July 25, 2006

Division of Dockets Management
Food and Drug Administration 1238 '06 JUL 25 P2:07
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

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The undersigned, on behalf of a client submits this petition under section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and 21 CFR § 314.93 and 21 CFR §10.30 to request the Commissioner of Food and Drugs to make a determination that the discontinued formulation of ELOXATIN® (Oxaliplatin for injection) containing sterile lyophilized powder in a vial, is suitable for submission as an Abbreviated New Drug Application (ANDA).

A. Action Requested

The petitioner requests the Commissioner of Food and Drugs to make a determination that the discontinued formulations of ELOXATIN® (Oxaliplatin for injection) containing Oxaliplatin 50 mg and 100 mg per vial were not discontinued for safety and efficacy reasons. The petitioner particularly requests the FDA to make a determination that the proposed generic product referring to the originally approved formulation (now discontinued) would not render the product less safe or effective than the currently marketed innovator's product. The petitioner further requests the FDA to accept Abbreviated New Drug Application (ANDA) for Oxaliplatin for Injection (hereinafter referred to as "proposed generic product") containing Oxaliplatin 50 mg /vial and 100 mg/ vial for the reasons discussed herein below.

B. Statement of Grounds

I. Background:

The active ingredient in ELOXATIN® (Oxaliplatin injection) is Oxaliplatin, an antineoplastic agent, that undergoes nonenzymatic conversion in physiologic solutions to active derivatives via displacement of the labile oxalate ligand. ELOXATIN® (Oxaliplatin injection), used in combination with infusional 5-FU/LV is indicated for adjuvant treatment of stage III colon cancer patients who have undergone complete resection of the primary tumor and for treatment of advanced carcinoma of the colon or rectum. ELOXATIN® was available in both forms viz. lyophilized powder for injection and aqueous solution. As both the forms were listed in orange book as RLD, the proposed generic product has been developed as lyophilized form. Now in the list for "Addition/Deletion for Prescription and OTC Drug Products Lists", updated on 14 July, 06, the lyophilized form of RLD, ELOXATIN® (Oxaliplatin for Injection) has been identified as discontinued. The concentration of lyophilized powder for injection for RLD and proposed generic product, after reconstitution is 5 mg/mL, which is identical with concentration of 5 mg/mL for aqueous solution. Additional inactive ingredient Lactose monohydrate, NF (450 mg Lactose monohydrate in 50 mg/vial and 900 mg Lactose monohydrate in 100 mg/vial) was present in ELOXATIN® (Oxaliplatin for Injection). Whereas in ELOXATIN® (Oxaliplatin injection) water for injection is an inactive ingredient. The

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current version of the Orange book now lists lyophilized powder for Injection, ELOXATIN® (Oxaliplatin for Injection) under Discontinued Drug Products section, indicating this product is no longer marketed.

Originally approved formulation: ELOXATIN® (Oxaliplatin for injection), containing oxaliplatin manufactured by Sanofi Aventis was first approved on August 9, 2002 under NDA 021492. The product was supplied in a clear glass, single use vials fitted with a elastomeric stoppers and aluminum flip off seals containing 50 mg or 100 mg of oxaliplatin as a sterile, preservative-free lyophilized powder for reconstitution. Recommended storage temperature was at 25°C under normal lighting conditions. Lactose monohydrate was present as an inactive ingredient. It was recommended that each vial of be reconstituted with 10 mL (for 50 mg vial) or 20 mL (for 100 mg vial) of Water for injection or 5 % Dextrose Injection, USP.

The reconstituted solution was further diluted in an infusion solution of 250-500mL of 5 % Dextrose Injection, USP. After reconstitution in the original vial the solution may be stored upto 24 hours under 2-8 °C. After final dilution with 250-500 mL of 5 % Dextrose Injection, USP the shelf life was 6 hours at room temperature or upto 24 hours at 2-8°C.

A copy of the first approved labeling is provided herewith as Exhibit I.

Second formulation: ELOXATIN® (Oxaliplatin injection), containing oxaliplatin manufactured by Sanofi Aventis was later on approved on January 31, 2005 under NDA 021759 this currently marketed product is supplied in clear, glass, single-use vials with gray elastomeric stoppers and aluminum flip-off seals containing 50 mg or 100 mg of oxaliplatin as a sterile preservative-free, aqueous solution at a concentration of 5 mg/mL. Water for Injection, USP is present as an inactive ingredient. The injection solution is further diluted in an infusion solution of 250-500mL of 5 % Dextrose Injection, USP. After dilution with 250-500 mL of 5 % Dextrose Injection, USP, the shelf life is 6 hours at room temperature or upto 24 hours at 2-8°C.

A copy of the labeling currently approved is provided herewith as Exhibit II.

II. Referencing discontinued labeling:

It is known from the Code of Federal Regulations that when an ANDA makes a reference to a discontinued label of a drug, FDA may still approve the ANDA upon determination that the formulation was not withdrawn for reasons of safety or effectiveness (21 U.S.C. Section 355 (j)(6) and 21 CFR §§ 314.122 and 314.161).[1] Similarly FDA is also authorized to approve an ANDA that omits in its labeling an indication or other aspects for the listed drug. The regulation 21 CFR § 314.94(a)(9)(iii)[2] permits ANDA application to seek approval for parenteral products that differ in inactive ingredient. The proposed generic formulation for Oxaliplatin for Injection is identical with discontinued formulation of ELOXATIN® (Oxaliplatin for Injection), in its dosage form and formula.

[1] Although the regulations are consistent with relief sought, this citizen petition is submitted pursuant to section 505(j)(2)(C) of the Federal Food Drug, and Cosmetic Act ("The FDC Act") and 21 CFR § 314.93.

