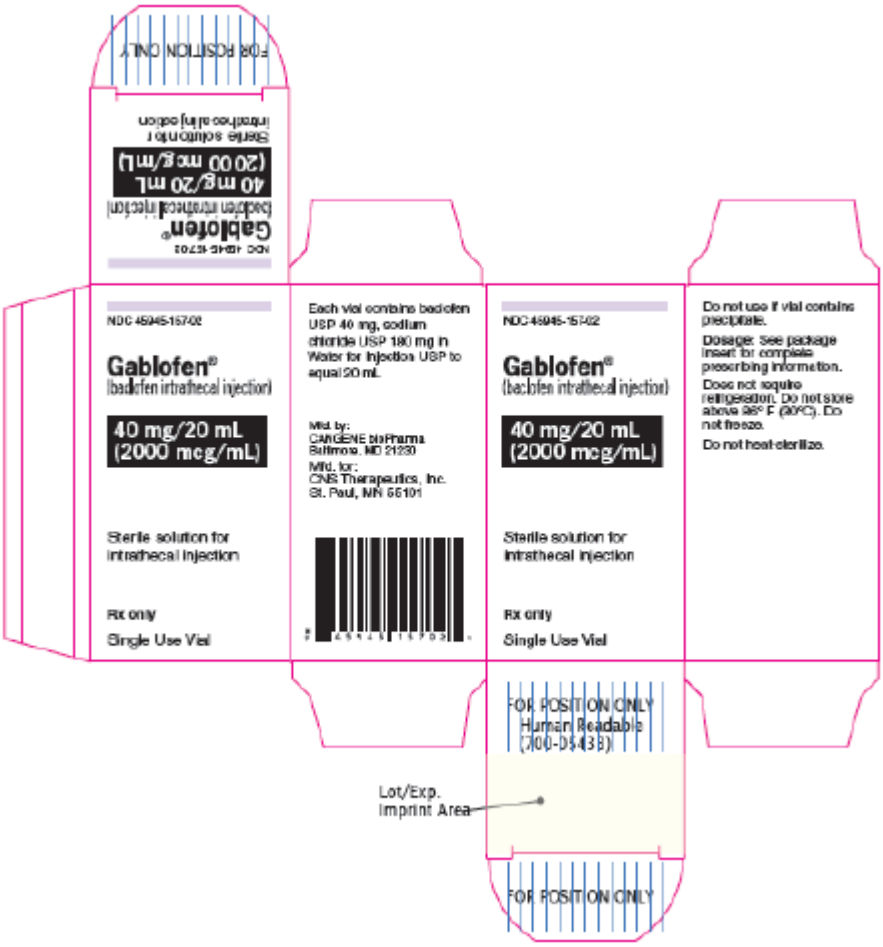
Syringe Carton (50 mcg/mL, 1 mL)

Appendix D. Carton Labeling (cont'd)



Carton Labeling (500 mcg/mL vial)

Appendix D. Carton Labeling (cont'd)



Carton Labeling (2000 mcg/mL vial)


(b) (4)

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22462	ORIG-1	CNS THERAPEUTICS INC	BACLOFEN INTRATHECAL INJ 0.05 MG/ML/0.5

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/s/

LORETTA HOLMES
05/03/2010

KRISTINA C ARNWINE
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05/04/2010

CAROL A HOLQUIST
05/05/2010

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:	April 21, 2010
To:	Russell Katz, MD, Director Division of Neurology Products
Through:	Kristina A. Toliver, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
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Application Type/Number:	NDA 022462
Applicant/Sponsor:	CNS Therapeutics, Inc.
OSE RCM #:	2010-867

1 INTRODUCTION

This re-assessment of the proprietary name is written in response to the anticipated approval of this NDA within 90 days from the date of this review. The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed proprietary name, Gablofen, acceptable in OSE Review # 2009-2141, dated January 28, 2010. The Division of Neurology Products did not have any concerns with the proposed name, Gablofen, and the Division of Drug Marketing, Advertising and Communication (DDMAC) found the name acceptable from a promotional perspective on November 19, 2009.

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DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, Gablofen, as of April 11, 2010.

The searches of the databases did not yield any additional names thought to look or sound similar to Gablofen and represent a potential source of drug name confusion.

