CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

022534Orig1s000

MEDICAL REVIEW(S)

CLINICAL REVIEW

Application Type	NDA 505(b)(2)
Submission Number	NDA 22534
Submission Code	Class 2, Resubmission
Letter Date	November 3, 2010
Stamp Date	November 3, 2010
PDUFA Goal Date	May 3, 2011
Reviewer Name	Kristen M. Snyder, MD
Clinical Team Leader	Patricia Cortazar, MD
Review Completion Date	April 8, 2011
Established Name	docetaxel
Trade Name	Docefrez
Reference NDA	20449
Therapeutic Class	Disruptor of microtubule network
Applicant	Sun Pharmaceutical Ind. Ltd
Priority Designation	Not Applicable
Formulation	IV
Dosing Regimen	Multiple (see product information, 2.1)
Indication	Multiple (see product information, 2.1)
Intended Population	Multiple (see product information, 2.1)

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1 Recommendations/Risk Benefit Assessment

1.1 Recommendation on Regulatory Action

This NDA for Docefrez, in accordance with section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, was submitted to request approval of the therapeutic equivalence of the proposed product to Taxotere®, as defined in the FDA orange book. The sponsor of NDA 20449 for Taxotere® is sanofi-aventis.

The exclusivity of the Taxotere® indications below has expired.

Breast Cancer

- Docetaxel Injection is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
- Docetaxel Injection in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Non-Small Cell Lung Cancer

- Docetaxel Injection as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy.
- Docetaxel Injection in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition.

Prostate Cancer

- Docetaxel Injection in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.

Gastric Adenocarcinoma

- Docetaxel injection in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

Head and Neck Cancer

- Docetaxel injection in combination with cisplatin and fluorouracil is indicated for the induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

No new clinical data was submitted for this NDA. The Taxotere NDA 20449 has been previously reviewed for efficacy and safety. The applicant submitted Docefrez for use in the following indications:

- **Breast Cancer (BC)**: single agent for locally advanced or metastatic BC after chemotherapy failure
- **Non-Small Cell Lung Cancer (NSCLC)**: single agent for locally advanced or metastatic NSCLC after platinum therapy failure
- **Hormone Refractory Prostate Cancer (HRPC)**: with prednisone in androgen independent (hormone refractory) metastatic prostate cancer

Therefore, the medical reviewer recommends approval of Docefrez as a single agent for the above indications (BC, NSCLC, HRPC). The recommendation for the application is approval with respect to the chemistry, manufacturing, and controls (CMC). See CMC reviews by Debasis Ghosh and Angelica Dorantes.

1.2 Risk Benefit Assessment

Please refer to NDA 20449.

2 Introduction and Regulatory Background

2.1 Product Information

Established Name: docetaxel

Proprietary Name: Docefrez

Applicant: Sun Pharmaceutical Industries. Ltd.
Executive Suite
P.O. Box 122304
Sharjah, United Arab Emirates

US Agent: Salamandra, LLC
Attention: Karin A. Kook, Ph.D.
4800 Hampden Lane, Suite 900
Bethesda, MD 20814-2998
Tel: (301) 652-6110
Fax: (301) 652-6739

Drug Class: Disruptor of microtubule network

Proposed Indications:

Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure

Non-Small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure

Hormone Refractory Prostate Cancer (HRPC): with prednisone in androgen independent (hormone refractory) metastatic prostate cancer.

Proposed Dosage and Administration

Administered IV over 1 hr every 3 weeks for the following cancers:

- BC, locally advanced or metastatic: 60-100 mg/m^2 single agent
- NSCLC: after platinum therapy failure: 75 mg/m^2 single agent
- HRPC: 75 mg/m^2 with 5 mg prednisone twice a day continuously

Reviewer's Comments: The pediatric use information for the reference listed product (RLP) is based on data submitted in response to a pediatric written request is protected by Pediatric Exclusivity under the Best Pharmaceuticals for Children Act (BPCA) until May 13, 2013. While the innovator product was issued a pediatric written request, fairly complied with the terms of the WR, and received pediatric exclusivity no pediatric indication was sought. The labeling provides information regarding safety and dosing (including dose-limiting toxicity). Similarly, the question of whether pediatric language in labeling should be "carved-out" or retained in 505(b)(2) applications resulted in a consult to the Pediatric and Maternal Health staff regarding another 505(b)(2) application (NDA 200795) and its RLP (Gemcitabine). The BPCA does not address the protected pediatric information of 505(b)(2) products, only generic products. Therefore, the PMH staff believes omitting pediatric language may be appropriate for a 505b2 product when removal of the language will not result in a safety concern for pediatric patients.

