

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

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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**

Proprietary Name Review--Final

Date: December 5, 2011
Application Type/Number: NDA 202331
Reviewer: Yelena Maslov, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis
Team Leader Irene Z. Chan, Pharm.D., BCPS, Team Leader
Division of Medication Error Prevention and Analysis
Division Director Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis
Drug Name and Strength(s): Edarbyclor
(Azilsartan Medoxomil and Chlorthalidone) Tablets
40 mg/12.5 mg and 40 mg/25 mg
Applicant/sponsor: Takeda, Inc.
OSE RCM #: #2011-2501

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1 INTRODUCTION

This re-assessment of the proposed proprietary name, Edarbyclor, is written in response to the anticipated approval of this NDA within 90 days from the date of this review. DMEPA found the proposed name, Edarbyclor, acceptable in OSE Review #2011-1244 dated July 12, 2011.

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 #2011-1244. Since the proposed product characteristics were altered (i.e., only 40 mg/12.5 mg and 40 mg/25 mg strengths will be available), we re-evaluated previous names of concern (See Appendix A). However, the searches of the databases did not yield any new names thought to look or sound similar to Edarbyclor 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 November 17, 2011.

OPDP re-reviewed the proposed name on September 28, 2011 and had no concerns regarding the proposed name from a promotional perspective.

3 CONCLUSIONS

The re-evaluation of the proposed proprietary name, Edarbyclor, did not identify any vulnerabilities that would result in medication errors with any additional name(s) noted in this review. Thus, DMEPA has no objection to the proprietary name, Edarbyclor, for this product at this time.

DMEPA considers this a final review; however, if approval of the NDA is delayed beyond 90 days from the date of this review, the Division of Cardiovascular and Renal 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, Phoung Nina Ton, OSE project manager, at 301-796-1648.

4 REFERENCES

1. *Maslov, Yelena. Proprietary Name Review for Edarbyclor, OSE Review #2011-1244.*

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/physician-resources/medical-science/united-states-adopted-names-council/naming-guidelines/approved-stems.page?>)

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 dissimilarity of the names and/ or use in clinical practice for the reasons described.

<p>Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets</p>	<p>Strength(s): 40 mg/12.5 mg and 40 mg/25 mg</p>	<p>Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily</p>
<p>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</p>	<p>Causes (could be multiple)</p>	<p>Prevention of Failure Mode</p>
<p>Ethacrynate Sodium Powder for Injection, 50 mg</p> <p><u>Usual Dose</u> 50 mg or 0.5 mg/kg to 1 mg/kg intravenously injected slowly once, may repeat after 2 to 4 hours (children) or 8 to 12 hours (adults) if needed</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and contain down stroke ‘y’ in similar positions. Additionally, the letter string ‘Ed-’ and the letter ‘l’ in Edarbyclor may appear similar to the corresponding letter string ‘Et-’ and the letter ‘t’ in Ethacrynate when scripted.</p> <p><u>Partial Numerical Overlap in Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength of 40 mg and Ethacrynate may have an achievable dose of 40 mg</p>	<p><u>Orthographic</u> Although both names contain the same number of upstrokes they are located in different positions. Additionally, the letter string ‘-arb’ lacks orthographic similarity with the corresponding letter string ‘-hacr-’ when scripted.</p> <p><u>Strength</u> 40 mg/12.5 mg, 40 mg/25 mg vs. 50 mg. Although there is partial overlap in strength and dose between the two products, Edarbyclor contains different strengths of Chlorthalidone (i.e., 12.5 mg and 25 mg) associated with the strength of Azilsartan (i.e., 40 mg). Thus, it is unlikely that the strength/dose of Chlorthalidone will be omitted.</p>

Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets	Strength(s): 40 mg/12.5 mg and 40 mg/25 mg	Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily
<p>Etidronate Disodium Tablets, 200 mg and 400 mg</p> <p><u>Usual Dose</u> 5 mg/kg/day to 10 mg/kg/day orally once daily for no longer than 6 months or 11 mg/kg/day to 20 mg/kg/day orally once daily for no longer than 3 months.</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and contain 4 upstrokes. Additionally, the letter string ‘Edarb-’ in Edarbyclor may appear similar to the corresponding letter string ‘Etidr-’ in Etidronate when scripted.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor contains a down stroke vs. the name Etidronate does not and the last upstrokes are located in different positions. Additionally, the letter string ‘-ylcor’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-onate’ when scripted.</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 200 mg and 400 mg.</p> <p><u>Usual Dose</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 5 mg/kg/day to 10 mg/kg/day or 11 mg/kg/day to 20 mg/kg/day. Thus, Etidronate dose will be specified.</p>
<p>Ed-Chlortan (Chlorpheniramine Maleate) Tablets, 4 mg</p> <p><u>Usual Dose</u> 4 mg orally every 4 hours to 6 hours, up to 24 mg in 24 hours</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Ed-’. Additionally, the letter ‘b’ and the letter string ‘-lor’ in Edarbyclor may appear similar to the corresponding letter ‘l’ and the letter string ‘-tan’ in Ed-chlortan.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes and 1 down stroke vs. the name Ed-Chlortan contains 5 upstrokes next to each other and no down strokes. Additionally, the letter strings ‘-ar-’ and ‘-yc-’ in Edarbyclor lack orthographic similarity to the corresponding letter strings ‘-ch’ and ‘-or-’ in Ed-Chlortan.</p> <p><u>Frequency of Administration</u> Once daily vs. every 4 to 6 hours</p> <p><u>Strength and Dose</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 4 mg. Thus, Edarbyclor’s strength or dose should be specified.</p>

<p>Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets</p>	<p>Strength(s): 40 mg/12.5 mg and 40 mg/25 mg</p>	<p>Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily</p>
<p>Valacyclovir Tablet, 500 mg and 1 g</p> <p><u>Usual Dose</u> 500 mg to 1 g orally twice daily to three times daily for 5 to 10 days depending on the indication</p>	<p><u>Orthographic</u> The letter strings ‘edar-’ and ‘-yclor’ in Edarbyclor may appear similar to the letter string ‘valac-’ and ‘-yclov’ in Valacyclovir when scripted if both names are scripted with a lower case first letter.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes the name Valacyclovir contains 3 upstrokes Additionally, although both names share the letter string ‘-yclo-’ the letter string appears in different positions of the names.</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 500 mg and 1 g</p> <p><u>Frequency of Administration</u> Once daily vs. twice daily to three times daily</p>
<p>Atacand (Candesartan) Tablets, 4 mg, 8 mg, 16 mg, and 32 mg</p> <p><u>Usual Dose</u> 4 mg to 32 mg orally once daily to twice daily</p>	<p><u>Orthographic</u> The letter strings ‘Edar-’ and ‘cl’ in Edarbyclor may appear similar to the corresponding letter string ‘atac-’ and the letter ‘d’ in Atacand when scripted if the letter ‘a’ is scripted in a lower case.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Both products may be administered once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Atacand when scripted (10 letters vs. 7 letters). Additionally, the letter string ‘-by-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-an-’ when scripted.</p> <p><u>Strength and Dose</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 4 mg, 8 mg, 16 mg, and 32 mg. Thus, the strength or dose for both products will be specified.</p>

Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets	Strength(s): 40 mg/12.5 mg and 40 mg/25 mg	Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily
<p>Edurant (Rilpivirine) Tablets, 25 mg</p> <p><u>Usual Dose</u> 25 mg orally once daily</p>	<p><u>Orthographic</u> Both names share the first letter string ‘Ed-’. Additionally, the letter string ‘-ar-’ and the letter ‘l’ in Edarbyclor may appear similar to the corresponding letter string ‘-ur-’ and the letter ‘t’ in Edurant.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Chlorthalidone strength of 25 mg, which overlaps with Edurant strength and dose of 25 mg.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Edurant when scripted (10 letters vs. 7 letters). Additionally, the letter string ‘-byc-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-an-’ in Edurant when scripted.</p>
<p>Etanercept Powder for Injection, 25 mg</p> <p>Injection, 25 mg/0.5 mL and 50 mg/mL</p> <p><u>Usual Dose</u> 50 mg/week either as 50 mg subcutaneously once a week or 25 mg twice a week up to 100 mg per week depending on the indication</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’. Additionally, the letter string ‘-dar-’ and the letter ‘l’ in Edarbyclor may appear similar to corresponding the letter string ‘tan-’ and the letter ‘t’ in Etanercept when scripted.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Chlorthalidone strength of 25 mg, which overlaps with Etanercept strength and dose of 25 mg.</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes and 1 down stroke in the middle of the name vs. the name Etanercept contains 3 upstrokes and 1 down stroke at the end of the name. Additionally, the letter string ‘-byc-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-ercep-’ in Etanercept when scripted.</p> <p><u>Frequency of Administration</u> Once daily vs. once weekly to twice daily</p>

<p>Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets</p>	<p>Strength(s): 40 mg/12.5 mg and 40 mg/25 mg</p>	<p>Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily</p>
<p>Idamycin PFS (Idarubicin HCl) Injection 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 12 mg/m² daily for 3 days by slow intravenous injection.</p>	<p><u>Orthographic</u> Both names share the letter string ‘-yc-’ in similar positions. Additionally, the letter string ‘eda-’ in Edarbyclor may appear similar to the letter string ‘eda’ in Edarbyclor when scripted, if both names are scripted with a lower case first letter.</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The letter strings ‘-rb-’ and ‘-lor-’ in Edarbyclor lack orthographic similarity to the corresponding letter ‘m’ and the letter string ‘-in’ in the name Idamycin. Additionally, Edarbyclor appears longer than Idamycin (10 letters vs. 8 letters). Also, Idamycin contains a modifier PFS.</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 40 mg/12.5 mg, 40 mg/25 mg vs. 12 mg/m² Thus, the doses for both products will be specified.</p>
<p>Etodolac Tablet, 400 mg and 500 mg</p> <p>Etodolac Capsule 200 mg and 300 mg</p> <p><u>Usual Dose</u> 200 mg to 400 mg orally every 6 to 8 hours up to 1000 mg daily</p> <p>Etodolac Extended-release Tablet, 400 mg, 500 mg, 600 mg</p> <p><u>Usual Dose</u> 400 mg to 1000 mg orally once daily</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’. Additionally, the letter string ‘-darb-’ in Edarbyclor may appear similar to the corresponding letter string ‘-todo-’ in Etodolac when scripted.</p> <p><u>Dosage Form</u> Both products are available as tablets</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Both products may be administered once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Etodolac when scripted (10 letters vs. 8 letters). Additionally, Edarbyclor contains a down stroke vs. Etodolac does not.</p> <p><u>Strength and Dose</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 400 mg and 500 mg (tablet) or 200 mg and 300 mg (capsule) and 400 mg, 500 mg, 600 mg (ER tablet). Thus, the strength and dose will be specified.</p>

Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets	Strength(s): 40 mg/12.5 mg and 40 mg/25 mg	Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily
<p>Adcetris^{***} (BLA 125388 and BLA 125399) (Brentuximab vedotin) Powder for Injection, 50 mg</p> <p><u>Usual Dose</u> 1.8 mg/kg over intravenous infusion over 30 minutes every three weeks</p>	<p><u>Orthographic</u> The letter string ‘Edarb-’ may appear similar to the corresponding letter string ‘adcet-’ when scripted if the letter ‘a’ is scripted in a lower case.</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Adcetris when scripted (10 letters vs. 8 letters). Additionally, the letter string ‘-yclor’ lacks orthographic similarity to the corresponding letter string ‘-ris’.</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 50 mg</p> <p><u>Frequency of Administration</u> Once daily vs. once every three weeks</p>
<p>Atopiclair Cream</p> <p><u>Usual Dose</u> Apply to affected, dry skin two to three times daily as needed and massage gently into the skin</p>	<p><u>Orthographic</u> The letter strings ‘Eda-’ and ‘-clor’ in Edarbyclor may appear similar to the corresponding letter strings ‘ato-’ and ‘-clair’ when scripted if the letter ‘a’ is scripted in a lower case.</p> <p><u>Phonetic</u> The letter string ‘-clor’ in Edarbyclor is phonetically similar to the letter string ‘-clair’ in Atopiclair</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes vs. the name Atopiclair contains 3 upstrokes. Additionally, the letter string ‘-rby-’ in Edarbyclor lacks orthographic similarity with the letter string ‘-pi-’ in Atopiclair.</p> <p><u>Phonetic</u> The letter string ‘Edarby-’ lacks phonetic similarity to the letter string ‘Atopi-’ in Atopiclair</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. single strength</p> <p><u>Usual Dose</u> 1 tablet vs. apply to affected skin</p> <p><u>Frequency of Administration</u> Once daily vs. two to three times daily</p>

