

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

125276

PROPRIETARY NAME REVIEW(S)



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

Date: December 22, 2009

To: Bob Rappaport, M.D., Director
Division of Analgesia, Anesthesia, and Rheumatology Products

Through: Zachary Oleszczuk, Pharm.D., Acting Team Leader
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From: Tara Turner, Pharm.D., Safety Evaluator *T Turner 12/22/09*
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): Actemra (Tocilizumab) Injection
80 mg/4 mL; 200 mg/10 mL; 400 mg/20 mL

Application Type/Number: BLA# 125276/0

Applicant: Hoffmann-LaRoche Inc.

OSE RCM #: 2009-1378

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1 INTRODUCTION

This re-assessment is written in response to the anticipated approval of BLA # 125276 within 90 days from the date of this review. DMEPA found the proposed name, Actemra, acceptable in OSE Review #2007-2566, dated July 28, 2008. Additionally, the Division of Drug Marketing, Advertising and Communications (DDMAC) found the name acceptable from a promotional perspective on October 20, 2009. Furthermore, the Review Division did not have any concerns with the proposed name, Actemra, during our initial review.

2 METHODS

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources (see Section 5) to identify names with orthographic and/or phonetic similarity to the proposed name that have been approved since the completion of the previous OSE proprietary name review. We used the same search criteria outlined in OSE Review #2007-2566 for the proposed proprietary name, Actemra. None of Actemra's product characteristics have been altered since the time of the last review. Thus, we did not re-evaluate previous names of concern.

Additionally, DMEPA searches the USAN stem list to determine if the name contains any USAN stems as of the last USAN updates. 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.

3 RESULTS

The searches of the databases yielded four new names (Zactima***, Bactrim, Coartem, and Akten), thought to look and/or sound similar to Actemra and represent a potential source of drug name confusion. The findings of the FMEA indicate that the proposed name, Actemra, is not likely to result in name confusion with any of the identified names for the reasons presented in Appendices A through C.

Additionally, DMEPA staff did not identify any United States Adopted Names (USAN) stems in the proposed proprietary name, as of December 9, 2009.

4 CONCLUSIONS AND RECOMMENDATIONS

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

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

5 REFERENCES

1. Turner, Tara. OSE Review #2007-2566: Proprietary Name, Label and Labeling Review for Actemra. 28 July 2008.

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 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.

Appendix B: Single strength products with multiple differentiating product characteristics

Product name with potential for confusion	Similarity to Product Name	Strength	Usual Dose	Other Differentiating Product Characteristics
Actemra (tocilizumab)		Injection (Vials): 80 mg/4 mL 200 mg/10 mL 400 mg/20 mL	8 mg/kg via intravenous infusion over 60 minutes once every 4 weeks	
Coartem (artemether and lumefantrine)	Look	Tablet : artemether 20 mg and lumefantrine 120 mg	Adult dosage: Tablets should be administered over 3 days for a total of 6 doses: an initial dose, second dose after 8 hours and then twice daily (morning and evening) for the following two days. For patients with bodyweight of 35 kg and above, 4 tablets per dose for a total of 6 doses.	<u>Dosage form:</u> Tablet vs. injection <u>Dose:</u> Weight based (1, 2, 3, or 4 tablets) vs. 8 mg/kg <u>Route of administration:</u> Oral vs. intravenous infusion <u>Frequency of administration:</u> Administer over 3 days for a total of 6 doses vs. once every 4 weeks
Akten (lidocaine hydrochloride)	Sound	Ophthalmic gel : 3.5%	2 drops applied to the ocular surface in the area of the planned procedure; additional anesthesia may be reapplied as needed	<u>Dosage form:</u> Ophthalmic gel vs. injection <u>Dose:</u> 2 drops vs. 8 mg/kg <u>Route of administration:</u> Ophthalmic (to ocular surface) vs. intravenous infusion <u>Frequency of administration:</u> Prior to procedure vs. once every 4 weeks

Appendix C: Product with overlap in dose and dosage form.

Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p>Actemra (tocilizumab)</p>	<p>Injection (Vials): 80 mg/4 mL 200 mg/10 mL 400 mg/20 mL</p>	<p>8 mg/kg via intravenous infusion over 60 minutes once every 4 weeks</p>
<p>Bactrim (sulfamethoxazole and trimethoprim)</p> <p>Bactrim Tablet : sulfamethoxazole 400 mg and trimethoprim 80 mg</p> <p>Bactrim DS Tablet : sulfamethoxazole 800 mg and trimethoprim 160 mg</p> <p>Bactrim Oral Suspension (discontinued-generics available): sulfamethoxazole 200 mg/5 mL and trimethoprim 40 mg/5mL</p> <p>Bactrim Injection (discontinued – generics available) : sulfamethoxazole 80 mg/mL and trimethoprim 16 mg/mL</p>	<p>Orthographic similarity ('actrim' vs. actemr')</p> <p>Overlapping dose (8 mg/kg)</p> <p>Overlapping dosage form (injection)</p>	<p>The orthographic differences in the names help to minimize the risk of medication errors in the usual practice setting. Although the names contain letters which may look similar when scripted ('actrim' vs. 'actemr'), the beginning letter 'B' helps to differentiate Bactrim from Actemra.</p> <p>The risk of medication errors is further reduced by the different frequencies of administration. The recommended dose of Bactrim injection is 8 to 10 mg/kg/day (based on the trimethoprim component) administered intravenously in 3 to 4 equally divided doses for up to 14 days. By contrast, the recommended dose of Actemra is 8 mg/kg administered via intravenous infusion once every four weeks.</p>



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

Date: July 28, 2008

To: Bob Rappaport, M.D., Director
Division of Anesthesia, Analgesia, and Rheumatology Products,
HFD-170

Through: Linda Kim-Jung, Pharm.D., Team Leader *LLK 7/29/08*
Denise Toyer, Pharm.D., Deputy Director *DT 7/29/08*
Division of Medication Error Prevention and Analysis, HFD-420

From: Tara Turner, Pharm.D., Safety Evaluator *TT 7/29/08*
Division of Medication Error Prevention and Analysis, HFD-420

Subject: Proprietary Name, Label, and Labeling Review

Drug Name(s): Actemra (Tocilizumab) _____ for Intravenous Infusion **b(4)**
20 mg/mL
80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL single-use vials

Application Type/Number: BLA # 125276/0

Licensee: Hoffman-La Roche Inc.

OSE RCM #: 2007-2566

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

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EXECUTIVE SUMMARY

The results of the Proprietary Name Risk Assessment found that the proposed name, Actemra, has some similarity to other proprietary and established drug names, but the findings of the FMEA indicates that the proposed name does not appear to be vulnerable to name confusion that could lead to medication errors. The Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name Actemra for this product at this time.

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

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed container labels and carton labeling are vulnerable to confusion that could lead to medication errors. We note needed improvements with respect to the prominence and presentation of important product information, as well as the clarity and completeness of the preparation and administration instructions. The Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

1 BACKGROUND

1.1 INTRODUCTION

This consult was written in response to a request from the Division of Anesthesia, Analgesia, and Rheumatology Products (HFD-170) for assessment of the proprietary name, Actemra, regarding potential name confusion with other proprietary or established drug names.

Additionally, container labels, carton and insert labeling, and patient information, were provided for review and comment. We note that the patient information will be addressed under separate cover by the Patient Labeling and Education Team of the Division of Risk Management.

We also note that the Licensee submitted a risk management plan which will be addressed under separate cover (OSE review# 2008-357).

1.2 PRODUCT INFORMATION

Actemra (tocilizumab) is indicated to reduce signs and symptoms in adult patients with moderately to severely active rheumatoid arthritis who are naïve to treatment with, or who had an inadequate response to, one or more Disease-Modifying Antirheumatic Drugs (DMARDs) or Tumor Necrosis Factor (TNF) antagonists. Actemra can be used alone or in combination with methotrexate or other DMARDs. The recommended dose for adults is 8 mg/kg given once every 4 weeks as a 60-minute single intravenous drip infusion. The dose should be diluted to 100 mL 0.9% Sodium Chloride Injection, USP. It should not be infused concomitantly in the same intravenous line with other drugs. The product is available in single use vials at a concentration of 20 mg/mL in the following sizes: 80 mg/4 mL, 200 mg/10 mL, 400 mg/20 mL. For each size the vials are packaged individually and in boxes of 4. Actemra must be refrigerated and protected from light.

2 METHODS AND MATERIALS

This section consists of two sections which describe the methods and materials used by medication error staff conducting a proprietary name risk assessment (see 2.1 Proprietary Name Risk Assessment) and label, labeling, and/or packaging risk assessment (see 2.2 Container Label, Carton and Insert Labeling

Risk Assessment). The primary focus for both of the assessments is to identify and remedy potential sources of medication error prior to drug approval. We define 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.¹

2.1 PROPRIETARY NAME RISK ASSESSMENT

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

For the proprietary name, Actemra, the medication error staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity (see Sections 2.1.1 for detail) and held an CDER Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name (see 2.1.1.2). We also conduct internal CDER prescription analysis studies (see 2.1.2), and, when provided, external prescription analysis studies results are considered and incorporated into the overall risk assessment (see detail 2.1.4).

