

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*

**205383Orig1s000**

**PROPRIETARY NAME REVIEW(S)**

---

**PROPRIETARY NAME REVIEW**

Division of Medication Error Prevention and Analysis (DMEPA)  
Office of Medication Error Prevention and Risk Management (OMEPRM)  
Office of Surveillance and Epidemiology (OSE)  
Center for Drug Evaluation and Research (CDER)

**\*\*\* This document contains proprietary information that cannot be released to the public\*\*\***

---

<b>Date of This Review:</b>	December 16, 2014
<b>Application Type and Number:</b>	NDA 205383
<b>Product Name and Strength:</b>	Oraltag (Iohexol) <span style="background-color: #cccccc; padding: 0 5px;">(b) (4)</span> Oral Solution 9.7 grams of Iohexol powder (4.5 grams of Iodine)
<b>Product Type:</b>	Single
<b>Rx or OTC:</b>	Rx
<b>Applicant/Sponsor Name:</b>	Interpharma Praha, A.S.
<b>Submission Date:</b>	September 30, 2014
<b>Panorama #:</b>	2014-37859
<b>DMEPA Primary Reviewer:</b>	Neil Vora, PharmD, MBA
<b>DMEPA Team Leader:</b>	Yelena Maslov, PharmD

---

## Contents

1	INTRODUCTION .....	1
1.1	Regulatory History.....	1
1.2	Product Information.....	1
2	RESULTS .....	2
2.1	Misbranding Assessment .....	2
2.2	Safety Assessment.....	2
3	CONCLUSIONS.....	4
3.1	Comments to the Applicant .....	4
4	REFERENCES.....	5
	APPENDICES .....	6

## 1 INTRODUCTION

This review evaluates the proposed proprietary name, Oraltag, from a safety and misbranding perspective. The sources and methods used to evaluate the proposed name are outlined in the reference section and Appendix A respectively. The Applicant submitted an external name study, conducted by [REDACTED] (b) (4) for this product.

### 1.1 REGULATORY HISTORY

The sponsor previously submitted the proposed proprietary name, Oraltag on June 4, 2013. At that time, the Division of Medication Error Prevention and Analysis (DMEPA) found the name, Oraltag acceptable from a safety perspective in OSE Review #2013-1319, dated August 30, 2013.

### 1.2 PRODUCT INFORMATION

The following product information is provided in the September 30, 2014 proprietary name submission.

- Intended Pronunciation: Oré al tag
- Active Ingredient: Iohexol
- Indication of Use: indicated for oral use in adults and children as an opacification agent during computed tomography of the abdomen and pelvis.
- Route of Administration: Oral
- Dosage Form: [REDACTED] (b) (4) oral solution
- Strength: 9.7 grams
- Dose and Frequency:
  - Adults: 4.5 to 9 grams of Iodine for one dose
  - Children: 1.62 to 6.750 grams of Iodine for one dose
    - Children (less than 3 years of age): maximum dose is 4.5 grams of Iodine
    - Children (3 to 18 years of age): maximum dose is 9 grams of Iodine
- How Supplied: 500 mL beverage bottle packaged in a [REDACTED] (b) (4) foil pouch
- Storage: Store at 20°C to 25°C (68°F to 77°F)
- Container and Closure Systems: 500 mL transparent polyethylene terephthalate beverage bottle. The secondary package is a [REDACTED] (b) (4) pouch made from a foil [REDACTED] (b) (4)

## 2 RESULTS

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

### 2.1 MISBRANDING ASSESSMENT

The Office of Prescription Drug Promotion (OPDP) determined that the proposed name would not misbrand the proposed product. DMEPA and the Division of Medical Imaging Products (DMIP) concurred with the findings of OPDP's assessment of the proposed name. Safety Assessment

The following aspects were considered in the safety evaluation of the name.

#### 2.1.1 *United States Adopted Names (USAN) Search*

There is no USAN stem present in the proprietary name<sup>1</sup>.

#### 2.1.2 *Components of the Proposed Proprietary Name*

The proposed proprietary name, Oraltag, incorporates the route of administration "Oral" in the proprietary name. DMEPA considered whether the inclusion of the route of administration would be misleading.

The applicant also stated that no other route of administration would be pursued for this product. The inclusion of the route was discussed in detail in OSE Review #2013-1319.

#### 2.2.3 *FDA Name Simulation Studies*

One hundred two practitioners participated in DMEPA's prescription studies. The responses did not overlap with any currently marketed products nor did the responses sound or look similar to any currently marketed products or any products in the pipeline. Below is a summary of the prescription study:

- In the voice prescription study, 19 of 81 participants correctly interpreted the prescription.
- In the written inpatient prescription study, 30 of 81 participants correctly interpreted the prescription.
- In the outpatient prescription study, 32 of 81 participants correctly interpreted the prescription.

---

<sup>1</sup>USAN stem search conducted on November 24, 2014.

***Common misinterpretations in the outpatient study include:***

- “z” for “g”
- “v” for “r”

***Common misinterpretations in the inpatient study include:***

- A space between the words “Oral” and “tag”
- The addition of the word “drink” after “Oraltag”
- “q” for “g”
- “z” for “g”
- “x” for “r”

***Common misinterpretations in the voice study include:***

- A space between the words “Oral” and “tag”
- The addition of a “-” between the words “Oral” and “tag”
- “x” for “g”
- The omission of the letter “l” from the name “Oral”
- “o” for “a” in the word “Oral”
- “e” for “a” in the word “tag”
- “c” for “g” in the word “tag”

Appendix B contains the results from the verbal and written prescription studies.

***2.2.4 Comments from Other Review Disciplines at Initial Review***

In response to the OSE, October 10, 2014 e-mail, the Division of Medical Imaging Products (DMIP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

***2.2.5 Phonetic and Orthographic Computer Analysis (POCA) Search Results***

Table 1 lists the number of names with the combined orthographic and phonetic score of  $\geq 50\%$  retrieved from our POCA search<sup>2</sup> organized as highly similar, moderately similar or low similarity for further evaluation. Table 1 also includes names identified from the FDA Prescription Simulation and (b) (4).

---

<sup>2</sup> POCA search conducted on November 24, 2014.

<b>Table 1. POCA Search Results</b>	<b>Number of Names</b>
Highly similar name pair: combined match percentage score $\geq 70\%$	1
Moderately similar name pair: combined match percentage score $\geq 50\%$ to $\leq 69\%$	85
Low similarity name pair: combined match percentage score $\leq 49\%$	12

### ***2.2.6 Safety Analysis of Names with Potential Orthographic, Spelling, and Phonetic Similarities***

Our analysis of the ninety-eight names contained in Table 1 determined zero names will pose a risk for confusion as described in Appendices C through H.

