CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

202270Orig1s000

PROPRIETARY NAME REVIEW(S)

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 202270

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Merck Sharp & Dohme Corp.
P.O. Box 1000, UG2C-50
North Wales, PA 19454-1099

Attention: Richard J. Swanson, Ph.D.
Senior Director, Worldwide Regulatory Affairs

Dear Dr. Swanson:

Please refer to your New Drug Application (NDA) dated September 23, 2010, received September 23, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Sitagliptin and Metformin Extended-release Tablets, 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg.

We also reference your Class 2 resubmission to your New Drug Application (NDA) dated August 3, 2011, and received August 3, 2011.

We also reference your original March 25, 2011, correspondence, received March 25, 2011, requesting review of your proposed proprietary name Janumet XR. Additionally, we also reference your August 16, 2011, correspondence, received August 16, 2011, requesting review of your proposed proprietary name, Janumet XR. We have completed our review of the proposed proprietary name, Janumet XR and have concluded that it is acceptable.

If **any** of the proposed product characteristics as stated in your August 16, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Margarita Tossa, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4053. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager, Raymond S. Chiang at (301) 796-1940

Sincerely,
{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology
Center for Drug Evaluation and Research

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/s/

CAROL A HOLQUIST
11/04/2011

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review--Final

Date:	November 1, 2011
Reviewer(s):	Richard Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader	Carlos Mena-Grillasca, RPh, Team Leader Division of Medication Error Prevention and Analysis
Division Director	Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
Drug Name(s):	Janumet XR (Sitagliptin and Metformin Extended-release) Tablets, 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg
Application Type/Number:	NDA 202270
Applicant:	Merck, Sharpe, and Dohme, Corp
OSE RCM #:	2011-3134

CONTENTS

1 INTRODUCTION

This re-assessment of the proposed proprietary name, Janumet XR, is written in response to the Request for Proprietary Name Review submitted August 18, 2011 and to the anticipated approval of this NDA within 90 days from the date of this review.

1.1 REGULATORY HISTORY

The Division of Medication Error Prevention and Analysis (DMEPA) found the proposed name, Janumet XR, acceptable in OSE Review 2011-1111 dated June 16, 2011. However, this application received a Complete Response on July 22, 2011 due to deficiencies identified during a facilities inspection. The Applicant submitted a response to the CR letter August 3, 2011 which includes information which is intended to address the identified deficiencies.

2 METHODS AND DISCUSSION

For re-assessments of proposed proprietary names, DMEPA searches a standard set of databases and information sources (see section 4) to identify names with orthographic and phonetic similarity to the proposed name that have been approved since the previous OSE proprietary name review. For this review we used the same search criteria described in OSE Review 2011-1111. Since none of the proposed product characteristics were altered we did not re-evaluate previous names of concern. The searches of the databases yielded one new name (Juvisync) thought to look or sound similar to Janumet XR and represent a potential source of drug name confusion.

Additionally, DMEPA searched the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. The Safety Evaluator did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of October 26, 2011.

DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proposed proprietary name, and focuses on the avoidance of medication errors. Failure mode and effects analysis was applied to determine if the proposed proprietary name could potentially be confused with Juvisync and lead to medication errors. This analysis determined that the name similarity between Janumet XR and the identified name was unlikely to result in medication error for the reasons presented in Appendix A.

Additionally, the Office of Prescription Drug Promotion re-reviewed the proposed name on August 25, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Janumet XR, did not identify any vulnerabilities that would result in medication errors with the additional name noted in this review. Thus, DMEPA has no objection to the proprietary name, Janumet XR, for this product at this time. Since the Applicant submitted a Request for Proprietary Name Review, the comments in 3.1 will be communicated to the Applicant via letter.

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

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

3.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Janumet XR, and have concluded that this name is acceptable for this product.

4 REFERENCES

1. **OSE Review 2011-1111, Janumet XR Proprietary Name Review, Abate, R. June 16, 2011.**

2. ***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.

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

   USAN Stems List contains all the recognized USAN stems.

4. ***Division of Medication Error Prevention and Analysis Proprietary Name Consultation Request***

   Compiled list of proposed proprietary names submitted to the Division of Medication Error Prevention and Analysis for review. The list is generated on a weekly basis from the Access database/tracking system.

Appendix A: Risk of medication errors due to product confusion minimized by the dissimilarity of the names and/or use in clinical practice for the reasons described.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg tablets** **One tablet (any strength but recommended strength is 100 mg/ 1000 mg) by mouth daily or two tablets (50 mg/500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**		**Other Failures to Consider with this product** ***Previously considered failures associated with the use of this product:*** • *Use of a modifier: a failure that the modifier may be dropped.* • *Using an alternative name: failure to identify duplicative therapy.*
	Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion **Causes (could be multiple)**	**Prevention of Failure Mode (name confusion)**
Juvisync (sitagliptin and simvastatin) 100 mg/10 mg, 100 mg/20 mg, and 100 mg/40 mg tablets Usual dose: One tablet by mouth once daily	**Orthographic similarity to the root name, Janumet:** Both names begin with the same letter (J), have a letter grouping at the beginning of the name that may appear similar when scripted (Juvis- vs. Janu-), and have similar length when scripted. **Product characteristics:** Both products include	Orthographic difference between these names stems from the fact that Juvisync includes the letter 'y' which provides a down stroke when scripted and lacks any modifier. Additionally, the name, Janumet XR, includes the letter 't' at the end of the root name which may provide an upstroke and/or a cross stroke when scripted and also includes the modifier 'XR" which provides added length to the name when scripted. These orthographic differences minimize the risk of confusion. In addition, both products are combination medications with strengths presented in terms of both drug components of the product. Although the strengths on the first and shared drug (sitagliptin) may overlap, the second strengths in the presentation are not similar and thus also provide differentiation. (10 mg, 20 mg, and 40 mg vs. 1000 mg)

	Sitagliptin as an active ingredient, share a numeric strength (100 mg) as part of a combination strength presentation, are oral tablets taken once a day, and are manufactured by Merck, Sharpe, and Dohme.	

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/s/

RICHARD A ABATE
11/01/2011

CARLOS M MENA-GRILLASCA
11/01/2011

CAROL A HOLQUIST
11/02/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202270

PROPRIETARY NAME REQUEST ACCEPTABLE

Merck Sharp & Dohme Corp.
P.O. Box 1000, UG2C-50
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Attention: Richard J. Swanson, PhD
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We also refer to your March 25, 2011, correspondence, received March 25, 2011, requesting review of your proposed proprietary name, Janumet XR, and we also refer to your June 22, 2011, correspondence, received June 22, 2011. We have completed our review of the proposed proprietary name, Janumet XR and have concluded that it is acceptable.

The proposed proprietary name, Janumet XR, 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.

If **any** of the proposed product characteristics as stated in your March 25, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Margarita Tossa, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4053. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Raymond Chiang at (301) 796-1940.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology

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/s/

MARGARITA V TOSSA
06/23/2011

CAROL A HOLQUIST
06/23/2011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Silver Spring, MD 20993

NDA 202270

PROPRIETARY NAME REQUEST
CONDITIONALLY ACCEPTABLE

Merck Sharp & Dohme Corp.
P.O. Box 1000, UG2C-50
North Wales, PA 19454-1099

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If you have any questions regarding the contents of this letter or any other aspects of the proprietary name review process, contact Margarita Tossa, Safety Regulatory Project Manager in the Office of Surveillance and Epidemiology, at (301) 796-4053. For any other information regarding this application contact the Office of New Drugs (OND) Regulatory Project Manager Patricia Madara at (301) 796-1249.