3 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Gablofen, is not vulnerable to name confusion that could lead to medication errors nor is the name considered promotional. Thus the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Gablofen, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Neurology Products should notify DMEPA because the proprietary name must be re-reviewed prior to the new approval date.

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/s/

LORETTA HOLMES
05/03/2010

KRISTINA C ARNWINE
05/04/2010

DENISE P TOYER
05/05/2010

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:	January 28, 2010
To:	Russell Katz, MD, Director Division of Neurology Products
Through:	Kristina C. Arnwine, PharmD, Team Leader Denise P. Toyer, PharmD, Deputy Director Division of Medication Error Prevention and Analysis (DMEPA)
From:	Loretta Holmes, BSN, PharmD, Safety Evaluator Division of Medication Error Prevention and Analysis (DMEPA)
Subject:	Proprietary Name Review
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Application Type/Number:	NDA 022462
Applicant:	CNS Therapeutics, Inc.
OSE RCM #:	2009-2141

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EXECUTIVE SUMMARY

Gablofen is the proposed proprietary name for Baclofen Injection (Intrathecal). This proposed name was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant. We sought input from pertinent disciplines involved with the review of this application and considered it accordingly. Our evaluation did not identify concerns that would render the name unacceptable based on the product characteristics and safety profile known at the time of this review. Thus, DMEPA finds the proposed proprietary name, Gablofen, conditionally acceptable for this product. If the NDA is not approved on or before April 30, 2010, the proposed name must be resubmitted for evaluation.

Additionally, if any of the proposed product characteristics as stated in this review are altered, DMEPA rescinds this finding and the name must be resubmitted for review. The conclusions upon re-review are subject to change.

1 BACKGROUND

1.1 INTRODUCTION

This review is in response to an October 29, 2009 request from CNS Therapeutics, Inc. for an assessment of the proposed proprietary name, Gablofen, regarding potential name confusion with other proprietary or established drug names in the usual practice settings.

Additionally, the container labels, carton and insert labeling are being evaluated for their potential contribution to medication errors under separate cover (OSE Review 2009-2164).

1.2 REGULATORY HISTORY

This NDA for Baclofen Injection (Intrathecal) is a 505(b)(2) application. The Reference Listed Drug is Lioresal (Baclofen Injection Intrathecal) NDA 020075. The Applicant intends to market the proposed product in the same concentrations as Lioresal (b) (4)

1.3 PRODUCT INFORMATION

Gablofen is a muscle relaxant and antispasticity agent indicated for spasticity of spinal cord origin and spasticity due to traumatic brain injury. Gablofen is administered through an intrathecal pump. Prior to pump inplantation and initiation of chronic infusion of Gablofen, patients must demonstrate a positive clinical response to a Gablofen bolus dose administered intrathecally in a screening trial (see Appendix B). After an adequate response to the screening trial and after the post-implant titration period, the usual maintenance dose range is from 12 mcg/day to 2003 mcg/day as a continuous infusion via intrathecal pump. Gablofen will be available in the following concentrations and package sizes: a single use syringe of 1 mL containing 50 mcg (50 mcg/ml) and single use vials of 10 mg/20 mL (500 mcg/mL), 40 mg/20 mL (2000 mcg/mL) (b) (4) Gablofen does not require refrigeration; do not store above 86˚F (30˚C); do not freeze.

Gablofen is available in multiple concentrations as stated above. Therefore, in order for a prescription to be complete, it would have to state the concentration since this information is important to know when dispensing Gablofen, administering the test dose(s), and filling and programming the intrathecal pump.

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all

proprietary names. Sections 2.1 and 2.2 identify specific information associated with the methodology for the proposed proprietary name, Gablofen.

2.1 SEARCH CRITERIA

For this review, particular consideration was given to drug names beginning with the letter 'G' 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.[1,2]

To identify drug names that may look similar to Gablofen the DMEPA staff also considers the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (8 letters), upstrokes (3, lower case letters 'b', 'l', and 'f'), downstrokes (one, lower case 'f'), cross strokes (one, lower case 'f'), and dotted letters (none). Additionally, several letters in Gablofen may be vulnerable to ambiguity when scripted (see Appendix C). As a result, the DMEPA staff also considers these alternate appearances when identifying drug names that may look similar to Gablofen.