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<p>Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets</p>	<p>Strength(s): 40 mg/12.5 mg and 40 mg/25 mg</p>	<p>Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily</p>
<p>Indiclor (Indium) Injection, 2 mCi/0.2 mL</p> <p><u>Usual Dose</u> 5 mCi In-111 over 10 minutes as intravenous injection within 4 hours following completion of Rituximab infusion.</p>	<p><u>Orthographic</u> Both names share the letter ‘d’ and the suffix ‘-clor’. Additionally, the letter ‘e’ in Edarbyclor may appear similar to the letter ‘i’ if the names are scripted with a lower case letters.</p> <p><u>Phonetic</u> Both names share the letter string ‘-clor’</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Indiclor when scripted (10 letters vs. 8 letters). Additionally, although both names share the letter ‘d’, they do not appear in similar positions.</p> <p><u>Phonetic</u> The letter string ‘Edabri-’ lacks phonetic similarity to the letter string ‘Indi-’</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. single strength</p> <p><u>Usual Dose</u> 1 tablet of 40 mg/12.5 mg, or 40 mg/25 mg vs. 5 mCi In-111 over 10 minutes</p>
<p>Idarubicin Injection, 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 12 mg/m² daily for 3 days by slow intravenous injection.</p>	<p><u>Orthographic</u> The letter string ‘edarb-’ in the name Edarbyclor appears similar to the corresponding letter string ‘idaryb-’ in Idarubicin when scripted if the first letters of the name are scripted in a lower case. Additionally, both names share the letter ‘c’ in similar positions.</p> <p><u>Phonetic</u> The letter string ‘edarby-’ in Edarbyclor is phonetically similar to the corresponding letter string ‘idarubi-’ in Idarubicin</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The letter ‘y’ and the letter string ‘lor’ in Edarbyclor lack orthographic similarity to the corresponding letter ‘i’ and the letter string ‘-in’ in Idarubicin</p> <p><u>Phonetic</u> The letter string ‘-clor’ in Edarbyclor lacks phonetic similarity to the letter string ‘-cin’ in Idarubicin.</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 40 mg/12.5 mg, 40 mg/25 mg vs. 12 mg/m² Thus, the doses for both products will be specified.</p>

Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets	Strength(s): 40 mg/12.5 mg and 40 mg/25 mg	Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily
<p>Edarbi (Azilsartan Medoxomil) Tablets, 40 mg and 80 mg</p> <p><u>Usual Dose</u> 40 mg to 80 mg orally once daily</p>	<p><u>Orthographic</u> Both names share the letter string ‘Edarb-’</p> <p><u>Phonetic</u> The letter string ‘Edarby-’ is phonetically similar to the name Edarbi.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength of 40 mg or 80 mg, which overlaps with Edarbi’s strength and dose of 40 mg or 80 mg.</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Edarbi when scripted (10 letters vs. 6 letters).</p> <p><u>Phonetic</u> The letter string ‘-clor’ in Edarbyclor lacks phonetic similarity with the name Edarbi</p> <p><u>Strength and Dose</u> Although there is a partial overlap in strength and dose between the two products, Edarbyclor also contains different strength of Chlorthalidone (i.e., 12.5 mg vs. 25 mg) associated with the strength of Azilsartan (i.e., 40 mg). Thus, it is unlikely that the strength/dose of Chlorthalidone will be omitted.</p>
<p>Acyclovir Capsule, 200 mg Tablet, 400 mg to 800 mg Suspension, 200 mg/5 mL</p> <p><u>Usual Dose</u> 200 mg to 400 mg orally 5 times daily for 7 to 10 days or 800 mg every 8 hours for 7 to 10 days</p> <p>Powder for Injection, 500 mg and 1000 mg Injection, 25 mg/mL and 50 mg/mL</p> <p><u>Usual Dose</u> 10 mg/kg to 15 mg/kg every 8 hours for 10 to 14 days</p>	<p><u>Orthographic</u> The letter ‘E’ and the letter string ‘-yclor’ in Edarbyclor appear similar to the letter ‘a’ and the letter string ‘yclov’ when scripted if the letter ‘a’ in scripted in a lower case</p> <p><u>Phonetic</u> Both names share the letter string ‘-yclo-’, however, the shared string in in different positions of the names.</p> <p><u>Dosage Form</u> Both products are available as tablets</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> Although both names share the letter string ‘-yclo-’, this letter string appears in different positions of the names. Additionally, the names Edarbyclor contains 4 upstrokes vs. the name Acyclovir contains 2 upstrokes.</p> <p><u>Phonetic</u> The names lack phonetic similarity.</p> <p><u>Frequency of Administration</u> Once daily vs. 5 times daily or every 8 hours</p> <p><u>Strength</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 200 mg (capsule), 400 mg and 800 mg (tablet) and 200 mg/5 mL (suspension). Thus, strength for Edarbyclor must be specified.</p>

<p>Proposed name: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets</p>	<p>Strength(s): 40 mg/12.5 mg and 40 mg/25 mg</p>	<p>Usual dose: 40 mg/12.5 mg to 40 mg/25 mg orally once daily</p>
<p>Ecuzumab Injection, 300 mg</p> <p><u>Usual Dose</u> 600 mg as intravenous infusion every 7 days for the first 4 weeks, followed for a single dose of 900 mg as intravenous infusion 7 days after the 4th dose, and then 900 mg intravenous infusion every 14 days.</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and the letter string ‘-abyc-’ in Edarbyclor may appear similar to the eltter string ‘-ulizu-’ in Ecuzumab when scritped</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes vs. the name Ecuzumab contains 3 upstrokes. Additionally, the letter string ‘-lor’ in Edarbyclor lacks orthographic similarity to the letter string ‘-mab’ in Ecuzumab.</p> <p><u>Strength and Dose</u> 40 mg/12.5 mg and 40 mg/25 mg vs. 300 mg</p>
<p>Cefaclor Capsule, 250 mg and 500 mg Powder for Suspension, 125 mg/5 mL, 187 mg/5 mL, 250 mg/5 mL, 375 mg/5 mL</p> <p><u>Usual Dose</u> Adults: 250 mg to 500 mg orally every 8 hours Children: 20 mg/kg to 40 mg/kg orally every 8 hours for 7 to10 days</p> <p>Extended-release Tablet, 573 mg and 500 mg</p> <p><u>Usual Dose</u> 375 mg to 500 mg orally every 12 hours for 7 to 10 days</p>	<p><u>Orthographic</u> Both names share the letter ‘a’ in similar positions. Additionally, both names share the letter string ‘-clor’ at the end of the names. Furthermore, the letter ‘e’ in Edarbyclor may appear similar to the letter ‘c’ in Cefaclor if both names are scripted in a lower case.</p> <p><u>Phonetic</u> Both names share the letter string ‘-clor’</p> <p><u>Dosage Form</u> Both products are available in solid dosage forms</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Cefaclor when scripted (10 letters vs. 8 letters). Additionally, the name Edarbyclor contains 4 upstrokes and 1 down stroke vs the name Cefaclor contains 2 upstrokes and 1 down stroke (if the letter ‘f’ in scripted as a down stroke) or 3 upstrokes and no down strokes (if the letter ‘f’ is scripted as an upstroke)</p> <p><u>Phonetic</u> The letter string ‘Edarby-’ lacks orthographic similarity to the letter string ‘Cefa-’</p> <p><u>Strength</u> 40 mg/12.5 mg, 40 mg/25 mg vs. 250 mg and 500 mg (capsule) and 125 mg/5 mL, 187 mg/5 mL, 250 mg/5 mL, 375 mg/5 mL (powder for suspension).</p> <p><u>Frequency of Administration</u> Once daily vs. every 8 hours or every 12 hours.</p>

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/s/

YELENA L MASLOV
12/05/2011

CAROL A HOLQUIST
12/05/2011

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

Proprietary Name Review

Date: July 12, 2011
Application Type/Number: NDA 202331
Reviewer: Yelena Maslov, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis
Team Leader Zachary Oleszczuk, Pharm.D., Team Leader
Division of Medication Error Prevention and Analysis
Division Director Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis
Drug Name and Strength(s): Edarbyclor
(Azilsartan Medoxomil and Chlorthalidone) Tablets
(b) (4) 40 mg/12.5 mg, 40 mg/25 mg,
and (b) (4)
Applicant/sponsor: Takeda, Inc.
OSE RCM #: #2011-1244

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

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1 INTRODUCTION

This review evaluates the proposed proprietary name, Edarbyclor, 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. The proposed product characteristics are provided in Section 1.2.

1.1 REGULATORY HISTORY

This review responds to a request from Takeda, Inc., dated April 13, 2011, for a safety and promotional assessment of the proposed proprietary name, Edarbyclor (NDA 202331). The proposed product is the subject of a 505 (b)(1) application, submitted to the FDA on February 24, 2011. The first proposed proprietary name, submitted in the IND stage under IND 077278, (b) (4) was found unacceptable by DMEPA on February 25, 2011 due to (b) (4). The second proposed proprietary name, (b) (4) was also found unacceptable by DMEPA due to (b) (4) and the Applicant was informed of DMEPA's decision via teleconference held on April 6, 2011.

1.2 PRODUCT INFORMATION

Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) tablets is an angiotensin II receptor blocker and a diuretic combination product indicated for the treatment of hypertension. Edarbyclor will be available in the following strengths: (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, and (b) (4). The product will be administered orally without regard to food. The usual starting dose is (b) (4) 40 mg/12.5 mg. The dose may be increased after 2 weeks to 4 weeks as needed to control blood pressure. The maximally effective dose is 40 mg/25 mg. Edarbyclor will be supplied in bottles containing 30 tablets or 90 tablets. The product must be dispensed in original container for light and moisture protection. Edarbyclor should be stored at 25°C (77°F), with temperature excursions permitted to 15°C-30°C (59°F -86°F).

2 RESULTS AND DISCUSSION

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 Cardiovascular and Renal Products (DCRP) concurred with the findings of DDMAC's promotional assessment of the proposed name.

2.2 SAFETY ASSESSMENT

2.2.1 United States Adopted Names (USAN) SEARCH

The United States Adopted Name (USAN) stem search conducted on May 24, 2011, identified that a USAN stem is not present in the proposed proprietary name.

2.2.2 Postmarketing Medication Error Data Evaluated

In order to evaluate the medication error risk due to potential confusion between the single-ingredient product, Edarbi, and the combination product, Edarbyclor, we considered whether confusion has occurred with similar products that use a modified version of the root name of a single active ingredient product and a suffix to identify a second active ingredient.

There are multiple antihypertensive and antidiabetic products that utilize this naming strategy. Combination antihypertensive products that contain hydrochlorothiazide typically use part of the root name of the single active ingredient and the suffixes “-retic” (i.e. Accupril/Accuretic, Quinapril/Quinaretic, Univasc/Uniretic, Tenormin/Tenoretic, Vasotec/Vaseretic, and Zestril/Zestoretic) or “-zide” (Aldactone/Aldactazide, Apresoline/Apresazide, Corgard/Corzide, Minipress/Minizide, Normodyne/Normozide).

Some currently marketed combination antidiabetic products use a similar naming strategy of using a modified version of the root name from a single active ingredient product in conjunction with the suffix “-met” to represent the metformin component (i.e., Avandia/Avandamet, Januvia/Janumet, and Prandin/Prandimet, (b) (4)).

2.2.2.1 Post-Marketing Experience with Antihypertensive Combination Products

We searched the FDA Adverse Event Reporting System (AERS) database to identify whether wrong drug errors occur with antihypertensive combination products that use modified root names and suffixes ‘retic’ or ‘zide’ to express Hydrochlorothiazide active ingredient. We searched the following product pairs: Accupril/Accuretic, Quinapril/Quinaretic, Univasc/Uniretic, Tenormin/Tenoretic, Vasotec/Vaseretic, Zestril/Zestoretic Aldactone/Aldactazide, Apresoline/Apresazide, Corgard/Corzide, Minipress/Minizide, Normodyne/Normozide. We used MedDRA High Level Group Term (HLGT) “Medication Errors”, High Level Term (HLT) “Medication Errors NEC”, and Preferred Term (PT) “Wrong Drug Administered”. No time limit was set.