### ***2.2.7 Communication of DMEPA's Analysis at Midpoint of Review***

DMEPA communicated our findings to the Division of Medical Imaging Products (DMIP) via e-mail on December 8, 2014. At that time we also requested additional information or concerns that could inform our review. Per e-mail correspondence from the DMIP on December 15, 2014, they stated no additional concerns with the proposed proprietary name, Oraltag.

## **3 CONCLUSIONS**

Given the detailed discussion in the previous OSE Review #2013-139, the proposed proprietary name is acceptable.

If you have further questions or need clarifications, please contact Vasantha Ayala, OSE project manager, at 240-402-5035.

### **3.1 COMMENTS TO THE APPLICANT**

We have completed our review of the proposed proprietary name, Oraltag, and have concluded that this name is acceptable.

If any of the proposed product characteristics as stated in your September 30, 2014 submission are altered prior to approval of the marketing application, the name must be resubmitted for review.

## 4 REFERENCES

1. **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.

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

POCA is a system that FDA designed. As part of the name similarity assessment, POCA is used to evaluate proposed names via a phonetic and orthographic algorithm. The proposed proprietary name is converted into its phonemic representation before it runs through the phonetic algorithm. Likewise, an orthographic algorithm exists that operates in a similar fashion. POCA is publicly accessible.

#### **Drugs@FDA**

Drugs@FDA is an FDA Web site that contains most of the drug products approved in the United States since 1939. The majority of labels, approval letters, reviews, and other information are available for drug products approved from 1998 to the present.

Drugs@FDA contains official information about FDA-approved *brand name* and *generic drugs*; *therapeutic biological products*, *prescription* and *over-the-counter* human drugs; and *discontinued drugs* (see Drugs @ FDA Glossary of Terms, available at [http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther\\_biological](http://www.fda.gov/Drugs/InformationOnDrugs/ucm079436.htm#ther_biological)).

#### **RxNorm**

RxNorm contains the names of prescription and many OTC drugs available in the United States. RxNorm includes generic and branded:

- Clinical drugs – pharmaceutical products given to (or taken by) a patient with therapeutic or diagnostic intent
- Drug packs – packs that contain multiple drugs, or drugs designed to be administered in a specified sequence

Radiopharmaceuticals, contrast media, food, dietary supplements, and medical devices, such as bandages and crutches, are all out of scope for RxNorm (<http://www.nlm.nih.gov/research/umls/rxnorm/overview.html#>).

#### **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.

## APPENDICES

### Appendix A

FDA's Proprietary Name Risk Assessment evaluates proposed proprietary names for misbranding and safety concerns.

1. **Misbranding Assessment:** For prescription drug products, OPDP assesses the name for misbranding concerns. . For over-the-counter (OTC) drug products, the misbranding assessment of the proposed name is conducted by DNCE. OPDP or DNCE evaluates proposed proprietary names to determine if the name is false or misleading, such as by making misrepresentations with respect to safety or efficacy. For example, a fanciful proprietary name may misbrand a product by suggesting that it has some unique effectiveness or composition when it does not (21 CFR 201.10(c)(3)). OPDP or DNCE provides their opinion to DMEPA for consideration in the overall acceptability of the proposed proprietary name.
2. **Safety Assessment:** The safety assessment is conducted by DMEPA, and includes the following:
  - a. Preliminary Assessment: 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.) See prescreening checklist below in Table 2\*. 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.<sup>3</sup>

---

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

**\*Table 2- Prescreening Checklist for Proposed Proprietary Name**

	Answer the questions in the checklist below. Affirmative answers to any of these questions indicate a potential area of concern that should be carefully evaluated as described in this guidance.
<b>Y/N</b>	<b>Is the proposed name obviously similar in spelling and pronunciation to other names?</b>
	Proprietary names should not be similar in spelling or pronunciation to proprietary names, established names, or ingredients of other products.
<b>Y/N</b>	<b>Are there medical and/or coined abbreviations in the proprietary name?</b>
	Proprietary names should not incorporate medical abbreviations (e.g., QD, BID, or others commonly used for prescription communication) or coined abbreviations that have no established meaning.
<b>Y/N</b>	<b>Are there inert or inactive ingredients referenced in the proprietary name?</b>
	Proprietary names should not incorporate any reference to an inert or inactive ingredient in a way that might create an impression that the ingredient's value is greater than its true functional role in the formulation (21 CFR 201.10(c)(4)).
<b>Y/N</b>	<b>Does the proprietary name include combinations of active ingredients?</b>
	Proprietary names of fixed combination drug products should not include or suggest the name of one or more, but not all, of its active ingredients (see 21 CFR 201.6(b)).
<b>Y/N</b>	<b>Is there a United States Adopted Name (USAN) stem in the proprietary name?</b>
	Proprietary names should not incorporate a USAN stem in the position that USAN designates for the stem.
<b>Y/N</b>	<b>Is this proprietary name used for another product that does not share at least one common active ingredient?</b>
	Drug products that do not contain at least one common active ingredient should not use the same (root) proprietary name.
<b>Y/N</b>	<b>Is this a proprietary name of a discontinued product?</b>
	Proprietary names should not use the proprietary name of a discontinued

product if that discontinued drug product does not contain the same active ingredients.
---

b. **Phonetic and Orthographic Computer Analysis (POCA):** Following the preliminary screening of the proposed proprietary name, DMEPA staff evaluates the proposed name against potentially similar names. In order to identify names with potential similarity to the proposed proprietary name, DMEPA enters the proposed proprietary name in POCA and queries the name against the following drug reference databases, Drugs@fda, CernerRxNorm, and names in the review pipeline using a 50% threshold in POCA. DMEPA reviews the combined orthographic and phonetic matches and group the names into one of the following three categories:

- Highly similar pair: combined match percentage score  $\geq 70\%$ .
- Moderately similar pair: combined match percentage score  $\geq 50\%$  to  $\leq 69\%$ .
- Low similarity: combined match percentage score  $\leq 49\%$ .