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

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

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

¹ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

² Institute for Healthcare Improvement (IHI). Failure Modes and Effects Analysis. Boston. IHI:2004.

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

2.1.1 Search Criteria

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

For this review, particular consideration was given to drug names beginning with the letter 'A' when searching to identify potentially similar drug names, as 75% of the confused drug names reported by the USP-ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{4,5}

To identify drug names that may look similar to Actemra, the Staff also consider the orthographic appearance of the name on lined and unlined orders. Specific attributes taken into consideration include the length of the name (seven letters), upstrokes (two: upper case letter 'A' and lower case letter 't'), downstrokes (none), cross-strokes (one, lower case 't') and dotted letters (none). Additionally, several letters in Actemra may be vulnerable to ambiguity when scripted, including the upper case letter 'A' may appear as upper case 'S'; lower case letter 'c' may appear as lower case 'a'; lower case 't' may appear as lower case 'r'; lower case 'e' may appear as a lower case 'i' or 'l'; lower case 'm' may appear as lower case 'n' or 'z'; lower case 'r' may appear as lower case 'n' or 'i'; and lower case 'a' may appear as a lower case 'c', 'ce', or 'ci'. As such, the Staff also consider these alternate appearances when identifying drug names that may look similar to Actemra.

When searching to identify potential names that may sound similar to Actemra, the Medication Error Staff search for names with similar number of syllables (3), stresses (ac-TEM-ra or AC-tem-ra), and placement of vowel and consonant sounds. In addition, several letters in Actemra may be subject to interpretation when spoken, including the letter 'A' may be interpreted as 'E'; the letter 'c' may be interpreted as 'k'; the letter 't' may be interpreted as 'd'; or the letter 'e' may be interpreted as 'i' or 'a'. The Sponsor's intended pronunciation of the proprietary name could not be expressly taken into consideration, as this was not provided with the proposed name submission.

The Staff also consider the product characteristics associated with the proposed drug throughout the identification of similar drug names, since the product characteristics of the proposed drug ultimately determine the use of the product in the clinical practice setting. For this review, the Medication Error Staff were provided with the following information about the proposed product: the proposed proprietary name (Actemra), the established name (tocilizumab), proposed indication (reduce signs and symptoms in adult patients with moderately to severely active rheumatoid arthritis), strength (20 mg/mL), dose (8 mg/kg), frequency of administration (once every 4 weeks), route (intravenous infusion), and dosage form

Appendix A provides a more detailed listing of the product characteristics the Medication Error Staff generally take into consideration.

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

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

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

b(4)

2.1.1.1 Database and information sources

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

2.1.1.2 CDER Expert Panel Discussion

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

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

2.1.2 CDER Prescription analysis studies

Three separate studies are conducted within the Centers of the FDA for the proposed proprietary name to determine the degree of confusion of Actemra 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 a total of 123 healthcare professionals (pharmacists, physicians, and nurses), and attempts to simulate the prescription ordering process. The results are used by the Safety Evaluator to identify any orthographic or phonetic vulnerability of the proposed name to be misinterpreted by healthcare practitioners.

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

Figure 1. Actemra Study (conducted on January 8, 2008)

HANDWRITTEN PRESCRIPTION AND MEDICATION ORDER	VERBAL PRESCRIPTION
<p>Inpatient Requisition #1:</p> <p><u>Actemra</u></p>	<p>“Actemra 10 vials”</p>
<p>Inpatient Requisition #2:</p> <p><u>Actemra</u></p>	

2.1.3 Safety Evaluator Risk Assessment of the Proposed Proprietary Name

Based on the criteria set forth in Section 2.1, the Safety Evaluator Risk Assessment applies their individual expertise gained from evaluating medication errors reported to FDA to conduct a Failure Modes and Effects Analysis and provide an overall risk of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ When applying FMEA to assess the risk of a proposed proprietary name, we seek to evaluate the potential for a proposed name to be confused with another drug name as a result of the name confusion and cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to look- or sound-alike drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

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

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

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

The Division of Medication Error Prevention will object to the use of proposed proprietary name when the one or more of the following conditions are identified in the Safety Evaluator’s Risk Assessment:

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

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

If none of these conditions are met, then we will not object to the use of the proprietary name. If any of these conditions are met, then we will object to the use of the proprietary name. The threshold set for objection to the proposed proprietary name may seem low to the Sponsor; however, the safety concerns set forth in criteria 1 through 5 are supported either by FDA Regulation or by external healthcare authorities, including the Institute of Medicine, World Health Organization, Joint Commission, and the Institute for Safe Medication Practices, who have examined medication errors resulting from look- or sound-alike drug names and called for Regulatory Authorities to address the issue prior to approval.