[2] 21 CFR § 314.94 (a)(9)(iii) : "Inactive ingredient changes permitted in drug products intended for parenteral use". An applicant may seek approval of a drug product that differs from the reference listed drug in preservative, buffer, or antioxidant provided that the applicant identifies and characterizes the differences and provides information demonstrating that the differences do not affect the safety or efficacy of the proposed generic drug product.

The proposed generic product is identical with currently approved ELOXATIN® (Oxaliplatin Injection) with respect to indication, active ingredient, strength and route of administration.

The petitioner is not aware of any documentation which establish that the lyophilized formulation ELOXATIN® (Oxaliplatin for Injection) was discontinued for safety or efficacy reasons. FDA's "Additions/Deletions for prescription and OTC Drug Products list " ELOXATIN® (Oxaliplatin for Injection) has been marked with symbol "@", which indicates "drugs that have been discontinued from marketing or that have has their approvals withdrawn for other than safety or efficacy reasons".

Proposed generic product:

The proposed generic product's formulation is identical to the discontinued formulation of ELOXATIN® (Oxaliplatin for Injection) and is supplied as a freeze-dried powder in a clear glass vial containing Oxaliplatin 50 mg/vial and 100 mg/vial

The formula of proposed generic product, which is subject of this petition, is provided in the following Table I.

Table I

Ingredients	**Oxaliplatin for Injection**	
	50 mg/vial	**100 mg/vial**
Oxaliplatin	50 mg	100 mg
Lactose Monohydrate	450 mg	900 mg
Water for injection	Quantity sufficient	Quantity sufficient

III. Conclusion

For all the reasons stated above in this statement grounds, the petitioner seeks FDA to make a determination that the discontinued formulation of ELOXATIN® (Oxaliplatin for Injection) was not voluntarily withdrawn by Sanofi for reasons of safety or effectiveness and that the use of that labeling by the proposed generic product would not render the proposed generic product less safe or effective and would be therapeutically equivalent to the currently marketed product, ELOXATIN® (Oxaliplatin injection).

Accordingly, this petition seeks a determination that the discontinued formulation of ELOXATIN ®(Oxaliplatin for Injection) is suitable for submission as an Abbreviated New Drug Application (ANDA).

C. Environmental Impact

This petition is entitled to a categorical exclusion under 21 CFR §§ 25.30 and 25.31

D. Economic Report

The petitioner agrees to provide an economic analysis if requested by the agency.

E. Certification

The undersigned certifies that, 'to the best knowledge and belief of the undersigned, this petition includes all information and review upon which the petitioner relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Sincerely,

Mr. Anthony Celeste
Sr. Vice President,
AAC Consulting Group/Kendle

Search results from the "OB_Rx" table for query on "021492."

Active Ingredient:	OXALIPLATIN
Dosage Form;Route:	INJECTABLE; IV (INFUSION)
Proprietary Name:	ELOXATIN
Applicant:	SANOFI AVENTIS US
Strength:	50MG/VIAL
Application Number:	021492
Product Number:	001
Approval Date:	Aug 9, 2002
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: View

Active Ingredient:	OXALIPLATIN
Dosage Form;Route:	INJECTABLE; IV (INFUSION)
Proprietary Name:	ELOXATIN
Applicant:	SANOFI AVENTIS US
Strength:	100MG/VIAL
Application Number:	021492
Product Number:	002
Approval Date:	Aug 9, 2002
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	

Patent and Exclusivity Info for this product: View

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Orange Book Data Updated Through May, 2006
Patent and Generic Drug Product Data Last Updated: July 06, 2006

Active Ingredient Search Results from "OB_Rx" table for query on "oxaliplatin."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
021759		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	100MG/20ML (5MG/ML)	ELOXATIN	SANOFI AVENTIS US
021492		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	100MG/VIAL	ELOXATIN	SANOFI AVENTIS US
021759		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	50MG/10ML (5MG/ML)	ELOXATIN	SANOFI AVENTIS US
021492		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	50MG/VIAL	ELOXATIN	SANOFI AVENTIS US

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Patent and Generic Drug Product Data Last Updated: July 06, 2006

Search results from the "OB_Rx" table for query on "021759."

Active Ingredient:	OXALIPLATIN
Dosage Form;Route:	INJECTABLE; IV (INFUSION)
Proprietary Name:	ELOXATIN
Applicant:	SANOFI AVENTIS US
Strength:	50MG/10ML (5MG/ML)
Application Number:	021759
Product Number:	001
Approval Date:	Jan 31, 2005
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	View

Active Ingredient:	OXALIPLATIN
Dosage Form;Route:	INJECTABLE; IV (INFUSION)
Proprietary Name:	ELOXATIN
Applicant:	SANOFI AVENTIS US
Strength:	100MG/20ML (5MG/ML)
Application Number:	021759
Product Number:	002
Approval Date:	Jan 31, 2005
Reference Listed Drug	Yes
RX/OTC/DISCN:	RX
TE Code:	
Patent and Exclusivity Info for this product:	View

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Orange Book Data Updated Through June, 2006
Patent and Generic Drug Product Data Last Updated: July 20, 2006

Active Ingredient Search Results from "OB_Rx" table for query on "Oxaliplatin."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
021759		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	100MG/20ML (5MG/ML)	ELOXATIN	SANOFI AVENTIS US
021759		Yes	OXALIPLATIN	INJECTABLE; IV (INFUSION)	50MG/10ML (5MG/ML)	ELOXATIN	SANOFI AVENTIS US

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