Using the criteria outlined in the check list (Table 3-5) that corresponds to each of the three categories (highly similar pair, moderately similar pair, and low similarity), DMEPA evaluates the name pairs to determine the acceptability or non-acceptability of a proposed proprietary name. The intent of these checklists is to increase the transparency and predictability of the safety determination of whether a proposed name is vulnerable to confusion from a look-alike or sound-alike perspective. Each bullet below corresponds to the name similarity category cross-references the respective table that addresses criteria that DMEPA uses to determine whether a name presents a safety concern from a look-alike or sound-alike perspective.

- For highly similar names, differences in product characteristics often cannot mitigate the risk of a medication error, including product differences such as strength and dose. Thus, proposed proprietary names that have a combined score of  $\geq 70$  percent are at risk for a look-alike sound-alike confusion which is an area of concern (See Table 3).
- Moderately similar names with overlapping or similar strengths or doses represent an area for concern for FDA. The dosage and strength information is often located in close proximity to the drug name itself on prescriptions and medication orders, and it can be an important factor that either increases or decreases the potential for confusion between similarly named drug pairs. The ability of other product characteristics to mitigate confusion (e.g., route, frequency, dosage form, etc.) may be limited when the strength or dose overlaps. We review such names further, to determine whether sufficient differences exist to prevent confusion. (See Table 4).
- Names with low similarity that have no overlap or similarity in strength and dose are generally acceptable (See Table 5) unless there are data to suggest that the

name might be vulnerable to confusion (e.g., prescription simulation study suggests that the name is likely to be misinterpreted as a marketed product). In these instances, we would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

- c. FDA Prescription Simulation Studies: DMEPA staff also conducts a prescription simulation studies using FDA health care professionals.

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.

- d. 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 OPDP'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.

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.

**Table 3. Highly Similar Name Pair Checklist (i.e., combined Orthographic and Phonetic score is  $\geq 70\%$ ).**

Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may render the names less likely to confusion, provided that the pair do not share a common strength or dose.			
<u>Orthographic Checklist</u>		<u>Phonetic Checklist</u>	
<b>Y/N</b>	Do the names begin with different first letters? <i>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</i>	<b>Y/N</b>	Do the names have different number of syllables?
<b>Y/N</b>	Are the lengths of the names dissimilar* when scripted?	<b>Y/N</b>	Do the names have different syllabic stresses?

	<i>*FDA considers the length of names different if the names differ by two or more letters.</i>		
Y/N	Considering variations in scripting of some letters (such as z and f), is there a different number or placement of upstroke/downstroke letters present in the names?	Y/N	Do the syllables have different phonologic processes, such vowel reduction, assimilation, or deletion?
Y/N	Is there different number or placement of cross-stroke or dotted letters present in the names?	Y/N	Across a range of dialects, are the names consistently pronounced differently?
Y/N	Do the infixes of the name appear dissimilar when scripted?		
Y/N	Do the suffixes of the names appear dissimilar when scripted?		

**Table 4: Moderately Similar Name Pair Checklist (i.e., combined score is  $\geq 50\%$  to  $\leq 69\%$ ).**

Step 1	<p>Review the DOSAGE AND ADMINISTRATION and HOW SUPPLIED/STORAGE AND HANDLING sections of the prescribing information (or for OTC drugs refer to the Drug Facts label) to determine if strengths and doses of the name pair overlap or are very similar. Different strengths and doses for products whose names are moderately similar may decrease the risk of confusion between the moderately similar name pairs. Name pairs that have overlapping or similar strengths or doses have a higher potential for confusion and should be evaluated further (see Step 2). Because the strength or dose could be used to express an order or prescription for a particular drug product, overlap in one or both of these components would be reason for further evaluation.</p> <p>For single strength products, also consider circumstances where the strength may not be expressed.</p>
--------	--

	<p>For any i.e. drug products comprised of more than one active ingredient, consider whether the strength or dose may be expressed using only one of the components.</p> <p>To determine whether the strengths or doses are similar to your proposed product, consider the following list of factors that may increase confusion:</p> <ul style="list-style-type: none"> <li>○ Alternative expressions of dose: 5 mL may be listed in the prescribing information, but the dose may be expressed in metric weight (e.g., 500 mg) or in non-metric units (e.g., 1 tsp, 1 tablet/capsule). Similarly, a strength or dose of 1000 mg may be expressed, in practice, as 1 g, or vice versa.</li> <li>○ Trailing or deleting zeros: 10 mg is similar in appearance to 100 mg which may potentiate confusion between a name pair with moderate similarity.</li> <li>○ Similar sounding doses: 15 mg is similar in sound to 50 mg</li> </ul>
<p>Step 2</p>	<p>Answer the questions in the checklist below. Affirmative answers to some of these questions suggest that the pattern of orthographic or phonetic differences in the names may reduce the likelihood of confusion for moderately similar names <u>with</u> overlapping or similar strengths or doses.</p>

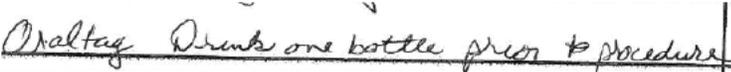
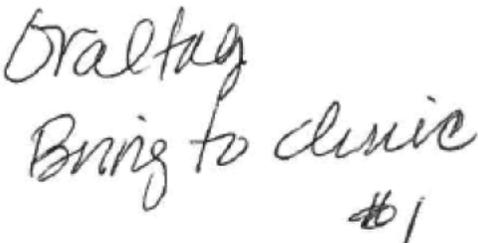
	<p>Orthographic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• Do the names begin with different first letters?</li> </ul> <p>Note that even when names begin with different first letters, certain letters may be confused with each other when scripted.</p> <ul style="list-style-type: none"> <li>• Are the lengths of the names dissimilar* when scripted?</li> </ul> <p>*FDA considers the length of names different if the names differ by two or more letters.</p> <ul style="list-style-type: none"> <li>• Considering variations in scripting of some letters (such as <i>z</i> and <i>f</i>), is there a different number or placement of upstroke/downstroke letters present in the names?</li> <li>• Is there different number or placement of cross-stroke or dotted letters present in the names?</li> <li>• Do the infixes of the name appear dissimilar when scripted?</li> <li>• Do the suffixes of the names appear dissimilar when scripted?</li> </ul>	<p>Phonetic Checklist (Y/N to each question)</p> <ul style="list-style-type: none"> <li>• Do the names have different number of syllables?</li> <li>• Do the names have different syllabic stresses?</li> <li>• Do the syllables have different phonologic processes, such as vowel reduction, assimilation, or deletion?</li> <li>• Across a range of dialects, are the names consistently pronounced differently?</li> </ul>
--	--	--

**Table 5: Low Similarity Name Pair Checklist (i.e., combined score is  $\leq 49\%$ ).**

In most circumstances, these names are viewed as sufficiently different to minimize confusion. Exceptions to this would occur in circumstances where, for example, there are data that suggest a name with low similarity is nonetheless misinterpreted as a marketed product name in a prescription simulation study. In such instances, FDA would reassign a low similarity name to the moderate similarity category and review according to the moderately similar name pair checklist.