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

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

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

2.2 LABEL AND LABELING RISK ASSESSMENT

The label and labeling of a drug product are the primary means by which practitioners and patients (depending on configuration) interact with the pharmaceutical product. The container labels and carton labeling communicate critical information including proprietary and established name, strength, form, container quantity, expiration, and so on. The insert labeling is intended to communicate to practitioners all information relevant to the approved uses of the drug, including the correct dosing and administration.

Given the critical role that the label and labeling has in the safe use of drug products, it is not surprising that 33 percent of medication errors reported to the USP-ISMP Medication Error Reporting Program may be attributed to the packaging and labeling of drug products, including 30 percent of fatal errors.⁷

Because Medication Error Prevention staff analyze reported misuse of drugs, we are able to use this experience to identify potential errors with all medication similarly packaged, labeled or prescribed. We use FMEA and the principles of human factors to identify potential sources of error with the proposed product labels and insert labeling, and provided recommendations that aim at reducing the risk of medication errors.

For this product the Licensee submitted on November 19, 2007 the following labels and labeling for our review (see Appendices I, J, and K for images):

- Container Label: 80 mg/4 mL vial
- Container Label: 200 mg/10 mL vial
- Container Label: 400 mg/20 mL vial
- Carton Labeling: 80 mg/4 mL vial
- Carton Labeling: 200 mg/10 mL vial

⁷ Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006. p275.

- Carton Labeling: 400 mg/20 mL vial
- Carton Labeling: 80 mg/4 mL (4 vials)
- Carton Labeling: 200 mg/10 mL (4 vials)
- Carton Labeling: 400 mg/20 mL (4 vials)
- Insert Labeling (no image) – revised version submitted July 25, 2008
- Patient Information (no image) – revised version submitted July 25, 2008

3 RESULTS

3.1 PROPRIETARY NAME RISK ASSESSMENT

3.1.1 Database and information sources

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

Twenty-seven of the names were thought to look like Actemra, which include: Activa, Antara, Alera, Actiza***, Aceta, Climara, Citracal, Sclerosol, Ciloxan, Actinex, Azactam, Actonel, Activase, Activia, ——— Ertaczo, Estrace, Octamide, Actamin, Acticin, Hetrazan, Sitrex, Acthar, Acetemra, Acutrim, Artemisia, and Actenacol. The remaining name, ——— was thought to sound like Actemra.

b(4)

Additionally, the Division of Medication Error Prevention did not identify any USAN stems in the name, Actemra, as of February 19, 2008.

3.1.2 Expert panel discussion

The Expert Panel reviewed the pool of names identified by Medication Error Prevention staff (see section 3.1.1. above) but did not identify any additional names with similarity to Actemra. Additionally, the Expert Panel noted that Actemra is currently available in several foreign countries.

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

3.1.3 CDER Prescription analysis studies

A total of 36 practitioners responded, but none of the responses overlapped with any existing or proposed drug names. Twenty-two percent of the participants (n=8) interpreted the name correctly as “Actemra”, with correct interpretation occurring more frequently in the first inpatient requisition study. The remainder of the participants misinterpreted the drug name. The majority of misinterpretations involved either the relocation of the ‘r’ to appear after the ‘t’ (Actrema; n=6) or the misinterpretation of the lower case ‘r’ as lower case ‘i’ (Actemia; n=5). See Appendix B for the complete listing of interpretations from the verbal and written prescription studies.

3.1.4 Safety evaluator risk assessment

Independent searches by the primary Safety Evaluator did not identify any additional names thought to look similar to Actemra and represent a potential source of drug name confusion. As such, a total of

twenty-eight names were analyzed to determine if the drug names could be confused with Actemra and if the drug name confusion would likely result in a medication error.

All of the identified names were determined to have some orthographic and/or phonetic similarity to Actemra, and thus determined to present some risk for confusion. Failure modes and effects analysis (FMEA) was then applied to determine if the proposed name, Actemra, could potentially be confused with any of the twenty-eight names and lead to medication error.

This analysis determined that the name similarity between Actemra and the identified names was unlikely to result in medication errors for all twenty-eight products. Twelve names were not considered further because they lack convincing orthographic and/or phonetic similarities with Actemra (Appendix C). Four names are for products with a different context of use than Actemra (Appendix D). Two names are proposed proprietary names for other products within the Agency which have not been approved or were approved under a different proprietary name, and thus were determined by FMEA to pose a minimal risk of error in the usual practice setting (Appendix E). Acetemra *** was a proposed name for the subject of this review, tocilizumab. The name was never reviewed because the sponsor did not submit additional information. One name is for a product that is no longer marketed in the U.S. (Appendix F). Aceta is an acetaminophen product that is available both as a tablet and as an elixir. However, no further information is available. Actenacol is a foreign natural medicine product that is available in Italy. It is used to treat gastrointestinal disorders.