We identified two medication errors (n=2) involving confusion between the products. One error (n=1) from 2001 reported confusion between Univasc and Uniretic. The case did not report any contributing factors. This error occurred only once in 2001 and appears transient. The second error (n=1) from 2004 reported confusion between Aldactone and Aldactazide. This case involved a refill for Aldactone that was filled with Aldactazide. This case did not report any contributing factors either. However, we suspect that this error occurred during product selection off the shelf, because this was a refill and did not require computer entry of the product.

2.2.2.2 Post-Marketing Experience with Antidiabetic Combination Products

DMEPA is aware that combination antidiabetic names and the single active ingredients products have been identified as source of drug name confusion. Avandia and Avandamet are listed in the USP’s Drug Error Finder as Look-alike/Sound-alike Drug Names. Januvia and Janumet are listed in ISMP’s List of Confused Drug Names.

Additionally, post-marketing reports of wrong drug medication errors as a result of name confusion have been documented in previous OSE reviews. OSE Review #2011-1111, dated June 15, 2011, identified five medication errors (n=5) involving confusion between Januvia and Janumet. One case was reported in 2007 and one case was reported in 2008 and the remaining three cases did not report the date. Although no detail regarding contributing factors were reported, we suspect the confusion could be due to orthographic and/or phonetic similarities between the two names. Both names contain the same length (7 letters). Additionally, both names share the prefix ‘Janu’ and the letter string ‘vi’ in Januvia appears similar to the letter string ‘me’ in Janumet when scripted. Although the name Janumet contains an upstroke letter ‘t’ at the end of the name, this upstroke may trail off when scripted or be overlooked and thus, may not necessarily prevent medication errors from occurring between the products.

DMEPA also identified twelve medication errors (n=12) involving confusion between Avandia and Avandamet OSE Review #2007-1775, dated November 5, 2009. Five cases (n=5) reported that Avandia and Avandamet look alike and one case reported that error occurred due to strength confusion between Avandia and Avandamet (4 mg vs. 4 mg/500 mg). Avandia and Avandamet share the prefix ‘Avand’ and the letter string ‘ia’ in Avandia may appear similar to the letter string ‘ame’ in Avandamet. Although the name Avandamet contains an upstroke letter ‘t’ at the end of the name, this upstroke may trail off when scripted or be overlooked and thus, may not necessarily prevent medication errors from occurring between the products.

2.2.3 Components of the Proposed Proprietary Name

Edarbyclor contains two active ingredients, Azilsartan Medoxomil and Chlorthalidone. Per the Applicant’s submission, there is no direct derivation of the proposed proprietary name. However, DMEPA considered whether the letter string ‘Edarb’ represents Azilsartan Medoxomil ingredient and the letter string ‘clor’ represents Chlorthalidone ingredient. A search of various databases listed in Reference Section 4, identified that the letter string ‘clor’ has been used in the proprietary name that contain Chlorthalidone (i.e., Clorpres). Thus, use of the suffix “clor” is appropriate for this product.

DMEPA also considered whether the name Edarbyclor is misleading pursuant to 21 CFR 201.6 (b) which states:

The labeling of a drug which contains two or more ingredients may be misleading by reason, among other reasons, of the designation of such drug in such labeling by a name which includes or suggests the name of one or more but not all such ingredients, even though the names of all such ingredients are states elsewhere in the labeling.

Because, the Edarbi portion of the name can be used to represent Azilsartan, and “clor” has been used for other Chlorthalidone containing products, the name is not misleading.

Although, we identified confusion between antihypertensive combination products and antidiabetic combination products with their single active ingredient product counterparts, the confusion found with those products is unlikely to occur with Edarbyclor and Edarbi for the reasons listed below.

Most of the name confusion errors we identified involved the antidiabetic combination products. These names use all or most of the proprietary name of the single active ingredient product and the suffix “met”. All of the combination products for the antidiabetic products that used this naming strategy were found unacceptable by DMEPA, but Avandimet, Prandimet, and Janumet, were approved despite our objection. Edarbyclor is more orthographically and phonetically different than the antidiabetic combination products compared to the single ingredient with the same route name (see Table 2 below):

Table 2: Name Similarities with Antidiabetic Products and the Single Ingredient Products.

Names	Percentage of Increased letters with addition of the Suffix	Differentiating Orthographic letters	Percentage of Different letters
Edarbyclor vs. Edarbi	66%	Addition of downstroke ‘y’ in the middle of the name and upstroke ‘l’ that is not located at the end of the name	50%
(b) (4)			
Janumet vs. Januvia	0%	Upstroke letter ‘t’ at the end of the name that may trail off when written	42%
Avanadmet vs. Avandia	42%	Addition of upstroke letter ‘t’ at the end of the name that may trail off when written	33%
Prandimet vs. Prandia	42%	Addition of upstroke letter ‘t’ at the end of the name that may trail off when written	30%

Although both products share the letter string ‘Edarb’, the remaining 5 letters of the name Edarbyclor are different. Additionally, the combination product, Edarbyclor appears longer than the name Edarbi when scripted (10 letters in the name Edarbyclor vs. 6 letters in the name Edarbi). Also, Edarbyclor contains four upstrokes whereas the single ingredient Edarbi product contains three upstrokes. The fourth upstroke, letter ‘l’ is located closer to the middle of the name; and thus, it will be less likely to trail off than if it appeared at the end of the name. Furthermore, Edarbyclor contains a down stroke letter ‘y’ in the sixth position of the name, whereas a monotherapy product, Edarbi contains a dotted letter ‘i’ in the sixth position of the name. Finally, the letter string ‘clor’ in Edarbyclor lacks phonetic similarity with any letter string in the name Edarbi. Thus, the length of the name Edarbyclor, the number of down strokes and upstrokes, and the letter string ‘clor’ help additional orthographic and phonetic differentiation between the two products.

DMEPA identified one medication error that we suspect was due to name confusion between combination antihypertensive products. That case involved the names Uniretic and Univasc. There were not enough details in the case to determine a definitive root cause, however we can not rule out that orthographic and phonetic similarity contributed to the confusion. The endings of each name differ, however, the overall length of the name remains similar (8 letters vs. 7 letters). This similar length in the name in addition to the overlapping beginning of the names and strengths may have contributed to this confusion. Similar to the comparison of the antidiabetic combination products, Edarbyclor is more orthographically and phonetically different from Edarbi than Uniretic is from Univasc. Edarbyclor is longer than Edarbi and has an additional upstroke and downstroke in the name.

Additionally, although both products share the letter string ‘Edarb’, we do not anticipate confusion between Edarbi and Edarbyclor during computer entry because of the aforementioned orthographic differences between the two names and the fact that the name Edarbyclor is so much longer than the name Edarbi. Additionally, the difference in this name pair starts appearing at the sixth character of each name. Although long names may be truncated in computer drop down menus it is unlikely that a drop down menu would contain only five characters, thus the difference in the names would likely be visible during order entry from a drop down menu.

Furthermore, although Edarbyclor and Edarbi may be placed near one another on the pharmacy shelf, we are recommending in a forthcoming Label and Labeling Review for Azilsartan Medoxomil and Chlorthalidone (OSE Review 2011-704) that the Applicant utilize different contrasting colors for the container labels that do not overlap with Edarbi or any of the strengths of the proposed product to help minimize the risk of product selection. Thus, this will help minimize errors due to product selection.

2.2.4 FDA Name Simulation Studies

Thirty practitioners participated in DMEPA’s prescription studies. See Appendix D for sample prescriptions used in a study and the complete listing of interpretations from the verbal and written prescription studies. None of the responses overlapped with other drug names. Sixteen participants interpreted the proposed proprietary name correctly as

‘Edarbyclor’ with three correct interpretations (n=3) occurring with inpatient orders and thirteen correct interpretations (n=13) occurring with outpatient orders. The remaining fourteen participants misinterpreted the name Edarbyclor. The most common misinterpretation occurred with five voice order participants misinterpreting the first letter ‘E’ as the letter ‘A’ and four inpatient order participants misinterpreting the letter ‘o’ as the letter ‘e’ (n=1), letter string ‘-ie-’ (n=2), or letter string ‘-ee-’ (n=1). Additionally, one participant stated the following: “The drug Edarbi was approved in February, 2011, with 40 mg dose. Could be confusing for phone scripts unless the proposed name is for a drug/drug combo with Edarbi.”

DMEPA noted that the confusion between Edarbi and Edarbyclor is unlikely for the reasons listed in Section 2.2.3 and Appendix F. Additionally, the proposed product is a drug combination with Edarbi (Azilsartan Medoxomil) and Chlorthalidone.

2.2.5 Comments from Other Review Disciplines

In response to the OSE email, dated April 25, 2011, the Division of Cardiovascular and Renal Products (DCRP) did not forward any concerns relating to the proposed name at the initial phase of the name review. However, in the email dated April 28, 2011, DCRP had the following comments regarding the name, Edarbyclor.

- DMEPA might have issues. There could be confusion with a name containing chloride.
- This name would not be confused with some drugs such as Ceclor (antibiotic Cefaclor) or Daraclor (antimalaria combination of daraprim and chloroquine). Although the reviewer stated these names would not be confused with the proposed name, Edarbyclor, we included these names in our evaluation.

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, Edarbyclor (see Appendix C). These names were identified by the primary reviewer, the DMEPA’s Expert Panel Discussion (EPD), other review disciplines (DCRP). The table also includes the names identified by Addison-Whitney that were not previously identified by DMEPA and require further evaluation.

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

Look Similar		Sound Similar		Look and Sound Similar	
<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>	<i>Name</i>	<i>Source</i>
(b) (4)	DMEPA EPD	Atopiclair	Primary reviewer/ External study	Indiclor	DMEPA EPD
Ethacrynate	DMEPA EPD	Klor-Con	External study	Idarubicin	DMEPA EPD
Edotreotide	DMEPA EPD	Ticagrelor	External study	Edarbi	DMEPA EPD
Ed-Chlortan	DMEPA EPD			Aldoclor	Primary reviewer
Eldercaps	DMEPA EPD			Edarbychlor	Primary reviewer
Eculizumab	DMEPA EPD			Acyclovir	External study
Daraclor	DCRP Reviewer			Cefaclor	DMEPA EPD/ External Study
Ceclor	DCRP Reviewer				
Atacand	Primary reviewer				
Edurant	Primary reviewer				
Edarbuet	Primary reviewer				
Etanercept	Primary reviewer				
Idamycin	Primary reviewer				
Etodolac	Primary reviewer				
Adcetris ^{***}	Primary reviewer				
Etidronate	Primary reviewer				
Valacyclovir	External Study				
Valsartan	Esxternal Study				

Our analysis of the twenty-eight names contained in Table 1 considered the information obtained in the previous sections along with the product characteristics for the names. We determined that all twenty-eight names will not pose a risk for confusion as described in Appendix E through F.

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

DMEPA communicated these findings to the Division of Cardiovascular and Renal Products (DCRP) via e-mail on June 10, 2011. At that time of the email, we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DCRP on June 15, 2011, the Division stated that they have no additional concerns or comments with the proposed proprietary name, Edarbyclor.

Additionally, DMEPA responded to DCRP's initial comments communicated to us via email on April 28, 2011, as follows:

- The Division noted that we might have an issue because the letter string 'clor' may mean chloride. However, during our search, we were unable to find any reference stating that 'clor' was an abbreviation for Chloride.
- The Division noted that the name Edarbyclor would not be confused with some drugs such as Ceclor (antibiotic Cefaclor) or Daraclor (antimalaria combination of daraprim and chloroquine). We agree. Our Failure Mode and Effect Analysis demonstrates that confusion between Edarbyclor and Ceclor or Edarbyclor and Daraclor is unlikely to occur (See Appendices E and F for specific details).

3 CONCLUSIONS

DMEPA concludes the proposed proprietary name is acceptable from both a promotional and safety perspective. 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.

The proposed proprietary name, Edurant, must be re-reviewed if NDA approval is delayed beyond 90 days.