**Appendix B: Prescription Simulation Samples and Results**

**Figure 1. Oraltag Study (Conducted on October 15, 2014)**

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p>  <p><u>Outpatient Prescription:</u></p> 	<p>Oraltag</p> <p>Bring to clinic</p> <p>Dispense #1</p>

**FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)**

259 People Received Study

102 People Responded

Study Name: Oraltag

Total	34	31	37	
<b>INTERPRETATION</b>	<b>OUTPATIENT</b>	<b>VOICE</b>	<b>INPATIENT</b>	<b>TOTAL</b>

?? OROTAGS	0	1	0	1
ORAL TAG	0	2	1	3
ORALTAG	32	19	30	81
ORAL-TAG	0	1	0	1
ORALTAG DRINK	0	0	1	1
ORALTAG?	0	1	0	1
ORALTAQ	0	0	2	2
ORALTAX	0	1	0	1
ORALTAZ	1	0	1	2
ORATAG	0	1	0	1
OROTAG	0	4	0	4
OROTEC	0	1	0	1
OVALTAG	1	0	0	1
OXALTAG	0	0	2	2

**Appendix C:** Highly Similar Names (e.g., combined POCA score is ≥70%)

No.	Proposed name: Oraltag Established name: iohexol Dosage form: (b) (4) oral solution Strength(s): 9.7 grams per 20 oz beverage bottle Usual Dose: 4.5 g – 9 g	POCA Score (%)	Orthographic and/or phonetic differences in the names sufficient to prevent confusion  Other prevention of failure mode expected to minimize the risk of confusion between these two names.	Product Characteristics:
1.	Orastat	71	The suffixes of this name pair have sufficient orthographic differences  The third syllables of this name pair sound different.	<b>Dosage Form:</b> Oral gel <b>Strength:</b> 20% <b>Dose:</b> Apply to affected area Over the counter product use

**Appendix D:** Moderately Similar Names (e.g., combined POCA score is ≥50% to ≤69%) with no overlap or numerical similarity in Strength and/or Dose

No.	Proposed Name	POCA Score (%)
1.	(b) (4) ***	64
2.	Auralgan	60
3.	Oracit	59
4.	Oralair 100	58
5.	Oralair 300	58
6.	Oralone	58
7.	(b) (4) ***	56
8.	Keralac	54
9.	(b) (4) ***	54
10.	Oraline	55
11.	Orvaten	54
12.	Oracea	52
13.	(b) (4) ***	52
14.	Oragesic	52

15.	(b) (4) ***	52
16.	OraQix	51
17.	(b) (4) ***	50
18.	Orabase	50
19.	Orajel Baby	50
20.	Orasep	50

**Appendix E:** Moderately Similar Names (e.g., combined POCA score is  $\geq 50\%$  to  $\leq 69\%$ ) with overlap or numerical similarity in Strength and/or Dose

No.	<p>Proposed name: Oraltag</p> <p>Established name: iohexol</p> <p>Dosage form: <sup>(b) (4)</sup> oral solution</p> <p>Strength(s): 9.7 grams per 20 oz beverage bottle</p> <p>Usual Dose: 4.5 g – 9 g</p>	POCA Score (%)	Prevention of Failure Mode
1.	Oravig	64	<p>The infix and suffix of this name pair have sufficient orthographic differences</p> <p>The third syllables of this name pair sound different.</p>
2.	Oretic	60	<p>The suffix of this name pair have sufficient orthographic differences</p> <p>The third syllables of this name pair sound different.</p>
3.	Relpax	60	<p>The prefix and suffix of this name pair have sufficient orthographic differences</p> <p>The first and second syllables of this name sound different. Oraltag contains an extra syllable.</p>
4.	Oreton	57	<p>The suffix of this name pair have sufficient orthographic differences</p> <p>The third syllables of this name pair sound different.</p>
5.	Moxatag	56	<p>The prefix and suffix of this name pair have sufficient orthographic differences</p> <p>The first and second syllables of this name pair sound different.</p>
6.	Orlistat	55	<p>The infix and suffix of this name pair have sufficient orthographic differences</p> <p>The second and third syllables of this name sound different.</p>
7.	Aralast	54	<p>The suffix of this name pair have sufficient orthographic differences</p> <p>The prefix of this name pair sound different.</p>

8.	Furalan	54	The prefix and suffix of this name pair have sufficient orthographic differences The prefix and suffix of this name pair sound different.
9.	Orabloc	54	The suffix of this name pair have sufficient orthographic differences The third syllables of this name pair sound different.
10.	Orange C	54	The suffixes of this name pair have sufficient orthographic differences. This name also contains a modifier "C" The second syllable of this name pair sounds different.
11.	Orapred	53	The suffixes of this name pair have sufficient orthographic differences. The last syllable of this name pair sound different.
12.	Delta D3	52	The prefix and suffix of this name pair have sufficient orthographic differences. This name also contains a modifier "D3" The first and second syllables of this name pair sound different.
13.	Zaltrap	51	The prefix and suffix of this name pair have sufficient orthographic differences The prefix and suffix of this name pair sound different. Oraltag contains an extra syllable.
14.	Aralen	50	The suffixes of this name pair have sufficient orthographic differences The first and third syllables of this name pair sound different.
15.	Ferralet TD	50	The prefix and suffix of this name pair have sufficient orthographic differences. This name also contains a modifier, "TD" The first and third syllables of this name pair sound different.

**Appendix F:** Low Similarity Names (e.g., combined POCA score is  $\leq 49\%$ )

No.	Name	POCA Score (%)
1.	Orbactiv	48
2.	Omtryg	40
3.	Purixan	34
4.	Otrexup	30
5.	Versacloz	28
6.	Fallback Solo	26
7.	Gilotrif	25
8.	Karbinal ER	24
9.	Epaned	20
10.	Vituz	20
11.	Nymalize	18
12.	Hemangeol	12

**Appendix G:** Names not likely to be confused or not used in usual practice settings for the reasons described.

No.	Name	POCA Score (%)	Failure preventions
1.	Orostat	64	Name found in RxNorm. No product characteristics available in common drug references.
2.	Eraldin	62	European drug not marketed in the U.S.