Sincerely,

{See appended electronic signature page}

Carol Holquist, RPh
Director
Division of Medication Error Prevention and Analysis
Office of Medication Error Prevention and Risk Management
Office of Surveillance and Epidemiology

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/s/

CAROL A HOLQUIST
06/16/2011

Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Surveillance and Epidemiology
Office of Medication Error Prevention and Risk Management

Proprietary Name Review

Date:	June 15, 2011
Reviewer:	Richard Abate, RPh, MS, Safety Evaluator Division of Medication Error Prevention and Analysis
Team Leader:	Lubna Merchant, MS, PharmD, Acting Team Leader Division of Medication Error Prevention and Analysis
Division Director:	Carol Holquist, RPh, Director Division of Medication Error Prevention and Analysis
Drug Names and Strengths:	Janumet XR (Sitagliptin and Metformin HCl Extended-release) Tablets 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg
Application Type/Number:	NDA 202270
Applicant:	Merck Sharp and Dohme Corp.
OSE RCM #:	2011-1111

*** This document contains proprietary and confidential information that should not be released to the public.***

This document contains proprietary data from the Institute for Safe Medication Practices (ISMP) and Quantros MedMARX which cannot be shared outside of the FDA. Users wanting this information must contact Matthew Grissinger, RPh, FISMP, FASCP, Director, Error Reporting Programs at ISMP

CONTENTS

1 INTRODUCTION

This review evaluates the proposed proprietary name, Janumet XR, from a safety and promotional perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A, respectively.

1.1 REGULATORY HISTORY

Janumet (sitagliptin and metformin HCl) tablets (NDA 022044) was approved March 30, 2007. Prior to approval of NDA 022044, the Division of Medication Error Prevention and Analysis evaluated the name, Janumet, in OSE review # 2006-462 dated March 15, 2007. DMEPA recommended not to use the proprietary name, Janumet, due to likely confusion with Januvia and Sinemet would result in medication errors. Since approval, medication errors have been reported between these name pairs.

1.2 PRODUCT INFORMATION

Janumet XR (Sitagliptin and Metformin HCl Extended-release) tablets is under evaluation for use as an adjunct to exercise and diet to improve glycemic control in adults with type 2 diabetes mellitus. These tablets are formulated to release sitagliptin immediately and have an extended-release mechanism for the metformin. Janumet XR will be available as 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg tablets. The dose is one (100 mg/1000 mg) tablet or two (50 mg/500 mg or 50 mg/1000 mg) tablets taken orally once a day but is determined by the amount of metformin the patient requires. The maximum daily dose is 100 mg of sitagliptin and 2000 mg of metformin. Janumet XR 50 mg/500 mg and 50 mg/1000 mg tablets will be marketed in bottles containing 60, 180, and 1000 tablets. The 100 mg/1000 mg tablets will be marketed in bottles containing 30, 90, and 100 tablets. Janumet XR is stored at room temperature.

2 RESULTS

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

2.1 PROMOTIONAL ASSESSMENT

DDMAC determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Metabolism and Endocrinology Products concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

The following aspects of the name are considered in the overall assessment.

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on April 21, 2011 identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Components of the Proposed Proprietary Name

The proposed proprietary name includes the modifier, XR, to represent the extended release properties of this formulation and differentiate it from the approved Janumet product. The modifier, XR, is used for extended release products only. In addition, the most recent use of this modifier has been with products administered once a day. Thus, the inclusion of the modifier in Janumet XR is appropriate for this product.

However, DMEPA noted the immediate release formulation and this proposed extended-release formulation share overlapping product characteristics that add to the potential for confusion between Janumet and Janumet XR. We discuss these findings in Section 3.

2.2.3 Postmarketing Medication Error Data Evaluated

Janumet is a marketed product. In addition, DMEPA found the proprietary name Janumet likely to be confused with Januvia and Sinemet resulting in medication errors in our review OSE review# 2006-462. Thus, DMEPA searched various databases for medication errors involving Janumet which would be relevant for this review. The results of these searches are described in the following subsections.

2.2.3.1 FDA Adverse Event Reporting System (AERS) Selection of Cases

DMEPA searched the Adverse Event Reporting System (AERS) database on March 29, 2011 using the following search terms: trade name "Janumet%"; verbatim terms "Janume%" and "Sitagliptin%," selecting only those sitagliptin terms that also included Metformin; and the MedDRA High Level Group Term (HLGT) "Medication Errors," and High Level Terms (HLT) "Product Label Issues" and "Product Quality Issues NEC." No time limit was set.

The reports were manually reviewed to determine if a medication error occurred. Duplicate reports were combined into cases. The cases that described a medication error were categorized by type of error. We reviewed the cases within each category to identify factors that contributed to the medication errors. If a root cause was associated with Janumet name confusion, the case was considered pertinent to this review. Reports excluded from the case series include those that did not describe a medication error, describe Janumet as a concomitant medication not involved in the medication error, or described a product complaint. The medication errors associated with the labels and labeling of Janumet will be discussed in DMEPA's review for the proposed labels and labeling of Janumet XR (OSE review # 2010-2299).

Following exclusions, the search yielded four relevant cases (n=4) of wrong drug medication errors. The ISR numbers for these cases appear in Appendix I.

- Confusion with Sinemet (n=2): These cases reported in 2007 Describe confusion between Sinemet and Janumet. The first case describes a pharmacist confusing an order for "Janumet 50 /500" for Sinemet and entered the incorrect medication into the pharmacy computer. However, the error was noted by a second pharmacist prior to dispensing the medication. In the remaining case, the pharmacist confused an order for Janumet 50 mg/500 mg as Sinemet, but called to clarify the dose with the prescriber who stated the medication should be Janumet.

- Confusion with Januvia (n=1): This case from 2007 noted the patient returned a professional sample bottle of Januvia 100 mg tablets stating the tablets appeared to be Janumet which he was to begin after he finished his current prescription of Metformin. The nurse checked the contents of the vial and reported its contents as 42 Janumet tablets and three Januvia tablets.
- Confusion between Jantoven, Januvia and Janumet (n=1): This 2008 case describes multiple prescribers requesting drug information on Jantoven believing it contained sitagliptin or indicated for diabetes mellitus, similar to Januvia or Janumet. The reporter noted several medication errors were avoided due to prescriber confusion but without providing further detail.

2.2.3.2 Institute of Safe Medication Practices Database Selection of Cases[***]

DMEPA requested the Institute of Safe Medication Practices (ISMP) search its databases for medication errors involving Janumet on May 12, 2011, specifically cases of name confusion. DMEPA excluded cases if they did not involve Janumet, name confusion with Janumet or medication error types such as wrong strength or wrong dose.

Following exclusions, the search yielded eight relevant cases. The cases did not describe the event or provide patient outcome. Evaluation of the cases noted were duplicates of cases identified in the AERS database. The remaining six medication error cases are listed below.