4 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 Database*** (<http://www.accessmedicine.com/drugs.aspx>)
Access Medicine contains full-text information from approximately 60 medical titles: it includes tables and references. Among the database titles are: Goodman and Gilman's The Pharmacological Basis of Therapeutics, Current Medical Diagnosis and Treatment, Tintinalli's Emergency Medicine, and Hurst's the Heart.
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. ***LabelDataPlus Database*** (<http://www.labeldataplus.com/index.php?ns=1>)
LabelDataPlus database covers a total of 36773 drug labels. This includes Human prescription drug labels as well as Active Pharmaceutical Ingredients (APIs), OTC

(Application and Monograph) drugs, Homeopathic drugs, Unapproved drugs, and Veterinary drugs.

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.¹

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

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

proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. 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.² 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		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
	Similar spelling	Identical prefix	• Names may appear similar

² Institute of Medicine. Preventing Medication Errors. The National Academies Press: Washington DC. 2006.

Look-alike		Identical infix Identical suffix Length of the name Overlapping product characteristics	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/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 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.³ 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

³ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

practice setting? And Are there any components of the name that may function as a source of error beyond sound/look-alike”

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 possess 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: Product Characteristics Provided for Edarbyclor

Edarbyclor
(Azilsartan Medoxomil and Chlorthalidone)
/eh-DAR-bih-clor/

Indication: Treatment of Hypertension

Route: Oral

Dosage Form: Tablet

Strength: (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4)

Dose: (b) (4) once daily

How supplied: in bottles of 30 tablets and 90 tablets

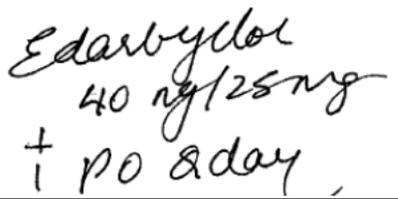
Applicant: Takeda Pharmaceuticals

Appendix C: Letters with Possible Orthographic or Phonetic Misinterpretation

Letters in Name, Edarbyclor	Scripted May Appear as	Spoken May Be Interpreted as
Capital 'E'	'a', 'C', 'I', 'L', 'S'	Any vowel
lower case 'e'	'a', 'c', 'i', 'l', 'o'	Any vowel
lower case 'd'	'b', 'el', 'al', 'f', 't'	't'
lower case 'a'	'el', 'd', 'o', 'u', 'n'	Any vowel
lower case 'r'	n, s, or v	'w'
lower case 'b'	'h', 'l', 'li', 'n', 't'	'p', 'v'
lower case 'y'	'f', 'p', 'u', 'v', 'x', 'z'	'e', 'i', 'u'
lower case 'c'	'a', 'e', 'i', 'z'	'k', 'z'
Lower case 'l'	'b', 't', 'e', 'i'	'n'
Lower case 'o'	'0', 'Q', 'a', 'e'	Any vowel

Appendix D: Prescription Simulation Samples and Results

Figure 1. Edarbyclor Study (Conducted on 04/22/2011)

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u> </p>	<p>Edarbyclor #30 40 mg/25 mg 1 po qday</p>
<p><u>Outpatient Prescription:</u> </p>	

FDA Prescription Simulation Responses.

Inpatient Medication Order	Outpatient Prescription	Voice Prescription
Edarbyclar	Edarbyclol	Adarbicor
Edarbycleer	Edarbyclor	Adarbicor
Edarbycler	Edarbyclor	Adarbicor
Edarbyclier	Edarbyclor	Adarbicor
Edarbyclier	Edarbyclor	Adarbicor
Edarbyclor	Edarbyclor	Darbecor
Edarbyclor	Edarbyclor	Darbicor
Edarbyclor	Edarbyclor	EdarbiChlor
	Edarbyclor	

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

Product Name	Similarity to Edarbyclor	Failure preventions
Valsartan	Look alike	Lacks sufficient orthographic similarity
Ceclor (Cefaclor)	Look alike	Lacks sufficient orthographic similarity
Ticagrelor	Sound alike	Lacks sufficient phonetic similarity
Klor-Con (Potassium Chloride)	Sound alike	Lacks sufficient phonetic similarity
(b) (4)		
Edotreotide	Look alike	This proprietary name is only found in Orphan Drugs and Fact and Comparisons databases, but not in any other commonly used databases listed in the Reference Section. This product was not approved by FDA. No product characteristics are available.
Edarbuet	Look alike	Additional name for Azilsartan Medoxomil and Chlorthalidone registered with USPTO, but not submitted to the FDA
Edarbyclor	Look alike and sound alike	Additional name for Azilsartan Medoxomil and Chlorthalidone registered with USPTO, but not submitted to the FDA
Daraclor (Pyrimethamine and Chloroquine)	Look alike	Foreign product marketed in Great Britain, Spain, Italy, and France, but no United States.
Eldercaps (multivitamin)	Look alike	The product is discontinued without a generic equivalent available
Aldoclor-150 and Aldoclor-250 (Methyldopa and Chlorthalidone)	Look and sound alike	The product is discontinued without a generic equivalent available

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

Appendix F: 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: Edarbyclor (Azilsartan Medoxomil and Chlorthalidone) Tablets	Strength(s): ^{(b) (4)} 40 mg/12.5 mg, 40 mg/25 mg, ^{(b) (4)}	Usual dose: ^{(b) (4)} 40 mg/25 mg orally once daily
Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion	Causes (could be multiple)	Prevention of Failure Mode
<p>Ethacrynate Sodium Powder for Injection, 50 mg</p> <p><u>Usual Dose</u> 50 mg or 0.5 mg/kg to 1 mg/kg intravenously injected slowly once, may repeat after 2 to 4 hours (children) or 8 to 12 hours (adults) if needed</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and contain down stroke ‘y’ in similar positions. Additionally, the letter string ‘Ed-’ and the letter ‘l’ in Edarbyclor may appear similar to the corresponding letter string ‘Et-’ and the letter ‘t’ in Ethacrynate when scripted.</p> <p><u>Partial Numerical Overlap in Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength of 40 mg and Ethacrynate may have an achievable dose of 40 mg</p>	<p><u>Orthographic</u> Although both names contain the same number of upstrokes they are located in different positions. Additionally, the letter string ‘-arb’ lacks orthographic similarity with the corresponding letter string ‘-hacr-’ when scripted.</p> <p><u>Strength</u> ^{(b) (4)} 40 mg/12.5 mg, 40 mg/25 mg, ^{(b) (4)} vs. 50 mg. Although there is partial overlap in strength and dose between the two products, Edarbyclor contains different strengths of Chlorthalidone (i.e., 12.5 mg and 25 mg) associated with the strength of Azilsartan (i.e., 40 mg). Thus, it is unlikely that the strength/dose of Chlorthalidone will be omitted.</p>

<p>Etidronate Disodium Tablets, 200 mg and 400 mg</p> <p><u>Usual Dose</u> 5 mg/kg/day to 10 mg/kg/day orally once daily for no longer than 6 months or 11 mg/kg/day to 20 mg/kg/day orally once daily for no longer than 3 months.</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and contain 4 upstrokes. Additionally, the letter string ‘Edarb-’ in Edarbyclor may appear similar to the corresponding letter string ‘Etidr-’ in Etidronate when scripted.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength (b) (4) 40 mg, (b) (4)</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor contains a down stroke vs. the name Etidronate does not and the last upstrokes are located in different positions. Additionally, the letter string ‘-ylcor’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-onate’ when scripted.</p>
<p>Ed-Chlortan (Chlorpheniramine Maleate) Tablets, 4 mg</p> <p><u>Usual Dose</u> 4 mg orally every 4 hours to 6 hours, up to 24 mg in 24 hours</p>	<p><u>Orthographic</u> Both names start with the letter string ‘Ed-’. Additionally, the letter ‘b’ and the letter string ‘-lor’ in Edarbyclor may appear similar to the corresponding letter ‘l’ and the letter string ‘-tan’ in Ed-chlortan.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength of 40 mg, which is similar to of Ed-Chlortan’s strength and dose of 4 mg.</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes and 1 down stroke vs. the name Ed-Chlortan contains 5 upstrokes next to each other and no down strokes. Additionally, the letter strings ‘-ar-’ and ‘-yc-’ in Edarbyclor lack orthographic similarity to the corresponding letter strings ‘-ch’ and ‘-or-’ in Ed-Chlortan.</p> <p><u>Frequency of Administration</u> Once daily vs. every 4 to 6 hours</p>

<p>Valacyclovir Tablet, 500 mg and 1 g</p> <p><u>Usual Dose</u> 500 mg to 1 g orally twice daily to three times daily for 5 to 10 days depending on the indication</p>	<p><u>Orthographic</u> The letter strings ‘edar-’ and ‘-yclor’ in Edarbyclor may appear similar to the letter string ‘valac-’ and ‘-yclov’ in Valacyclovir when scripted if both names are scripted with a lower case first letter.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes the name Valacyclovir contains 3 upstrokes. Additionally, although both names share the letter string ‘-yclo-’ the letter string appears in different positions of the names.</p> <p><u>Strength</u> [redacted] (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, [redacted] (b) (4) vs. 500 mg and 1 g</p> <p><u>Frequency of Administration</u> Once daily vs. twice daily to three times daily</p>
<p>Atacand (Candesartan) Tablets, 4 mg, 8 mg, 16 mg, and 32 mg</p> <p><u>Usual Dose</u> 4 mg to 32 mg orally once daily to twice daily</p>	<p><u>Orthographic</u> The letter strings ‘Edar-’ and ‘cl’ in Edarbyclor may appear similar to the corresponding letter string ‘atac-’ and the letter ‘d’ in Atacand when scripted if the letter ‘a’ is scripted in a lower case.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbyclor may be dosed at the Azilsartan Medoxomil strength of 40 mg [redacted] (b) (4)</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Both products may be administered once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Atacand when scripted (10 letters vs. 7 letters). Additionally, the letter string ‘-by-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-an-’ when scripted.</p>

<p>Edurant (Rilpivirine) Tablets, 25 mg</p> <p><u>Usual Dose</u> 25 mg orally once daily</p>	<p><u>Orthographic</u> Both names share the first letter string ‘Ed-’. Additionally, the letter string ‘-ar-’ and the letter ‘l’ in Edarbyclor may appear similar to the corresponding letter string ‘-ur-’ and the letter ‘t’ in Edurant.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Chlorthalidone strength of 25 mg, which overlaps with Edurant strength and dose of 25 mg.</p> <p><u>Dosage Form</u> Tablets</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Edurant when scripted (10 letters vs. 7 letters). Additionally, the letter string ‘-byc-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-an-’ in Edurant when scripted.</p>
<p>Etanercept Powder for Injection, 25 mg</p> <p>Injection, 25 mg/0.5 mL and 50 mg/mL</p> <p><u>Usual Dose</u> 50 mg/week either as 50 mg subcutaneously once a week or 25 mg twice a week up to 100 mg per week depending on the indication</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’. Additionally, the letter string ‘-dar-’ and the letter ‘l’ in Edarbyclor may appear similar to corresponding the letter string ‘tan-’ and the letter ‘t’ in Etanercept when scripted.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Chlorthalidone strength of 25 mg, which overlaps with Etanercept strength and dose of 25 mg.</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes and 1 down stroke in the middle of the name vs. the name Etanercept contains 3 upstrokes and 1 down stroke at the end of the name. Additionally, the letter string ‘-byc-’ in Edarbyclor lacks orthographic similarity to the corresponding letter string ‘-ercep-’ in Etanercept when scripted.</p> <p><u>Route of Administration</u> Oral vs. subcutaneous</p> <p><u>Frequency of Administration</u> Once daily vs. once weekly to twice daily</p>