3.	Ultratag	58	European drug not marketed in the U.S.
4.	Orelox	55	European drug not marketed in the U.S.
5.	Oradent	54	Name found in RxNorm. No product characteristics available in common drug references.
6.	Orlenta	54	Product that is discontinued with no generic equivalent available.
7.	Orabid	52	Name found in RxNorm. No product characteristics available in common drug references.
8.	Oratuss	52	European drug not marketed in the U.S.
9.	Oratuss 12	52	European drug not marketed in the U.S.
10.	Aquatag		Product that is discontinued with no generic equivalent available.
11.	Coracten	50	European drug not marketed in the U.S.
12.	Duralutin	50	Product that is discontinued with no generic equivalent available.
13.	One-Alpha		European drug not marketed in the U.S.
14.	Orlept	50	European drug not marketed in the U.S.
15.	Otoalgan	50	Name found in RxNorm. No product characteristics available in common drug references.

**Appendix H:** Names not likely to be confused due to notable spelling, orthographic and phonetic differences.

No.	Name	POCA Score (%)
1.	Norel AD	58
2.	Norel SD	56
3.	Pyril Tann-12	56
4.	Uristat	56
5.	(b) (4) ***	55
6.	Rilutek	55
7.	Urealac	55
8.	Duratan	54
9.	Uro-Mag	54
10.	Valomag	54
11.	Xarelto	54
12.	Coal Tar	53
13.	Alamag	52
14.	Aler-Tab	52
15.	Drolban	52
16.	Ferratab	52
17.	Norel DM	52
18.	Portalac	52
19.	Respa-GF	52
20.	Riastap	52
21.	Robalog	52
22.	Surelac	52
23.	Trilog	52
24.	Uritact	52
25.	Xalatan	52

26.	Norel LA	51
27.	Cortastat	50
28.	Cortastat 10	50
29.	Curretab	50
30.	Formalaz	50
31.	Lorelco	50
32.	Norel CS	50
33.	Rantec	50
34.	Roclatan ***	50
35.	Valpax	50

-----  
**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
-----

/s/  
-----

NEIL H VORA  
12/16/2014

YELENA L MASLOV  
12/17/2014

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

**Proprietary Name Review**

Date: August 30, 2013

Reviewer: Kevin Wright, PharmD  
Division of Medication Error Prevention and Analysis

Team Leader: Yelena Maslov, PharmD  
Division of Medication Error Prevention and Analysis

Division Director: Carol A. Holquist, RPh.  
Division of Medication Error Prevention and Analysis

Drug Name and Strength: Oraltag (Iohexol) (b) (4) Oral Solution  
9 mg of Iodine to 21 mg of Iodine per 500 mL

Application Type/Number: NDA 205383

Applicant/Sponsor: Interpharma Praha as

OSE RCM #: 2013-1319

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

## CONTENTS

1	INTRODUCTION.....	1
1.1	Product Information.....	1
2.2	Safety Assessment.....	2
2	DISCUSSION .....	3
3	CONCLUSION .....	4
3.1	Comments to the Applicant.....	5
4	REFERENCES.....	6
	APPENDICES.....	9

## 1 INTRODUCTION

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

### 1.1 PRODUCT INFORMATION

The following product information is provided in the June 4, 2013 proprietary name submission.

- Intended pronunciation: Oré al tag
- Active Ingredient: Iohexol
- Indication of Use: is indicated for oral use in adults and children as an opacification agent during computed tomography of the abdomen and pelvis.
- Route of Administration: Oral
- Dosage Form: (b) (4) Oral Solution
- Strength: 9.7 grams
- Dose and Frequency:
  - Adults: 4.5 to 9 grams of Iodine for one dose
  - Children: 1.62 to 6.750 grams of Iodine for one dose
    - Children (less than 3 years of age): maximum dose is 4.5 grams of Iodine
    - Children (3 to 18 years of age): maximum dose is 9 grams of Iodine
- How Supplied: 500 mL beverage bottle packaged in a (b) (4) foil pouch
- Storage: store at 20°C to 25°C (68°F to 77°F)
- Container and Closure Systems: 500 mL transparent polyethylene terephthalate beverage bottle. The secondary package is a (b) (4) pouch made from a foil (b) (4)

## 2. RESULTS

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

### 2.1 PROMOTIONAL ASSESSMENT

The Office of Prescription Drug Promotion OPDP determined the proposed name is acceptable from a promotional perspective. DMEPA and the Division of Medical Imaging Products concurred with the findings of OPDP's promotional assessment of the proposed name.

## **2.2 SAFETY ASSESSMENT**

The following aspects were considered in the safety evaluation of the name.

### ***2.2.1 United States Adopted Names (USAN) SEARCH***

The August 6, 2013 search of the United States Adopted Name (USAN) stems did not identify that a USAN stem is present in the proposed proprietary name.

### ***2.2.2 Components of the Proposed Proprietary Name***

The proposed proprietary name, Oraltag, incorporates the route of administration “Oral” in the proprietary name.

### ***2.2.3 FDA Name Simulation Studies***

Seventy-four practitioners participated in DMEPA’s prescription studies. The interpretations did not overlap with any currently marketed products nor did the misinterpretations sound or look similar to any currently marketed products or any products in the pipeline. In the written studies, 32 of 47 participants correctly interpreted the prescription. Common misinterpretations in the written study were substitution of ‘taz’ and ‘tay’ for ‘tag’ and ‘oval’ for ‘oral’. In the voice study, 11 of the 27 participants correctly interpreted the prescription. Common misinterpretations in the voice study include: ‘oro’, ‘aural’ for ‘oral’. We have considered these variations in our look-alike and sound-alike searches and analysis (see Appendix B). Appendix C contains the results from the verbal and written prescription studies.

### ***2.2.4 Comments from Other Review Disciplines at Initial Review***

In response to the OSE, June 21, 2013 e-mail, the Division of Medical Imaging Products (DMIP) did not forward any comments or concerns relating to the proposed proprietary name at the initial phase of the review.

### ***2.2.5 Failure Mode and Effects Analysis of Similar Names***

Appendix B lists possible orthographic and phonetic misinterpretations of the letters appearing in the proposed proprietary name, Oraltag. Table 1 lists the names identified by the primary reviewer, the Expert Panel Discussion (EPD), and other review disciplines to have potential orthographic, phonetic, or spelling similarity to the proposed proprietary name, Oraltag. Table 1 also includes the potentially similar names identified by (b) (4) that require further evaluation by DMEPA. Our analysis of the 19 names contained in Table 1 determined all 19 names will not pose a risk for confusion as described in Appendices D through E.

