# CENTER FOR DRUG EVALUATION AND RESEARCH

***APPLICATION NUMBER:***

# 205917Orig1s000

# CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

10/27/14

| Clinical Pharmacology Review | |
|---|---|
| **NDA** | 205917 |
| **Submission Date:** | June 7, 2013 |
| **Goal Date:** | November 18, 2014 |
| **Brand Name:** | N/A |
| **Generic Name:** | Paricalcitol Injection |
| **Formulation/Strength:** | Injectable/2 mcg per mL, 5 mcg per mL, 10 mcg per 2 mL (5 mcg per mL) |
| **OCP Reviewer:** | Zhihong Li, Ph.D. |
| **OCP Team Leader:** | Immo Zadezensky, Ph.D. |
| **OCP Division:** | Division of Clinical Pharmacology 2 |
| **OND Division:** | Division of Metabolism and Endocrinology Products |
| **Sponsor:** | Hikma Pharmaceutical Co. Ltd. |
| **Dosing regimen:** | Initial dose: 0.04 mcg/kg to 0.1 mcg/kg (2.8 – 7 mcg) administered as a bolus dose no more frequently than every other day. The dose may be increased by 2 to 4 mcg at 2- to 4-week intervals. |
| **Indication:** | Prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5 |

In accordance with 21 CFR§314.54(a)(1)(iii) and under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355), Exela Pharma Sciences LLC submitted a New Drug Application (NDA) for Paricalcitol Injection, 2 mcg / mL and 5 mcg / mL for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5. The sponsor identified Abbott's Zemplar (paricalcitol) Injection under NDA 20819 as the reference listed drug (RLD).

Exela's formulation contains 35% v/v alcohol, whereas the concentration of alcohol is 20% v/v in Abbott's ZEMPLAR (paricalcitol) Injection. In addition, Exela's formulation contains sorbitol solution, 70%, at a concentration of 7% v/v, whereas Abbott's ZEMPLAR (paricalcitol) Injection contains propylene glycol at a concentration of 30% v/v.

No new clinical data is presented in support of the proposed drug product Paricalcitol Injection; the sponsor requests a waiver of *in vivo* Bioavailability/Bioequivalence requirements. The biowaiver request will be evaluated by the Office of New Drug Quality Assessment (ONDQA) – Biopharmaceutics.

## DETAILED LABELING RECOMMENDATIONS

The label is based on Zemplar label. Sections with recommendations from Clinical Pharmacology are included.

Texts are deleted (~~crossed out~~) and new wording added in red fonts, as follows:

2 Page(s) of Draft Labeling have been Withheld in Full as b4 (CCI/TS) immediately following this page

**Attachment I: Clinical Pharmacology Filing Memo**

# Office of Clinical Pharmacology

## *New Drug Application Filing and Review Form*

*General Information About the Submission*

| | Information | | Information |
|---|---|---|---|
| **NDA/BLA Number** | **205917** | **Brand Name** | |
| **OCP Division (I, II, III, IV, V)** | **II** | **Generic Name** | **Paricalcitol Injection** |
| **Medical Division** | **DMEP** | **Drug Class** | **Calcitriol analog, vitamin D active form** |
| **OCP Reviewer** | **Zhihong Li** | **Indication(s)** | **Prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5** |
| **OCP Team Leader** | **Immo Zadezensky** | **Dosage Form** | **Injection** |
| **Pharmacometrics Reviewer** | | **Dosing Regimen** | **Initial dose: 0.04 mcg/kg to 0.1 mcg/kg (2.8 – 7 mcg) administered as a bolus dose no more frequently than every other day. The dose may be increased by 2 to 4 mcg at 2- to 4-week intervals** |
| **Date of Submission** | **6/10/2013** | **Route of Administration** | **Intravenous** |
| **Estimated Due Date of OCP Review** | **3/2/2014** | **Sponsor** | **Hikma Pharmaceutical Co. Ltd.** |
| **Medical Division Due Date** | | **Priority Classification** | **Standard** |
| **PDUFA Due Date** | **4/10/2014** | | |