<p>Idamycin PFS (Idarubicin HCl) Injection 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 12 mg/m² daily for 3 days by slow intravenous injection.</p>	<p><u>Orthographic</u> Both names share the letter string ‘-yc-’ in similar positions. Additionally, the letter string ‘eda-’ in Edarbyclor may appear similar to the letter string ‘eda’ in Edarbyclor when scripted, if both names are scripted with a lower case first letter.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength [REDACTED] ^{(b) (4)}</p> <p>[REDACTED] Additionally, Edarbyclor may be dosed at Chlorthalidone strength of 12.5 mg, which may overlap with Idamycin PFS achievable dose.</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The letter strings ‘-rb-’ and ‘-lor-’ in Edarbyclor lack orthographic similarity to the corresponding letter ‘m’ and the letter string ‘-in’ in the name Idamycin. Additionally, Edarbyclor appears longer than Idamycin (10 letters vs. 8 letters). Also, Idamycin contains a modifier PFS.</p>
<p>Etodolac Tablet, 400 mg and 500 mg</p> <p>Etodolac Capsule 200 mg and 300 mg</p> <p><u>Usual Dose</u> 200 mg to 400 mg orally every 6 to 8 hours up to 1000 mg daily</p> <p>Etodolac Extended-release Tablet, 400 mg, 500 mg, 600 mg</p> <p><u>Usual Dose</u> 400 mg to 1000 mg orally once daily</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’. Additionally, the letter string ‘-darb-’ in Edarbyclor may appear similar to the corresponding letter string ‘-todo-’ in Etodolac when scripted.</p> <p><u>Dosage Form</u> Both products are available as tablets</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength of [REDACTED] ^{(b) (4)} 40 mg, [REDACTED] ^{(b) (4)}</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Both products may be administered once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Etodolac when scripted (10 letters vs. 8 letters). Additionally, Edarbyclor contains a down stroke vs. Etodolac does not.</p>

<p>Adcetris^{***} (BLA 125388 and BLA 125399) (Brentuximab vedotin) Powder for Injection, 50 mg</p> <p><u>Usual Dose</u> 1.8 mg/kg over intravenous infusion over 30 minutes every three weeks</p>	<p><u>Orthographic</u> The letter string 'Edarb-' may appear similar to the corresponding letter string 'adcet-' when scripted if the letter 'a' is scripted in a lower case.</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Adcetris when scripted (10 letters vs. 8 letters). Additionally, the letter string '-yclor' lacks orthographic similarity to the corresponding letter string '-ris'.</p> <p><u>Strength</u> (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4) vs. 50 mg</p> <p><u>Frequency of Administration</u> Once daily vs. once every three weeks</p>
<p>Atopiclair Cream</p> <p><u>Usual Dose</u> Apply to affected, dry skin two to three times daily as needed and massage gently into the skin</p>	<p><u>Orthographic</u> The letter strings 'Eda-' and '-clor' in Edarbyclor may appear similar to the corresponding letter strings 'ato-' and '-clair' when scripted if the letter 'a' is scripted in a lower case.</p> <p><u>Phonetic</u> The letter string '-clor' in Edarbyclor is phonetically similar to the letter string '-clair' in Atopiclair</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes vs. the name Atopiclair contains 3 upstrokes. Additionally, the letter string '-rby-' in Edarbyclor lacks orthographic similarity with the letter string '-pi-' in Atopiclair.</p> <p><u>Phonetic</u> The letter string 'Edarby-' lacks phonetic similarity to the letter string 'Atopi-' in Atopiclair</p> <p><u>Strength</u> (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4) vs. single strength</p> <p><u>Usual Dose</u> 1 tablet vs. apply to affected skin</p> <p><u>Frequency of Administration</u> Once daily vs. two to three times daily</p>

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

<p>Indiclor (Indium) Injection, 2 mCi/0.2 mL</p> <p><u>Usual Dose</u> 5 mCi In-111 over 10 minutes as intravenous injection within 4 hours following completion of Rituximab infusion.</p>	<p><u>Orthographic</u> Both names share the letter ‘d’ and the suffix ‘-clor’. Additionally, the letter ‘e’ in Edarbyclor may appear similar to the letter ‘i’ if the names are scripted with a lower case letters.</p> <p><u>Phonetic</u> Both names share the letter string ‘-clor’</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength [REDACTED]^{(b) (4)}</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Indiclor when scripted (10 letters vs. 8 letters). Additionally, although both names share the letter ‘d’, they do not appear in similar positions.</p> <p><u>Phonetic</u> The letter string ‘Edabri-’ lacks phonetic similarity to the letter string ‘Indi-’</p> <p><u>Usual Dose</u> 1 tablet vs. 5 mCi In-111 over 10 minutes</p>
<p>Idarubicin Injection, 5 mg/5 mL, 10 mg/10 mL, 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> 12 mg/m² daily for 3 days by slow intravenous injection.</p>	<p><u>Orthographic</u> The letter string ‘edarb-’ in the name Edarbyclor appears similar to the corresponding letter string ‘idaryb-’ in Idarubicin when scripted if the first letters of the name are scripted in a lower case. Additionally, both names share the letter ‘c’ in similar positions.</p> <p><u>Phonetic</u> The letter string ‘edarby-’ in Edarbyclor is phonetically similar to the corresponding letter string ‘idarubi-’ in Idarubicin</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbyclor may be dosed at Azilsartan Medoxomil strength [REDACTED]^{(b) (4)}</p> <p>[REDACTED] Additionally, Edarbyclor may be dosed at Chlorthalidone strength of 12.5 mg, which may overlap with Idarubicin’s achievable dose.</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The letter ‘y’ and the letter string ‘lor’ in Edarbyclor lack orthographic similarity to the corresponding letter ‘i’ and the letter string ‘-in’ in Idarubicin</p> <p><u>Phonetic</u> The letter string ‘-clor’ in Edarbyclor lacks phonetic similarity to the letter string ‘-cin’ in Idarubicin.</p>

<p>Edarbi (Azilsartan Medoxomil) Tablets, 40 mg and 80 mg</p> <p><u>Usual Dose</u> 40 mg to 80 mg orally once daily</p>	<p><u>Orthographic</u> Both names share the letter string ‘Edarb-’</p> <p><u>Phonetic</u> The letter string ‘Edarby-’ is phonetically similar to the name Edarbi.</p> <p><u>Partial Overlap in Strength and Dose</u> Edarbylcor may be dosed at Azilsartan Medoxomil strength of 40 mg (b) (4)</p> <p><u>Route of Administration</u> Oral</p> <p><u>Frequency of Administration</u> Once daily</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Edarbi when scripted (10 letters vs. 6 letters).</p> <p><u>Phonetic</u> The letter string ‘-clor’ in Edarbyclor lacks phonetic similarity with the name Edarbi</p> <p><u>Strength and Dose</u> Although there is a partial overlap in strength and dose between the two products, Edarbyclor also contains different strength of Chlorthalidone (i.e., 12.5 mg vs. 25 mg) associated with the strength of Azilsartan (i.e., 40 mg). Thus, it is unlikely that the strength/dose of Chlorthalidone will be omitted.</p>
<p>Acyclovir Capsule, 200 mg Tablet, 400 mg to 800 mg Suspension, 200 mg/5 mL</p> <p><u>Usual Dose</u> 200 mg to 400 mg orally 5 times daily for 7 to 10 days or 800 mg every 8 hours for 7 to 10 days</p> <p>Powder for Injection, 500 mg and 1000 mg Injection, 25 mg/mL and 50 mg/mL</p> <p><u>Usual Dose</u> 10 mg/kg to 15 mg/kg every 8 hours for 10 to 14 days</p>	<p><u>Orthographic</u> The letter ‘E’ and the letter string ‘-yclor’ in Edarbyclor appear similar to the letter ‘a’ and the letter string ‘yclov’ when scripted if the letter ‘a’ in scripted in a lower case</p> <p><u>Phonetic</u> Both names share the letter string ‘-yclo-’, however, the shared string in in different positions of the names.</p> <p><u>Dosage Form</u> Both products are available as tablets</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbylcor may be dosed at the Azilsartan Medoxomil strength of (b) (4) 40 mg, (b) (4)</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> Although both names share the letter string ‘-yclo-’, this letter string appears in different positions of the names. Additionally, the names Edarbyclor contains 4 upstrokes vs. the name Acyclovir contains 2 upstrokes.</p> <p><u>Phonetic</u> The names lack phonetic similarity.</p> <p><u>Frequency of Administration</u> Once daily vs. 5 times daily or every 8 hours</p>

<p>Eculizumab Injection, 300 mg</p> <p><u>Usual Dose</u> 600 mg as intravenous infusion every 7 days for the first 4 weeks, followed for a single dose of 900 mg as intravenous infusion 7 days after the 4th dose, and then 900 mg intravenous infusion every 14 days.</p>	<p><u>Orthographic</u> Both names start with the letter ‘E’ and the letter string ‘-abyc-’ in Edarbyclor may appear similar to the eltter string ‘-ulizu-’ in Eculizumab when scripted</p>	<p><u>Orthographic</u> The name Edarbyclor contains 4 upstrokes vs. the name Eculizumab contains 3 upstrokes. Additionally, the letter string ‘-lor’ in Edarbyclor lacks orthographic similarity to the letter string ‘-mab’ in Eculizumab.</p> <p><u>Strength</u> (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4) vs. 300 mg</p> <p><u>Usual Dose</u> 1 tablet vs. 600 mg or 900 mg</p>
<p>Cefaclor Capsule, 250 mg and 500 mg Powder for Suspension, 125 mg/5 mL, 187 mg/5 mL, 250 mg/5 mL, 375 mg/5 mL</p> <p><u>Usual Dose</u> Adults: 250 mg to 500 mg orally every 8 hours Children: 20 mg/kg to 40 mg/kg orally every 8 hours for 7 to 10 days</p> <p>Extended-release Tablet, 573 mg and 500 mg</p> <p><u>Usual Dose</u> 375 mg to 500 mg orally every 12 hours for 7 to 10 days</p>	<p><u>Orthographic</u> Both names share the letter ‘a’ in similar positions. Additionally, both names share the letter string ‘-clor’ at the end of the names. Furthermore, the letter ‘e’ in Edarbyclor may appear similar to the letter ‘c’ in Cefaclor if both names are scripted in a lower case.</p> <p><u>Phonetic</u> Both names share the letter string ‘-clor’</p> <p><u>Dosage Form</u> Both products are available in solid dosage forms</p> <p><u>Partial Similarity in Strength and Dose</u> Edarbylcor may be dosed at the Chlorthalidone strength of (b) (4) 40 mg, (b) (4)</p> <p><u>Route of Administration</u> Oral</p>	<p><u>Orthographic</u> The name Edarbyclor appears longer than the name Cefaclor when scripted (10 letters vs. 8 letters). Additionally, the name Edarbyclor contains 4 upstrokes and 1 down stroke vs the name Cefaclor contains 2 upstrokes and 1 down stroke (if the letter ‘f’ in scripted as a down stroke) or 3 upstrokes and no down strokes (if the letter ‘f’ is scripted as an upstroke)</p> <p><u>Phonetic</u> The letter string ‘Edarby-’ lacks orthographic similarity to the letter string ‘Cefa-’</p> <p><u>Frequency of Administration</u> Once daily vs. every 8 hours or every 12 hours.</p>

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/s/

YELENA L MASLOV
07/12/2011

ZACHARY A OLESZCZUK
07/12/2011

CAROL A HOLQUIST
07/12/2011

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

Date: February 25, 2011

Application Type/Number: IND 077278

Through: Zachary Oleszczuk, Pharm.D., Team Leader
Carol Holquist, R.Ph., Director
Division of Medication Error Prevention and Analysis

From: Yelena Maslov, Pharm.D., Safety Evaluator
Division of Medication Error Prevention and Analysis

Subject: Proprietary Name Review

Drug Name(s): (b) (4) (Azilsartan Medoxomil and Chlorthalidone) Tablets
(b) (4) 40 mg/12.5 mg,
40 mg/25 mg, (b) (4)

Applicant/sponsor: Takeda Pharmaceuticals North America

OSE RCM #: 2010-1909

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

Reference ID: 2909995

Reference ID: 3064443

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EXECUTIVE SUMMARY

This review summarizes DMEPA's evaluation of the proposed proprietary name, (b) (4) for Azilsartan Medoxomil and Chlorthalidone tablets. Our evaluation determined the proposed proprietary name, (b) (4) is vulnerable to name confusion that could lead to medication errors due to the use of the ambiguous and error prone nature of the modifier, (b) (4). Thus, we object to the use of the proposed proprietary name, (b) (4) as outlined in Section 4. DMEPA will notify the Applicant of these findings via letter.

1 BACKGROUND

1.1 INTRODUCTION

This review responds to a request from Takeda Pharmaceuticals North America, dated August 30, 2010, for a safety and promotional assessment of the proposed proprietary name, (b) (4).