For five names (Actonel, Actamin, Azactam, Octamide, and Activase) it was determined that medication errors were unlikely because the products do not overlap in strength or dosage with Actemra (see Appendix G). We note that Octamide has been discontinued as a brand name product and is no longer available in the U.S. However, generic equivalents are available.

The remaining name (Acthar) had some numerical overlap with Actemra in dosage and strength, but analysis of the failure modes did not determine the effect of this similarity to result in medication errors in the usual practice setting (see Appendix H).

3.2 LABEL AND LABELING RISK ASSESSMENT

Review of the container labels and carton and insert labeling identified several areas of vulnerability that could lead to medication error, specifically with respect to the prominence and presentation of important product information, as well as the clarity and completeness of the preparation and administration instructions.

3.2.1 General Comments

The strength is only provided in terms of total drug content.

The strength is presented in two locations.

The dosage form is listed inconsistently.

The route of administration is presented without prominence.

The storage requirements are presented without prominence.

3.2.2 Insert Labeling

In the Dosage and Administration Section, there is no statement regarding a maximum dose which should not be exceeded regardless of patient weight.

The preparation instructions are unclear.

There is no information regarding whether or not the intravenous line needs to be flushed.

There is an all-encompassing list of compatible infusion bags and bottles.

3.2.3 Patient Information

We have no comments at this time.

4 DISCUSSION

4.1 PROPRIETARY NAME RISK ASSESSMENT

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

The findings of the Proprietary Name Risk Assessment are based upon current understanding of factors that contribute to medication errors involving name confusion. Although we believe the findings of the Risk Assessment to be robust, our findings do have limitations. First, because our assessment involves a limited number of practitioners, it is possible that the analysis did not identify a potentially confusing name. Also, there is some possibility that our Risk Assessment failed to consider a circumstance in which confusion could arise. However, we believe that these limitations are sufficiently minimized by the use of an Expert Panel and the Prescription Studies that involved 123 FDA practitioners.

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

4.2 LABEL AND LABELING RISK ASSESSMENT

The results of the Label and Labeling Risk Assessment found that the presentation of information and design of the proposed carton labeling and container labels appears to be vulnerable to confusion that could lead to medication errors. We note needed improvements with respect to the prominence and presentation of important product information, as well as the clarity and completeness of the preparation and administration instructions.

Specifically, we found that important information is presented in a manner that lacks prominence. On the container labels, the route of administration is presented on the side panel and thus is unavailable when looking at the principal display panel of the vial. Since this information is vital to the proper use of the product, relocating it to the principal display panel will increase its prominence. Similarly, the route of administration is presented in small, lightweight font on the carton labeling and container labels. Increasing the size and weight of the font will increase its prominence and help to minimize the risk of wrong route of administration errors. Also, the storage requirements are presented in a similar small, lightweight font, which makes it difficult to read and could result in the drug not being refrigerated.

Our analysis also revealed information that is presented in an inconsistent or otherwise confusing manner. On the container labels and carton labeling, the strength is presented in terms of total drug content (i.e. 80 mg/4 mL). It is also important to present the strength in terms of mg per mL (i.e. 20 mg/mL). This helps the healthcare practitioner accurately calculate the amount of drug to withdraw from the vial at the point of preparation. Further, there is a secondary statement of strength on the side panel of the container label and on the principal display panel of the carton labeling ("Vial contains 80 mg in 4 mL"). This is redundant because the strength is already presented immediately beneath the established name. Also, on

the carton labeling, the single use statement is presented twice. The removal of duplicative information will decrease the crowding and improve the readability of important information such as the route of administration and the storage conditions. Additionally, we note that on the container labels and carton labeling, the established name is presented as "tocilizumab sterile solution". However, on the insert labeling it is presented as "tocilizumab _____ for intravenous infusion". This information should be presented consistently across all product labeling. We contacted the CMC reviewer for this application, Gerald Feldman, and in an e-mail dated July 3, 2008, he suggested that the established name be changed to "tocilizumab sterile solution for intravenous infusion". The CDER Labeling and Nomenclature Committee could also provide input on the established name and dosage form to ensure that the dosage form used is consistent with other CDER approved biologics and drugs.