Because the RLP (Taxotere®) is not indicated for use in the pediatric population and toxicities seen in pediatric patients were similar to those seen in adults, Docefrez, if used in the pediatric oncology population, is unlikely to pose a significant or unknown safety risk.

Premedication Regimen

- Oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg twice a day) for 3 days starting 1 day before administration

- HRPC: oral dexamethasone 8 mg at 12, 3, and 1 hr before treatment

For dosage adjustments during treatment see full prescribing information.

Dosage Forms and Strengths

- Single use vial 80 mg docetaxel and Diluent for 80 mg
- Single use vial 20 mg docetaxel and Diluent for 20 mg

Contraindications

- Hypersensitivity to docetaxel injection or polysorbate 80
- Neutrophil counts of <1500 cells/mm^3

Warnings and Precautions

- Acute myeloid leukemia: In patients who received docetaxel, doxorubicin and cyclophosphamide, monitor for delayed myelodysplasia or myeloid leukemia.
- Cutaneous reactions: Reactions including erythema of the extremities with edema followed by desquamation may occur. Severe skin toxicity may require dose adjustment
- Neurologic reactions: Reactions including. paresthesia, dysesthesia, and pain may occur. Severe neurosensory symptoms require dose adjustment or discontinuation if persistent.
- Asthenia: Severe asthenia may occur and may require treatment discontinuation.
- Pregnancy: Fetal harm can occur when administered to a pregnant woman. Women of childbearing potential should be advised not to become pregnant when receiving DOCEFREZ

Adverse Reactions

The most common adverse reactions are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions, and myalgia.

2.2 Availability of Proposed Active Ingredient in the United States

Taxotere® (docetaxel) is marketed in the US. Docefrez is to be marketed in the US.

2.3 Summary of Resubmission Regulatory Activity Related to Submission

The applicant received tentative approval February 23, 2010.

2.4 Pediatric Waiver

Pediatric exclusivity of Taxotere® ended on November 14, 2010.

2.5 Other Relevant Background Information

Table 1: Patent Data for TAXOTERE Injection Concentrate

Patent Number	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Certification	21 CFR Reference
4814470	May 14, 2010	X	X	Paragraph II	314.50(i)(1)(i)(A)(3)
4814470*PED	Nov 14, 2010				
5438072	Nov 22, 2013		X	Paragraph IV	314.50(i)(1)(i)(A)(4)
5438072*PED	May 22, 2014				
5698582	Jul 03, 2012		X	Paragraph IV	314:50(i)(1)(i)(A)(4)
5698582*PED	Jan 03, 2013				
5714512	Jul 03, 2012		X	Paragraph IV	314.50(i)(1)(i)(A)(4)
5714512*PED	Jan 03, 2013				
5750561	Jul 03, 2012		X	Paragraph IV	314.50(i)(1)(i)(A)(4)
5750561*PED	Jan 3, 2013				

Table 2: Exclusivity Data* for TAXOTERE Injection Concentrate

Exclusivity Code	Exclusivity Definition	Exclusivity Expiration	Action if not Expired
I-429	For use in combination with prednisone for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.	May 19, 2007	Expired
I-436	For use in combination with doxorubicin and cyclophosphamide for the adjuvant treatment of patients with operable node-positive breast cancer.	Aug 18, 2007	Expired
I-490	For use in combination with Cisplatin and 5-FU for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease	Mar 22, 2009	Expired

I-519	For use in combination with Cisplatin and 5-FU in patients with inoperable HNSCC prior to definitive treatment.	Oct 17, 2009	Expired
I-542	Expansion of patient population for head and neck cancer from “inoperable” patients to all patients.	Sep 28, 2010	Expired
I-543	For use in combination with Cisplatin and 5-FU in patients with advanced HNSCC prior to definitive treatment.	Sep 28, 2010	Expired
PED	Pediatric exclusivity	Mar 28, 2011	Carved Out
M-61	Revisions to labeling based on data submitted in response to pediatric written request	May 13, 2013	Carved Out
PED	Pediatric exclusivity	Nov 13, 2013	Carved Out

3 Significant Efficacy/Safety Issues Related to Other Review Disciplines

Please refer to NDA 20449 CMC, Pharmacology/Toxicology, and Clinical Pharmacology reviews, NDA 22534 CMC reviews, and the labeling.

