

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

***APPLICATION NUMBER:***

**21-119**

**APPROVAL LETTER**



NDA 21-119  
PMA P990048  
PMA P990049

APR 12 2000

QLT PhotoTherapeutics  
Attention: David Mitchell, Director 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 new drug application (NDA) and pre-market applications (PMA) dated August 14, 1999, submitted under sections 505(b) and 515 of the Federal Food, Drug, and Cosmetic Act for Visudyne (verteporfin for injection), 15 mg, for the Coherent Opal Photoactivator Laser Console and LaserLink Adapter (P990049), and for the Zeiss VISULAS 690s laser and VISULINK PDT adapter (P990048).

We acknowledge receipt of your submissions dated October 18, November 2 and 15, and December 10, 1999, and January 21, 2000, to PMA P990048; December 3 and 10, 1999, to PMA P990049; and February 1, 8, and 18, March 2, 3, 6, 7, 24 (two), 30, and 31, and April 3 (two), 5, and 7, 2000 to NDA 21-119. Your submission of February 18, 2000, constituted a complete response to our February 11, 2000, action letter.

These applications provide for the treatment of age-related macular degeneration in patients with predominantly classic subfoveal choroidal neovascularization.

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

The sale, distribution, and use of these devices are restricted to prescription use in accordance with 21 CFR 801.109 within the meaning of section 520(e) of the Federal Food, Drug, and Cosmetic Act (the act) under the authority of section 515(d)(1)(B)(ii) of the act. FDA has also determined that, to ensure the safe and effective use of the device, the devices are further restricted within the meaning of section 520(e) under the authority of section 515(d)(1)(B)(ii) insofar as the sale, distribution, and use must not violate sections 502(q) and (r) of the act.

NDA 21-119  
PMA P990048  
PMA P990049  
Page 2

The Center for Devices and Radiological Health (CDRH) will notify the public of its decision to approve your PMA by making available a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at <http://www.fda.gov/cdrh/pmapage.html>. Written requests for this information can also be made to the Dockets Management Branch, (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Room 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by requesting an opportunity for administrative review, either through a hearing or review by an independent advisory committee, under section 515(g) of the Federal Food, Drug, and Cosmetic Act.

The final printed labeling (FPL) for Visudyne must be consistent with the draft labeling submitted April 7, 2000. Marketing the product with FPL that is not consistent with the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case 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 NDA 21-119." Approval of this submission by FDA is not required before the labeling is used.

You are reminded that, as soon as possible and before commercial distribution of your devices, you must submit amendments to these PMA submissions with copies of all approved labeling in final printed form.

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 in final print. Please send one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmologic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20857

NDA 21-119  
PMA P990048  
PMA P990049  
Page 3

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

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 for the drug product. Failure to comply with the conditions of approval for the devices invalidates this approval order. Commercial distribution of a device that is not in compliance with these conditions is a violation of the act.

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

Sincerely,

/S/

4/12/00

Robert DeLap, M.D., Ph.D.  
Director  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

**APPEARS THIS WAY  
ON ORIGINAL**

**CENTER FOR DRUG EVALUATION AND  
RESEARCH**

*APPLICATION NUMBER:*  
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**APPROVABLE LETTER**



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FEB 11 2000

QLT PhotoTherapeutics  
Attention: David Mitchell, Director Regulatory Affairs  
c/o Jonathan S. Kahan  
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555 Thirteenth Street, NW  
Washington, D.C. 20004-1109

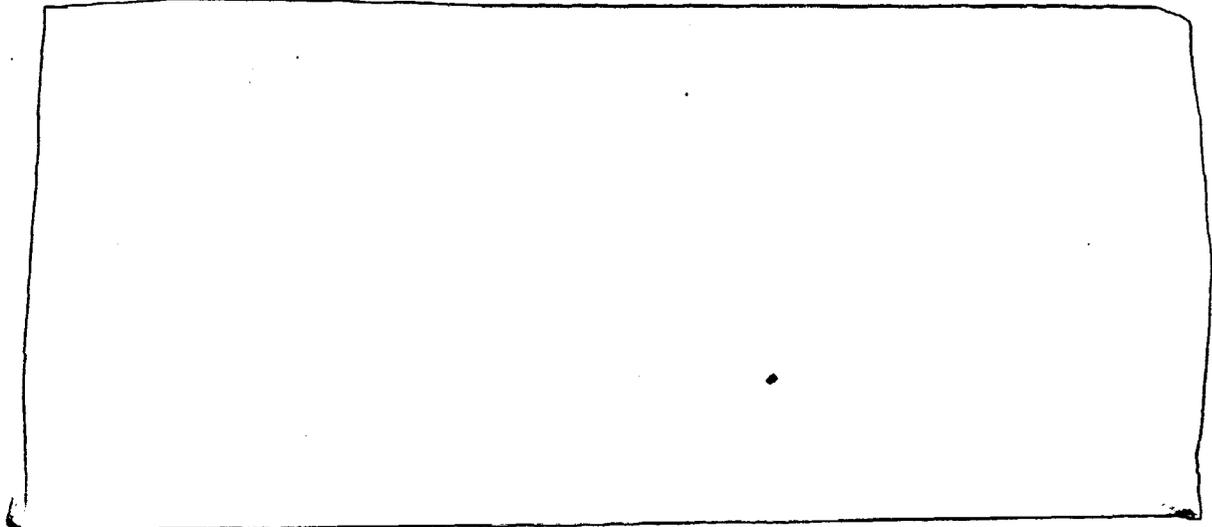
Dear Mr. Mitchell:

Please refer to your new drug application (NDA) dated August 14, 1999, received August 16, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Visudyne (verteporfin for injection) Ocular Injection.

We acknowledge receipt of your submissions dated May 28, August 14 and 20, September 8 and 23, October 6 (two), 12 (two), 14, 18 (two) and 26, November 1, 3, 5, 9, 10, 24, 26, 29 (two) and 30, December 1, 10 and 14, 1999, January 28 and 31, 2000.

We have completed the review of this application as amended above, and it is approvable. Your January 28, 2000, submission may address certain of the remaining deficiencies in this application, but that submission is still under review. Deficiencies in this application that must be adequately addressed before this application may be approved include the following:

1. The methods to be used in, and the facilities and controls used for, the manufacture, processing, packing, and holding of the drug substance and drug product are inadequate to preserve its identity, strength, quality, purity, and stability. Specifically,
  - a. Critical steps in the manufacturing process have not been adequately described including details about the international shipping of unstable materials. In addition, the testing results that document the acceptability of these materials for subsequent steps in the process have not been submitted.



**SUMMARY of SHIPPING CONDITIONS and MATERIAL TESTING  
DURING SITE TRANSFERS of PRODUCT-RELATED SUBSTANCES**

MATERIAL	TRANSFER SITES		SHIPPING CONDITIONS	TESTING	
	Manuf.	Recipient		Complete	Limited (List Tests)
			RESTRICTED		
			RESTRICTED		
Verteporfin					
Verteporfin for Injection			Not applicable		

Please confirm that the information already entered in the table is correct; otherwise, make corrections as well as additions. List all special shipping conditions for the different transfers, e.g., dry ice for presome shipment and, if correct, inclusion of temperature recording device. For sites receiving materials, list the testing sites and the tests that are performed, e.g., Appearance, ID-UV, and Assay-HPLC, or their SOP numbers.

*This page of the document  
contains confidential  
information that will not  
be included in the  
redacted portion of the  
document for the public to  
obtain.*

We very highly recommend that you refer to the Sterilization Process Validation Information Guidance issued by the FDA in the past to prepare your response. It is also available at the FDA/CDER/Guidance website, at the following URL: <http://www.fda.gov/cder/guidance/index.htm>. The document *Submission Documentation for Sterilization Process Validation in Applications for Human and Veterinary Drug Products, November 1994*, is number 18, under Chemistry guidances.

3. The proposed labeling requires revisions. Please submit revised labeling consistent with the attached proposed labeling. If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.
4. This application was linked at the time of its submission with Premarket applications (PMA) [redacted] and PMA [redacted]. Deficiencies have been noted in these applications and the deficiencies conveyed to you in letters dated October 12 and December 17, 1999.

As required under 21 CFR 314.50(d)(5)(vi)(b), in response to this approvable letter, please submit updated safety information collected from your ongoing and recently completed clinical studies. This information should include the visual acuity information of patients after two years of treatment with your product.

Inspections of the manufacturing facilities for your NDA and PMAs have been ongoing. We remind you that the facilities, controls for the manufacturing, processing, packing and holding of the drug substance and drug product must be in compliance with current good manufacturing practice regulations as described in 21 CFR 210 and 211.

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 send one copy to the Division of Anti-Inflammatory, Analgesic and Ophthalmic Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising, and Communications, HFD-40  
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 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.

The drug product may not be legally marketed until you have been notified in writing that the application is approved.

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

Sincerely,

*RSI*

11 FEBRUARY 2000

Robert DeLap, M.D., Ph.D.  
Director  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

Enclosures: Draft Labeling