UCB, Inc. - 1950 Lake Park Drive, Smyrna, Georgia 30080

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

CITIZEN PETITION

The undersigned submits this petition on behalf of UCB, Inc. (UCB) pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act (FDCA) and in accordance with 21 C.F.R. §10.30 to request that the Commissioner of Food and Drugs take the actions described below.

UCB markets a product containing the active ingredient lacosamide [(R)-2-acetoamido-N-benzyl-3-methoxy-propionamide] under the trade name Vimpat®. When FDA approved lacosamide, it was a new chemical entity (NCE) and was thus entitled to 5 years of NCE exclusivity.[1] FDA started the clock running on lacosamide's exclusivity on October 28, 2008, the date that it approved lacosamide's new drug application (NDA).[2] However, UCB could not commercially market lacosamide until June 9, 2009. UCB lost the benefit of 223 days of lacosamide's NCE exclusivity due to the time it took FDA to request, and the U.S. Drug Enforcement Administration (DEA) to complete, scheduling the drug under the Controlled Substances Act (CSA).[3]

In this petition UCB adopts the rationale provided by Eisai, Inc. (Eisai) in the Citizen Petition that it submitted to FDA dated July 25, 2013, which was assigned docket number FDA-2013-P-0884 (Eisai's Petition).[4] Unlike the products at issue in Eisai's Petition, lacosamide is the subject of at least sixteen pending abbreviated new drug applications (ANDAs) that are seeking FDA's approval to market generic versions of UCB's Vimpat® product. The timing of

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[1] 21 U.S.C. §355(c)(3)(E) and 21 U.S.C. §355(j)(5)(F).

[2] Exhibit A, relevant portion of FDA's publication titled *Approved Drug Products With Therapeutic Equivalence Evaluations* (the "Orange Book"), available at: http://www.accessdata.fda.gov/Scripts/cder/ob/docs/patexclnew.cfm?Appl_No=022253&Product_No=001&table1=OB_Rx

[3] 155 Cong. Rec. H6969 (daily ed. Jun. 17, 2009); Docket DEA-325F, pertaining to lacosamide's scheduling, received pursuant to 5 U.S.C. §801(a)(1)(A) on June 9, 2009.

[4] Exhibit B, Eisai Petition.

FDA's approval of the ANDAs could potentially be affected by the outcome of this petition. Based on the FDA approval date of October 28, 2008, UCB's five years of NCE exclusivity would expire on October 28, 2013, and the 30 month stay on the approvals of ANDAs whose filers have been sued would expire on April 28, 2016. Adding the 223 days lost pending CSA scheduling would move those dates to June 9, 2014 and December 7, 2016, respectively.

I. Action Requested

UCB respectfully requests that FDA take the following action:

1. determine that the NCE exclusivity for lacosamide began on June 9, 2009, and thus will end on June 9, 2014;

2. confirm that the Agency will stay approval of ANDAs Nos. 204682, 204787, 204839, 204857, 204873, 204874, 204855, 204921, 204947, 204974, 204980, 204986, 204994, 204999, 205006, 205011, 205026, 205031, 205237, and any additional ANDA that meets the criteria under 21 U.S.C. §355(j)(5)(B)(iii), absent another specified event under 21 U.S.C. §355(j)(5)(B)(iii), until December 7, 2016; and

3. respond substantively to this petition within 150 days of its submission.

II. Statement of Grounds

FDA accepted UCB's NDAs for lacosamide on November 29, 2007. As it must, UCB included with its applications certifications agreeing not to market the product that is the subject of the NDAs until the DEA makes a final scheduling decision.[5] On October 28, 2008, FDA approved two NDAs for lacosamide, which UCB markets under the trade name Vimpat® as an adjunctive therapy in patients ages 17 years and older for the treatment of partial-onset seizures.[6] As lacosamide was a NCE, UCB was granted 5 years of exclusivity,[7] which FDA triggered the same day that it approved lacosamide's NDAs. Although lacosamide's exclusivity had started to run, as FDA noted in the approval letters, UCB could not commercially market lacosamide until

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[5] Exhibit C, Form FDA 356h, submitted by UCB with its NDAs. Applicants for NDAs, UCB included, are required to submit with their applications Form FDA 356h, which includes the certification, "If this application applies to a drug product that FDA has proposed for scheduling under the Controlled Substances Act, I agree not to market the product until the Drug Enforcement Administration makes a final scheduling decision." 21 C.F.R. §314.101(d).