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

Look Similar					
Aquatag	EPD	Moxatag	Both	Octagam	External Study
Orabloc	EPD	Oracea	External Study	Orajel	EPD
Oral-Ivy	EPD	Oralmat (Drops)	EPD	Oralone	EPD
(b) (4)	EPD	Oralyte	Both	Orapred	EPD
Orasone	External Study	Oraspan	External Study	Oratuss	EPD
Oravig	External Study	Oretic	External Study	Orthovisc	External Study
Ultratag	EPD				

### 2.2.7 Communication of DMEPA’s Analysis at Midpoint of Review

DMEPA communicated our findings to the Division of Medical Imaging Products via e-mail on August 23, 2013. At that time we also requested additional information or concerns that could inform our review.

## 2 DISCUSSION

The approval of this NDA will introduce a nonsterile formulation of Iohexol to the marketplace. We examined the following factors for the proposed product from the medication error perspective:

### 1. Iohexol Product Line

Oraltag is a 505(b)(2) application for the reference listed drug, Omnipaque (Iohexol). Omnipaque is a sterile solution indicated for use in adults and children for various imaging procedures utilizing different routes of administration (e.g. intrathecally, intravenously, and orally). Conversely, Oraltag is indicated for use in adults and children as an opacification agent during computed tomography of the abdomen and pelvis.

Wrong medication errors involving Oraltag and Omnipaque would result in a patient receiving a non-sterile solution instead of sterile solution via the parenteral or

intrathecal route of administration. This error could result in bodily harm or even death of the patient. Therefore, the Applicant has proposed the route of administration be incorporated into the proprietary name. Since it is not uncommon for a contrast agent to have multiple routes of administrations (intravenous, intrathecal, intra-arterial), inclusion of ‘oral’ in the proprietary may help practitioners recognize that this formulation of Iohexol is unique and for oral administration only unlike the reference listed product, Omnipaque or other contrast imaging agents. However, we have no evidence confirming that inclusion of the route in this name will in fact minimize wrong route errors nor did the applicant supply data to support this conclusion. There are other features of this product’s design that may also aid practitioners in the identification of this product as an oral formulation. The container closure system looks similar to a water bottle rather than a vial for injection, the established name of the product includes “Oral Suspension”, the route of administration appears on the PDP of the label as “For Oral Use Only” and the product is labeled as “Nonsterile”. Thus, these measures in totality should distinguish this oral product from the intravenous products.

DMEPA considered whether the inclusion of the route of administration would be misleading. Considering, Oraltag is indicated for oral use only we determined the inclusion of “oral” would not be misleading. (b) (4)

## 2. Inclusion of the Route of Administration (i.e. Oral) in the Proprietary Name

DMEPA generally discourages Applicants from incorporating the route of administration into the proprietary name because the inclusion of the route of administration in the proprietary name limits the use of the name to a particular route of administration which may be misleading for future product line extensions.<sup>1</sup>

(b) (4)

Thus, at this point in time the name is not misleading. If the Applicant were to pursue a different route of administration for this product, Oraltag could not be used as the proprietary name for the different route of administration because it may lead to wrong route of administration errors.

## 3 CONCLUSION

The proposed proprietary name is acceptable from both a promotional and safety perspective.

If you have further questions or need clarifications, please contact Sandra Rimmel, OSE project manager, at 301-796-245

---

<sup>1</sup> PDUFA Pilot Project: Proprietary Name Review Concept Paper. September 2008.

### **3.1 COMMENTS TO THE APPLICANT**

We have completed our review of the proposed proprietary name, Oraltag, and have concluded that this name is acceptable.

The proposed proprietary name must be re-reviewed 90 days prior to approval of the NDA. The results are subject to change. If any of the proposed product characteristics as stated in your June 4, 2013 submission are altered, the name must be resubmitted for review.

## 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. This database also lists the orphan drugs.

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

USPTO provides information regarding patent and trademarks.

8. ***Clinical Pharmacology Online*** ([www.clinicalpharmacology-ip.com](http://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.

**9. *Data provided by Thomson & Thomson's SAEGIS™ Online Service, available at ([www.thomson-thomson.com](http://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.

**10. *Natural Medicines Comprehensive Databases ([www.naturaldatabase.com](http://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.

**11. *Access Medicine ([www.accessmedicine.com](http://www.accessmedicine.com))***

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

**12. *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.

**13. *Red Book ([www.thomsonhc.com/home/dispatch](http://www.thomsonhc.com/home/dispatch))***

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

**14. *Lexi-Comp ([www.lexi.com](http://www.lexi.com))***

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

**15. *Medical Abbreviations ([www.medilexicon.com](http://www.medilexicon.com))***

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

**16. *CVS/Pharmacy ([www.CVS.com](http://www.CVS.com))***

This database contains commonly used over the counter products not usually identified in other databases.

**17. *Walgreens ([www.walgreens.com](http://www.walgreens.com))***

This database contains commonly used over the counter products not usually identified in other databases.

**18. Rx List ([www.rxlist.com](http://www.rxlist.com))**

RxList is an online medical resource dedicated to offering detailed and current pharmaceutical information on brand and generic drugs.

**19. Dogpile ([www.dogpile.com](http://www.dogpile.com))**

Dogpile is a [Metasearch](#) engine that searches multiple search engines including Google, Yahoo! and Bing, and returns the most relevant results to the search.

**20. Natural Standard (<http://www.naturalstandard.com>)**

Natural Standard is a resource that aggregates and synthesizes data on complementary and alternative medicine.

## 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 OPDP. OPDP 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. OPDP 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.<sup>2</sup>

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

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

DMEPA uses the clinical expertise of its staff to anticipate the conditions of the clinical setting where the product is likely to be used based on the characteristics of the proposed product. DMEPA considers the product characteristics associated with the proposed product throughout the risk assessment because the product characteristics of the proposed may provide a context for communication of the drug name and ultimately determine the use of the product in the *usual* clinical practice setting.

---

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

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

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).