### *Clin. Pharm. and Biopharm. Information*

| | "X" if included at filing | Number of studies submitted | Number of studies reviewed | Critical Comments If any |
|---|---|---|---|---|
| **STUDY TYPE** | | | | |
| **Table of Contents present and sufficient to locate reports, tables, data, etc.** | **X** | | | |
| **Tabular Listing of All Human Studies** | **NA** | | | |
| **HPK Summary** | **NA** | | | |
| **Labeling** | **X** | | | |
| **Reference Bioanalytical and Analytical Methods** | | | | |
| **I. Clinical Pharmacology** | **NA** | **0** | | |
| **Mass balance:** | | | | |
| **Isozyme characterization:** | | | | |
| **Blood/plasma ratio:** | | | | |
| **Plasma protein binding:** | | | | |
| **Pharmacokinetics (e.g., Phase I) -** | | | | |
| **Healthy Volunteers-** | | | | |
| single dose: | | | | |
| multiple dose: | | | | |
| **Patients-** | | | | |
| single dose: | | | | |
| multiple dose: | | | | |
| **Dose proportionality -** | | | | |
| fasting / non-fasting single dose: | | | | |
| fasting / non-fasting multiple dose: | | | | |

| | | | | |
|---|---|---|---|---|
| **Drug-drug interaction studies -** | | | | |
| In-vivo effects on primary drug: | | | | |
| In-vivo effects of primary drug: | | | | |
| In-vitro: | | | | |
| **Subpopulation studies -** | | | | |
| ethnicity: | | | | |
| gender: | | | | |
| pediatrics: | | | | |
| geriatrics: | | | | |
| renal impairment: | | | | |
| hepatic impairment: | | | | |
| **PD -** | | | | |
| Phase 2: | | | | |
| Phase 3: | | | | |
| **PK/PD -** | | | | |
| Phase 1 and/or 2, proof of concept: | | | | |
| Phase 3 clinical trial: | | | | |
| **Population Analyses -** | | | | |
| Data rich: | | | | |
| Data sparse: | | | | |
| **II. Biopharmaceutics** | | | | |
| **Absolute bioavailability** | | | | |
| **Relative bioavailability -** | | | | |
| solution as reference: | | | | |
| alternate formulation as reference: | | | | |
| **Bioequivalence studies -** | | | | |
| traditional design; single / multi dose: | | | | |
| replicate design; single / multi dose: | | | | |
| **Food-drug interaction studies** | | | | |
| **Bio-waiver request based on BCS** | | | | |
| **BCS class** | | | | |
| **Dissolution study to evaluate alcohol induced dose-dumping** | | | | |
| **III. Other CPB Studies** | | | | |
| **Genotype/phenotype studies** | | | | |
| **Chronopharmacokinetics** | | | | |
| **Pediatric development plan** | | | | |
| **Literature References** | | | | |
| **Total Number of Studies** | | **0** | | |

On **initial** review of the NDA/BLA application for filing:

| | Content Parameter | Yes | No | N/A | Comment |
|---|---|---|---|---|---|
| **Criteria for Refusal to File (RTF)** | | | | | |
| 1 | Has the applicant submitted bioequivalence data comparing to-be-marketed product(s) and those used in the pivotal clinical trials? | | | X | |
| 2 | Has the applicant provided metabolism and drug-drug interaction information? | | X | | |
| 3 | Has the sponsor submitted bioavailability data satisfying the CFR requirements? | | | X | |
| 4 | Did the sponsor submit data to allow the evaluation of the validity of the analytical assay? | | | X | |
| 5 | Has a rationale for dose selection been submitted? | | | X | |
| 6 | Is the clinical pharmacology and biopharmaceutics section of the NDA organized, indexed and paginated in a manner to allow substantive review to begin? | | | X | |
| 7 | Is the clinical pharmacology and biopharmaceutics section of the NDA legible so that a substantive review can begin? | | | X | |
| 8 | Is the electronic submission searchable, does it have appropriate hyperlinks and do the hyperlinks work? | X | | | |