1.2 PRODUCT INFORMATION

(b) (4) (Azilsartan Medoxomil and Chlorthalidone) tablets is an angiotensin II receptor blocker and a diuretic combination product indicated for the treatment of hypertension. (b) (4) will be available in the following strengths: (b) (4). The product will be administered orally once daily without regard to food. Phase III trials are currently ongoing to determine the starting dose for the product. However, it is expected that the maximum daily dose will be (b) (4) taken once daily. It is expected that (b) (4) will be supplied in bottles of 30 or 90 tablets. (b) (4) should be stored at 25°C (77°F), with temperature excursions permitted to 15°C-30°C (59°F -86°F).

2 METHODS AND MATERIALS

Appendix A describes the general methods and materials used by the Division of Medication Error Prevention and Analysis (DMEPA) when conducting a proprietary name risk assessment for all proprietary names. Sections 2.1, 2.2, and 2.3 identify specific information associated with the methodology for the proposed proprietary name, (b) (4).

2.1 SEARCH CRITERIA

For this review particular consideration was given to drug names beginning with the letter (b) (4) when searching to identify potentially similar drug root names, as 75% of the confused drug name reported by the ISMP Medication Error Reporting Program involve pairs beginning with the same letter.^{1,2}

Because omission of a modifier (b) (4) is cited in literature as a common cause of medication error, DMEPA also considers the proposed root name, (b) (4) without modifiers, as well as the proposed name (b) (4) as complete name.

To identify drug names that may look similar to (b) (4) DMEPA safety evaluators also consider the orthographic appearance of the root name (b) (4) and modifier (b) (4) on lined and unlined orders.

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

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

Additionally, since the modifier alone can be a source of confusion, we consider its current use on the market, potential to be misinterpreted, and appropriateness for the proposed product.

Specific attributes taken into consideration to identify drug names that may look similar to (b) (4) (b) (4) include the length of the proposed proprietary name, (b) (4) (b) (4) upstrokes (b) (4) downstrokes (b) (4) cross strokes (b) (4) and dotted letters (b) (4). Additionally, several in the proposed root name (b) (4) may be vulnerable to ambiguity when scripted (See Appendix B).

When searching to identify potential names that may sound similar to (b) (4) DMEPA (b) (4) safety evaluators search for the names with the similar number of syllables (b) (4) stresses (b) (4) and placement of vowel and consonant sounds in the name. Additionally, DMEPA safety evaluators consider that pronunciation of the part of the name (b) (4) can vary (See Appendix B). The Applicant's intended pronunciation (b) (4) (b) (4) was also take into consideration, as it as included in the Proprietary Name review Request. Moreover, names are often mispronounced or spoken with regional accents and dialects, so other pronunciations of the names are considered.

2.2 FDA PRESCRIPTION ANALYSIS STUDIES

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, the following inpatient and verbal orders were communicated during FDA prescription studies conducted on October 13, 2010.

Figure 1: (b) (4) study samples

HANDWRITTEN REQUISITION MEDICATION ORDER	VERBAL PRESCRIPTION
<p style="text-align: center;"><u>MEDICATION ORDER</u></p> <p>(b) (4) PD 80</p>	<p style="text-align: center;">(b) (4)</p> <p style="text-align: center;">#30 1 PO QD</p>
<p style="text-align: center;"><u>OUTPATIENT PRESCRIPTION</u></p> <p>(b) (4) 40mg/113.5mg</p> <p>#30 take 1 + po Daily</p>	

2.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

For this product, the Applicant referred to an external evaluation of the proposed proprietary name, (b) (4) for a single ingredient Azilsartan product under (b) (4) conducted by (b) (4). The Division of Medication Error Prevention and Analysis conducts an independent analysis and evaluation of the data provided, and responds to the overall finding of

the assessment. When the external proprietary name risk assessment identifies potentially confusing names that were not captured in DMEPA's database searches or in the Expert Panel Discussion, these names are included in the Safety Evaluator's Risk Assessment and analyzed independently by the Safety Evaluator to determine if the potentially confusing name could lead to medication errors in the usual practice settings.

After the Safety Evaluator has determined the overall risk associated with the proposed name, the Safety Evaluator compares the findings to their overall assessment with the findings of the proprietary name risk assessment submitted by the Applicant. The Safety Evaluator then determines whether the Division's risk assessment concurs or differs with the findings. When the proprietary name risk assessments differ, the Division of Medication Error Prevention and Analysis provides a detailed explanation of these differences.

3 RESULTS

The following sections describe the findings of database and information source searches, FDA prescription studies, expert panel discussion, and external proprietary name risk assessment.

3.1 DATABASE AND INFORMATION SOURCES

DMEPA safety evaluators search yielded a total of sixteen names (n=16) as having some similarity to the proposed name, (b) (4)

Fourteen names (n=14) of the 16 were thought to look like (b) (4) by the safety evaluators. These names are Etodolac, Idarubicin, FL CLD, Carbic D, (b) (4) Etrafon, (b) (4) ED-TLC, Edge-OB, Elidel, Aldara, Advil Cold, Embeda, and Epivir.

The remaining two name (n=2) were thought to look like and sound like (b) (4). These names are Edluar and Darbid.

Additionally, DMEPA safety evaluators did not identify any United States Adopted Names (USAN) stems in the proposed proprietary names, as of January 5, 2011.

3.2 EXPERT PANEL DISCUSSION

The Expert Panel reviewed the pool of names identified by DMEPA safety evaluators (See Section 3.1 above) and noted no additional names thought to have orthographic or phonetic similarity to the name (b) (4).

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

3.3 EXTERNAL PROPRIETARY NAME RISK ASSESSMENT

In the proposed name risk assessment submitted by the Applicant for (b) (4), (b) (4) found the proprietary root name, (b) (4) acceptable.

(b) (4) identified and evaluated three names (Elavil, Advair, and Darbepoetin) for their potential similarity to the root name, (b) (4). Elavil and Advair were considered to look similar to the proposed name, while Darbepoetin was considered to sound similar to the proposed name. Elavil was also identified by DMEPA's primary safety evaluator as a look-alike name. Since, Advair and Darbepoetin were not identified by DMEPA safety evaluators, these names were considered in our overall evaluation.

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

The Applicant also searched several databases for products that contain the modifier (b) (4) and did not identify any names of concern related specifically to the modifier. However, the Applicant did not evaluate the modifier for its potential to contribute to medication errors.

3.4 FDA PRESCRIPTION ANALYSIS STUDIES

A total of 41 practitioners responded to the prescription analysis studies. Five respondents interpreted the proposed name correctly as (b) (4) with correct interpretation occurring with inpatient (n=2) and voice prescriptions (n=3). Two practitioners misinterpreted the modifier (b) (4) as 'HCTZ' (n=1) and 'UD' (n=1). Three practitioners noted that there was a modifier with the use of the question mark; however, the practitioners were unable to interpret the modifier. Additionally, participants omitted the modifier and did not note that a modifier was present. The remaining thirty one participants misinterpreted the name, (b) (4) with the majority of the misinterpretations from the voice orders occurring with the last letter of the root name (b) (4) misinterpreted as (b) (4), n=6). See Appendix C for the complete listing of interpretations from the verbal and written prescription studies.

3.5 COMMENTS FROM THE DIVISION OF CARDIOVASCULAR AND RENAL PRODUCTS

3.5.1 Initial Phase of Review

In response to an OSE email on September 14, 2010 Division of Cardiovascular and Renal Products (DCRP) did not have any comments or concerns regarding the proposed proprietary name, (b) (4) at the initial point of review.

3.5.2 Midpoint Phase of Review

DMEPA notified DCRP via email on January 5, 2011 that the proprietary name, (b) (4) is vulnerable to confusion that could lead to medication errors due to the ambiguous and error prone nature of the modifier (b) (4). Per email correspondence on January 10, 2011, DCRP stated that they have no objections to DMEPA's safety assessment of (b) (4).

3.6 SAFETY EVALUATOR RISK ASSESSMENT OF THE PROPOSED PROPRIETARY NAME

The primary safety evaluator identified sixteen additional names (n=16), which were thought to look similar to (b) (4) and represent a potential source of drug name confusion. These names are Chantix, Eleaf, Enbrel, Ebrex 600, Efasin, Endodan, Evista, Idarac, Aclasta***, (b) (4) Aclovate, Elavil, Inderal, and (b) (4).

Thus, a total of 34 names were identified for the potential similarity to the proposed name, (b) (4) (16 names from database and information source searches, 3 from external study, and 16 by the primary safety evaluator).

Additionally, the review of the modifier (b) (4) identified (b) (4) as a standard abbreviation for (b) (4).

(b) (4) Additionally, (b) (4) stands for (b) (4).

Furthermore, the modifier (b) (4) is orthographically similar to the abbreviation for (b) (4) and another modifier (b) (4).

³ Medical Abbreviations Dictionary [Internet]. MediLexicon International Ltd; © 2004-2011 [cited 2011 Feb 11]. Available from <http://www.ncbi.nlm.nih.gov/books/NBK7269/#A53635>

⁴ Davis, Neli. Medical Abbreviations, 15th Edition [Internet]. Neli Davis Associates © 2011 [cited 2011 Feb 11]. Available from <http://www.medabbrev.com/>

4 DISCUSSION

The proprietary name, (b) (4) was evaluated from a safety and promotional perspective based on the product characteristics provided by the Applicant.

4.1 PROMOTIONAL ASSESSMENT

DDMAC did not find the name, (b) (4) promotional. DMEPA and DCRP concurred with this finding.

4.2 SAFETY ASSESSMENT

The safety assessment considered the orthographic and phonetic similarity of the proposed proprietary name to currently marketed drugs, the acceptability of the modifier, and other aspects of the name that might be a source of confusion.

4.2.1 Look-Alike and Sound-Alike Assessment

A total of 34 names were identified and evaluated as being potentially similar to the proposed name, (b) (4)

Seventeen (n=17) of the 34 names were eliminated from the further analysis for the following reasons: six names (n=6) lack orthographic or phonetic similarity to (b) (4) one name (n=1) is a product in a foreign country, one name (n=1) was not found in any of the commonly used databases listed in Reference section, three names (n=3) are the products withdrawn or discontinued from the US market without generic equivalent, and six names (n=6) have never been marketed (See Appendices D through H).

Failure Mode and Effect Analysis (FMEA) was then applied to determine whether the proposed proprietary name could potentially be confused with the remaining 17 names; and thereby, lead to medication errors. This analysis determined that the name similarity between (b) (4) was unlikely to result in medication errors with all 17 of the remaining products for the reasons presented in Appendices I through K.

4.2.2 Modifier 'CLD' Assessment

The root name (b) (4) stands for the Azilsartan component and the modifier (b) (4) stands for Chlorthalidone as stated by the Applicant in their request for proprietary name review, dated August 30, 2010. There are some names that include modifier to represent an active ingredient. However, the abbreviation (b) (4) has never been used in conjunction with the proprietary drug name to represent Chlorthalidone. The Applicant did not provide data to support that the modifier (b) (4) is not error prone and conveys the intended meaning of Chlorthalidone. Thus, it is unknown whether medical professionals will readily understand the meaning of the modifier. This argument was supported by the prescription studies.

The proposed modifier (b) (4) will not be misinterpreted as a numerical strength because the letters of the modifiers are not orthographically or phonetically similar to any numbers. However, the letter string (b) (4) is an abbreviation for multiple medical and pharmaceutical terms described in Section 3.6. Since this abbreviation has multiple established meanings in clinical practice, it may be interpreted in many different ways including being confused with another product (b) (4)

(b) (4) or a laboratory value (b) (4)
(b) (4) As such, we discourage the use of such abbreviations in proprietary names.

Additionally, the proposed modifier (b) (4) looks similar to the abbreviation (b) (4) and modifier (b) (4) when scripted and as such may be misinterpreted. The abbreviation (b) (4) is used on written

prescriptions as an abbreviation for (b) (4). Additionally, (b) (4) is a modifier that is used for (b) (4). Due to the numerous ways in which the modifier (b) (4) can be misinterpreted, DMEPA does not consider (b) (4) an appropriate modifier for this product.

5 CONCLUSIONS AND RECOMMENDATIONS

The proprietary name risk assessment did not find the proposed name (b) (4) promotional, but vulnerable to name confusion that could lead to medication errors due to the use of the modifier (b) (4). Therefore, we do not recommend the use of the name, (b) (4) for this product. The Applicant will be notified of this finding via letter and will be requested to submit an alternate proprietary name for review.