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We noted confusing information in the insert labeling. In the Dosage and Administration Section, the usual recommended dose is listed as 8 mg/kg given once every 4 weeks. There is no indication as to whether there is a maximum dose which should not be exceeded regardless of patient weight. This information is necessary for calculating safe doses for all patients. According to the instructions for preparing the intravenous infusion, the healthcare professional is instructed to withdraw a volume equal to 0.4 mL per kg of the patient's body weight from a 100 mL bag or bottle of 0.9% sodium chloride for injection. Then the healthcare professional is to add the patient's dose of Actemra into the infusion bag or bottle. This description is confusing because it involves a secondary calculation, which increases the potential for calculation errors. The labeling needs to inform practitioners that the total final volume of Actemra and sodium chloride for injection must be 100 mL. Therefore, the appropriate volume of sodium chloride must be removed from the bag prior to adding the Actemra dose. In the Administration instructions, it is stated that Actemra should not be infused concomitantly in the same intravenous line with other drugs. However, no instructions are given as to whether the intravenous line needs to be flushed before and after the Actemra dose. Finally, we questioned if there are particular infusion bags or bottles in which Actemra should not be diluted. The labeling lists polypropylene, polyethylene and polyvinyl chloride infusion bags and polypropylene, polyethylene and glass infusion bottles, which appears to be all encompassing. Practitioners would only need this information if there is a limitation to the use of a specific type of bag or bottle.

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

5 CONCLUSIONS

The Proprietary Name Risk Assessment findings indicate that the proposed name, Actemra, does not appear to be vulnerable to name confusion that could lead to medication errors. As such, the Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name, Actemra, for this product at this time.

The Label and Labeling Risk Assessment findings indicate that the presentation of information and design of the proposed carton labeling and container labels introduces vulnerability to confusion that could lead to medication errors. The Division of Medication Error Prevention and Analysis believes the risks we have identified can be addressed and mitigated prior to drug approval, and provides recommendations in Section 6 that aim at reducing the risk of medication errors.

6 RECOMMENDATIONS

6.1 COMMENTS TO THE DIVISION

6.1.1 *Proprietary Name*

1. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review.
2. If the product approval is delayed beyond 90 days from the date of this review, the proposed name must be resubmitted for evaluation.
3. We recommend that Richard Lostritto of the Labeling and Nomenclature Committee be consulted on the correct established name and dosage form of this product. It is currently inconsistently presented throughout the labels and labeling [redacted] and he would be able to provide guidance as to whether the proposal of "tocilizumab [redacted] for intravenous infusion" is consistently used throughout CDER.

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We would appreciate feedback on the final outcome of this review. We would be willing to meet with the Division for further discussion, if needed. Please copy us on any communication to the licensee with regard to this review. If you have further questions or need clarifications, please contact Darrell Jenkins, project manager, at 301-796-0558.

6.2 COMMENTS TO THE LICENSEE

6.2.1 *Proprietary Name*

1. The Division of Medication Error Prevention and Analysis does not object to the use of the proprietary name Actemra for this product at this time.
2. If any of the proposed product characteristics as stated in this review are altered prior to approval of the product, we rescind this Risk Assessment finding, and recommend that the name be resubmitted for review. This name will be re-evaluated 90 days prior to approval.

6.2.2 *Labels and Labeling*

A. General Comments

1. Add a statement of strength in terms of mg/mL immediately beneath the total drug content as follows:
80 mg/4 mL
(20 mg/mL)
2. Remove the duplicate statements of strength (e.g., vial contains 400 mg in 20 mL) from the side panel of the container label and the principal display panel of the carton labeling. This will provide additional space on the labels and labeling so that the prominence of other important information can be increased.
3. Be consistent in the presentation of the established name across all product labels and labeling.

4. Increase the prominence of the route of administration on all of the product labeling.
5. Increase the prominence of the storage requirements in order to ensure this product is refrigerated.

B. Container Label

Relocate the route of administration to the principal display panel so that it is apparent when reading the trade and established name and strength. This location will also help minimize the risk of wrong route of administration errors.

C. Insert Labeling

1. Add information regarding whether or not there is a maximum dose regardless of patient weight.
2. Clarify the preparation instructions in terms of the amount of sodium chloride to withdraw from the bag or bottle prior to adding the Actemra dose so that a secondary calculation is not required.
3. Add information regarding whether or not it is necessary to flush the intravenous line before and after the Actemra dose, since it should not be infused concomitantly in the same intravenous line with other drugs.
4. Clarify whether there are particular infusion bags or bottles in which Actemra should not be diluted. The exceptions should be listed in lieu of the list in its entirety.