| Criteria for Assessing Quality of an NDA (Preliminary Assessment of Quality) | | | | | |
|---|---|---|---|---|---|
| | **Data** | | | | |
| 9 | Are the data sets, as requested during pre-submission discussions, submitted in the appropriate format (e.g., CDISC)? | | | X | |
| 10 | If applicable, are the pharmacogenomic data sets submitted in the appropriate format? | | | X | |
| | **Studies and Analyses** | | | | |
| 11 | Is the appropriate pharmacokinetic information submitted? | | | X | |
| 12 | Has the applicant made an appropriate attempt to determine reasonable dose individualization strategies for this product (i.e., appropriately designed and analyzed dose-ranging or pivotal studies)? | | | X | |
| 13 | Are the appropriate exposure-response (for desired and undesired effects) analyses conducted and submitted as described in the Exposure-Response guidance? | | | X | |
| 14 | Is there an adequate attempt by the applicant to use exposure-response relationships in order to assess the need for dose adjustments for intrinsic/extrinsic factors that might affect the pharmacokinetic or pharmacodynamics? | | | X | |
| 15 | Are the pediatric exclusivity studies adequately designed to demonstrate effectiveness, if the drug is indeed effective? | | | X | |
| 16 | Did the applicant submit all the pediatric exclusivity data, as described in the WR? | | | X | |
| 17 | Is there adequate information on the pharmacokinetics and exposure-response in the clinical pharmacology section of the label? | | | X | |
| | **General** | | | | |
| 18 | Are the clinical pharmacology and biopharmaceutics studies of appropriate design and breadth of investigation to meet basic requirements for approvability of this product? | | | X | |
| 19 | Was the translation (of study reports or other study information) from another language needed and provided in this submission? | | | X | |

**IS THE CLINICAL PHARMACOLOGY SECTION OF THE APPLICATION FILEABLE?**
**YES**

If the NDA/BLA is not fileable from the clinical pharmacology perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

None.

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/s/

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ZHIHONG LI
10/24/2014

IMMO ZADEZENSKY
10/27/2014

| BIOPHARMACEUTICS REVIEW<br>Office of New Drug Quality Assessment | | | |
|---|---|---|---|
| **Application No.:** | NDA 205-917 | **Reviewer:**<br>Assadollah Noory, PhD | |
| **Submission Dates:** | June 7, 2013, September 1, 2013 | | |
| **Division:** | Division of Pulmonary, Allergy and Rheumatology Products | **Team Leader:**<br>Tapash Ghosh, PhD | |
| **Applicant:** | HIKMA Pharmaceuticals Co, LTD | **Acting Supervisor:**<br>Richard Lostritto, PhD | |
| **Trade Name:** | Paricalcitol Injection | **Date Assigned:** | December 4, 2013 |
| **Established Name:** | Paricalcitol Injection | **Date of Review:** | January 3, 2014 |
| **Indication:** | Indicated for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5 | **Type of Submission:** Original New Drug Application – 505(b)(2) | |
| **Dosage form/ strengths** | Solution for Injection, single-use vial 2 mcg/mL, 5 mcg/mL | | |
| **Route of Administration** | IV injection | | |
| **Type of Review:** | Biowaiver Request | | |

**SUBMISSION:**

HIKMA Pharmaceuticals Co, LTD is seeking approval for their Paricalcitol injection 2 mcg/mL and 5 mcg/mL single use vials. In this 505(b)(2) application the sponsor is requesting a waiver of conducting *in vivo* bioavailability/bioequivalence studies for their intra-venous Paricalcitol Injection product. This new product is similar to the RLD (Abbot's Zemplar (paricalcitol) 2 mcg/mL and 5 mcg/mL solutions for injection) with some differences as described in the following Tables.