- Confusion with Januvia (n=3)
- Confusion with Jantoven (n=2)
- Confusion with Sinemet (n=1)

2.2.3.3 Merck Database Selection of cases

DMEPA requested Merck provide reports from their company database that described confusion involving Janumet regardless of patient outcome in an email dated May 23, 2011. Merck provided six reports of medication errors, three of which were relevant to this review. DMEPA's evaluation of the cases noted them to be duplicates of cases identified in the AERS search.

2.2.4 FDA Name Simulation Studies

Thirty-five practitioners participated in DMEPA's prescription studies. However, one respondent recorded the responses to all the included samples incorrectly. Therefore, the responses provided by this participant were discarded from this simulation study (April 15, 2011). We utilized the responses from the remaining 34 participants for this review. See Appendix D for the complete listing of interpretations from the verbal and written prescription studies. We noted one respondent misinterpreted the 'J' as an 'S' similar to

[***] **This document contains proprietary data from the Institute for Safe Medication Practices (ISMP) and Quantros MedMARX databases which cannot be shared outside of the FDA. ***

Sinemet. However, 31 of the 34 respondents interpreted the name correctly as "Janumet XR."

2.2.5 Comments from Other Review Disciplines

The Division of Metabolism and Endocrinology Product (DMEP) did not forward any comments or concerns relating to the proposed name at the initial phase of the name review.

DMEPA communicated our findings to the DMEP at the NDA wrap-up meeting May 24, 2011. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the Division of Metabolic and Endocrinology Products on May 31, 2011, they stated no additional concerns with the proposed proprietary name, Janumet XR.

2.2.6 Failure Mode and Effects Analysis of Similar Names

Table 1 lists the names with orthographic, phonetic, or spelling similarity to the proposed proprietary name, Janumet XR (see Appendix C). These names were identified by the primary reviewer, the Expert Panel Discussion (EPD), other review disciplines.

Table 1: Collective List of Potentially Similar Names (DMEPA, EPD and Other Disciplines)

Look Similar		**Look and Sound Similar**	
Name	***Source***	***Name***	***Source***
Anumed HC	EPD search	Granumed	EPD search for look and primary SE for sound
Anumed	EPD search	Jantoven	EPD search for look and primary SE for sound/ AERS
Anzemet	EPD search	Janumet	EPD search
Cesamet	EPD search	Januvia	EPD search/ AERS
Fioricet	EPD search	Janumet XR	EPD search
Fiorinal	EPD search	Jolivette	EPD search
Fortamet	EPD search	Prandimet	EPD search look and primary SE sound
Ganirelix Acetate	EPD search		
Glumetza	EPD search		
Jenest -28	EPD search		
Taclonex	EPD search		

Look Similar			
Name	***Source***		
Tavist	EPD search		
Tonocard	EPD search		
Lamictal XR	EPD search		
Namenda XR	EPD search		
Sinemet	EPD search/AERS		
Sinemet CR	EPD search		
Tagamet	EPD search		
Tagamet HB	EPD search		
Tanoral	EPD search		
Temovate	EPD search		
Timentin	EPD search		
Travasol	EPD search		

Our analysis of the 30 names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics. We determined the proposed name, Janumet XR, would perpetuate the previously identified confusion with Januvia, Jantoven, and Sinemet (including Sinemet CR) as described in Appendix E-G. We also noted the safety concerns of handling this product with an alternative name in Appendix H. We discuss our findings in Section 3 below.

3 DISCUSSION

Prior to the initial approval of Janumet (NDA 022044), DMEPA concluded that the name Janumet was unacceptable due to its potential to be confused with Januvia and Sinemet. However, the Division approved the name for market. Since marketing, errors with these name pairs have occurred as well as confusion with Jantoven. The majority of the reported medication errors occurred at the launch of the product with the last case reported in 2009. Due to postmarketing errors, the Institute for Safe Medication Practice (ISMP) placed Janumet on their list of confused drug names.[1]

The name, Janumet, was a root cause to these medication errors because of its similarity to Jantoven, Januvia and Sinemet. However, it is also likely that the relatively short time between the launch of Januvia and Janumet (six months) as well as the minimal number of proprietary names beginning with the letter 'J' also contributed to some of the medication errors. Furthermore, it appears healthcare providers have become more

[1] ISMP's List of Confused Drug Names, http://www.ismp.org/Tools/confuseddrugnames.pdf, cited June 14, 2011.

familiar with the name Janumet in practice as medication errors related to name confusion have not been reported to any of the searched database in the past two years. Finally, the adverse events associated with these medication errors have not been reported or were minimal. As such, it would be difficult to revise the name, Janumet, at this point and time due to existing confusion.

Since the proposed product contains an extended-release formulation for the metformin component of Janumet, there are basically two options for naming this formulation 1) Janumet with the addition of a modifier and 2) a different proprietary name. Each option poses a risk for confusion as described in the following sections, 3.1 and 3.2. However, the risk of harm and likelihood of error may be less than if the product were marketed as Janumet XR. Therefore, given the precedent for using this naming convention, and that the modifier 'XR' complies with the more recent criteria for acceptability (i.e. frequency of administration of once daily) and 31 of 34 respondents to the FDA prescription studies interpreted the name correctly as "Janumet XR," Janumet XR is an acceptable proprietary name for Sitagliptin and Metformin Extended-release tablets.

3.1 JANUMET PLUS MODIFIER 'XR'

Currently, the immediate-release tablet is available in strengths of 50 mg/500 mg and 50 mg/1000 mg administered twice a day (see Appendix G). The modifier 'XR' is used to differentiate the sitagliptin and extended-release metformin HCl formulation from the currently marketed sitagliptin and metformin immediate-release formulation. This modifier is commonly used for product line extensions to distinguish an extended-release formulation taken once daily from the immediate-release base brand (e.g. Cipro XR, Augmentin XR, Actoplus Met XR or Glucophage XR). Additionally, we have no reports of confusion with respect to misinterpretation of XR.

However, postmarketing experience with product line extensions where Applicants have used a modifier in conjunction with an already marketed root name demonstrates medication errors. The errors are generally the result of prescribers omitting the modifier when prescribing the product, healthcare providers overlooking the modifier, or healthcare providers mistakenly selecting the wrong product on electronic computer menus when prescribing medicines electronically.[2] Additionally, computer selection errors may occur in the pharmacy when dispensing the product if the modifier is overlooked, particularly since the strengths of the immediate and extended-release Janumet overlap (50 mg/
500 mg and 50 mg/1000 mg). If the modifier 'XR' is omitted or overlooked from a medication order of Janumet 50 mg/500 mg or 50 mg/1000 mg, it is highly probable that the immediate-release Janumet Tablets will be dispensed since Janumet has overlapping 50 mg/500 mg and 50 mg/1000 mg product strengths with Janumet XR. Thus, patients will receive an immediate-release metformin product with the dosing frequency (i.e. once daily) of the extended-release product, possibly resulting in hyperglycemia.

[2] Lesar TS. Prescribing Errors Involving Medication Dosage Forms. *J Gen Intern Med.* 2002; 17(8): 579-587.

Lastly, selection errors may occur if the products are stored side-by-side in pharmacies. However, the potential for such errors may be mitigated through well-differentiated container labels and carton labeling. This risk will be considered further in our forthcoming labeling review.