7 REFERENCES

1. *Adverse Events Reporting System (AERS)*

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

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

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

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

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

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

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

5. *AMF Decision Support System [DSS]*

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

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

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

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

Drugs@FDA contains most of the drug products approved since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present. Drugs@FDA contains official information about FDA approved brand name and generic drugs and therapeutic biological products; prescription and over-the-counter human drugs and therapeutic biologics, discontinued drugs and “Chemical Type 6” approvals.

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

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

9. United States Patent and Trademark Office <http://www.uspto.gov>.

Provides information regarding patent and trademarks.

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

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

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

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

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

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

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

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

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

List contains all the recognized USAN stems.

15. Red Book Pharmacy's Fundamental Reference

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

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

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

17. Medical Abbreviations Book

Contains commonly used medical abbreviations and their definitions.

APPENDICES

Appendix A:

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

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

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

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

Appendix B:

Actemra CDER Prescription Study Responses

Inpatient Requisition #1	Inpatient Requisition #2	Voice Prescription
Acetemia	Acetamice	Actrama
Aceterna	Acetemia	Actrama
Actemia	Actemace	Actrema
Actemia	Actemia	Actrema
Actemra	Actemia	Actrema
Actemra	Actemia	Actrema
actemra	Actemice	Actrema
Actemra	Actemice	Actrema
Actemra	Actemid	Actremma
Actemra	Actemsa	Actremma
Actemra		Actremma
Actemra		Actrima
		Ectrema
		Ectrema

Appendix C: Names lacking convincing look-alike and/or sound-alike similarities with Actemra

Proprietary Name	Similarity to Actemra
Antara	Look
Alera	Look
Climara	Look
Citracal	Look
Sclerosol	Look
Ciloxan	Look
—	Look
Ertaczo	Look
Estrace	Look
Acticin	Look
Hetrazan	Look
Sitrex	Look

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Appendix D: Products with a different context of use than Actemra

Proprietary Name	Similarity to Actemra	Type of Product/Use
Activa	Look	Surgical treatment (deep brain stimulation) for Parkinson's Disease
Activia	Look	Low fat yogurt with probiotic culture (<i>Bifidus regularis</i>) to help regulate the digestive system
Artemisia	Look	Natural product used for a variety of disorders
Acutrim	Look	Natural medicine product (Acutrim Natural AM; Acutrim Natural PM); Acutrim was also an over the counter weight loss aid (discontinued)

Appendix E: Proposed proprietary names for products not approved or approved with another name

Proprietary Name	Similarity to Actemra	Disposition of Name
Actiza***	Look	Name found unacceptable; approved as Evoclin
_____	Sound	Name found unacceptable; application received not approvable action

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Appendix F: Product that is no longer marketed in the U.S.

Proprietary Name	Similarity to Actemra	Generics available?
Actinex (masoprocol)	Look	No

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

Product name with potential for confusion	Similarity to Proposed Proprietary Name	Strength	Usual Dose (if applicable)
<p>Actemra (tocilizumab) <hr/>for Intravenous Infusion</p>		<p>Vials: 80 mg/4 mL 200 mg/10 mL 400 mg/20 mL</p>	<p>8 mg/kg once every 4 weeks as a 60-minute single intravenous drip infusion</p>
<p>Actonel (risedronate)</p>	Look	<p>Tablets: 5 mg; 30 mg; 35 mg; 75 mg; 150 mg</p>	<p>Treatment of Osteoporosis in Postmenopausal Women: 5 mg daily, 35 mg once a week, 75 mg taken on two consecutive days each month, or 150 mg once a month Prevention of Osteoporosis in Postmenopausal Women: 5 mg daily, or 35 mg once a week Men with Osteoporosis: 35 mg once a week Treatment and Prevention of Glucocorticoid-Induced Osteoporosis: 5 mg daily Paget's Disease: 30 mg daily for 2 months</p>
<p>Actamin (acetaminophen)</p>	Look	<p>Tablets : 325 mg and 500 mg</p>	<p>325 mg to 650 mg every 4 to 6 hours as needed or 1000 mg taken 2 to 4 times per day (not to exceed 4 grams per day)</p>
<p>Azactam (aztreonam)</p>	Look	<p>Injection: 1 gram per vial 2 grams per vial 1 gram/50 mL container 2 grams/50 mL container</p>	<p>500 mg, 1 gram, or 2 grams intravenously or intramuscularly every 8 or 12 hours; 2 grams every 6 or 8 hours</p>
<p>Octamide (metoclopramide) *Brand name product has been discontinued. Generic products are available.</p>	Look	<p>Injection: 5 mg/mL (2 mL, 10 mL, 30 mL vials)</p>	<p>Prevention of post-operative nausea and vomiting: 10 mg intramuscularly or intravenously near the end of the surgical procedure. Repeat every 4 to 6 hours as necessary. If required, a 20 mg dose may be used. Prevention of nausea and vomiting induced by cancer chemotherapy:</p>