| | **ZEMPLAR (paricalcitol) Injection (RLD)** | **Exela's Paricalcitol Injection** |
|---|---|---|
| **Strength(s)** | 2 µg/mL and 5 µg/mL | 2 µg/mL and 5 µg/mL |
| **Configurations/ Label Claim** | 2 µg / 1 mL<br>5 µg / 1 mL<br>5 µg / 2 mL | 2 µg / 1 mL<br>5 µg / 1 mL<br>5 µg / 2 mL |
| **Active Ingredient** | Paricalcitol, USP | Paricalcitol, USP |
| (b) (4) | Propylene Glycol<br>Alcohol | Sorbitol<br>Alcohol |
| | Water for Injection | Water for Injection |
| **Dosage Form** | Injection, solution | Injection, solution |
| **Route of Administration** | Intravenous | Intravenous |

| **Ingredients** | **Exela's Formulation** | **Abbott Laboratories Formulation[1]** |
|---|---|---|
| **Paricalcitol, USP** | 2 µg/mL or 5 µg/mL | 2 µg/mL or 5 µg/mL |
| **Alcohol,** (b) (4) **USP** | 35% v/v | 20% v/v |
| **Propylene Glycol, USP** | | 30% v/v |
| **Sorbitol Solution, 70%, USP** | 7% v/v | |
| **Water for Injection, USP** | q.s. | q.s. |

[1] Information regarding Abbot Laboratories Zemplar ® (paricalcitol) Injection formulation was obtained from the current package insert, vial label, and carton.

**BIOPHARMACEUTICS INFORMATION:**

***Reviewer's Comment:***

***The proposed product has three differences from the RLD, namely inclusion of 7% v/v Sorbitol Solution, 70%, USP, elimination of propylene glycol, USP and increasing the alcohol, (b) (4), USP concentration to 35% v/v compared to 20% v/v in the RLD.***

***7% v/v Sorbitol Solution, 70%, USP and 35% v/v alcohol, (b) (4), USP have been used in previous IV formulations as documented in the Agency's "Inactive Ingredient Search for Approved Drug Products" database. In addition, no other discipline raised any other safety concern for these changes during the mid-cycle meeting held on March 6, 2014.***

***In summary, the differences in formulation between the RLD and the new product are not expected to have any impact on its efficacy, or safety. Therefore, the request for a waiver of conducting an in-vivo bioavailability study for the proposed drug products, Paricalcitol Solution for Injection single-use vial (2 mcg/mL, 5 mcg/mL) for IV administration is granted.***

**RECOMMENDATION:**

The Office of New Drug Quality Assessment Completed the review of Biopharmaceutics portion of this NDA pertaining to a biowaiver request and recommends the approval of NDA 205-917.

| **Signature** | **Signature** |
|---|---|
| Assadollah Noory, Ph.D. | Tapash Ghosh, Ph.D. |
| Biopharmaceutics Reviewer | Team Leader |
| Office of New Drug Quality Assessment | Office of New Drug Quality Assessment |

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/s/

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ASSADOLLAH NOORY
03/06/2014

TAPASH K GHOSH
03/06/2014

# CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FILING FORM/CHECKLIST FOR NDA/BLA or Supplement

# Office of Clinical Pharmacology

## *New Drug Application Filing and Review Form*

***General Information About the Submission***

| | Information | | Information |
|---|---|---|---|
| **NDA/BLA Number** | **205917** | **Brand Name** | |
| **OCP Division (I, II, III, IV, V)** | **II** | **Generic Name** | **Paricalcitol Injection** |
| **Medical Division** | **DMEP** | **Drug Class** | **Calcitriol analog, vitamin D active form** |
| **OCP Reviewer** | **Zhihong Li** | **Indication(s)** | **Prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5** |
| **OCP Team Leader** | **Immo Zadezensky** | **Dosage Form** | **Injection** |
| **Pharmacometrics Reviewer** | | **Dosing Regimen** | **Initial dose: 0.04 mcg/kg to 0.1 mcg/kg (2.8 – 7 mcg) administered as a bolus dose no more frequently than every other day.<br>The dose may be increased by 2 to 4 mcg at 2- to 4-week intervals** |
| **Date of Submission** | **6/10/2013** | **Route of Administration** | **Intravenous** |
| **Estimated Due Date of OCP Review** | **3/2/2014** | **Sponsor** | **Hikma Pharmaceutical Co. Ltd.** |
| **Medical Division Due Date** | | **Priority Classification** | **Standard** |
| **PDUFA Due Date** | **4/10/2014** | | |