When searching to identify potential names that may sound similar to Gablofen, the DMEPA staff search for names with similar number of syllables (three), stresses (GAB-lo-fen, gab-LO-fen, or gab-lo-FEN), and placement of vowel and consonant sounds. Additionally, the DMEPA staff considers that pronunciation of parts of the name can vary (see Appendix C). The Applicant provided their intended pronunciation (găb´-lō-fĕn) of the proprietary name in the proposed name submission and, therefore, it was taken into consideration. However, names are often mispronounced and/or spoken with regional accents and dialects, so other potential pronunciations of the name are considered.

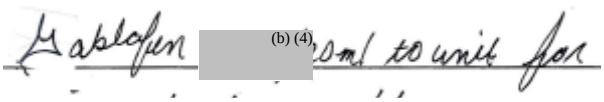
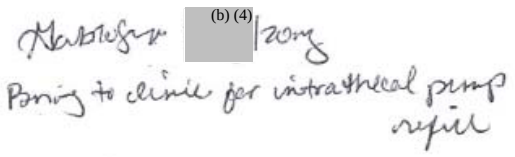
2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient medication order, outpatient and verbal prescription was communicated during the FDA prescription studies.

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

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

Figure 1. Gablofen Prescription Study (conducted on November 23, 2009)

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
Inpatient Medication Order: 	"Gablofen (b) (4) 20 mg Bring to clinic for intrathecal pump refill"
Outpatient Prescription*:  ***Please note the strength was erroneosly transcribed as (b) (4) /20 mg instead of the correct strength of (b) (4) 20 mL.***	

3 RESULTS

3.1 DATABASE AND INFORMATION SOURCES

The searches yielded a total of 13 names as having some similarity to the name Gablofen. Ten of the names were thought to look like Gablofen. These include Relafen, Gallium, Gabarone, Gabitril, Galardin, Gabadone, Gualaquin, Carbatol, Salagen, and Subutex. The remaining 3 names, Baclofen, Gabapentin, and Capoten were thought to look and sound similar to Gablofen.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name as of December 7, 2009.

3.2 CDER EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA staff (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to Gablofen.

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

3.3 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 21 practitioners responded but none of the responses overlapped with any existing or proposed drug names. Three of the participants interpreted the name correctly as "Gablofen" with correct interpretation occurring in both the inpatient written studies (n=2) and the outpatient written studies (n=1). The remainder of the written responses misinterpreted the drug name. In the verbal studies, all responses were misspelled phonetic variations of the proposed name, Gablofen. One respondent in the inpatient written study stated the name was "too close to Gabapentin". Gabapentin was identified in the database searches. See Appendix D for the complete listing of interpretations from the verbal and written prescription studies.

3.4 COMMENTS FROM THE DIVISION OF NEUROLOGY PRODUCTS (DNP)

3.4.1 Initial Phase of Review

In response to the OSE November 19, 2009 e-mail, the Division of Neurology Products stated "DNP has no objections to the proposed proprietary name."

3.4.2 Midpoint of Review

DMEPA notified DNP via e-mail that we had no objections to the proposed proprietary name, Gablofen, on January 14, 2010. In the same e-mail, we asked the Division if they had any concerns that the proposed name contained the letters "lofen" which are also contained in the established name (baclofen) of the drug. Per e-mail correspondence from DNP on January 19, 2010 in response to our questions, they stated "DNP is fine with the proposed proprietary name Gablofen."

3.5 SAFETY EVALUATOR RISK ASSESSMENT

Independent searches by the primary Safety Evaluator identified 3 additional names which were thought to look or sound similar to Gablofen and represent a potential source of drug name confusion. The names identified to have look-alike similarities are Silodosin and Dacogen. The name, Gamophen, was identified to have sound-alike similarities.

When compiling the list of potentially similar drug names, we note that attempts to identify the drug name Gualaquin were unsuccessful. We determined the name was misspelled during the search process (i.e., Gualaquin for Qualaquin). Thus we evaluated Qualaquin rather than Gualaquin.

4 DISCUSSION

4.1 PROMOTIONAL REVIEW

DDMAC did not find the name, Gablofen, promotional. DMEPA and the Division of Neurology Products concurred with this assessment.

4.2 SAFETY REVIEW

The Division of Neurology Products did not identify any factors that render the name unacceptable (e.g., clinical, chemistry, etc.).