With any of the above mentioned errors involving confusion between the immediate and extended-release Janumet, the potential exists for patients to receive an under dose of metformin (immediate-release product dosed once daily). However, the DMEP medical officer noted adverse events are not likely if the extended-release formulation is administered rather than immediate release Janumet. This may be due to the clinical effects of metformin are not immediate. Additionally, the daily dose of both medications is the same and sitagliptin is immediate release in both products.

Since healthcare practitioners may not recognize the dosing frequency differences between Janumet and Janumet XR based on the inclusion of the 'XR' modifier alone, DMEPA recommends that the Applicant alert practitioners and patients on the proper use of these products and clearly communicate the available strengths and dosing frequency for both product formulations. Furthermore, the Applicant attempted to utilize the container labels and carton labeling as a means to differentiate the products and help minimize confusion. DMEPA will address labels and labeling separately under OSE Review #2010-2299.

3.2 USE OF AN ALTERNATE NAME

To decrease the potential risk of confusion between Janumet and Janumet XR, another option to consider is the use of an alternate name. However, there are also risks associated with using dual proprietary names. The use of a new proprietary name for the sitagliptin and extended-release metformin product poses a risk of concomitant therapy of these medications if practitioners and patients fail to recognize that both products contain sitagliptin and metformin leading to overdose of both sitagliptin and metformin. These overdoses could have significant adverse events associated with them including hypoglycemia and diarrhea, and potentially pancreatitis. Additionally, type 2 diabetic patients likely receive multiple medications in the treatment their condition which also increases the risk of concomitant administration with the use of a dual trade name.

In summary, these findings indicate there may be risk of medication errors in both scenarios, but the risk of harm and likelihood of error may be less than if the product were marketed as Janumet XR. Therefore, given the precedent for using this naming convention, and that the modifier 'XR' complies with the more recent criteria for acceptability (i.e. frequency of administration of once daily), Janumet XR is an acceptable proprietary name for Sitagliptin and Metformin Extended-release tablets.

4 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable. However, 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.

Additionally, the proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA.

If you have further questions or need clarifications, please contact Margarita Tossa, OSE project manager, at 301-796-4053.

4.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, Janumet XR, and have concluded that it is acceptable.

The proposed proprietary name, Janumet XR, 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.

If **any** of the proposed product characteristics as stated in your March 25, 2011, submission are altered prior to approval of the marketing application, the proprietary name should be resubmitted for review.

5 REFERENCES

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

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

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

   POCA is a database which was created for the Division of Medication Error Prevention and Analysis, FDA. 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.

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

   Drug Facts and Comparisons is a compendium organized by therapeutic course; it 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)***

   The FDA Orange Book provides a compilation of approved drug products with therapeutic equivalence evaluations.

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

   USPTO provides information regarding patent and trademarks.

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

   Clinical Pharmacology contains full monographs for the most common drugs in clinical use, plus mini monographs covering investigational, less common, combination, nutraceutical and nutritional products. It also 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)***

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

12. ***Access Medicine (www.accessmedicine.com)***

    Access Medicine® from McGraw-Hill contains full-text information from approximately 60 titles; it includes tables and references. Among the titles are: Harrison's Principles of Internal Medicine, Basic & Clinical Pharmacology, and Goodman and Gilman's The Pharmacologic Basis of Therapeutics.

13. ***USAN Stems (http://www.ama-assn.org/ama/pub/about-ama/our-people/coalitions-consortiums/united-states-adopted-names-council/naming-guidelines/approved-stems.shtml)***

    USAN Stems List contains all the recognized USAN stems.

14. ***Red Book Pharmacy's Fundamental Reference***

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

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

    Lexi-Comp is a web-based searchable version of the Drug Information Handbook.

16. ***Medical Abbreviations Book***

    Medical Abbreviations Book contains commonly used medical abbreviations and their definitions.

17. Reviews

OSE Review #2006-462, Proprietary Name review for Janumet, Smith-Jones, T. March 15, 2007.

18. Medication Error Databases

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 post-marketing 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.

*QUANTROS MedMarx****

QUANTROS MedMarx is a national, Internet-accessible database that hospitals and health care systems use to track and trend adverse drug reactions and medication errors. Hospitals and health care systems participate in QUANTROS MedMarx voluntarily and subscribe to it on an annual basis. QUANTROS MedMarx is a quality improvement tool, which facilitates productive and efficient documentation, reporting, analysis, tracking, trending, and prevention of adverse drug events.

*** **This is confidential and proprietary data from the Quantros MedMARX database through an agreement with the Institute of Safe Medication Practices (ISMP) and cannot be shared outside of the FDA.*****

APPENDICES

Appendix A

FDA's Proprietary Name Risk Assessment considers the promotional and safety aspects of a proposed proprietary name. The promotional review of the proposed name is conducted by DDMAC. DDMAC evaluates proposed proprietary names to determine if they are overly fanciful, so as to misleadingly imply unique effectiveness or composition, as well as to assess whether they contribute to overstatement of product efficacy, minimization of risk, broadening of product indications, or making of unsubstantiated superiority claims. DDMAC provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.

The safety assessment is conducted by DMEPA. DMEPA staff search a standard set of databases and information sources to identify names that are similar in pronunciation, spelling, and orthographically similar when scripted to the proposed proprietary name. Additionally, we consider inclusion of USAN stems or other characteristics that when incorporated into a proprietary name may cause or contribute to medication errors (i.e., dosing interval, dosage form/route of administration, medical or product name abbreviations, names that include or suggest the composition of the drug product, etc.). 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]

Following the preliminary screening of the proposed proprietary name, DMEPA gathers to discuss their professional opinions on the safety of the proposed proprietary name. This meeting is commonly referred to the Center for Drug Evaluation and Research (CDER) Expert Panel discussion. DMEPA also considers other aspects of the name that may be misleading from a safety perspective. DMEPA staff conducts a prescription simulation studies using FDA health care professionals. When provided, DMEPA considers external proprietary name studies conducted by or for the Applicant/Sponsor and incorporates the findings of these studies into the overall risk assessment.

The DMEPA primary reviewer assigned to evaluate the proposed proprietary name is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name and misleading nature of the proposed proprietary name with a focus on the avoidance of medication errors.

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. DMEPA considers the product characteristics associated with the proposed product 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.

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

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. DMEPA considers how these product characteristics may or may not be present in communicating a product name throughout the medication use system. Because drug name confusion can occur at any point in the medication use process, DMEPA 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.[4] The product characteristics considered for this review appears in Appendix B1 of this review.

The DMEPA considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA compares the proposed proprietary name with the proprietary and established name of existing and proposed drug products and names currently under review at the FDA. DMEPA 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. DMEPA examines the phonetic similarity using patterns of speech. If provided, DMEPA will consider the Sponsor's intended pronunciation of the proprietary name. However, DMEPA also considers a variety of pronunciations that could occur in the English language because the Sponsor has little control over how the name will be spoken in clinical practice. The orthographic appearance of the proposed name is evaluated using a number of different handwriting samples. DMEPA applies expertise gained from root-cause analysis of postmarketing 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).

