DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-504

Vyteris, Inc.
13-01 Pollitt Drive
Fair Lawn, NJ 07410

Attention: George M. Baskinger
Manager, Quality Management and Regulatory Compliance

Dear Mr. Baskinger:

Please refer to your new drug application (NDA) dated September 25, 2002, received September 25, 2002, and submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for LidoSite™ Topical System comprised of the LidoSite™ Patch (Lidocaine HCl / Epinephrine topical iontophoretic patch) 10%/0.1% and the LidoSite™ Controller.

We acknowledge receipt of your submissions dated May 9, June 4 and 21, July 8, August 26, and December 18, 2002, February 26, March 10, 11 (2), 19, and 31, April 29, May 1, 15 (2), and 27, June 5, 13(2), 16, 20, 24, and 28, July 14(2), 15, and 18 (2), August 1, 8 and 20, September 8, November 8, 18, 21, 25, and 26, 2003, and January 30, March 18, 27, and 31, April 2, 5, 24, and 28, and May 3, 4 and 6, 2004.

The November 8, 2003, submission constituted a complete response to our July 25, 2003, action letter.

This new drug application provides for the use of LidoSite™ Topical System as a topical local anesthetic delivery system indicated for use on normal intact skin to provide local analgesia for superficial dermatological procedures such as venipuncture, intravenous cannulation, and laser ablation of superficial skin lesions, on patients 5 years of age and older.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the attached labeling (package insert), with the following minor revisions listed below and the labeling submitted April 24, 2004 (controller carton, supplemental controller carton and controller label) and April 28, 2004 (pouch primary, pouch patch carton, supplemental pouch patch carton labels and printed patch film).

1. On the Instruction Sheet:

    a. Change Item 3h from "the application site may not be fully anesthetized" to "the medication may not have been delivered to the application site."

    b. Change the footer of the instruction sheet from "Each patch contains Lidocaine HCl (10%), Epinephrine (0.1%)" to "Lidocaine HCl/Epinephrine topical iontophoretic patch 10%/ 0.1%.

2. Include the NDC number in the HOW SUPPLIED section of the package insert and on the immediate carton and container labels.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert), and the labeling submitted April 24, 2004 (controller carton, supplemental controller carton and controller label) and April 28, 2004 (pouch primary, pouch patch carton, supplemental pouch patch carton labels and printed patch film). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit the copies of final printed labeling (FPL) electronically, according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-504." Approval of this submission by FDA is not required before the labeling is used.

All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We are deferring submission of your pediatric studies for ages 0 to 5 years until November 2007.

Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

POST MARKETING COMMITMENT

1. Deferred pediatric study under PREA for the indication of local analgesia for superficial dermatological procedures such as venipuncture, intravenous cannulation, and laser ablation of superficial skin lesions in pediatric patients ages birth to 5 years.

   Final Report Submission: April 2007

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated **"Required Pediatric Study Commitment.**"

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "Postmarketing Study Protocol," "Postmarketing Study Final Report," or "Postmarketing Study Correspondence."

We also remind you of your agreements to the following:

1. Accrual of data for commercial batches of drug product for the cathode and anode probe tack, the apparent compressive modulus of the reservoirs (electrodes), the probe tack of the adhesive, and the anode-specific and cathode-specific conductivities with data based on eight lots of subcomponents.

2. Development, validation, and establishment of an *in-vitro* drug release test method as part of the drug product specifications. The method will be submitted as a Prior Approval Supplement within eighteen months from the date of the action letter.

In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

Please submit one market package of the drug product when it is available.

We have not completed validation of the regulatory methods. However, we expect your continued cooperation to resolve any problems that may be identified.

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kimberly Compton, Regulatory Project Manager, at (301) 827-7432.

Sincerely,

{See appended electronic signature page}

Bob Rappaport, M.D.
Director
Division of Anesthetic, Critical Care and
Addiction Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Bob Rappaport

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