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			<p>1 to 2 mg/kg intravenously 30 minutes before chemotherapy. May be repeated twice at 2-hour intervals. If vomiting continues, 3 further doses may be given at 3-hour intervals. After vomiting has been suppressed, a maintenance dose of 1 mg/kg may be given, at 3-hour intervals for 3 additional doses.</p> <p>Treatment of diabetic gastroparesis:</p> <p>10 mg intravenously or intramuscularly four times per day, 30 minutes before meals and at bedtime for 2 to 8 weeks.</p> <p>Treatment of gastroesophageal reflux disease and associated lesions due to erosive esophagitis:</p> <p>10 mg intravenously or intramuscularly up to four times per day, 30 minutes before meals and at bedtime.</p> <p>For use as a diagnostic aid during gastrointestinal radiography and to facilitate intestinal intubation:</p> <p>10 mg IV as a single dose</p>
<p>Activase (alteplase)</p>	<p>Look</p>	<p>Powder for injection: 50 mg vial 100 mg vial</p>	<p>Acute myocardial infarction:</p> <p>Accelerated Infusion The recommended total dose is based upon patient weight, not to exceed 100 mg. For patients weighing > 67 kg, the recommended dose administered is 100 mg as a 15 mg intravenous bolus, followed by 50 mg infused over the next 30 minutes, and then 35 mg infused over the next 60 minutes.</p> <p>For patients weighing ≤ 67 kg, the recommended dose is administered as a 15 mg intravenous bolus, followed by 0.75 mg/kg infused over the next 30 minutes not to exceed 50 mg, and then 0.50 mg/kg over the next 60 minutes not to exceed 35 mg.</p> <p>3-Hour Infusion The recommended dose is 100 mg</p>

			<p>administered as 60 mg in the first hour (of which 6 to 10 mg is administered as a bolus), 20 mg over the second hour, and 20 mg over the third hour. For smaller patients (< 65 kg), a dose of 1.25 mg/kg administered over 3 hours, as described above, may be used.</p> <p>Acute stroke:</p> <p>The recommended dose is 0.9 mg/kg (not to exceed 90 mg total dose) infused over 60 minutes with 10% of the total dose administered as an initial intravenous bolus over 1 minute.</p> <p>Pulmonary embolism:</p> <p>The recommended dose is 100 mg administered by intravenous infusion over 2 hours. Heparin therapy should be instituted or reinstated near the end of or immediately following the Activase infusion when the partial thromboplastin time or thrombin time returns to twice normal or less.</p>
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Appendix H: Potential confusing name with numerical overlap in strength or dose

Failure Mode: Name confusion	Causes (could be multiple)	Effects
<p style="text-align: center;">Actemra (tocilizumab) for Intravenous Infusion</p>	<p>80 mg/4 mL 200 mg/10 mL 400 mg/20 mL</p>	<p>Usual dose: 8 mg/kg once every 4 weeks as a 60-minute single intravenous drip infusion</p>
<p>HP Acthar Gel (repository corticotropin injection) 80 units/mL *Acthar powder for injection has been discontinued.</p>	<p>Orthographic similarity ('Act') and ('ra' vs. 'ar')</p> <p>Numerically similar strengths (80 mg/4 mL vs. 80 units/mL)</p> <p>Numerically similar doses (8 mg/kg vs. 80 units)</p> <p>Overlapping storage requirements (refrigeration)</p>	<p>Orthographic differences as well as differing product characteristics minimize the likelihood of medication errors in the usual practice settings.</p> <p><i>Rationale:</i></p> <p>Actemra and Acthar begin with the same three letters 'Act'. However, the ending of the names is very different ('emra' vs. 'har'). Although they have a similar number of letters (7 vs 6), Actemra appears much longer because of the 'em' in the middle of the name. This serves as a differentiator. Further, the risk of medication errors is reduced by the differing product characteristics. Actemra and Acthar differ in terms of route of administration (intravenous infusion vs. intramuscular or subcutaneous injection); frequency of administration (once every 4 weeks vs. every 24 to 72 hours); setting of use (both may be administered in the hospital or clinic but HP Acthar gel may also be administered on an outpatient basis by the patient or a caregiver); and distribution (HP Acthar Gel is only available through specialty pharmacy distribution).</p>

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6 Page(s) Withheld

 Trade Secret / Confidential (b4)

✓ Draft Labeling (b4)

 Draft Labeling (b5)

 Deliberative Process (b5)