In total, 16 names were identified as potential sources of confusion and evaluated by DMEPA. Four of the 16 names were not evaluated further for the following reasons: one name lacked orthographic and/or phonetic similarity, one is the name of a discontinued product with no available generics, one is the name of a product that is not currently marketed, and one name is the established name for Gablofen (see Appendices E through G).

Failure mode and effects analysis (FMEA) was then applied to determine if the proposed name could potentially be confused with the remaining 12 names and lead to medication errors. This analysis determined that the name similarity between Gablofen was unlikely to result in medication errors with any of the 12 products for the reasons presented in Appendix H.

5 CONCLUSIONS AND RECOMMENDATIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Gablofen, is not promotional nor is it vulnerable to name confusion that could lead to medication errors. Thus, the Division of Medication Error Prevention and Analysis (DMEPA) has no objection to the proprietary name, Gablofen, for this product at this time.

However, if any of the proposed product characteristics as stated in this review are altered prior to approval of the product, DMEPA rescinds this Risk Assessment finding and the name must be resubmitted for review. In 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. If the approval of this application is delayed beyond April 30, 2010, the proposed name must be reevaluated. If you have further questions or need clarifications, please contact Laurie Kelley, OSE Project Manager, at 301-796-5068.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Gablofen, and have concluded that it is acceptable. Gablofen will be re-reviewed 90 days prior to the approval of the NDA. If we find the name unacceptable following the re-review, we will notify you.

6 REFERENCES

1. Micromedex Integrated Index (http://csi.micromedex.com)

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

2. 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 the Division of Medication Error Prevention and Analysis, FDA.

3. Drug Facts and Comparisons, online version, St. Louis, MO (http://factsandcomparisons.com)

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

4. FDA Document Archiving, Reporting & Regulatory Tracking System [DARRTS]

DARRTS is a government database used to organize Applicant and Sponsor submissions as well as to store and organize assignments, reviews, and communications from the review divisions.

5. Division of Medication Errors Prevention and Analysis proprietary name consultation requests

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

6. 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, generic drugs, therapeutic biological products, prescription and over-the-counter human drugs and discontinued drugs and "Chemical Type 6" approvals.

7. 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.

8. U.S. Patent and Trademark Office (http://www.uspto.gov)

Provides information regarding patent and trademarks.

9. Clinical Pharmacology Online (www.clinicalpharmacology-ip.com)

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.

10. 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 trade names that are used in about 50 countries worldwide. The data is provided under license by IMS HEALTH.

11. Natural Medicines Comprehensive Databases (www.naturaldatabase.com)

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

12. Stat!Ref (www.statref.com)

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.

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

List contains all the recognized USAN stems.

14. Red Book Pharmacy's Fundamental Reference

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

15. Lexi-Comp (www.lexi.com)

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

16. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. [3]

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

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. DMEPA bases

[3] National Coordinating Council for Medication Error Reporting and Prevention. http://www.nccmerp.org/aboutMedErrors.html. Last accessed 10/11/2007.

the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail. [4] DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used 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. Accordingly, the DMEPA staff considers the product characteristics associated with the proposed drug throughout the risk assessment because 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 proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, 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, DMEPA staff 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.[5] DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly in spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines 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 even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g.,"T" may look like "F," lower case 'a' looks like a lower case 'u,' etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the Applicant's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Applicant has little control over how the name will be spoken in clinical practice.

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

[5] Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

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	• 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 Down strokes Cross-stokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	• Names may look similar when scripted, and lead to drug name confusion in written communication
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	• Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than 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. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches 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 the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA 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 DMEPA staff review the USAN stem list to determine if any USAN stems are present within the

proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

DMEPA conducts an Expert Panel Discussion to gather CDER professional opinions on the safety of the proposed product and the proposed proprietary name. The Expert Panel is composed of Division of Medication Errors Prevention (DMEPA) staff and representatives from the Division of Drug Marketing, Advertising, and Communications (DDMAC). The Expert Panel also discusses potential concerns regarding drug marketing and promotion related to the proposed names.

The primary Safety Evaluator presents the pooled results of the DMEPA staff 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 primary Safety Evaluator to supplement the pooled results, or general advice to consider when reviewing the proposed proprietary name.