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*
	Similar spelling	Identical prefix Identical infix Identical suffix	• Names may appear similar in print or electronic media and lead to drug name

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

Look-alike		Length of the name Overlapping product characteristics	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/Similar shape Upstrokes Down strokes Cross-strokes 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, DMEPA 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 searches 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. A standard description of the databases used in the searches is provided in the reference section of this review. To complement the process, the DMEPA uses 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, DMEPA reviews 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. DMEPA also evaluates if there are characteristics included in the composition that may render the name unacceptable from a safety perspective (abbreviation, dosing interval, etc.).

2. Expert Panel Discussion

DMEPA gathers gather CDER professional opinions on the safety of the proposed product and discussed the proposed proprietary name (Expert Panel Discussion). 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). We also consider input from other review disciplines (OND, ONDQA/OBP). 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 database and information searches to the Expert Panel for consideration. Based on the clinical and professional experiences of the Expert Panel members, the Panel may recommend additional 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 Simulation 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/or 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 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 record their interpretations of the orders which are recorded electronically.

4. Comments from Other Review Disciplines

DMEPA requests the Office of New Drugs (OND) and/or Office of Generic Drugs (OGD), ONDQA or OBP for their comments or concerns with the proposed proprietary name, ask for any clinical issues that may impact the DMEPA review during the initial phase of the name review. Additionally, when applicable, at the same time DMEPA

requests concurrence/non-concurrence with DDMAC's decision on the name. The primary Safety Evaluator addresses any comments or concerns in the safety evaluator's assessment.

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

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

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, considers all aspects of the name that may be misleading or confusing, conducts a Failure Mode and Effects Analysis, and provides an overall decision on acceptability dependent on their 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.[5] 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 Appendix B1 of this review. 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? And Are there any components of the name that may function as a source of error beyond sound/look-alike"***

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

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 or because of some other component of the name. 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.

Moreover, 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 Overall 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)].

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 but involve a naming characteristic that when incorporated into a proprietary name, may be confusing, misleading, cause or contribute to medication errors.

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 generally recommends that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for 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 Sponsor 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/Sponsor. However, the safety concerns set forth in criteria a through e above are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), the Joint Commission, and the Institute for Safe Medication Practices (ISMP). These organizations have examined medication errors resulting from look- or sound-alike drug names, confusing, or misleading 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 preventable source of medication error that, in many instances, the Agency and/or Sponsor 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. Sponsors have undertaken higher-leverage strategies, such as drug name changes, 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 approving the error-prone proprietary name. Moreover, even after Sponsors' 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.

Appendix B: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Janumet XR	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'J'	I, T, or Z	'N'
lower case 'j'	b, c, e, or i	'n'
lower case 'a'	a, c u, or v	any vowel
lower case 'n'	n, s, t, or v	'w'
lower case 'u'	g, p, y, or z	'k'
lower case 'm'	'rn,' 'nn,' n, v, w, 'wi,' 'vi,' 'onc,' or z	n
lower case 'e'	c, i, or l	any vowel
lower case 't'	a, n, or r	'c' or followed by a silent 'e'
Capital 'X'	d, f, K, P, t, U, V, or Y	the letter 'S'
lower case 'x'	a, d, skinny f, k, n, p, r, t, v, or y	the letter 's'
Capital 'R'	B, Pr, or K	
Lower case 'r'	s, n, e, or v	

Appendix C: Prescription Simulation Samples and Results

Figure 1. Janumet XR Study (Conducted on April 15, 2011)

Handwritten Requisition Medication Order	Verbal Prescription
Medication Order: Janumet XR 100/1000 PO qday	Janumet XR 100 slash 1000 mg tablets Take one tablet by mouth daily Dispense 30
Outpatient Prescription: Janumet XR 50/500 ii PO qdaily #60	

FDA Prescription Simulation Responses.

INPATIENT	STRENGTH	VOICE	STRENGTH	OUTPATIENT	STRENGTH
JANUMET XR	100/1000	JANUMET SR	100/1000	JANUMET XR	50/500
JANUMET XR	100/1000	JANUMET XR	100/1000mg	JANUMET XR	50/500
JANUMET XR	100/1000	Janumet XR	100/1000mg	JANUMET XR	50/500
JANUMET XR	100/1000	Janumet XR	100/1000mg	JANUMET XR	50/500
Janumet XR	100/1000 m	Janumet XR		JANUMET XR	50/500
Janumet XR	100/1000	Janumet XR	100/10	JANUMET XR 50/500 II PO QDAILY #60	
SANUMET XR	100/1000	Janumet XR	100/1000mg	Janumet XR	50/500
		Janumet XR	100/1000mg	Janumet XR	50/500 mg
		Janumet XR	100/1000mg	Janumet XR	50/500
		Janumet XR	100/1000mg	Janumet XR	50/500
		Januvmet XR	100/1000 m	Janumet XR	50/500
		janumet xr	100/1000mg	Janumet XR	50/500

	janumet xr 100/1000 mg 1 poqd	#30	Janumet XR	50/500
			Tanumet XR	50/500

Appendix D: Proprietary names not likely to be confused or not used in usual practice settings for the reasons described.

Proprietary Name	Active Ingredient	Similarity to Janumet XR	Failure preventions
Janumet XR	Sitagliptin and Metformin HCL extended-release	Look and sound	Trademark licensed to this Applicant and associated with the product in this application on Google.com searches.
Jenest 28	Norethindrone and Ethinyl estradiol	Look	Discontinued branded generic oral contraceptive. Unable to identify generic equivalents to this product.
Tanoral	Chlorpheniramine Tannate, Phenylephrine Tannate and Pyrilamine Tannate	Look	Discontinued unapproved product with no equivalent products marketed
Tonocard	Tocainide HCl	Look	Discontinued product with no equivalent product marketed.

Appendix E: Risk of medication errors due to product confusion minimized by dissimilarity of the names and/ or use in clinical practice for the reasons described.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Anu-Med HC (Hydrocortisone Acetate) 25 mg suppository Usual dose: One suppository rectally twice daily. Anu-Med (Phenylephrine HCl) 0.25 % suppository Usual dose: One suppository rectally up to four times daily.	Orthographic similarity: Both names include a similar letter grouping (anumed vs. –anumet), and both name include a modifier (HC vs. XR) Phonetic similarity: Both root names include three syllables; the root names rhyme and may include a modifier which have as similar sounding first letter when spoken (H vs. X).	Orthographic difference: Janumet XR begins with the letter 'J' which provides an additional letter at the beginning of the name as well as providing a possible down stroke. Phonetic difference: Janumet XR begins with the letter 'J' which provides a consonant sound at the beginning of the name not heard in Anumed. Additionally, the second letter in the modifier do not sound similar (R vs. C) when spoken. Strength: Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Anumed is a suppository which the modifier distinguishes the active ingredient and strength of the product. Dosage form and route of administration: Rectal suppository vs. oral extended-release tablet