### *Clin. Pharm. and Biopharm. Information*

| | "X" if included at filing | Number of studies submitted | Number of studies reviewed | Critical Comments If any |
|---|---|---|---|---|
| **STUDY TYPE** | | | | |
| **Table of Contents present and sufficient to locate reports, tables, data, etc.** | **X** | | | |
| **Tabular Listing of All Human Studies** | **NA** | | | |
| **HPK Summary** | **NA** | | | |
| **Labeling** | **X** | | | |
| **Reference Bioanalytical and Analytical Methods** | | | | |
| **I. Clinical Pharmacology** | **NA** | **0** | | |
| **Mass balance:** | | | | |
| **Isozyme characterization:** | | | | |
| **Blood/plasma ratio:** | | | | |
| **Plasma protein binding:** | | | | |
| **Pharmacokinetics (e.g., Phase I) -** | | | | |
| **Healthy Volunteers-** | | | | |
| single dose: | | | | |
| multiple dose: | | | | |
| **Patients-** | | | | |
| single dose: | | | | |
| multiple dose: | | | | |
| **Dose proportionality -** | | | | |
| fasting / non-fasting single dose: | | | | |
| fasting / non-fasting multiple dose: | | | | |
| **Drug-drug interaction studies -** | | | | |
| In-vivo effects on primary drug: | | | | |
| In-vivo effects of primary drug: | | | | |

File name: 5_Clinical Pharmacology and Biopharmaceutics Filing Form/Checklist for NDA_BLA or Supplement 090808

# CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FILING FORM/CHECKLIST FOR NDA/BLA or Supplement

| | | | | |
|---|---|---|---|---|
| In-vitro: | | | | |
| **Subpopulation studies -** | | | | |
| ethnicity: | | | | |
| gender: | | | | |
| pediatrics: | | | | |
| geriatrics: | | | | |
| renal impairment: | | | | |
| hepatic impairment: | | | | |
| **PD -** | | | | |
| Phase 2: | | | | |
| Phase 3: | | | | |
| **PK/PD -** | | | | |
| Phase 1 and/or 2, proof of concept: | | | | |
| Phase 3 clinical trial: | | | | |
| **Population Analyses -** | | | | |
| Data rich: | | | | |
| Data sparse: | | | | |
| **II. Biopharmaceutics** | | | | |
| **Absolute bioavailability** | | | | |
| **Relative bioavailability -** | | | | |
| solution as reference: | | | | |
| alternate formulation as reference: | | | | |
| **Bioequivalence studies -** | | | | |
| traditional design; single / multi dose: | | | | |
| replicate design; single / multi dose: | | | | |
| **Food-drug interaction studies** | | | | |
| **Bio-waiver request based on BCS** | | | | |
| **BCS class** | | | | |
| **Dissolution study to evaluate alcohol induced dose-dumping** | | | | |
| **III. Other CPB Studies** | | | | |
| **Genotype/phenotype studies** | | | | |
| **Chronopharmacokinetics** | | | | |
| **Pediatric development plan** | | | | |
| **Literature References** | | | | |
| **Total Number of Studies** | | **0** | | |

On **initial** review of the NDA/BLA application for filing:

| | Content Parameter | Yes | No | N/A | Comment |
|---|---|---|---|---|---|
| **Criteria for Refusal to File (RTF)** | | | | | |
| 1 | Has the applicant submitted bioequivalence data comparing to-be-marketed product(s) and those used in the pivotal clinical trials? | | | X | |
| 2 | Has the applicant provided metabolism and drug-drug interaction information? | | X | | |
| 3 | Has the sponsor submitted bioavailability data satisfying the CFR requirements? | | | X | |
| 4 | Did the sponsor submit data to allow the evaluation of the validity of the analytical assay? | | | X | |
| 5 | Has a rationale for dose selection been submitted? | | | X | |
| 6 | Is the clinical pharmacology and biopharmaceutics section of the NDA organized, indexed and paginated in a manner to allow substantive review to begin? | | | X | |
| 7 | Is the clinical pharmacology and biopharmaceutics section of the NDA legible so that a substantive review can begin? | | | X | |
| 8 | Is the electronic submission searchable, does it have appropriate hyperlinks and do the hyperlinks work? | X | | | |

File name: 5_Clinical Pharmacology and Biopharmaceutics Filing Form/Checklist for NDA_BLA or Supplement 090808

# CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FILING FORM/CHECKLIST FOR NDA/BLA or Supplement

| Criteria for Assessing Quality of an NDA (Preliminary Assessment of Quality) | | | | | |
|---|---|---|---|---|---|
| | **Data** | | | | |
| 9 | Are the data sets, as requested during pre-submission discussions, submitted in the appropriate format (e.g., CDISC)? | | | X | |
| 10 | If applicable, are the pharmacogenomic data sets submitted in the appropriate format? | | | X | |
| | **Studies and Analyses** | | | | |
| 11 | Is the appropriate pharmacokinetic information submitted? | | | X | |
| 12 | Has the applicant made an appropriate attempt to determine reasonable dose individualization strategies for this product (i.e., appropriately designed and analyzed dose-ranging or pivotal studies)? | | | X | |
| 13 | Are the appropriate exposure-response (for desired and undesired effects) analyses conducted and submitted as described in the Exposure-Response guidance? | | | X | |
| 14 | Is there an adequate attempt by the applicant to use exposure-response relationships in order to assess the need for dose adjustments for intrinsic/extrinsic factors that might affect the pharmacokinetic or pharmacodynamics? | | | X | |
| 15 | Are the pediatric exclusivity studies adequately designed to demonstrate effectiveness, if the drug is indeed effective? | | | X | |
| 16 | Did the applicant submit all the pediatric exclusivity data, as described in the WR? | | | X | |
| 17 | Is there adequate information on the pharmacokinetics and exposure-response in the clinical pharmacology section of the label? | | | X | |
| | **General** | | | | |
| 18 | Are the clinical pharmacology and biopharmaceutics studies of appropriate design and breadth of investigation to meet basic requirements for approvability of this product? | | | X | |
| 19 | Was the translation (of study reports or other study information) from another language needed and provided in this submission? | | | X | |

**IS THE CLINICAL PHARMACOLOGY SECTION OF THE APPLICATION FILEABLE?**
**YES**

If the NDA/BLA is not fileable from the clinical pharmacology perspective, state the reasons and provide comments to be sent to the Applicant.

Please identify and list any potential review issues to be forwarded to the Applicant for the 74-day letter.

None.

| | |
|---|---|
| Zhihong Li, Ph.D. | 9/12/2014 |
| Reviewing Clinical Pharmacologist | Date |
| Immo Zadezensky, Ph.D. | 9/12/2014 |
| Team Leader/Supervisor | Date |

File name: 5_Clinical Pharmacology and Biopharmaceutics Filing Form/Checklist for NDA_BLA or Supplement 090808

# CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS FILING FORM/CHECKLIST FOR NDA/BLA or Supplement

**RECOMMENDATIONS:**

- This NDA application is fileable from a clinical pharmacology perspective
- No comments in the 74-day letter

**BACKGROUND:**

In accordance with 21 CFR§314.54(a)(1)(iii) and under Section 505(b)(2) of the Federal Food, Drug and Cosmetic Act (21 U.S.C. 355), the sponsor submitted a New Drug Application (NDA) for Paricalcitol Injection, 2 mcg / mL and 5 mcg / mL for the prevention and treatment of secondary hyperparathyroidism associated with chronic kidney disease Stage 5. The sponsor identified Abbott's Zemplar (paricalcitol) Injection under NDA 20819 as the reference listed drug (RLD).

Exela's formulation contains 35% v/v alcohol, whereas the concentration of alcohol is 20% v/v in Abbott's ZEMPLAR (paricalcitol) Injection. In addition, Exela's formulation contains sorbitol solution, 70%, at a concentration of 7% v/v, whereas Abbott's ZEMPLAR (paricalcitol) Injection contains propylene glycol at a concentration of 30% v/v.

No new clinical data is presented in support of the proposed drug product Paricalcitol Injection; the sponsor requests a waiver of *in vivo* Bioavailability/Bioequivalence requirements. The biowaiver request will be evaluated by the Office of New Drug Quality Assessment (ONDQA) – Biopharmaceutics.

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/s/

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ZHIHONG LI
09/12/2013

IMMO ZADEZENSKY
09/12/2013