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and outpatient prescriptions are written, each consisting of a combination of marketed and unapproved drug products, including the proposed name. These orders are optically scanned and one prescription is delivered to a random sample of the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are 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 send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

DMEPA requests the Office of New Drugs (OND) or Office of Generic Drugs (OGD) Regulatory Division responsible for the application for their comments or concerns with the proposed proprietary name and any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

The OND or OGD Regulatory Division is contacted a second time following our analysis of the proposed proprietary name. At this point, DMEPA conveys their decision to accept or reject the name. The OND or OGD Regulatory Division is requested to concur/not concur with DMEPA's final decision.

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment 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, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, 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 orthographically or phonetically similar 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 primary Safety Evaluator must analyze the use of the product at all points in the medication use system. Because the proposed product is has not been marketed, the primary Safety Evaluator anticipates the use of the product in the usual practice settings by considering the clinical and product characteristics listed in Section one. 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 Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

> ***"Is the proposed proprietary name 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 the proposed proprietary name 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 posses similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes 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 not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name 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 the use of an alternate proprietary name.

DMEPA will object to the use of proposed proprietary name when the primary Safety Evaluator identifies one or more of the following conditions in the Risk Assessment:

a. 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 PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].

b. DMEPA 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)].

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

c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.

d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.

e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, 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 and another drug product.

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

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

The threshold set for objection to the proposed proprietary name may seem low to the Applicant. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), Joint Commission on Accreditation of Hospitals (JCOAH), and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or Applicant can identify and rectify prior to approval to avoid patient harm.

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Applicants have undertaken higher-leverage strategies, such as drug name changes, in the past but at great financial cost to the Applicant and at the expense of the public welfare, not to mention the Agency's credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Applicants' have changed a product's proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners' vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA 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 Section 4 for limitations of the process).

Appendix B: Gablofen Screening Dosing

Prior to pump implantation and initiation of chronic infusion of Baclofen Injection (Intrathecal), patients must demonstrate a positive clinical response to a Baclofen Injection (Intrathecal) bolus dose administered intrathecally in a screening trial. The screening trial employs Baclofen Injection (Intrathecal) at a concentration of 50 mcg/ mL. A 1 mL syringe (50 mcg/ mL) is available for use in the screening trial. The screening procedure is as follows. An initial bolus containing 50 micrograms in a volume of 1 milliliter is administered into the intrathecal space by barbotage over a period of not less than one minute. The patient is observed over the ensuing 4 to 8 hours. A positive response consists of a significant decrease in muscle tone and/ or frequency and/or severity of spasms. If the initial response is less than desired, a second bolus injection may be administered 24 hours after the first. The second screening bolus dose consists of 75 micrograms in 1.5 milliliters. Again, the patient should be observed for an interval of 4 to 8 hours. If the response is still inadequate, a final bolus screening dose of 100 micrograms in 2 milliliters may be administered 24 hours later.

Pediatric Patients: The starting screening dose for pediatric patients is the same as in adult patients, i.e., 50 mcg. However, for very small patients, a screening dose of 25 mcg may be tried first.

Patients who do not respond to a 100 mcg intrathecal bolus should not be considered candidates for an implanted pump for chronic infusion.

Appendix C: Letters with possible orthographic or phonetic misinterpretation

Letters in proposed name "Contrave"	When scripted may appear as:	When spoken may be interpreted as:
Capital 'G'	'C', 'D', or 'S'	'C' or 'K'
lower case 'a'	'ce', 'ci', 'o' or 'u'	'ah' or 'ay'
lower case 'b'	'h', 'l', 'li', 'lo' or 'n'	't' or 'v'
lower case 'l'	'e', undotted 'i', or uncrossed 't'	
lower case 'o'	'a', 'e' or 'u	'oh' or 'ah'
lower case 'f'	'g, 'p' or 't'	'ph' or 's'
lower case 'e'	'a', undotted 'i' or 'l'	
lower case 'n'	'h', 'm', 'r' or 'v'	'em'
'Gab-'		'Cab-', 'Grab-', 'Gav-' or 'Kab-'
'-lo-'		'-le-' or '-low-'
'-fen'		'-fin', '-phen' or '-phin'

Appendix D: FDA Prescription Study Responses

Inpatient Medication Order	Outpatient Medication Order	Voice Prescription
Gablafen	Gablofen	Camlofen
Gablafen	Gablogin	Camlophed
Gablafen (too close to gabapentin)	Gabtogen	Gablefin
Gablafin	Gabtogran	Gablophen
Gablafin	Gabtogro	Gabophen
Gablafin	Gabtosen	Gabophen
gablofen		Gabosen
Gablofen		

Appendix E: Names Lacking Orthographic and/or Phonetic Similarity.