5.1 COMMENTS TO THE APPLICANT

We have completed our review of the proposed proprietary name, (b) (4) and concluded that this name is unacceptable.

The proposed proprietary name is unacceptable because the proposed modifier can be misinterpreted and cause confusion. Since you have not provided data to support the modifier (b) (4) is not error prone and conveys the intended meaning of Chlorthalidone to healthcare providers, we have determined it is unacceptable for the following reasons:

1. The proposed modifier (b) (4) is an abbreviation for multiple medical and pharmaceutical terms such as (b) (4). Additionally, (b) (4) stands for (b) (4). Since the abbreviation (b) (4) has multiple established meanings in clinical practice, it may be interpreted in many ways including being confused with another product (b) (4) or a laboratory value (b) (4). As such, we discourage the use of such abbreviations in proprietary names.
2. The proposed modifier (b) (4) is subject to misinterpretation upon scripting. (b) (4) looks similar to the abbreviation (b) (4) and modifier (b) (4) when scripted. The abbreviation (b) (4) is used on written prescriptions as an abbreviation for (b) (4). Additionally, (b) (4) is a modifier that is used for (b) (4). Since the proposed modifier (b) (4) can appear similar to other known abbreviations and modifiers we discourage the use of this modifier.
3. The proposed modifier (b) (4) has never been used in an approved proprietary name to represent the active ingredient Chlorthalidone. Since this modifier has never been used in conjunction with an approved proprietary name, it is likely health care practitioners will not understand the intended meaning of the modifier or may confuse it for the above referenced medical abbreviations for (b) (4).

We note that you have not proposed an alternate proprietary name for review. If you intend to have a proprietary name for this product, we recommend that you submit a new request for a proposed proprietary name review. (See the Guidance for Industry, *Contents of a Complete Submission for the Evaluation of Proprietary Names*, <http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM075068.pdf> and “PDUFA Reauthorization Performance Goals and Procedures Fiscal Years 2008 through 2012”.)

6 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. ***The Document Archiving, Reporting, and Regulatory Tracking System (DARRTS)***

DARRTS is a government database used to track individual submissions and assignments in 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. ***Stat!Ref (www.statref.com)***

Stat!Ref contains full-text information from approximately 30 texts; it includes tables and references. Among the database titles are: Handbook of Adverse Drug Interactions, Rudolphs Pediatrics, Basic Clinical Pharmacology, and Dictionary of Medical Acronyms Abbreviations.

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

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.

APPENDICES

Appendix A:

FDA's Proprietary Name Risk Assessment considers the potential for confusion between the proposed proprietary name and the proprietary and established names of drug products existing in the marketplace and those pending IND, NDA, BLA, and ANDA products currently under review by the Center. DMEPA defines a medication error as any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.⁵

For the proposed proprietary name, DMEPA staff search a standard set of databases and information sources to identify names with orthographic and phonetic similarity and hold a Center for Drug Evaluation and Research (CDER) Expert Panel discussion to gather professional opinions on the safety of the proposed proprietary name. DMEPA staff also conducts internal

⁵ National Coordinating Council for Medication Error Reporting and Prevention. <http://www.nccmerp.org/aboutMedErrors.html>. Last accessed 10/11/2007.

CDER prescription analysis studies. When provided, DMEPA considers external prescription analysis study results and incorporate into the overall risk assessment.

The Safety Evaluator assigned to the Proprietary Name Risk Assessment is responsible for considering the collective findings, and provides an overall risk assessment of the proposed proprietary name. DMEPA bases the overall risk assessment on the findings of a Failure Mode and Effects Analysis (FMEA) of the proprietary name, and focuses on the avoidance of medication errors.

FMEA is a systematic tool for evaluating a process and identifying where and how it might fail.⁶ DMEPA uses FMEA to analyze whether the drug names identified with orthographic or phonetic similarity to the proposed proprietary name could cause confusion that subsequently leads to medication errors in the clinical setting. DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product.

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

Typical product characteristics considered when identifying drug names that could potentially be confused with the proposed proprietary name include, but are not limited to; established name of the proposed product, proposed indication of use, dosage form, route of administration, strength, unit of measure, dosage units, recommended dose, typical quantity or volume, frequency of administration, product packaging, storage conditions, patient population, and prescriber population. Because drug name confusion can occur at any point in the medication use process, DMEPA staff considers the potential for confusion throughout the entire U.S. medication use process, including drug procurement, prescribing and ordering, dispensing, administration, and monitoring the impact of the medication.⁷ DMEPA provides the product characteristics considered for this review in section one.

The Division of Medication Error Prevention and Analysis considers the spelling of the name, pronunciation of the name when spoken, and appearance of the name when scripted. DMEPA also compares the spelling of the proposed proprietary name with the proprietary and established name of existing and proposed drug products because similarly spelled names may have greater likelihood to sound similar to one another when spoken or look similar to one another when scripted. DMEPA staff also examines the orthographic appearance of the proposed name using a number of different handwriting samples. Handwritten communication of drug names has a long-standing association with drug name confusion. Handwriting can cause similarly and even dissimilarly spelled drug name pairs to appear very similar to one another. The similar appearance of drug names when scripted has led to medication errors. The DMEPA staff applies expertise gained from root-cause analysis of such medication errors to identify sources of ambiguity within the name that could be introduced when scripting (e.g., “T” may look like “F,”

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

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

lower case ‘a’ looks like a lower case ‘u,’ etc). Additionally, other orthographic attributes that determine the overall appearance of the drug name when scripted (see Table 1 below for details). In addition, the DMEPA staff compares the pronunciation of the proposed proprietary name with the pronunciation of other drug names because verbal communication of medication names is common in clinical settings. If provided, DMEPA will consider the 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.

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 Down strokes Cross-strokes Dotted letters Ambiguity introduced by scripting letters Overlapping product characteristics	<ul style="list-style-type: none"> 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	<ul style="list-style-type: none"> Names may sound similar when pronounced and lead to drug name confusion in verbal communication

Lastly, the DMEPA staff also considers the potential for the proposed proprietary name to inadvertently function as a source of error for reasons other than name confusion. Post-marketing experience has demonstrated that proprietary names (or components of the proprietary name) can be a source of error in a variety of ways. Consequently, DMEPA considers and evaluates these broader safety implications of the name throughout this assessment and the medication error staff provides additional comments related to the safety of the proposed proprietary name or product based on professional experience with medication errors.

1. Database and Information Sources

DMEPA staff conducts searches of the internet, several standard published drug product reference texts, and FDA databases to identify existing and proposed drug names that may sound-alike or look-alike to the proposed proprietary name using the criteria outlined in Section 2.1. Section 6 provides a standard description of the databases used in the searches. To complement the process, the DMEPA staff use a computerized method of identifying phonetic and orthographic similarity between medication names. The program, Phonetic and Orthographic Computer Analysis (POCA), uses complex algorithms to select a list of names from a database that have some similarity (phonetic, orthographic, or both) to the trademark being evaluated. Lastly, the DMEPA staff review the USAN stem list to determine if any USAN stems are present within the proprietary name. The individual findings of multiple safety evaluators are pooled and presented to the CDER Expert Panel.

2. CDER Expert Panel Discussion

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

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

3. FDA Prescription Analysis Studies

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

In order to evaluate the potential for misinterpretation of the proposed proprietary name in handwriting and verbal communication of the name, inpatient medication orders and/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 the 123 participating health professionals via e-mail. In addition, a verbal prescription is recorded on voice mail. The voice mail messages are then sent

to a random sample of the participating health professionals for their interpretations and review. After receiving either the written or verbal prescription orders, the participants send their interpretations of the orders via e-mail to DMEPA.

4. Comments from the OND review Division or Generic drugs

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

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

5. Safety Evaluator Risk Assessment of the Proposed Proprietary Name

The primary Safety Evaluator applies his/her individual expertise gained from evaluating medication errors reported to FDA, conducts a Failure Mode and Effects Analysis, and provides an overall risk assessment of name confusion. Failure Mode and Effects Analysis (FMEA) is a systematic tool for evaluating a process and identifying where and how it might fail.⁸ When applying FMEA to assess the risk of a proposed proprietary name, DMEPA seeks to evaluate the potential for a proposed proprietary name to be confused with another drug name because of name confusion and, thereby, cause errors to occur in the medication use system. FMEA capitalizes on the predictable and preventable nature of medication errors associated with drug name confusion. FMEA allows the Agency to identify the potential for medication errors due to orthographically or phonetically similar drug names prior to approval, where actions to overcome these issues are easier and more effective than remedies available in the post-approval phase.

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

In the initial stage of the Risk Assessment, the Safety Evaluator compares the proposed proprietary name to all of the names gathered from the above searches, Expert Panel Discussion, and prescription studies, external studies, and identifies potential failure modes by asking:

“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting?”

An affirmative answer indicates a failure mode and represents a potential for the proposed proprietary name to be confused with another proprietary or established drug name because of look- or sound-alike similarity. If the answer to the question is no, the Safety Evaluator is not

⁸ Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

convinced that the names possess similarity that would cause confusion at any point in the medication use system, thus the name is eliminated from further review.

In the second stage of the Risk Assessment, the primary Safety Evaluator evaluates all potential failure modes to determine the likely *effect* of the drug name confusion, by asking:

“Could the confusion of the drug names conceivably result in medication errors in the usual practice setting?”

The answer to this question is a central component of the Safety Evaluator’s overall risk assessment of the proprietary name. If the Safety Evaluator determines through FMEA that the name similarity would not ultimately be a source of medication errors in the usual practice setting, the primary Safety Evaluator eliminates the name from further analysis. However, if the Safety Evaluator determines through FMEA that the name similarity could ultimately cause medication errors in the usual practice setting, the Safety Evaluator will then recommend the use of an alternate proprietary name.

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

- a. DDMAC finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with DDMAC’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].
- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product.

If DMEPA objects to a proposed proprietary name on the basis that drug name confusion could lead to medication errors, the primary Safety Evaluator uses the FMEA process to identify strategies to reduce the risk of medication errors. DMEPA is likely to recommend that the Sponsor select an alternative proprietary name and submit the alternate name to the Agency for DMEPA to review. However, in rare instances FMEA may identify plausible strategies that could reduce the risk of medication error of the currently proposed name. In that instance, DMEPA may be able to provide the 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 Sponsor. However, the safety concerns set forth in criteria a through e are supported either by FDA regulation or by external healthcare authorities, including the Institute of Medicine (IOM), World Health Organization (WHO), 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 and called for regulatory authorities to address the issue prior to approval. Additionally, DMEPA contends that the threshold set for the Proprietary Name Risk Assessment is reasonable because proprietary drug name confusion is a predictable and a preventable source of medication error that, in many instances, the Agency and/or 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. . (See Section 4 for limitations of the process).