4 Sources of Clinical Data

Refer to NDA 20449.

5 Review of Efficacy

Refer to NDA 20449.

6 Review of Safety

Refer to NDA 20449.

7 Appendices

7.1 Literature Review/References

Refer to NDA 20449.

7.2 Labeling Recommendations

See final labeling and carton and container labels. The clinical safety and efficacy are based on the Taxotere® (NDA 20449) labeling. Although the applicant proposed all removal of any reference to acute myeloid leukemia and/or myelodysplasia we asked this to remain in the labeling given the likelihood that Docefrez will be used in combination therapy and thus patients may be at a similar risk of developing acute myeloid leukemia

and/or myelodysplasia. The clinical team is in agreement with the final approved labeling, carton and container labels.

7.3 Advisory Committee Meeting

None

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/s/

KRISTEN M SNYDER
04/13/2011

PATRICIA CORTAZAR
04/13/2011

Summary Review for Regulatory Action

Date	(electronic stamp)
From	Anthony J. Murgo, M.D., M.S.; DDOP, Acting DDD
Subject	Acting Deputy Director Summary
NDA 505(b)(2)	# 22-534
Applicant Name	Sun Pharma Global FZE
Date of Submission	April 23, 2009
PDUFA Goal Date	February 23, 2010 (Standard)
Proprietary Name / Established (USAN) Name	Docefrez™ Injection/Docetaxel Injection
Dosage Forms / Strength	• 20 mg (b) (4) single-use vial and diluent • 80 mg (b) (4) single-use vial and diluent
Proposed Indication(s)	1. Breast cancer 2. Non-small cell lung cancer 3. Prostate cancer (b) (4)
Action/Recommended Action for NME:	Tentative Approval

Material Reviewed/Consulted OND Action Package, including:	
Medical Officer Review	X
Statistical Review	
Pharmacology Toxicology Review	X
CMC Review/OBP Review	X
Microbiology Review	X
Clinical Pharmacology Review	X
DDMAC	X (labeling)
DSI	
CDTL Review	
OSE/DMEPA	X (labeling)
OSE/DDRE	
OSE/DRISK	X (labeling)
Other	

OND=Office of New Drugs
DDMAC=Division of Drug Marketing, Advertising and Communication
OSE= Office of Surveillance and Epidemiology
DMEPA=Division of Medication Error Prevention and Analysis
DSI=Division of Scientific Investigations
DDRE= Division of Drug Risk Evaluation
DRISK=Division of Risk Management
CDTL=Cross-Discipline Team Leader

Signatory Authority Review

1. Introduction

This 505(b)(2) NDA is for DOCEFREZ (docetaxel) for Injection. The sponsor is Sun Pharma and the reference listed drug (RLD) is Taxotere (docetaxel) Injection, 20 and 80 mg vials (NDA 20449; sponsor Sanofi-Aventis). The current 505(b)(2) application does not include clinical studies and relies on the FDA's findings of safety and effectiveness for Taxotere® for Injection (NDA 20-449). Since there are no new clinical data, the review focused on CMC and non-clinical pharmacology and toxicology information.

2. Background

The following summarizes the difference between Sun Pharma Docefrez (docetaxel) and the RLD: The RLD Taxotere® under NDA 20-449 is a solution formulation (40mg base/mL), which is reconstituted with sterile WFI, USP. In the case of Sun Pharma's docetaxel, the drug is formulated as a lyophilized powder, which is initially diluted with a different excipient, 35.4% w/w ethanol in polysorbate 80. The contents of the two single-use vials (20 mg/ (b) (4) and 80 mg (b) (4) strengths) are intended for reconstitution and further dilution in 5% dextrose or 0.9% sodium chloride prior to administration by intravenous infusion.

Docetaxel is an antineoplastic agent with anti-tumor activity against a variety of solid tumors. The (b) (4) Head and Neck cancer indication is not requested. The exclusivity for the RLD's Head and Neck cancer indication is due to expire on September 28, 2010.