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Anzemet (Dolasetron) 50 mg and 100 mg tablets Usual dose Oral: Post-operative Nausea and Vomiting – One tablet (100 mg) by mouth once within two hours of surgery. Chemotherapy induced nausea and vomiting: One tablet (100 mg) by mouth once two hours prior to chemotherapy. 12.5 mg/0.625 mg, 100 mg/ 5 mL, and 500 mg/25 mL vials Usual dose injection: Chemotherapy induced nausea and vomiting: 100 mg once intravenously 30 minutes prior to chemotherapy. Post-operative Nausea and Vomiting: 12.5 mg intravenously once 15 minutes prior to the cessation of anesthesia (prevention) or once as soon as nausea or vomiting presents.	Orthographic similarity to Janumet: Both names include seven letters and have a similar length when scripted and include a letter grouping that appears similar when scripted (-emet vs. –umet) Phonetic similarity to Janumet: Both names include three syllables, and the names rhyme. Numerically similar strength: 50 mg and 100 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/ 1000 mg. Similar Dose: one tablet Dosage form: oral tablet.	Orthographic difference: Janumet XR begins with the letter 'J' which provides an additional letter at the beginning of the name as well as providing a possible down stroke. Janumet XR includes a modifier "XR' which adds length to the name. Anzemet includes the letter 'z' which may be scripted with a down stroke. Phonetic difference: Janumet XR begins with the letter 'J' which provides a consonant sound at the beginning of the name not heard in Anzemet and includes a modifier which adds two syllables to the name. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Frequency of use: Anzemet in the oral formulation is administered once prior to chemo or surgery, while Janumet XR is a chronic medication which is dosed daily.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Cesamet (Nabilone) 1 mg capsules Usual dose: One to two capsules (1 mg to 2 mg) by mouth twice daily during chemotherapy regimen, may increase to a maximum of 2 mg three times a day.	Orthographic similarity to Janumet: Both names include seven letters and have a similar length when scripted and include a letter grouping that appears similar when scripted (-amet vs. –umet) Both are oral solid dosage forms.	Orthographic difference: The beginning in each name appears different (C vs. J), and Janumet XR includes a modifier, 'XR,' which adds length to the name. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Cesamet is a single strength product with no numeric overlap in strength or dose compared to Janumet XR. Additionally, Cesamet is administered twice or three times daily.
Fioricet (Butalbital, Acetaminophen, and Caffeine) 50 mg/325 mg/40 mg tablets Usual dose: One or two tablets every four hours as needed for headache.	Orthographic similarity to Janumet: The names begin a similar appearing letter when scripted (F vs. J) and end with the same two letters (-et). Finally, the letters in between provide no upstrokes or down strokes when scripted. Both products are oral tablets.	Orthographic difference: The letter "F" provides a cross stroke at the beginning of the name, Fioricet. Janumet XR includes the modifier, 'XR,' which adds length to the name. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Fioricet is a combination product in one configuration of three active ingredients. Thus, it is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Fiorinal (Butalbital, Aspirin and caffeine) 50 mg/325 mg/40 mg capsules Usual dose: One or two capsules every four hours as needed for headache.	Orthographic similarity to Janumet: The names begin a similar appearing letter when scripted (F vs. J) and end with letters that provide upstrokes (l vs. t). Finally, the letters in between provide no upstrokes or down strokes when scripted. Both products are oral solid dosage forms.	Orthographic difference: The letter "F" provides a cross stroke at the beginning of the name, Fiorinal. Janumet XR includes the letter 't' at the end of the name providing a cross stroke and includes the modifier, 'XR,' which adds length to the name. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Fiorinal is a combination product in one configuration of three active ingredients. Thus, it is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Fortamet (Metformin HCL) 500 mg and 1000 mg extended-release tablet Usual dose: One tablet by mouth once daily with evening meal.	Orthographic similarity to Janumet: The names begin a similar appearing letter when scripted (F vs. J) and include a letter grouping that appears similar when scripted (-amet vs. –umet). Numerically similar strength: 500 mg and 1000 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/ 1000 mg. Both are Metformin HCl containing extended-release tablets taken by mouth once daily.	Orthographic difference: The letter "F" provides a cross stroke at the beginning of the name, Fortamet, and also includes the letter 't' in the middle of the name providing a cross stroke as well as an additional upstroke. Janumet XR includes the modifier, 'XR,' which adds length to the name. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Fortamet includes only one active ingredient.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Ganirelix Ganirelix Acetate 250 mcg/0.5 mL prefilled syringe Usual dose: Inject one syringe (250 mcg) subcutaneously once daily	Orthographic similarity to Janumet: The names begin with letters that may appear similar when scripted (G vs. J) and end with a letter which provides a cross stroke (x vs. t). Both are administered once a day.	Orthographic difference: Granirelix includes two additional letters (nine vs. seven) which adds length when scripted and includes the letter 'l' which provides an upstroke in the middle of the name. Janumet XR includes the modifier, 'XR.' Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Ganirelix is a single strength injection formulation administered subcutaneously for short durations (7-14 days) during fertility treatments.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Glumetza (Metformin HCL) 500 mg and 1000 mg extended-release tablet Usual dose: One tablet by mouth once daily with evening meal.	Orthographic similarity to Janumet: The names begin with letters that may appear similar when scripted (G vs. J) and share the letter grouping (umet). Numerically similar strength: 500 mg and 1000 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/ 1000 mg. Both are Metformin HCl containing extended-release tablets taken by mouth once daily	Orthographic difference: Glumetza includes the letter 'l' providing an upstroke in the second position and two letters following the shared letter grouping. One of these l letters is 'z' which may provide a down stroke when scripted. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Glumetza includes only one active ingredient and thus the strength represents Metformin only.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Granumed (Castor oil, Peru Balsam, and Trypsin) 788 mg/87 mg and 0.12 mg per gram topical spray Usual dose: Apply spray to wound twice daily or with each dressing change.	Orthographic similarity to Janumet: The names begin with letters that may appear similar when scripted (G vs. J) and share the letter grouping (anume) and end with a letter which provides an upstroke (d vs. t) Phonetic Similarity to Janumet: The names include three syllables and each syllable is very similar making the names rhyme.	Orthographic difference: Janumet XR includes the modifier, 'XR,' which adds length to the name. Phonetic difference: Granumed begins with a different sounding consonant sound ("Gr" vs. "J"). Janumet XR includes the modifier, 'XR,' which adds two more syllables to the name. Janumet XR is a combination product oral extended-release tablet with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Granumed is a combination topical spray product in one configuration of three active ingredients. Thus, it is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug.
Jolivette (norethindrone) 0.35 mg tablets Usual dose: One tablet by mouth daily.	Orthographic similarity to Janumet: Both names begin with the same letter followed by a similar appearing vowel (Jo vs. Ja) and both include a letter group that may appear similar (-ivet- vs. –met). Both are oral tablets taken daily.	Orthographic difference: Janumet XR includes no upstrokes in the middle of the name and includes a modifier, XR. Jolivette includes a total of four letters which provide upstrokes. Two if these letters are 't' which also provide cross strokes. Strength: 0.35 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg. Janumet XR is a combination product oral extended-release tablet with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Jolivette is an oral contraceptive in one strength presentation which provides a complete prescription without using the strength.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Lamictal XR (Lamotrigine) 25 mg, 50 mg, 100 mg, 200 mg, and 300 mg Extended-release tablets Usual dose: One or two tablets (25 mg to 600 mg) by mouth daily.	Orthographic similarity: The names share a letter grouping that appears similar when scripted (amict vs. umet) and include the modifier XR. Both are extended-release tablets taken once daily. Numerically similar strength: 50 mg and 100 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/ 1000 mg.	Orthographic difference: Janumet XR begins with the letter 'J' which provide a down stroke when scripted. Lamictal XR includes the letters '-al' following the noted shared letter grouping which provides an additional upstroke in the name. Although the products have similar strengths, Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler.
Namenda XR (memantine HCl) 7 mg, 14 mg, 21 mg, and 28 mg extended-release tablets Usual dose: One tablet (28 mg) by mouth daily.	Orthographic similarity: the names include a letter grouping which may appear similar when scripted (amend. vs. umet) and include the modifier, XR. Both are extended-release tablets taken once daily.	Orthographic difference: Namenda XR begins with the letter 'N' which appears different compare to the 'J' in Janumet and includes the letter 'a' after the upstroke provided by the letter 'd.' Strength: 7 mg, 14 mg, 21 mg, and 28 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Namenda XR is an approved product but never marketed by the applicant as of May 2011.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Prandimet (Repaglinide and Metformin HCL) 1 mg/500 mg and 2 mg/ 500 mg tablets Usual dose: One or two tablets by mouth twice daily.	Orthographic similarity to Janumet: the names include two letter groupings that are the same (-an-) or that appear similar when scripted (-imet vs. –umet). Phonetic Similarity to Janumet: the names include three syllables, and the names rhyme. Both products are oral tablets containing two active ingredients including Metformin HCl. Numerically similar strengths: 1 mg/**500** mg and 2 mg/**500** mg vs. 50 mg/**500** mg.	Orthographic difference: Prandimet includes the beginning letters 'Pr' which appear different when compared to the 'J' in Janumet XR. Prandimet also includes the letter 'd' in the fifth position providing an upstroke in the middle of the name. Janumet XR includes the modifier, XR, which adds additional length to the name. Phonetic difference: Prandimet includes different sounding consonants at the beginnings of the first ("pr' vs. "j") and ('d' vs. 'n') second syllables. Janumet XR includes the modifier 'XR' which provides two additional syllables. Although the second strength may overlap, the first strength does not and this is the strength healthcare providers usually refer to initially. The appropriate Prandimet strength may be identified with only the first strength as the Metformin dose is the same in both presentations. Janumet XR requires both strengths for a complete prescription or ability to order the product from a wholesaler.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Taclonex (Calcipotriene and Betamethasone) 0.005%/0.064% ointment and topical suspension Usual dose: Apply a small amount to affected area once daily.	Orthographic similarity to Janumet: The names have letter groupings at the beginning (Ta- vs. Ja-) and end of the name (-onex vs. -umet) that may appear similar when scripted. Both products are administered once daily.	Orthographic difference: Taclonex includes the letter 'l' which provides an upstroke in the middle of the name. Janumet XR includes the modifier, 'XR,' which adds length to the name. Janumet XR is a combination product oral extended-release tablet with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Taclonex is a combination topical product in one configuration of two active ingredients. Thus, it is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug. However, Taclonex is available in two topical dosage form, thus the dosage form is required for a complete prescription or ability to order the product from a wholesaler.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Tagamet and Tagamet HB (Cimetidine) 200 mg, 300 mg, 400 mg and 800 mg tablets; 300 mg/ 5 mL oral solution; 300 mg/ 2 mL and 1200 mg/8 mL vials Usual dose for Tagamet HB: One tablet (200 mg) by mouth one time to treat or prevent acid indigestion, no more than two tablets in 24 hours. Usual dose for Tagamet: One tablet (400 mg) by mouth twice daily One tablet (800 mg) by mouth daily at bed time. *(Prescription Tagamet tablets are discontinued, but generic equivalents are available on the market.)* Injection: 300 mg (2 mL) intravenously or intramuscularly every six or eight hours.	Orthographic similarity: The names include seven letters and may have similar length when scripted, the names begin with letters that may appear similar when scripted (Ta- vs. Ja-); the names include a letter grouping at the end of the name which may appear similar when scripted (-amet vs. umet); and the names include modifiers that may appear similar when scripted (HB vs. XR). Both products are available as oral tablets.	Orthographic difference: Tagamet includes the letter 'g' which provides a down stroke in the middle of the name. Janumet XR includes the letter 'J' which may provide a down stroke when scripted at the beginning of the name. Strength of oral tablet: 200 mg, 300 mg, 400 mg and 800 mg vs. 50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg. Janumet XR is a combination product with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Tavist (Clemastine Fumerate) 1.34 mg tablets Usual dose: One tablet by mouth every 12 hours.	Orthographic similarity to Janumet: The names have letter groupings at the beginning (Tav- vs. Jan-) and end with the same letter (t). Both products are oral tablets.	Orthographic difference: In the name Janumet, the letter grouping (-ume-) between the noted beginning and the 't' at the end adds length to the name when compared to (-is-) in Tavist. Tavist is a single ingredient tablet in one strength presentation which does not numerically overlap with Janumet. It is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug. Janumet XR is a combination product oral extended-release tablet with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler.
Temovate (Clobetasol Propionate) 0.05% cream, emollient cream and topical solution. Usual dose: Apply a small amount of cream to affected area topically twice daily. Apply a small amount of topical solution to the scalp twice daily.	Orthographic similarity to Janumet: The names includes two letter groupings that appear similar when scripted, one at the beginning of the name (Tem- vs. Jan-) and one at the end (-ovat- vs. –umet).	Orthographic difference: Janumet XR includes the modifier, XR, which adds additional length to the name. Temovate includes the letter 'e' after the letter 't.' Janumet XR is a combination product oral extended-release tablet with two active ingredients requiring both strengths for a complete prescription or ability to order the product from a wholesaler. Temovate is a single ingredient product in one strength presentation but in three dosage forms. Thus, it is likely the strength will be omitted during the use of this product as it is not needed for a complete prescription or acquisition of the drug. However, the dosage form is required for a complete prescription or acquisition of the product from a wholesaler.