---

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

**Table 1.** Criteria Used to Identify Drug Names that Look- or Sound-Similar to a Proposed Proprietary Name.

<b>Type of Similarity</b>	<b>Considerations when Searching the Databases</b>		
	<i>Potential Causes of Drug Name Similarity</i>	<i>Attributes Examined to Identify Similar Drug Names</i>	<i>Potential Effects</i>
Look-alike	Similar spelling	Identical prefix Identical infix Identical suffix Length of the name Overlapping product characteristics	<ul style="list-style-type: none"> <li>Names may appear similar in print or electronic media and lead to drug name confusion in printed or electronic communication</li> <li>Names may look similar when scripted and lead to drug name confusion in written communication</li> </ul>
	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	<ul style="list-style-type: none"> <li>Names may look similar when scripted, and lead to drug name confusion in written communication</li> </ul>
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"> <li>Names may sound similar when pronounced and lead to drug name confusion in verbal communication</li> </ul>

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 Office of Prescription Drug Promotion (OPDP). 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 OPDP'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.<sup>4</sup> 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

---

<sup>4</sup> Institute for Healthcare Improvement (IHI). Failure Mode and Effects Analysis. Boston. IHI:2004.

characteristics listed in Section 1.2 of this review. The Safety Evaluator then analyzes the proposed proprietary name in the context of the usual practice setting and works to identify potential failure modes and the effects associated with the failure modes.

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

***“Is the proposed proprietary name convincingly similar to another drug name, which may cause practitioners to become confused at any point in the usual practice setting? And are there any components of the name that may function as a source of error beyond sound/look-alike?”***

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. OPDP finds the proposed proprietary name misleading from a promotional perspective, and the Review Division concurs with OPDP’s findings. The Federal Food, Drug, and Cosmetic Act provides that labeling or advertising can misbrand a product if misleading representations are made or suggested by statement, word, design, device, or any combination thereof, whether through a PROPRIETARY name or otherwise [21 U.S.C 321(n); See also 21 U.S.C. 352(a) & (n)].
- b. DMEPA identifies that the proposed proprietary name is misleading because of similarity in spelling or pronunciation to another proprietary or established name of a different drug or ingredient [CFR 201.10.(C)(5)].

- c. FMEA identifies the potential for confusion between the proposed proprietary name and other proprietary or established drug name(s), and demonstrates that medication errors are likely to result from the drug name confusion under the conditions of usual clinical practice.
- d. The proposed proprietary name contains an USAN (United States Adopted Names) stem.
- e. DMEPA identifies a potential source of medication error within the proposed proprietary name. For example, the proprietary name may be misleading or, inadvertently, introduce ambiguity and confusion that leads to errors. Such errors may not necessarily involve confusion between the proposed drug and another drug product but involve a naming characteristic that when incorporated into a proprietary name may be confusing, misleading, cause or contribute to medication errors.

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

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

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

Furthermore, post-marketing experience has demonstrated that medication errors resulting from drug name confusion are notoriously difficult to rectify post-approval. Educational and other post-approval efforts are low-leverage strategies that have had limited effectiveness at alleviating medication errors involving drug name confusion. Sponsors have undertaken higher-leverage strategies, such as drug name changes, in the

past but at great financial cost to the Sponsor and at the expense of the public welfare, not to mention the Agency’s credibility as the authority responsible for approving the error-prone proprietary name. Moreover, even after Sponsors’ have changed a product’s proprietary name in the post-approval phase, it is difficult to eradicate the original proprietary name from practitioners’ vocabulary, and as a result, the Agency has continued to receive reports of drug name confusion long after a name change in some instances. Therefore, DMEPA believes that post-approval efforts at reducing name confusion errors should be reserved for those cases in which the potential for name confusion could not be predicted prior to approval.

**Appendix B:** Letters and Letter Strings with Possible Orthographic or Phonetic Misinterpretation

Letters in Name,	Scripted May Appear as	Spoken May Be Interpreted as
Upper case letter ‘O’	A, Q, 0, U, D	Oh
Lower case ‘o’	a, c, e, u	Oh
Lower case ‘r’	s, n, e, ,v	
Lower case ‘a’	el, ci, cl, d, o, u	Any Vowel
Lower case ‘l’	L	
Lower case ‘t’	f, i, l, x	d, f, p, pt, v
Lower case ‘a’	el, ci, cl, d, o, u	Any Vowel
Lower case ‘g’	q, j, s	k, j
Letter strings		
tag		tab

**Appendix C: Prescription Simulation Samples and Results**

**Figure 1. Oraltag Study (Conducted on June 20, 2013)**

Handwritten Requisition Medication Order	Verbal Prescription
<p><u>Medication Order:</u></p> <p>Oraltag send to radiology #1</p>	<p>Oraltag Bring to clinic #2</p>
<p><u>Outpatient Prescription:</u></p> <div data-bbox="196 709 915 1150" style="border: 1px solid black; padding: 5px;"><p>Patient _____ Date _____ Address _____</p><p><b>R</b></p><p>Oraltag #2 bring to clinic</p><p>Refill(s): _____ Dr. <u>Ose</u> DEA No. _____ Address _____ Telephone _____</p></div>	

**FDA Prescription Simulation Responses (Aggregate 1 Rx Studies Report)**

					190 People Received Study
					74 People Responded
Study Name: Oraltag					
<b>Total</b>	<b>27</b>	<b>27</b>	<b>20</b>	<b>74</b>	
<b>INTERPRETATION</b>	<b>OUTPATIENT</b>	<b>VOICE</b>	<b>INPATIENT</b>	<b>TOTAL</b>	
AURALTAG	0	1	0	1	
ORAL TAG	0	7	0	7	
ORAL TAG #2	0	1	0	1	
ORALTAB	0	1	0	1	
ORALTAG	25	11	7	43	
ORALTAG # 2	0	1	0	1	
ORALTAG #2	2	1	0	3	
ORALTAQ	0	0	1	1	
ORALTAY	0	0	4	4	
ORALTAZ	0	0	1	1	
ORALTRAG	0	0	1	1	
ORALTRAY	0	0	1	1	
ORATAG	0	1	0	1	
OROLTRAY	0	0	1	1	
OROTAG	0	3	0	3	
OVALTAY	0	0	2	2	
OVALTAZ	0	0	2	2	