The specific indications proposed for DOCEFREZ are as follows:

- Breast cancer in patients with locally advanced or metastatic cancer following failure of prior chemotherapy (b) (4)
- Non-small cell lung cancer (NSCLC), locally advanced or metastatic, following failure of platinum-based therap (b) (4)
- Prostate cancer in combination with prednisolone for treatment of androgen independent (hormone refractory) metastatic cancer (b) (4)

3. CMC

The major CMC issue was related to level of one drug substance impurity (b) (4) Sun Pharma has requested the qualification of impurity (b) (4) in

the drug substance (see non-clinical Pharmacology/Toxicology review below). The rest of the drug substance impurities at release are controlled at or below ICHQ3A.

The proposed shelf-life of (b) (4) (when stored between 2°C-8°C [36°F-46°F], protected from bright light) is acceptable.

I concur with the conclusions reached by the chemistry review (signed 2/17/10) regarding the acceptability of the perspective of chemistry, manufacturing, and controls of the drug product and drug substance. Manufacturing site inspections were acceptable.

4. Nonclinical Pharmacology/Toxicology

There were two areas in the pharmacology/toxicology review of note, one pertaining to the qualification of one of the impurities and the other pertaining to a 2009 Citizen's Petition submitted by Sanofi-Aventis.

All Docefrez impurities/degradants (b) (4) were found to be within ICH Q3B(R2) (b) (4). However, the (b) (4) impurity was qualified in a toxicology study in mice, bridging the reference listed drug (RLD) to Docefrez.

The Citizen's Petition submitted to the agency by Sanofi raised the concern (b) (4) Therefore, the Petition does not apply to Docefrez.

I concur with the conclusions reached by the pharmacology/toxicology review (signed 2/18/10) that there are no outstanding pharmacology/toxicology issues that preclude approval.

5. Clinical Pharmacology/Biopharmaceutics

I concur with the conclusions reached by the clinical pharmacology/biopharmaceutics review (signed 01/15/2010) that there are no outstanding clinical pharmacology issues and that the application is acceptable from that discipline's perspective.

6. Clinical Microbiology

N/A

7. Clinical/Statistical-Efficacy

Not applicable. This 505(b)(2) application does not include clinical studies and relies on the FDA's findings of safety and effectiveness for Taxotere® for Injection (NDA 20-449).

8. Safety

Not applicable.

9. Advisory Committee Meeting

Not applicable.

10. Pediatrics

A full pediatric waiver request was submitted with NDA 22534 application. The waiver was granted by PeRC on November 19, 2009 because there are very few pediatric patients, if any, with the proposed indications (i.e., breast cancer, lung cancer, prostate cancer (b) (4)).

11. Other Relevant Regulatory Issues

All the RLD exclusivities are expired except for the Head and Neck cancer indications, but the Head and Neck indications are not included in this 505(b)(2) application. However, there is a 30-month stay on a Civil Action on patent infringement against this application, which does not end until February 20, 2012.

12. Labeling

Multiple FDA disciplines have reviewed the drug labeling, including the package insert, patient PPI, and carton and container labels. Recommended revisions have been shared with the sponsor for comment. Final revisions of the labeling will be attached to the action letter.

13. Decision/Action/Risk Benefit Assessment

Regulatory Action:
Because the 30-month stay on a Civil Action against this application does not end until February 20, 2012, a tentative approval will be issued.

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22534	ORIG-1	SUN PHARMA GLOBAL FZE	DOCEFREZ INJECTION (20/80 MG/VIAL)

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/s/

ANTHONY J MURGO
02/22/2010

CLINICAL REVIEW

Application Type	NDA 505(b)(2)
Submission Number	22534
Submission Code	000
Letter Date	Apr 23, 2009
Stamp Date	Apr 28, 2009
PDUFA Goal Date	Jan 10, 2010
Reviewer Name	Qin Ryan, MD, PhD
Clinical Team Leader	V. Ellen Maher, MD
Review Completion Date	May. 29, 2009
Established Name	docetaxel
Trade Name	Docetaxel Injection
Reference NDA	20449
Therapeutic Class	Microtubule disregulator and antineoplastic
Applicant	Salamandra LLC
Priority Designation	S
Formulation	IV
Dosing Regimen	Multiple (see product information, 2.1)
Indication	Multiple (see product information, 2.1)
Intended Population	Multiple (see product information, 2.1)

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1 Recommendations/Risk Benefit Assessment

1.1 Recommendation on Regulatory Action

This NDA for docetaxel injection, in accordance with section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, was submitted to request approval of therapeutic equivalence of the proposed product to Taxotere, as defined in the FDA orange book. The sponsor of NDA 20449 for Taxotere is sanofi-aventis. The exclusivity of the indications below has expired.