Proposed name: **Janumet XR** **Sitagliptin and Metformin HCl Extended release tablets**	**Strength:** **50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose:** **One tablet (any strength but recommended strength is 100 mg/1000 mg) by mouth daily or two tablets (50 mg/ 500 mg and 50 mg/1000 mg) by mouth daily. Maximum daily dose 100 mg of sitagliptin or 2000 mg of metformin HCl**
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of name confusion	**Causes (could be multiple)**	**Prevention of Failure Mode;(name confusion)**
Timentin (Ticarcillin disodium and Clavulanate Potassium) 3.1 g vials and premixed bags Usual dose: 3.1 g intravenously every 4 hours, dose reduced for renal function to 2 g intravenously every 4 hours or every 8 hours. Pediatric dosing: (< 60 kg): 50 mg/kg based on ticarcillin per dose intravenously every 4 hours.	Orthographic similarity Janumet: The names include beginning letter groupings that may appear similar when scripted (Timen- vs. Janum-)	Orthographic difference: The endings of the names (-tin vs. -et) differ in appearance. Strength 3.1 g vs. 50 mg/500 mg, 50 mg/1000 mg, 100 mg/1000 mg Dosage form and route of administration: injection in a premixed bag or powder for injection in a vial for intravenous administration vs. an oral extended release tablet.
Travasol (Amino Acids) injection 5.5%, 8.5% and 10 % Usual dose: Amino acids are ordered as part of a parenteral nutrition supplement administered intravenously. The daily dose of protein varies based on the patients condition.(0.5 g/kg to 1.5 g/kg)	Orthographic similarity Janumet: Both names have a similar length (eight letters vs. seven letters), begin with a similar appearing letter (T vs. J) and end with a letter providing the only other upstroke in the name (l vs. t)	Orthographic difference: Janumet ends with the letter 't' which may provide cross stroke when scripted. Janumet XR includes the modifier, XR, which adds additional length to the name. Strengths: 5.5%, 8.5% and 10 % vs. 50 mg/500 mg, 50 mg/1000 mg, 100 mg/1000 mg Dose: 0.5g/kg to 1.5 g/kg (ordered as g of amino acid in a TPN solution) vs. one or two tablets. Dosage form and route of administration: Injection administered intravenously as part of a parenteral nutrition solution vs. oral extended-release tablets.