[6] Exhibit D: Letter from FDA dated October 28, 2008, approving NDAs Nos. 22253 and 22254.

[7] 21 U.S.C. §355(c)(3)(E) and 21 U.S.C. §355(j)(5)(F).

the DEA finalized its scheduling under the CSA and lacosamide's label was amended to reflect the schedule.[8]

On December 2, 2008, 35 days after FDA triggered lacosamide's exclusivity, the Assistant Secretary for Health of the Department of Health and Human Services (HHS) sent to the Administer of DEA a request to place lacosamide into schedule V of the CSA. Lacosamide was not scheduled until May 21, 2009, and the Department of Justice's letter to each House of the Congress and the Comptroller General, transmitting the final rule scheduling lacosamide, was received on June 9, 2009.[9] As a result of the time to request and receive lacosamide's CSA scheduling, 223 days of NCE exclusivity was lost.

A trigger date of October 28, 2008 means lacosamide's NCE exclusivity is set to expire on October 28, 2013.[10] Based on that expiry date, companies seeking to market generic versions of products containing lacosamide were permitted to, and did, submit ANDAs to FDA on or after October 28, 2012.[11] UCB received nineteen letters from sixteen companies, each informing UCB that the respective sender had submitted at least one ANDA under section 505(j) of the FDCA, 21 U.S.C. §355(j), seeking approval to market a generic version of UCB's Vimpat® product. Included in each of the ANDAs was a certification, pursuant to 21 U.S.C. §355(j)(2)(A)(vii)(IV) (Certification), that the patents listed in FDA's Orange Book were, in the sender's opinion and to the best of its knowledge, invalid and/or will not infringed by the proposed generic product(s). In response, UCB and other plaintiffs commenced lawsuits against each ANDA filer within 45 days of receiving notice of each Certification.[12] Accordingly, approval of the ANDAs is currently stayed until April 28, 2016, which is the date prescribed by 21 U.S.C. §355(j)(5)(F)(ii), absent another specified event under 21 U.S.C. §355(j)(5)(B)(iii).

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[8] Letter from FDA, *supra*, note 6, heading titled "Controlled Substance Class."

[9] 5 U.S.C. §801(a)(1)(A).

[10] 21 U.S.C.A. §355(j)(5)(F)(ii).

[11] *Id.*

[12] Exhibits E-1 to E-16, letters dated August 12, 2013, submitted to Dr. Kathleen Uhl, Acting Director, Office of Generic Drugs at FDA on behalf of UCB and other plaintiffs in the lawsuits.

III. Argument

UCB adopts the rationale in the Eisai Petition. In compliance with FDA's guidance[13] and 21 C.F.R. §10.20(c)'s requirement that "[i]information referred to or relied upon in a submission is to be included in full and may not be incorporated by reference, unless previously submitted in the same proceeding," UCB reiterates that rationale below.

A. NCE Is An Important Statutory Right

NCE exclusivity is a valuable statutory right that FDA has recognized as "a critical incentive for drug development that advances FDA's goal of protecting and promoting public health."[14] According to FDA, shortening the exclusivity would "cause irreparable harm to the regulatory process by undermining the benefits to the public and to FDA of the marketing exclusivity that the FDCA affords to drug sponsors" and "would stifle rather than encourage innovation, to the detriment of the public."[15] Despite these statements, here FDA triggered lacosamide's NCE exclusivity before the drug could be legally marketed, shortening the exclusivity to the irreparable harm of UCB.

B. Drug Scheduling Is Outside UCB's Control

Scheduling of a FDA-approved drug that the Agency determines has abuse potential, like lacosamide, is outside of the applicant's (UCB's) control. FDA initiates the scheduling process by the Assistant Secretary for Health of HHS informing the Administrator of DEA that a drug may have abuse potential, preparing a medical and scientific evaluation regarding the drug, and recommending on what schedule the drug should be placed. The DEA Administrator reviews the submission and decides whether the drug should be controlled and, if so, onto which schedule placed. DEA's proposed scheduling is published in the Federal Register, allowing a

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[13] FDA, Guidance for Industry, Citizen Petitions and Petitions for Stay of Action Subject to Section 505(q) of the Federal Food, Drug, and Cosmetic Act (June 2011), available at http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM079353.pdf.