Name	Similarity to Gablofen
Carbatol	Look

Appendix F: Drug products that are discontinued or not currently marketed

Proprietary Name	Similarity to Gablofen	Status and Date
Gamophen (Hexachlorophene) Soap 2% OTC product	Sound	This NDA application was withdrawn in 1978. There are no generic equivalent products available.
Galardin (Matrix Metalloproteinase Inhibitor)	Look	This is an orphan drug that has not received marketing approval by the Agency. It is indicated for the treatment of corneal ulcers. No other product information readily available.

Appendix G: Drug name that is the established name for the product

Name	Similarity to Gablofen	Comments
Baclofen	Look and Sound	Bacofen is the established name for Gablofen and will, therefore, unlikely be a source of medication errors.

Appendix H: Products with numerical overlap or similarity in strength, dose or achievable dose with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Gablofen	Strength	Signa	Differentiating Product Characteristics (Gablofen vs. Product)
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Gabarone (Gabapentin) Tablets	Look	100 mg, 300 mg, and 400 mg	300 mg to 800 mg orally three times per day	The ending letters of the names ("lofen" vs. "arone") look different. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets *Frequency of administration*: bolus test dose once or continuous infusion vs. three times per day

Product name with potential for confusion	Similarity to Gablofen	Strength	Signa	Differentiating Product Characteristics (Gablofen vs. Product)
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Gabapentin (established name, multiple generics available, brand name product is Neurontin) Tablets Capsules Oral Solution	Look and Sound	Tablets: 100 mg, 300 mg, 400 mg, 600 mg, and 800 mg Capsules: 100 mg, 300 mg, and 400 mg Oral solution: 250 mg/5 mL	300 mg to 800 mg orally three times per day	The ending letters look different ('lofen" vs. "apentin"). Additionally, Gabapentin, which contains 10 letters, appears longer in length when scripted as compared to Gablofen which contains eight letters. The ending syllables of the names sound different ("lo-fen") vs. (-ba-pen-tin"). Additionally, Gabapentin contains four syllables vs. Gablofen which contains three which also helps to differentiate the names. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets, capsules, and oral solution *Frequency of administration*: bolus test dose once or continuous infusion vs. three times per day

Product name with potential for confusion	Similarity to Gablofen	Strength	Signa	Differentiating Product Characteristics (Gablofen vs. Product)
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Gabitril (Tiagabine) Tablets	Look	2 mg, 4 mg, 12 mg, and 16 mg	32 mg to 56 mg orally per day in two to four divided doses	The ending letters of the names ("lofen" vs. "itril") look different *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets *Frequency of administration*: bolus test dose once or continuous infusion vs. twice daily, three times per day, or four times per day
Salagen (Pilocarpine Hydrochloride) Tablets	Look	5 mg and 7.5 mg	5 mg orally taken three or four times per day. The usual dosage range is 15-30 mg per day. (Not to exceed 10 mg per dose).	Gablofen has two upstroke letters "bl" located next to each other vs. the letter "l" in Salagen helps to differentiate the names and make Gablofen appear longer in length. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets *Frequency of administration*: bolus test dose once or continuous infusion vs. three or four times per day

Product name with potential for confusion	**Similarity to Gablofen**	**Strength**	**Signa**	**Differentiating Product Characteristics (Gablofen vs. Product)**
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Subutex (Buprenorphine) Tablets	Look	2 mg and 8 mg	12 mg to 16 mg orally once daily	The ending letters of the names ("lofen" vs. "utex") look different. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets
Capoten (Captopril) Tablets	Look and Sound	12.5 mg, 25 mg, 50 mg, and 100 mg	25 mg to 150 mg orally twice daily or three times per day	The letters "bl" in Gablofen vs. "po" in Capoten look different. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets *Frequency of administration*: bolus test dose once or continuous infusion vs. two or three times per day

