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OVERNIGHT DOCUMENT 9/6/13

Division of Dockets Management
Food and Drug Administration (HFA-305)
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, Maryland 20852

CITIZEN PETITION

Dear Sir or Madam:

This petition is submitted in quadruplicate pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (FDC Act), and 21 CFR 314.93, and in accordance with 21 CFR §10.20 and 21 CFR §10.30, to request that the Food and Drug Administration (FDA) determine that Capecitabine Tablets in strengths of 300 mg and 1000 mg are suitable for submission in an Abbreviated New Drug Application (ANDA).

A. Action Requested

The petitioner requests that Commissioner of the Food and Drug Administration make a determination that Capecitabine Tablets, 300 mg and 1000 mg, are suitable for submission in an ANDA. The Reference Listed Drug (RLD) upon which this petition is based is XELODA® (capecitabine) Tablets, 500 mg of HOFMANN LA ROCHE, which FDA initially approved on April 30, 1998 under NDA No. 020896. XELODA is also approved and available in a 150 mg strength (see copy of the page from the current edition of the Electronic Orange Book provided in **Attachment 1**). Therefore, the petitioner seeks a change in strength (from 500 mg to 300 mg and 1000 mg).

B. Statement of Grounds

Section 505(j)(2)(A) of the Federal Food, Drug and Cosmetic Act permits the submission of an ANDA for a new drug that differs in strength from the listed drug after FDA has approved a petition submitted pursuant to FDC Act §505(j)(2)(C). The RLD for the proposed drug product is XELODA® (capecitabine) Tablets, 500 mg. XELODA is also available in a 150 mg strength. Capecitabine converts to 5-fluorouracil (5-FU), which indirectly inhibits thymidylate formation and is approved for several indications. The proposed drug products represent the same dosage form and route of administration and differ only in strength from that of the RLD. The following table provides a comparison of the two drug products:

Product Name	Dosage Form	Route of Administration	Strengths
XELODA® (capecitabine)	Film-coated Tablet	Oral	RLD: 500 mg Additional strength: 150 mg
Proposed Capecitabine	Film-coated Tablet	Oral	300 mg and 1000 mg

Petitioner's proposed drug products in the new 300 mg and 1000 mg strengths do not pose questions of safety or efficacy. The uses, dosage form, and route of administration are the same as those of the RLD. The only difference between the proposed product and the RLD is the strength. The proposed new strengths are consistent with the RLD labeling in several respects.

Following are excerpts from the Dosage and Administration section of the RLD labeling:

Monotherapy (Metastatic Colorectal Cancer, Adjuvant Colorectal Cancer, Metastatic Breast Cancer)

The recommended dose of XELODA (capecitabine) Tablets is 1250 mg/m² administered orally twice daily (morning and evening; equivalent to 2500 mg/m² total daily dose) for 2 weeks followed by a 1-week rest period given as 3-week cycles (**see Table 1**).

Table 1: XELODA (capecitabine) Dose Calculation According to Body Surface Area

Dose Level 1250 mg/m² Twice a Day		Number of Tablets to be Taken at Each Dose (Morning and Evening)	
Surface Area (m²)	**Total Daily Dose* (mg)**	**150 mg**	**500 mg**
≤ 1.25	3000	0	3
1.26-1.37	3300	1	3
1.38-1.51	3600	2	3
1.52-1.65	4000	0	4
1.66-1.77	4300	1	4
1.78-1.91	4600	2	4
1.92-2.05	5000	0	5
2.06-2.17	5300	1	5
≥ 2.18	5600	2	5

*Total Daily Dose divided by 2 to allow equal morning and evening doses

Dose Management Guidelines

General

XELODA (capecitabine) dosage may need to be individualized to optimize patient management. Patients should be carefully monitored for toxicity and doses of XELODA (capecitabine) should be modified as necessary to accommodate individual patient tolerance to treatment. Toxicity due to XELODA (capecitabine) administration may be managed by symptomatic treatment, dose interruptions and adjustment of XELODA (capecitabine) dose. Once the dose has been reduced, it should not be increased at a later time. Doses of XELODA (capecitabine) omitted for toxicity are not replaced or restored; instead the patient should resume the planned treatment cycles.

The range of total daily doses that is described in the Dosing and Administration section for monotherapy is 3000 mg to 5600 mg.

Other dosing instructions are given for the management of adverse reactions, for use in special populations (e.g., renal impairment) and for giving capecitabine in combination with other agents. These other dosing instructions include adjustment of the daily dose by a suggested percentage. The Dosing and Administration section in its entirety can be found in **Attachment 2** (XELODA Tablets full prescribing information).

The proposed 300 mg and 1000 mg strengths would provide additional strengths for prescribing physicians to choose from, and thereby, make it easier to dose the patient according to the individualized dosing recommendations. This wider choice of dosage strengths would also presumably increase compliance and reduce medication errors because patients may not have to take multiple tablets to

achieve the desired dose. For example, a patient could take a single 300 mg tablet instead of two 150 mg tablets, a single 1000 mg tablet instead of two 500 mg tablets, or two 1000 mg tablets instead of four 500 mg tablets.

There should be no question of safety or efficacy raised with regard to the requested proposed new drug product as the uses, dose, dosage form, and route of administration are the same as that of the reference listed drug. The draft labeling of the proposed drug product **(see Attachment 3)** is the same as that of the approved reference listed drug product's labeling **(see Attachment 2)** with the exception of the addition of the 300 mg and 1000 mg strengths in the "Description" and "How Supplied" section and any manufacturer related information.

Inapplicability of the Pediatric Research Equity Act (PREA '7). PREA, which is codified at FDC Act §505B, does not apply to a new strength, such as the ones proposed in this Petition. See FDC Act §505B(a)(l)(A). As such, PREA should not serve as an impediment to FDA granting this Petition.

For the foregoing reasons, Petitioner requests that FDA find that Capecitabine Tablets, 300 mg and 1000 mg, are suitable for submission in an ANDA.

C. Environmental Impact

The environmental impact report on the action requested in this petition is not required under 21 CFR §25.31.

D. Economic Impact Statement

Pursuant to 21 CFR § 10.30(b), economic impact information to this petition is to be submitted only when requested by the Commissioner. If requested, the economic impact statement will be submitted.

E. Certification

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

Respectfully Submitted:

Joan Janulis

Joan Janulis, RAC
Vice President

JJ/pk

Attachments:
1. Page Showing the RLD in the 25th Edition of Electronic Orange Book
2. XELODA Tablets Full Prescribing Information
3. Draft Labeling of Proposed Drug Product

cc: Martin Shimer

Petition Capecitabine Tablets 090613

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