[14] Exhibit F: Memorandum In Support of Defendant's Motion for Stay Pending Appeal, *Tummino v. Hamburg*, No. 12-CV-763 (ERK/VVP), D.I. 91-1 at 16 (E.D.N.Y. May 1, 2013).

[15] *Id.* at 15.

comment period before a final order is published that sets the effective date for imposing the CSA's requirements.[16]

UCB lost 223 days of lacosamide's NCE exclusivity while FDA and DEA completed its scheduling: 35 days before FDA sent its scheduling request to DEA; 98 days before DEA publishing its proposed scheduling in the Federal Register[17]; 72 days before DEA published the final rule; and 18 days for the final rule to go into effect.[18]

C. The "Effective" Date That Should Trigger Exclusivity Is The Date That The Drug Can Be Legally Marketed

FDA's regulations contemplate different "approval" dates, and equate an "effective" approval to the ability to legally market the product. First, the regulations define the "date of approval" for exclusivity as the date on FDA's letter approving the new drug *unless* final printed labeling or other material require approval.[19] Therefore, situations where the dates of the approval letter and the date triggering exclusivity differ are contemplated. Second, these regulations explicitly state that the "'date of approval' refers only to a final approval and not to a tentative approval that may become *effective* at a later date."[20] "Effective" means the ability to market the product: "[a] new drug product ... may not be marketed until an approval is effective."[21] Third, FDA has recognized that exclusivity begins when a product can be legally marketed: "[a] requirement in the approval letter for submission (but not for approval) of final printed labeling or other material that may delay the actual initiation of marketing of the product is not relevant to the determination of the date of approval, *so long as the product could be legally marketed.*"[22,23]

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[16] 21 U.S.C. §811(a)-(c); *See also* Exhibit G: Excerpt of U.S. Dept. of Justice, DEA, Drugs of Abuse, A DEA Resource Guide (2011 Ed.), pp. 8-10, available at http://www.justice.gov/dea/docs/drugs_of_abuse_2011.pdf.

[17] 74 F.R. 10205-207 (March 10, 2009).

[18] 74 F.R. 23789-90 (May 21, 2009); *supra*, note 3.

[19] 21 C.F.R. §314.108(a).

[20] *Id.* (emphasis added).

[21] 21 C.F.R. §314.105(a).

[22] 54 F.R. 28872, 28898 (July 10, 1989) (emphasis added).

Here, although lacosamide's NDAs received nominally "final" approval on October 28, 2008, that approval was not the "effective" approval necessary to trigger exclusivity, because the drug could not be legally marketed until after CSA scheduled the drug, and lacosamide's label revised to reflect that scheduling.[24]

D. Triggering NCE Exclusivity On The Date The Drug Can Be Marketed Avoids Disparate Treatment

Triggering NCE exclusivity on the date that the drug can be legally marketed ensures that a NCE receives its full 5 years of Congressionally-mandated exclusivity. FDA's triggering of NCE exclusivity on the day it sends an approval letter results in NCEs receiving varying amounts less than the mandated 5 years. For example, Lunesta and Vyvanse each lost approximately 3.5 months of their NCE exclusivity to scheduling; Lyrica and Nucynta 7 months; Vimpat 8 months; Lusedra 11 months; and Belviq one year.[25]

E. Pending ANDAs Should Not Weigh Against The Requested Actions

That companies have already submitted ANDAs on or about October 28, 2012—something that would not have been permitted until at least June 9, 2013 if FDA triggered

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[23] In 54 F.R. 28898, FDA cites two cases where the courts upheld its interpretation that the "date of approval" is the date FDA sends the approval letter. Neither case applies here: In *Mead Johnson Pharmaceutical Group v. Bowen*, 838 F.2d 1332 (D.C. Cir. 1988), FDA requested that the company submit revised labeling, but did not prohibit the company marketing the drug. It was the company that decided to wait for FDA's approval before marketing its product. *Id.* at 1336. In *Norwich Eaton Pharmaceuticals, Inc. v. Bowen*, 808 F.2d 486 (6th Cir. 1987), FDA explicitly told the company that it could market its drug while it underwent CSA re-scheduling, but the company chose not to until rescheduling was complete. That UCB did not market lacosamide upon receiving approval of its NDAs was not a business decision, but rather because FDA's Form FDA 356h prohibited it, as FDA reminded UCB in the approval letters. Notably, both cases FDA relied on predate FDA Form 356h.