Product name with potential for confusion	**Similarity to Gablofen**	**Strength**	**Signa**	**Differentiating Product Characteristics (Gablofen vs. Product)**
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Silodosin (established name for Rapaflo) Capsules	Look	4 mg and 8 mg	4 mg or 8 mg orally once daily	The letter "f" in Gablofen helps to differentiate the names because it is in the third position from the end of the name and has an upstroke and downstroke characteristic (depending on how scripted) vs. the letter "s" in Silodosin which is in the same position but does not have an upstroke or downstroke characteristic. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. capsules.

Product name with potential for confusion	**Similarity to Gablofen**	**Strength**	**Signa**	**Differentiating Product Characteristics (Gablofen vs. Product)**
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Dacogen (Decitabine) for Injection	Look	50 mg vial	15 mg/m^2 intravenously every 8 hours for three days every 6 weeks	The upstroke of the letters "bl" in Gablofen help to differentiate the names. *Frequency of administration*: bolus test dose once or continuous infusion vs. every 8 hours *Context of use*: Although a Gablofen dose could potentially overlap with a dose of Dacogen, Dacogen is an antineoplastic agent so a prescription for it would likely state the mg/m^2 dose as well as the calculated dose. Furthermore, an order for Dacogen would likely be written on a special chemotherapy order sheet or it would be stated on the order that it is chemotherapy.
Gallium Nitrate (established name for Ganite) Injection	Look	500 mg/20 mL (25 mg/mL)	100 mg/m^2 to 200 mg/m^2 intravenously daily for 5 days	The ending letters of the names ("ofen" vs. "ium") look different. *Compound name*: Gallium Nitrate is a compound name which also helps to differentiate it from Gablofen when scripted. *Frequency of administration*: bolus test dose once or continuous infusion vs. daily for 5 days

Product name with potential for confusion	**Similarity to Gablofen**	**Strength**	**Signa**	**Differentiating Product Characteristics (Gablofen vs. Product)**
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Relafen (Nabumentone) Tablets *This NDA application has been withdrawn, however, there are multiple generics available*	Look	500 mg and 750 mg	1500 mg to 2000 mg per day in one or two divided doses	The beginning letters of the names ("Gab" vs. "Re") look different. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. tablets
Gabadone (glutamate, 5-hydroxytrypto-phan, choline bitartrate, GABA, glutamate, grape seed extract, gingko biloba, and cocoa powder) Capsules Medical Food product	Look	Not available	1 or 2 capsules orally, every night at bedtime.	The ending letters of the names ("lofen" vs. "adone") look different *Dosage units*: A prescription for Gabadone would specify the dose based on the number of capsules and not the strength since it contains multiple ingredients. Although the number of mL or number of vials of Gablofen could overlap with the number of Gabadone capsules, a Gablofen prescription would likely state the dosage unit (i.e., mg in this case) on a prescription. *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. capsule

Product name with potential for confusion	**Similarity to Gablofen**	**Strength**	**Signa**	**Differentiating Product Characteristics (Gablofen vs. Product)**
Gablofen (Baclofen Injection) Intrathecal	**N/A**	**0.05 mg per 1 mL (50 mcg/mL)** **10 mg/20 mL 0.5 mg/mL (500 mcg/mL)** **40 mg/20 mL 2 mg/mL (2,000 mcg/mL)** (b) (4)	**Test dose: 50 mcg, 75 mcg, or 100 mcg bolus intrathecally, each as a one time dose** **Maintenance dose: 12 mcg to 2003 mcg per day via continuous infusion via intrathecal pump**	**N/A**
Qualaquin (Quinine Sulfate) Capsules	Look	324 mg	648 mg (2 capsules) orally every 8 hours for 7 days	The ending letters of the names ("ofen" vs. "aquin") look different. Qualaquin appears longer in length when scripted as compared to Gablofen *Frequency of admnistration*: bolus test dose once or continuous infusion vs. every 8 hours *Route of administration*: Intrathecal vs. oral *Dosage form*: Injection vs. capsules

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22462	ORIG-1	CNS THERAPEUTICS INC	BACLOFEN INTRATHECAL INJ 0.05 MG/ML/0.5

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/s/

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