CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

022555Orig1s000

Trade Name:	**CYSVIEW for INTRAVESICAL SOLUTION, 100 mg**
Generic Name:	**Hexaminolevulinate Hydrochloride**
Sponsor:	**Photocure ASA (Cato Research, Ltd.)**
Approval Date:	**May 28, 2010**
Indications:	For use in the cystoscopic detection of non-muscle invasive papillary cancer of the bladder among patients suspected or known to have lesion(s) on the basis of a prior cystoscopy.

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APPLICATION NUMBER:

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APPROVAL LETTER

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 22555 **NDA APPROVAL**

Cato Research, Ltd (for Photocure ASA)
Attn: Lynda Sutton, Chief Regulatory Officer
4364 S. Alston Ave.
Durham, NC 27713-2220

Dear Ms. Sutton (for Photocure ASA):

Please refer to your New Drug Application (NDA) 22555, dated and received March 31, 2010, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Cysview (hexaminolevulinate hydrochloride) for Intravesical Solution, 100 mg, indicated for use in the cystoscopic detection of non-muscle invasive papillary cancer of the bladder among patients suspected or known to have lesion(s) on the basis of a prior cystoscopy. Cysview is part of a combination product in association with the Karl Storz D-Light C Photodynamic Diagnostic (PDD) system to perform cystoscopy with the blue light setting (Mode 2) as an adjunct to the white light setting (Mode 1). The Karl Storz D-Light C PDD system is the subject of a premarket application (PMA).

We acknowledge receipt of your NDA submissions April 9; May 17, 20, 25 and 26, 2010.

The NDA submission of March 31, 2010, constituted a complete response to our action letter of December 30, 2009.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling and label texts. A separate FDA letter will issue concurrently for the PMA for Karl Storz D-Light C PDD system.

LABELING RX

As soon as possible, but no later than 14 days from the date of this letter, submit, via the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at: http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the enclosed labeling (text for package insert). Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at: http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible via publicly available labeling repositories.

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels that are identical to the enclosed carton and immediate container labels as soon as they are available, but no more than 30 days after they are printed. Submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)". Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22555**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for this application because necessary studies are impossible or highly impracticable. Cysview does not represent a meaningful therapeutic (clinical) benefit (as defined in 21 CFR 314.55 (c)(5)) for pediatric patients because the number of pediatric patients with bladder cancer is extremely low. The drug is not likely to be used in a substantial number of pediatric patients. For the same reason, studies in the pediatric population would not be feasible.

POSTMARKETING STUDY COMMITMENTS SUBJECT TO REPORTING REQUIREMENTS UNDER SECTION 506B

We remind you of your postmarketing commitments in your submission dated May 20, 2010, listed below:

1642-1 A prospective, randomized, controlled clinical trial that will assess the safety and efficacy of repetitive use of Cysview in the detection of bladder cancer.

Final Protocol Submission:	May 2011
Trial Completion:	July 2015
Final Report Submission:	July 2015

1642-2 A prospective, randomized, controlled clinical trial that will assess the safety and efficacy of Cysview in the detection of carcinoma *in situ* of the bladder.

Final Protocol Submission:	May 2011
Trial Completion:	July 2015
Final Report Submission:	July 2015

You may address both of these postmarketing commitments by the completion of a single, well-designed clinical trial that addresses the individual trial expectations, as listed above.

Submit clinical protocols to your IND 51224, for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all trial 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/trials, number of patients entered into each study/trial. All submissions, including supplements, relating to these postmarketing commitments should be prominently labeled "**Postmarketing Commitment Protocol**," "**Postmarketing Commitment Final Report**," or "**Postmarketing Commitment Correspondence**."

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in *triplicate hard copies*, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert, at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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

If you decide to issue a letter communicating important safety-related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

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

All submissions/correspondences should be submitted to the FDA CDER – Division of Medical Imaging Products in ***triplicate*** hard copies with a cover letter and Form FDA 1571 or 356(h), along with an **electronic copy on CD-Rom (PDF)**, as follow:

Courier/Overnight/Postal
Rafel Dwaine Rieves, M.D., Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research
U.S. Food and Drug Administration
Attention: FDA Central Document Room
5901-B Ammendale Road
Beltsville, MD 20705-1266

Or solely electronic submission via Gateway / Global Submit Review (GSR) – See the following links for information and assistance:

http://www.fda.gov/ForIndustry/ElectronicSubmissionsGateway/default.htm

http://www.fda.gov/Drugs/DevelopmentApprovalProcess/FormsSubmissionRequirements/ElectronicSubmissions/ucm153574.htm

If you have any questions regarding NDA 22555, contact Ms. Thuy M. Nguyen, M.P.H., Senior Regulatory Health Project Manager, at (301) 796-2050 or Thuy.Nguyen@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Rafel Dwaine Rieves, M.D.
Director
Division of Medical Imaging Products
Office of Drug Evaluation IV
Center for Drug Evaluation and Research
U.S. Food and Drug Administration

Enclosures: Content of Labeling, Carton, Container, and Vial Labels

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22555	ORIG-1	PHOTOCURE ASA	HEXVIX

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

/s/

THUY M NGUYEN
05/28/2010

RAFEL D RIEVES
05/28/2010