[24] The label approved concurrent with lacosamide's NDAs omits section 9.1 (Exhibit H), which pertains to scheduling, and was revised to reflect lacosamide's scheduling (Exhibit I), before the drug could be legally marketed. *See also* 21 C.F.R. §201.57(a)(2) "For controlled substances, the controlled substance symbol designating the schedule in which the controlled substance is listed must be included…" and 21 C.F.R. §314.70(b)(2)(v)(C).

[25] Exhibit J: FDA/DEA Session on Scheduling, Douglas C. Throckmorton, MD, Deputy Director for Regulatory Programs, CDER, FDA, April 6, 2011, p. 2, available at: http://www.fdli.org/docs/default-document-library/dea-scheduling-combined-v4.pdf?sfvrsn=0. *See also* Exhibit B, Eisai Petition.

lacosamide's NCE exclusivity *after* UCB was legally able to commercially market its drug—should not weigh against granting UCB's requested relief. Companies relied on the October 28, 2013 expiration date of lacosamide's NCE exclusivity to file their ANDAs. In accordance with the Drug Price Competition and Patent Term Restoration Act, litigations were commenced and FDA's approval of the ANDAs stayed for 30 months—until April 28, 2016. UCB is not requesting a change in the *status quo*, only that the 30-month stay of the pending ANDAs approval be extended from April 28, 2016 until December 7, 2016. The litigations involving those ANDAs are ongoing, so the ANDA filers have already had the benefit of filing applications and beginning the process of challenging the lacosamide patent. If the litigations conclude, or another triggering event under 21 U.S.C. §355(j)(5)(B)(iii) occurs, the requested action will not prevent final FDA approval of those pending ANDAs.

F. The Petition Meets The Criteria For A Response Within 150 Days

UCB's petition meets the criteria necessary to require that FDA provide a substantive response within 150 days.[26,27] Specifically, this petition is submitted after September 27, 2007 pursuant to 21 C.F.R. §10.30; ANDAs are currently pending; the requested action may delay approval of the pending ANDAs; and does not fall within any of the exceptions described in section 505(q)(4).

G. Conclusion

Consistent with congressional intent, FDA's regulations and the Agency's recognition of the importance of NCE exclusivity, the appropriate date to trigger lacosamide's NCE exclusivity period is June 9, 2009, the date on which the drug could be legally commercially marketed.

IV. Environmental Impact

This petition is categorically exempt from the requirement for an environmental assessment or an environmental impact statement pursuant to 21 C.F.R. §§25.30 and 25.31.

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[26] 21 U.S.C. §355(q)(1)(F) as amended by the FDA Safety and Innovation Act §1135 (Pub. L. 112-144, 126 Stat. 993).

[27] FDA Guidance, *supra*, note 13 at pp. 4-7.

V. Economic Impact

Information on the economic impact of the petition will be provided upon request.

Certification

I certify that, to my best knowledge and belief: (a) this petition includes all information and views upon which the petition relies; (b) this petition includes representative data and/or information known to the petitioner which are unfavorable to the petition; and (c) I have taken reasonable steps to ensure that any representative data and/or information which are unfavorable to the petition were disclosed to me. I further certify that the information upon which I have based the action requested herein first became known to the party on whose behalf this petition is submitted on or about the following date: Early August, 2013 when, upon learning of the filing of the Eisai Petition, UCB recognized that it had experienced similar circumstances to Eisai, and that UCB likewise had a basis to pursue restoration of lost exclusivity with respect to Vimpat®. If I received or expect to receive payments, including cash and other forms of consideration, to file this information or its contents, I received or expect to receive those payments from the following persons or organizations: UCB. I verify under penalty of perjury that the foregoing is true and correct as of the date of the submission of this petition.

Respectfully submitted,

Patricia A Fritz
VP, Corporate Affairs & Operations