Breast Cancer
- Docetaxel Injection is indicated for the treatment of patients with locally advanced or metastatic breast cancer after failure of prior chemotherapy.
- Docetaxel Injection in combination with doxorubicin and cyclophosphamide is indicated for the adjuvant treatment of patients with operable node-positive breast cancer.

Non-Small Cell Lung Cancer
- Docetaxel Injection as a single agent is indicated for the treatment of patients with locally advanced or metastatic non-small cell lung cancer after failure of prior platinum-based chemotherapy.
- Docetaxel Injection in combination with cisplatin is indicated for the treatment of patients with unresectable, locally advanced or metastatic non-small cell lung cancer who have not previously received chemotherapy for this condition.

Prostate Cancer
- Docetaxel Injection in combination with prednisone is indicated for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.

Gastric Adenocarcinoma
- Docetaxel injection in combination with cisplatin and fluorouracil is indicated for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of the gastroesophageal junction, who have not received prior chemotherapy for advanced disease.

No new clinical data was submitted for this NDA. The Taxotere NDA 20449 has been previously reviewed for efficacy and safety. Therefore, the medical reviewer recommends approval (if pharmacological equivalence is established) for all of the above indications.

The exclusivity for the following indication will expire on September 28, 2010.

Head and Neck Cancer
- Docetaxel injection in combination with cisplatin and fluorouracil is indicated for induction treatment of patients with locally advanced squamous cell carcinoma of the head and neck (SCCHN).

1.2 Risk Benefit Assessment

Please refer to NDA 20449.

2 Introduction and Regulatory Background

2.1 Product Information

Established Name: docetaxel

Proprietary Name: Docefrez

Applicant: Salamandra LLC
4800 Hampden Ln, Suite 900
Bethesda, MD 20814
Tel: (301) 652-6100
Fax: (301) 652-6739
kkook@salamandra.net

Drug Class: Microtubule disregulator and antineoplastic

Proposed Indications:

Breast Cancer (BC): single agent for locally advanced or metastatic BC after chemotherapy failure (b) (4)

Non-Small Cell Lung Cancer (NSCLC): single agent for locally advanced or metastatic NSCLC after platinum therapy failure (b) (4)

Hormone Refractory Prostate Cancer (HRPC): with prednisone in androgen independent (hormone refractory) metastatic prostate cancer.

(b) (4)

Proposed Dosage and Administration

Administered IV over 1 hr every 3 weeks for the following cancers:

- BC, locally advanced or metastatic: 60-100 mg/m^2 single agent.

(b) (4)

- NSCLC: chemotherapy-naïve: 75 mg/m^2 (b) (4)
- HRPC: 75 mg/m^2 with 5 mg prednisone twice a day continuously

(b) (4)

Reviewer: The applicant did not apply for the Taxotere indication "NSCLC: single agent for locally advanced or metastatic NSCLC after platinum therapy failure." The exclusivity has expired for this indication.

The applicant also did not apply for the following indications, still under exclusivity.

Induction chemotherapy of inoperable SCCHN followed by radiotherapy: 75 mg/m2 followed by cisplatin 75 mg/m2 IV (day 1), followed by fluorouracil 750 mg/m2 per day as a continuous 24-hr IV infusion (days 1-5) for 4 cycles.

Induction chemotherapy followed by chemoradiotherapy of locally advanced SCCHN: 75 mg/m2 followed by cisplatin 100 mg/m2 IV (day 1), followed by fluorouracil 1000 mg/m2 per day as a continuous 24-hr IV infusion (days 1-4) for 3 cycles.

Premedication Regimen

- Oral corticosteroids such as dexamethasone 16 mg per day (e.g., 8 mg twice a day) for 3 days starting 1 day before administration
- HRPC: oral dexamethasone 8 mg, at 12, 3, and 1 hr before treatment

For dosage adjustments during treatment see full prescribing information.