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

No.	Proprietary Name	Active Ingredient	Similarity to Oraltag	Failure preventions
1.	Aquatag		Look	The pair have sufficient orthographic and/or phonetic differences
2.	Moxatag	Amoxicillin	Look	The pair have sufficient orthographic and/or phonetic differences
3.	Octagam	Immune Globulin IV, IVIG, IGIV	Look	The pair have sufficient orthographic and/or phonetic differences
4.	Orabloc	Articaine and Epinephrine	Look	The pair have sufficient orthographic and/or phonetic differences
5.	Oracea	Doxycycline	Look	The pair have sufficient orthographic and/or phonetic differences
6.	Orajel	Benzocaine	Look	The pair have sufficient orthographic and/or phonetic differences
7.	Oral-Ivy	Toxicodendron	Look	The pair have sufficient orthographic and/or phonetic differences
8.	Oralmat Drops	Rye extract	Look	Name identified in Natural Medicines database. Unable to find product characteristics in commonly used drug databases
9.	(b) (4)	Iohexol (b) (4) Oral Solution	Look	Applicant withdrew the proprietary name, (b) (4) Applicant has proposed the proprietary name, Oraltag. The subject of this review
10.	Oralyte	Electrolyte Solution	Look	The pair have sufficient orthographic and/or phonetic differences
11.	Orapred	Prednisolone	Look	The pair have sufficient orthographic and/or phonetic differences

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

No.	Proprietary Name	Active Ingredient	Similarity to Oraltag	Failure preventions
12.	Orasone	Prednisone	Look	The pair have sufficient orthographic and/or phonetic differences
13.	Oraspan	Ferrous fumarate and Vitamin C and Vitamin B <sub>1</sub>	Look	The pair have sufficient orthographic and/or phonetic differences
14.	Oratuss	Carbetapentane and Guaifenesin	Look	The pair have sufficient orthographic and/or phonetic differences
15.	Orectic	Hydrochlorothiazide	Look	The pair have sufficient orthographic and/or phonetic differences
16.	Orthovisc	Sodium Hyaluronate	Look	The pair have sufficient orthographic and/or phonetic differences
17.	Ultratag	Technetium Tc99m Red Blook Cell Kit	Look	The pair have sufficient orthographic and/or phonetic differences

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

No.	<p><b>Proposed name:</b> Oraltag (Iohexol <sup>(b)(4)</sup> Oral Solution)</p> <p><b>Dosage Form:</b> <sup>(b)(4)</sup> Oral Solution</p> <p><b>Strength:</b> 9.7 g (4.5 g of Iodine)</p> <p><b>Usual Dose:</b> <b>Adults:</b> 500 mL to 1,000 mL (4.5 g Iodine to 9 g Iodine) <b>Children:</b> 180 mL (neonates) 120 mL to 300 mL (infants and toddlers)</p>	<p><b>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</b></p> <p><b>Causes (could be multiple)</b></p>	<p><b>Prevention of Failure Mode</b></p> <p><b>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</b></p>
1.	<p>Oralone (Triamcinolone)</p> <p>Dosage form: Dental Paste</p> <p>Strength: 0.1%</p> <p>Usual dose: Apply to affected area(s) two to three times daily</p>	<p><u>Orthographic Similarities to Oraltag</u></p> <ul style="list-style-type: none"> <li>- The names Oraltag and Oralone share the letter string ‘Oral’.</li> <li>- When scripted Oraltag and Oralone are identical in length, 7 letters.</li> </ul> <p><u>Dosage form</u></p> <p>-Both products are available as a single dosage form, the dosage form maybe omitted when prescribed.</p> <p><u>Strength</u></p> <p>-Both products are available as a single strength products, the strength maybe omitted when prescribed.</p>	<p><u>Orthographic Differences</u></p> <ul style="list-style-type: none"> <li>- When scripted the letter string ‘-tag’ in Oraltag looks different than ‘-one’ in Oralone.</li> <li>- When scripted Oraltag has a different shape than Oralone. Oraltag has two upstrokes (‘l’ and ‘t’) in the 4<sup>th</sup> and 5<sup>th</sup> positions. Whereas, Oralone has one upstroke (‘l’) in the 4<sup>th</sup> position. Additionally, Oraltag has a downstroke (‘g’) in the 7<sup>th</sup> position.</li> </ul> <p><u>Frequency of Administration</u></p> <ul style="list-style-type: none"> <li>- Once daily administration compared to two to three times a day administration.</li> </ul> <p><u>Differing Product Characteristics</u></p> <ul style="list-style-type: none"> <li>-Dose (120 mL, 180 mL, 300, or 500 mL daily versus take as directed three times daily)</li> </ul>

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

No.	<p><b>Proposed name:</b> Oraltag (Iohexol <sup>(b) (4)</sup> Oral Solution)</p> <p><b>Dosage Form:</b> Oral Solution</p> <p><b>Strength:</b> 9.7 g (4.5 g of Iodine)</p> <p><b>Usual Dose:</b> <b>Adults:</b> 500 mL to 1,000 mL (4.5 g Iodine to 9 g Iodine) <b>Children:</b> 180 mL (neonates) 120 mL to 300 mL (infants and toddlers)</p>	<p><b>Failure Mode: Incorrect Product Ordered/ Selected/Dispensed or Administered because of Name confusion</b></p> <p><b>Causes (could be multiple)</b></p>	<p><b>Prevention of Failure Mode</b></p> <p><b>In the conditions outlined below, the following combination of factors, are expected to minimize the risk of confusion between these two names</b></p>
2.	<p>Oravig (Miconazole) Dosage form: Buccal Tablet</p> <p>Strength: 50 mg</p> <p>Usual dose: Apply one buccal tablet to upper gum daily for 14 days</p>	<p><u>Orthographic Similarities to Oraltag</u> - The names Oraltag and Oravig share the letter string ‘Ora’. - When scripted the names appear similar in length, 6 letters versus 7 letters. - Oraltag and Oravig have a downstroke (‘g’) in the last position.</p> <p><u>Dosage form</u> -Both products are available as a single dosage form, the dosage form maybe omitted when prescribed.</p> <p><u>Dosage</u> Numerical similarity overlap in dose 500 mL versus 50 mg</p> <p><u>Frequency of Administration</u> -Both products are dosed once daily.</p> <p><u>Strength</u> -Both products are available as a single strength products, the strength maybe omitted when prescribed.</p>	<p><u>Orthographic Differences</u> - When scripted the letter string ‘-lta’ in Oraltag looks different than ‘-vi’ in Oralone. - When scripted Oraltag has a different shape than Oralone. Oraltag has two upstrokes (‘l’ and ‘t’) in the 4<sup>th</sup> and 5<sup>th</sup> positions. Whereas, Oravig does not contain any upstrokes.</p>

-----  
**This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.**  
-----

/s/  
-----

CAROL A HOLQUIST on behalf of KEVIN WRIGHT  
08/30/2013  
Signing on behalf of Kevin Wright

CAROL A HOLQUIST  
08/30/2013