Appendix F: Janumet and Janumet XR product characteristics

Proprietary name	Janumet	Janumet XR
Established name	Sitagliptin and Metformin HCl	Sitagliptin and Metformin HCl extended-release
Dosage Form	Immediate-release tablets	Extended-release tablets
Indication	An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment of both medications is appropriate.	An adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus when treatment of both medications is appropriate.
Route of Administration	Oral	Oral
Strength	50 mg/500 mg and 50 mg/1000 mg	50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg
Frequency	Twice daily	Once daily
Dose	One tablet	One tablet or two tablets
Maximum daily dose	100 mg Sitagliptan or 2000 mg of Metformin	100 mg Sitagliptan or 2000 mg of Metformin

Appendix G: Failure Mode and Effects Analysis for the confused names reported in medication error cases

Janumet XR (Sitagliptin and Metformin Extended-release) tablets	**50 mg/500 mg, 50 mg/1000 mg, and 100 mg/1000 mg**	**Usual dose: One tablet (any strength) or two tablets (50 mg/500 mg and 50 mg/ 1000 mg) by mouth once daily.**		
Failure Mode: Name confusion	**Causes**	**Effects**	**Detectability if error occurs**	**Regulatory approaches to managing this risk**
Jantoven (Warfarin Sodium) 1 mg, 2 mg, 2.5 mg, 3 mg, 4 mg, 5 mg, 6 mg, 7.5 mg, and 10 mg tablets Usual dose: One tablet by mouth once daily. Medication errors identified: AERS database – 1 cases ISMP databases – 2 additional cases	Orthographic and phonetic similarity of these names. Oral tablets taken once daily	Jantoven is an oral anticoagulant therefore patients receiving this medication in error are at higher risk for bleeding. Patients who receive Janumet in error do not have the anticoagulation needed to prevent clots and are at increased risk of ischemic stroke or PE. In addition, these patients are likely to experience hypoglycemia.	**Medium:** The strengths have some numeric similarity, but Janumet is a combination product that requires both strengths for a complete prescription or the ability to order the appropriate strength from a wholesaler. One pharmacist overlooked the dose (50 mg/100 mg) in one report and started the patient on the inpatient anticoagulation protocol, but the error was noted by nurse when anticoagulation therapy started.	Find the proposed name, Janumet XR, unacceptable. Recommend use of an alternative name for this product. Allow the use of Janumet XR and monitor for the recurrence of medication errors involving name confusion with Janumet.

Sinemet (Carbidopa and Levodopa) 10 mg/100 mg, 25 mg/100 mg, and 25 mg/250 mg tablets Usual dose: One or two tablets by mouth three or four times daily. (Maximum daily dose of 200 mg of Carbidopa) Sinemet CR 25 mg/100 mg and 50 mg/200 mg extended-release tablets Usual dose: one or two tablets (200 to 400 mg levodopa) by mouth twice daily or three times daily. Medication errors identified: AERS database – 1 case ISMP databases- 1 additional case	Orthographic similarity: The names contain seven letters and have similar length; the beginning letter in each name may appear similar when scripted (S vs. J); four of the last five letters are the same (-nemet vs. -numet); and both include a two letter modifier (CR vs. XR) that includes the letter 'R.' Phonetic similarity: The names contain three syllables including the second and third which are nearly the same when spoken making the names rhyme; and the modifiers sound similar with a common letter "R." Numerically similar strengths – 50 mg/200 mg and 10 mg/ 100 mg vs. 50 mg/500 mg and 50 mg/1000 mg Oral solid dosage forms (tablets and extended-release tablets vs. extended-release tablets)	Patients receiving Sinemet CR in place of Janumet XR may not experience any noticeable adverse events. In fact in one of the reported cases the patient received several doses of Sinemet before asking what the new medication was. However, the omission the Janumet XR will result in hyperglycemia.	**Medium:** The products should be stored separately on the pharmacy shelf as they begin with letters that are separated alphabetically. However, both products are marketed by the same applicant who has a standard container label presentation (trade dress). If a written prescription is misread, verification of the filled prescription may not identify the error prior to dispensing	Find the proposed name, Janumet XR, unacceptable. Recommend use of an alternative name for this product. Allow the use of Janumet XR and monitor for the recurrence of medication errors involving name confusion with Janumet.

Januvia (Sitagliptin) 25 mg, 50 mg and 100 mg tablets Usual dose: One tablet by mouth daily. Medication errors identified: AERS database – 1 case ISMP databases – 3 additional cases	Orthographic similarity to Janumet: The names begin with the same three letters (Jan-) and include seven letters Similar numeric strength: 50 mg and 100 mg vs. 50 mg/500 mg, 50 mg/ 1000 mg and 100 mg/ 1000 mg Shared active ingredient: Sitagliptin Both are oral tablets manufactured by the same Applicant.	The modifier XR may be dropped by prescribers. The products are very similar but the added metformin is needed to help control hyperglycemia.	**Medium:** The similar initial strength of 50 mg and 100 mg sitagliptin appears in both products. However, Janumet XR is a combination product that requires both strengths for a complete prescription or ability to order from a wholesaler.	Find the proposed name, Janumet XR, unacceptable. Recommend use of an alternative name for this product. Allow the use of Janumet XR and monitor for the recurrence of medication errors involving name confusion with Janumet.

Appendix H: Failure mode and effects analysis of the use of an alternative proprietary name for this product.

Use of an Alternative Proprietary name for this NDA				
Failure Mode: Unidentified sitagliptin and metformin therapy	**Causes**	**Effects**	**Delectability**	**Managing the Risk**
Alternative proprietary name for the extended-release formulation	Unrecognized proprietary name of Sitagliptin and Metformin HCl extended- release oral tablets when medication reconciliation is completed. Healthcare providers unaware that Sitagliptin and Metformin HCl products are available as an extended-release oral formulation as well as an immediate release tablet formulation.	Duplicate therapy leads to overdoses of sitagliptin and metformin and likely increase the risk of adverse events related to sitagliptin and metformin, like hypoglycemia and indigestion and diarrhea.	**Low:** This error is unlikely to be detected before it occurs.	Recommend alternative name. Cannot justify a change to an alternative name for NDA 022044 as there have been no serious AE's associated with name confusion. Allow the proposed name Janumet XR and monitor for a recurrence of medication errors involving name confusion with Janumet.

Appendix I: IRS numbers of cases retrieved from AERS

5466623 5483880 5659105 5885513

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/s/

RICHARD A ABATE
06/15/2011

LUBNA A MERCHANT
06/15/2011

CAROL A HOLQUIST
06/16/2011