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

Appendix B:

Table 1: Letters with possible orthographic or phonetic misinterpretation

Letters in the root name,	Scripted may appear as	Spoken may be interpreted as
(b) (4)		

Letters in modifier,	Scripted may appear as	Spoken may be interpreted as
(b) (4)		

Appendix C: FDA Prescription study for (b) (4) from 10/13/2010

Figure 1: (b) (4) study samples

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order</u></p> <p>(b) (4) 1 po qd</p>	<p>(b) (4)</p> <p>#30 1 po qd</p>
<p><u>Outpatient Prescription</u></p> <p>(b) (4) 40mg/12.5mg</p> <p>#30 take 1 to po daily</p>	

Table 1: Responses to prescription study

Inpatient Medication Order 10/13/2010	Outpatient Prescription Order 10/13/2010	Voice Prescription
(b) (4)		

Appendix D: Names of products that lack convincing orthographic and/or phonetic similarity

Drug Product Name	Drug Product Name
Ebrex 600	Epivir
Efasin	Aclovate
Evista	ED-TLC

Appendix E: Product Name marketed in a foreign country

Name	Similarity to (b) (4)	Product Description
Idarac (Floctafenine) Tablets 200 mg and 400 mg	Look alike	Non-steroidal anti-inflammatory drug (NSAID) used for management of acute, mild-to moderate pain marketed in France, Pakistan, and Thailand

Appendix F: Proprietary Name of the Product Not Found in any of the commonly Used Databases listed in Reference Section (Section 6)

Proprietary Name	Similarity to (b) (4)	Active Ingredients	Marketed Product	Database Found
Advil Cold	Look Alike	Unknown	Does not appear to be marketed	None, the product is only available as Advil Cold and Sinus

Appendix G: Names of the products discontinued or withdrawn from the United States market that have no generic equivalents

Proprietary Name	Similarity to (b) (4)	Status
Edge OB (Prenatal Multi-vitamin and Multimineral) Tablets	Look alike	Discontinued without generic equivalent
Carbic D (Carbinoxamine Maleate and Pseudoephedrine HCl) Syrup 2 mg/30 mg per 5 mL	Look alike	Discontinued without generic equivalent
Darbid (Isopropamide Iodide) Tablets'	Look alike and Sound Alike	Withdrawn from market by the Applicant without generic equivalent

Appendix H: Names of the products that have never been marketed

Proprietary Name	Similarity to (b) (4)	Status of a Product Name (b) (4)
Aclasta*** (Zolendroic Acid)	Look alike	(b) (4)
		(b) (4)

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Appendix I: Names of the products with no overlap in dose and/or strength

Product name with potential for confusion	Similarity to (b) (4)	Dosage Form and Strength	Usual Dose (If applicable)
(b) (4) (Azilsartan Medoxomil and Chlorthalidone)	N/A	Tablets: (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4)	Take (b) (4) orally once daily
Advair (Fluticasone Propionate and Salmeterol Xinafoate)	Look alike	Powder for Inhalation: 100 mcg/50 mcg per actuation 250 mcg/50 mcg per actuation 500 mcg/50 mcg per actuation Inhalation Aerosol: 45 mcg/21 mcg per actuation 115 mcg/21 mcg per actuation 230 mcg/21 mcg per actuation	1 inhalation orally twice daily 2 inhalations orally twice daily
Etodolac	Look alike	Tablet: 400 mg and 500 mg Capsule: 200 mg, 300 mg Extended Release Tablet: 400 mg, 500 mg, 600 mg	400 mg to 500 mg orally twice daily 200 mg to 300 mg orally twice daily 400 mg to 600 mg tablet orally once daily
Chantix (Varenicline)	Look alike	Tablets: 0.5 mg and 1 mg Chantix Starting Month PAK: 11 tablets of 0.5 mg and 42 tablets of 1 mg Chantix Continuing Month Pak: 56 tablets of 1 mg	Days 1 to 3: Take 0.5 mg once daily Days 4 through 7: Take 0.5 mg 2 times daily Days 8 through end of treatment: Take 1 mg 2 times daily
Edluar (Zolpidem Tartrate)	Look alike and sound alike	Sublingual Tablet: 5 mg and 10 mg	Take 5 mg to 10 mg under the tongue at bedtime
Elidel (Pimecrolimus)	Look alike	Cream: 1%	Apply to affected area twice daily
Aldara (Imiquimod)	Look alike	Cream: 5%	Actinic Keratosis: Apply to affected area two times per week, prior to bedtime Genital and Perianal warts: Apply a thin layer to affected area three times per week at bedtime
Eleaf (Avobenzone, Octinoxate, Octocrylene, Oxybenzone, and Zinc Oxide)	Look alike	Cream	Apply prior to sun exposure

Endodan (Oxycodone and Aspirin)	Look alike	Tablets: 5 mg/325 mg	Take 1 tablet every 6 hours as needed for pain; maximum dose of aspirin 4 g per day
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Appendix K: Potentially confusing names with overlap in strength, but analysis indicates low potential for confusion

Failure Mode: Name Confusion	Causes (can be multiple)	Rationale for Failure Mode Prevention
(b) (4) (Azilsartan Medoxomil and Chlorthalidone) Tablets (b) (4) 40 mg/12.5 mg, 40 mg/25 mg, (b) (4)	N/A	Take (b) (4) (b) (4) orally once daily
Etrafon* (Perphenazine HCl and Amitriptyline) Tablets 2 mg/10 mg and 2 mg/25 mg *Proprietary name is discontinued, however, generic products are still available <u>Usual Dose</u> Take 1 tablet orally twice daily	<u>Orthographic</u> (b) (4) <u>Route of Administration</u> Orally <u>Numerical overlap in Strength</u> (b) (4)	<u>Orthographic</u> (b) (4) Additionally, (b) (4) contains a modifier vs. Etrafon does not. <u>Frequency of Administration</u> Once daily vs. Twice daily

<p>Embeda (Morphine Sulfate and Naltrexone HCl) Extended Release Capsules: 30 mg/1.2 mg, 50 mg/2 mg, 60 mg/2.4 mg, 80 mg/3.2 mg, 100 mg/4 mg</p> <p><u>Usual Dose</u> Take 1 tablet orally twice daily</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Route of Administration</u> Orally</p> <p><u>Partial Numerical Overlap in Strength</u> (b) (4)</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Strength and Dose</u> (b) (4)</p> <p>(b) (4) also contains different strengths of Chlorthalidone (i.e., 12.5 mg and 25 mg). Thus, the strength of Chlorthalidone would have to be specified on a prescription for (b) (4)</p>
<p>Enbrel (Etanercept) Injection: 25 mg/0.5 mL, 50 mg/0.5 mL, 50 mg/mL (Sureclick)</p> <p>Kit: 25 mg</p> <p><u>Usual Dose</u> Ankylosing Spondylitis, Psoriatic Arthritis, and Rheumatoid Arthritis: Inject 50 mg subcutaneously every week</p> <p>Plaque Psoriasis: Inject 50 mg subcutaneously 2 times weekly for 3 months, then reduce to 50 mg weekly</p> <p>Children Juvenile idiopathic Arthritis: 0.8 mg/kg subcutaneous weekly</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Partial Numerical Overlap in Strength</u> (b) (4) may be dosed at a strength of Chlorthalidone that overlaps with Enbrel 25 mg/0.5 mL strength if the strength for Azilsartan is omitted e.g. (b) (4) 25 mg vs. Enbrel 25mg</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Dosage Form</u> Tablet vs. Injection</p> <p><u>Route of Administration</u> Orally vs. Subcutaneous Injection</p> <p><u>Frequency of Administration</u> Once daily vs. once weekly</p> <p><u>Strength and Dose</u> Although there is a partial overlap in the strength and dose between the two products, (b) (4) also contains (b) (4)</p>

<p>Elavil* (Amitriptiline HCl) Tablet 10 mg, 25 mg, 50 mg, 75 mg, 100 mg, 150 mg</p> <p>*Proprietary name is discontinued, however, generic products are still available</p> <p><u>Usual Dose</u> Take 1 tablet orally once daily to three times daily</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Route of Administration</u> Orally</p> <p><u>Partial Numerical Overlap in Strength</u> (b) (4) may be dosed at strengths of Chlorthalidone that overlap with Elavil strengths: 25 mg and 50 mg, if the strength for Azilsartan is omitted e.g. (b) (4) vs. Elavil 25 mg</p> <p><u>Frequency of Administration</u> Both products can be administered once daily.</p>	<p><u>Orthographic</u> (b) (4) The letter string (b) (4) lacks similarity with the letter string '-vil' in Elavil when scripted. Additionally, (b) (4) contains a modifier (b) (4) whereas Elavil does not.</p> <p><u>Strength and Dose</u> Although there is a partial overlap in the strength and dose between the two products, (b) (4) also contains (b) (4)</p>
<p>Idarubicin Injection 5 mg/5 mL; 10 mg/10 mL; 20 mg/20 mL (1 mg/mL)</p> <p><u>Usual Dose</u> Inject 12 mg/m² daily for 3 days by slow intravenous injection over 10 to 15 minutes</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Partial Numerical Overlap in Strength and Dose</u> (b) (4) may be ordered at the strength of (b) (4)</p> <p><u>Frequency of administration</u> Both products should be administered daily, although Idarubicin should be administered daily for 3 days only.</p>	<p><u>Orthographic</u> (b) (4) Idarubicin contains 10 letters; thus, making the name Idarubicin much longer. Additionally, (b) (4) contains a modifier (b) (4) whereas Idarubicin does not.</p> <p><u>Dosage Form</u> Tablets vs. Injection</p> <p><u>Strength and Dose</u> Although there is a partial overlap in the strength and dose between the two products, (b) (4) also contains different strengths of Chlorthalidone (i.e., 12.5 mg and 25 mg). Thus, the strength of Chlorthalidone would have to be specified on a prescription for (b) (4)</p> <p><u>Route of Administration</u> Orally vs. Intravenously</p> <p><u>Usual Dose</u> 1 Tablet vs. 12 mg/m² over 10 to 15 minutes.</p>

<p>FL CLD #5</p> <p>Each Tablet Supplies: Bayberry 85mg, Yarrow 85mg, Echinacea 45mg, Fenugreek 45mg, Ginger Root 45mg, Myrrh Gum 45mg, Catnip 45mg, Slippery Elm Bark 45mg. In a base of 6x Cell (tissue) Salts: Ferric Phosphate, Potassium Chloride, Sodium Chloride, Calcium Phosphate, Silicea.</p> <p><u>Usual Dose</u> Take 1 to 2 tablets three times daily</p>	<p><u>Orthographic</u> (b) (4)</p> <p><u>Dosage Form</u> Tablet</p> <p><u>Overlap in Usual Dose</u> Both products may be administered as 1 tablet</p> <p><u>Route of Administration</u> Both products should be administered orally.</p>	<p><u>Orthographic</u> (b) (4)</p> <p>(b) (4) Additionally, FL CLD contains another modifier '#5'</p> <p><u>Frequency of administration</u> Once daily vs. three times daily</p> <p><u>Strength and Dose</u> The strength and dose of both active ingredients of (b) (4) have to be included on a prescription.</p>
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*** This document contains proprietary and confidential information that should not be released to the public.

<p>Inderal (Propranolol HCl) Tablets 20 mg, 40 mg, 60 mg, 80 mg</p> <p><u>Usual Dose</u> Take 1 to 3 tablets orally 2 times daily (Dose range: 40 mg to 320 mg per day)</p> <p>Inderal (Propranolol HCl) Oral Solution: 20 mg/5 mL and 40 mg/ 5 mL</p> <p><u>Usual dose</u> 2.5 mL (½ teaspoonful) to 10 mL (2 teaspoonfuls) orally twice daily</p>	<p>Orthographic (b) (4)</p> <p><u>Dosage Form</u> Both products are available as tablets</p> <p>Partial Numerical Overlap in Strength (b) (4)</p> <p><u>Route of Administration</u> Both products should be administered orally.</p>	<p>Orthographic (b) (4)</p> <p><u>Strength and Dose</u> Although there is a partial overlap in the strength and dose between the two products, (b) (4) also contains different strength of Chlorthalidone (i.e., 12.5 mg and 25 mg) associated with each strength of Azilsartan (b) (4). Thus, it is unlikely that the strength/dose of either active ingredient will be omitted.</p> <p><u>Frequency of Administration</u> Once daily vs. twice daily</p>
<p>Darbepoetin alpha Injection 25 mcg/0.42 mL; 25 mcg/mL; 40 mcg/0.4 mL; 40 mcg/mL; 60 mcg/0.3 mL; 60 mcg/mL; 100 mcg/0.5 mL; 100 mcg/mL; 150 mcg/0.3 mL; 150 mcg/0.75 mL; 200 mcg/0.4 mL; 200 mcg/mL; 300 mcg/0.6 mL; 300 mcg/mL; 500 mcg/mL</p> <p><u>Usual Dose</u> 0.45 mcg/kg subcutaneously or intravenously weekly</p>	<p>Phonetic (b) (4)</p> <p><u>Numerical Overlap in strength</u> Both products contain numbers 25 and 40 as part of their strengths.</p>	<p>Phonetic (b) (4)</p> <p><u>Dosage Form</u> Tablet vs. Injection</p> <p><u>Route of Administration</u> Orally vs. subcutaneously or intravenously</p> <p><u>Frequency of Administration</u> Daily vs. weekly.</p>

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/s/

ZACHARY A OLESZCZUK on behalf of YELENA L MASLOV
02/25/2011

ZACHARY A OLESZCZUK
02/25/2011

CAROL A HOLQUIST
02/25/2011

Reference ID: 2909995

Reference ID: 3064443