

**CENTER FOR DRUG EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

21-119/S-001

APPROVAL LETTER



NDA 21-119/S-001

QLT Inc.

Attention: David Mitchell, Sr. Manager Regulatory Affairs

c/o Jonathan S. Kahan

Hogan and Hartson

555 Thirteenth Street, NW

Washington, D.C. 20004-1109

Dear Mr. Mitchell:

Please refer to your supplemental new drug application dated August 14, 2000, received August 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Visudyne (verteporfin for injection), 15 mg.

We acknowledge receipt of your submissions dated January 29, February 19 and 23, April 13, and August 20 and 21, 2001. We also refer to our approvable letter of February 2, 2001, to which your February 23, 2001, submission was a complete response.

This supplemental new drug application provides for the use of Visudyne (verteporfin for injection) therapy for the treatment of patients with predominantly classic subfoveal choroidal neovascularization due to macular degeneration, presumed ocular histoplasmosis or pathologic myopia.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted August 20, 2001).

Please submit the copies of final printed labeling (FPL) electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA* (January 1999). 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. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-119/S-001." Approval of this submission by FDA is not required before the labeling is used.

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Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We are waiving the pediatric study requirement for this action on this application.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit 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, Maryland 20857

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Lori M. Gorski, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

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APPLICATION NUMBER:
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APPROVABLE LETTER



NDA 21-119/S-001

FEB 2 2001

QLT Inc.
Attention: David Mitchell, Sr. Manager Regulatory Affairs
c/o Jonathan S. Kahan
Hogan and Hartson
555 Thirteenth Street, NW
Washington, D.C. 20004-1109

Dear Mr. Mitchell:

Please refer to your supplemental new drug application dated August 14, 2000, received August 14, 2000, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Visudyne (verteporfin for injection), 15 mg.

We acknowledge receipt of your submissions dated August 21, October 2, and December 8, 2000.

This supplemental new drug application proposes the use of Visudyne for the treatment of patients with predominantly classic subfoveal choroidal neovascularization.

We have completed the review of this application, as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

1. Study OCR 004 was prematurely submitted prior to its first scheduled interim analysis. Additionally, the statistical analysis did not include a control group. Please provide a final study report for the presumed ocular histoplasmosis patients (Study OCR 004) including at a minimum: the 12-month visual acuity data listings, a summary table of changes in visual acuity from baseline, and an appropriate statistical comparison to a control group. If there are any differences between the inclusion/exclusion criteria of the control group and the original study group, please clearly identify them and identify any expected impact on the analyses.
2. The 24-month visual acuity data for the VIP studies should have been available at the time of the submitted safety update. Please provide the 24-month visual acuity data for the pathologic myopia study VIP-PM and VIP-AMD patients (Studies OCR 003-PM and -AMD) including data listings and summary tables for visual acuity (15-letter responder rate and mean change in visual acuity from baseline).

3. Patient V13P51 in study OCR 003 PM was noted to have colon cancer. Provide a summary of all gastrointestinal cancers found in all studies of verteporfin for injection.
4. An incomplete listing of adverse reactions appears to have been provided. Specifically, only 4 of 5 pages of Table 47 (Page 146-149 of the Pathologic Myopia Study Report OCR 003 PM) have been submitted. Please provide the complete listing.

Under 21 CFR 314.50(d)(5)(vi)(b), we request that you update your NDA by submitting all safety information you now have regarding your new drug. The safety update should include data from all nonclinical and clinical studies of the drug under consideration regardless of indication, dosage form, or dose level.

We will continue to work with you on the proposed labeling for this product.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit 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, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of the other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with this division to discuss what further steps need to be taken before the application may be approved.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with these changes prior to approval of this supplemental application.

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If you have any questions, call Lori M. Gorski, Project Manager, at (301) 827-2090.

Sincerely,

{See appended electronic signature page}

Wiley A. Chambers, M.D.

Deputy Director

Division of Anti-Inflammatory, Analgesic and

Ophthalmic Drug Products, HFD-550

Office of Drug Evaluation V

Center for Drug Evaluation and Research