Dosage Forms and Strengths

- 20 mg (b) (4) vial and diluent
- 80 mg (b) (4) vial and diluent

Contraindications

- Hypersensitivity to Docetaxel Injection or polysorbate 80
- Neutrophil counts of <1500 cells/mm^3

Warnings and Precautions

- Acute myeloid leukemia

- Fetal harm can occur when administered to a pregnant woman. Women of childbearing potential should be advised not to become pregnant when taking Docetaxel Injection
- Asthenia

Adverse Reactions
The most common adverse reactions are infections, neutropenia, anemia, febrile neutropenia, hypersensitivity, thrombocytopenia, neuropathy, dysgeusia, dyspnea, constipation, anorexia, nail disorders, fluid retention, asthenia, pain, nausea, diarrhea, vomiting, mucositis, alopecia, skin reactions, and myalgia.

2.2 Availability of Proposed Active Ingredient in the United States

Taxotere is marketed in the US.

2.3 Summary of Presubmission Regulatory Activity Related to Submission

Dec 18, 2007, original IND (b) (4) was submitted.

June 16, 2008: Pre-IND meeting to discuss NDA submission plan

Apr 23, 2009: Salamandra LLC submitted NDA 22534.

2.4 Pediatric Waiver

A full pediatric waiver request was submitted with NDA 22534 submission. The waiver is granted because there are very few pediatric patients, if any, which would have breast cancer, lung cancer, prostate cancer (b) (4)

2.5 Other Relevant Background Information

Refer to NDA 20449

Table 1: Patent Data for TAXOTERE Injection Concentrate

Patent Number	Patent Expiration	Drug Substance Claim	Drug Product Claim	Patent Certification	21 CFR Reference
4814470	14 May 2010	X	X	Paragraph II	314 50(i)(1)(i)(A)(3)
5438072	22 Nov 2013	X		Paragraph IV	314.50(i)(1) (i)(A)(4)
5698582	03 Jul 2012	X		Paragraph IV	314:50(i)(1)(i)(A)(4)
5714512	03 Jul 2012	X		Paragraph IV	314.50(i)(1)(i)(A)(4)
5750561	03 Jul 2012	X		Paragraph IV	314.50(i)(1)(i)(A)(4)

Table 2: Exclusivity Data* for TAXOTERE Injection Concentrate

Exclusivity Code	Exclusivity Definition	Exclusivity Expiration
I-429	For use in combination with prednisone for the treatment of patients with androgen independent (hormone refractory) metastatic prostate cancer.	May 19, 2007
I-436	For use in combination with doxorubicin and cyclophosphamide for the adjuvant treatment of patients with operable node-positive breast cancer.	Aug 18, 2007
I-490	For use in combination with Cisplatin and 5-FU for the treatment of patients with advanced gastric adenocarcinoma, including adenocarcinoma of prior chemotherapy for advanced disease	Mar 22,2009
I-519	For use in combination with Cisplatin and 5-FU in patients with inoperable HNSCC prior to definitive treatment.	Oct 17, 2009
I-542	Expansion of patient population for head and neck cancer from "inoperable" patients to all patients.	Sep 28, 2010
I-543	For use in combination with Cisplatin and 5-FU in patients with advanced HNSCC prior to definitive treatment.	Sep 28, 2010

* No exclusivity information remains in Orange Book for NSCLC indication.

3 Significant Efficacy/Safety Issues Related to Other Review Disciplines

Please refer to NDA 20449 CMC, Pharmacology/Toxicology, and Clinical Pharmacology reviews, NDA 22534 CMC review, and the label.

4 Sources of Clinical Data

Refer to NDA 20449.

5 Review of Efficacy

Refer to NDA 20449.

6 Review of Safety

Refer to NDA 20449.

7 Appendices

7.1 Literature Review/References

Refer to NDA 20449.

7.2 Labeling Recommendations

See final label.

7.3 Advisory Committee Meeting

None

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22534	ORIG-1	SUN PHARMA GLOBAL FZE	DOCEFREZ INJECTION (20/80 MG/VIAL)

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/s/

QIN C RYAN
11/16/2009

VIRGINIA E MAHER
11/19/2009