SUMMARY OF SAFETY AND EFFECTIVENESS DATA

VISUDYNE (verteporfin for injection) and the applicants Coherent Opal Photoactivator Laser Console and the LaserLink Adapter comprise a combination product as defined in 21 CFR 3.2(e). The primary mode of action for the combination has been determined to be that of a drug and the Center for Drug Evaluation and Research (CDER) has been given administrative jurisdiction over the combination. Accordingly, information pertaining to the clinical studies to support the approval of the light device system described in PMA No. 990049 is contained within the New Drug Application (NDA) No. 21-119.

I. GENERAL INFORMATION

Device Generic Name:	Diode Laser
Device Trade Name:	Coherent Opal Photoactivator Laser Console and LaserLink Adapter
Applicant's Name and Address:	Mr. Jonathan Kahan Hogan & Hartson c/o QLT PhotoTherapeutics, Inc 555 Thirteenth Street, N.W. Washington, D.C. 20004-1109
Laser Manufacture Name and Address:	Coherent Medical Group Coherent, Inc. 2400 Condensa Street Santa Clara, California 95051-0901
PMA Number:	P990049
NDA Number:	21-119

Date of Panel Recommendation:	As a component of a combination therapy, this device was presented and reviewed at the Dermatologic and Ophthalmic Drug Advisory Committee Meeting of the Center for Drug Evaluation and Research on November 17, 1999
Date of Notice of Approval:	April 12, 2000

II. INDICATIONS FOR USE

The Coherent Opal Photoactivator Laser Console and LaserLink Adapter are intended for use in VISUDYNE therapy as sources of photoactivation of VISUDYNE™ (verteporfin for injection) for the treatment of age-related macular degeneration (AMD) in patients with predominantly classic subfoveal choroidal neovascularization (CNV).

Refer to the VISUDYNE Package Insert for information and instructions for use of the drug and for information on laser power, duration, and light dose.

Refer to the Coherent Opal Photoactivator Laser System Operator Manual for information regarding use and operation of the laser system.

III. DEVICE DESCRIPTION

The Coherent Opal Photoactivator is a semiconductor diode laser that provides power output of up to 300 mW of light at 689 nm. Dosimetry limits, including fluence and intensity, may be selected by the operator and displayed on the control panel.

The Coherent Opal Photoactivator is comprised of an Aluminum Gallium Indium Phosphor, (AlGaInP), diode (treatment laser) emitting 689 nm, a diode laser (aiming beam) emitting 635 nm, control electronics and software, power supply, regulatory compliance safety features (i.e. safety shutter, safety interlocks, key lock switch, etc.), and a self-contained forced air cooling system. Laser energy is delivered to the patient through a fiber optic delivery system mated to slit lamp instruments.

IV. ALTERNATIVE PRACTICES AND PROCEDURES

Age-related macular degeneration (AMD) causes severe, irreversible vision loss and is the leading cause of blindness in individuals older than 50 years in the Western World. Most patients have the non-neovascular or "dry" form, characterized by drusen and atrophic changes in the retinal pigment epithelium (RPE). Eighty to 90 percent of the severe vision loss due to AMD, however, is attributable to the neovascular or exudative form, also known as the "wet" form, which is characterized by choroidal neovascularization or CNV. In CNV, the newly-formed vessels are accompanied by proliferation of fibrous tissue that can destroy photoreceptors within 3-24 months as the areas of leakage become increasingly fibrosed and scarred, causing photoreceptors to atrophy resulting in extensive central scotoma. Without treatment, most affected eyes will have poor central vision (<20/200) within 2 years.

Various experimental therapies have been tried for CNV secondary to AMD but have thus far failed to show promising results. These therapies include interferon alpha, tissue plasminogen activator, and thalidomide. External beam radiation therapy has also been explored, with conflicting results, and the best-designed study to date has shown no effect. Surgical removal of neovascular lesions is under evaluation in randomized clinical trials. Another potential treatment, still in preliminary stages, is retrovirus-mediated gene transfer.

The only accepted treatment for neovascular AMD is laser photocoagulation. Several studies have shown that thermal laser photocoagulation is effective in treating CNV which is situated >200 μm from the foveal center (extrafoveal CNV) or within 1 to 200 μm from the foveal center (juxtafoveal CNV). When the CNV has extended to involve the geometric center of the foveal avascular zone (subfoveal CNV), the benefit of laser photocoagulation becomes much less clear since the destruction of photoreceptors overlying the area of the central fovea resulted in immediate vision loss. No substantial treatment benefit was observed until an average follow-up of 18 months after treatment has been reached.

Laser photocoagulation is indicated only for well-demarcated extrafoveal and juxtafoveal CNV lesions as well as for small, well-demarcated CNV subfoveal lesions that include a component of classic CNV, which account for approximately 10-20% of the patients who present with this disease. Recurrences following standard laser treatment occur in approximately 50% of cases.

V. MARKETING HISTORY

The Coherent Opal Photoactivator has not been marketed internationally or domestically, but the first generation Coherent Opal Photoactivator (Ocular Photoactivation Diode Laser System [OPDL]) has been used by ophthalmologists in a number of international Phase I/II and III clinical investigations for photodynamic therapy (PDT).

The Coherent Opal Photoactivator is comprised of the Coherent Opal Laser Console and Coherent Opal LaserLink. The Coherent Opal LaserLink is the result of modifications of the Coherent LaserLink Slit Lamp Delivery Adapter that has been marketed in various configurations throughout the world since 1993. The original LaserLink delivery adapter was approved and cleared for domestic distribution by the Food and Drug Administration under Premarket Notification (510K) #K932468 for indications in ophthalmology and otology. Approximately, 1,558 Coherent LaserLink Slit Lamp Delivery Adapters have been distributed worldwide to date by Coherent since initial distribution in 1993.

VI. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Please refer to the information in the VISUDYNE™ NDA (NDA 21-119) for full and summarized reports on the safety and effectiveness of this combination product.

Potential adverse effects of the Coherent Opal Photoactivator could be related to inappropriate dosages or improper use of the device. Such events should not occur if the conditions and instructions for use are followed, as fully described in the VISUDYNE Package Insert and Coherent Opal Operator Manual.

If the laser power should drop so that the light dose delivered to tissue was below that needed to activate verteporfin, the treatment would fail. Conversely, if the laser power should be greater than expected, so that an excess light dose was delivered to tissue, some areas of adjacent normal tissue that should have been spared treatment could be damaged. The inclusion of a broken-fiber sensor within the Coherent Opal LaserLink to test fiber transmission from the laser console is intended to reduce these possible events.

VII. SUMMARY OF NON-CLINICAL STUDIES AND CLINICAL STUDIES

The non-clinical and clinical data for verteporfin and the specifications for the Coherent Opal Photoactivator used in the clinical investigations form the combination product application as defined in the Safe Medical Devices Act of 1990.

Full and summarized reports of the clinical studies of verteporfin under the conditions of use described in the labeling are presented in the VISUDYNE™ NDA (NDA 21-119). See the attachment for a summary of the clinical data obtained during this trial.

VIII. Conclusions Drawn from the Studies

The in vivo and in vitro nonclinical studies together with the clinical investigation reported in NDA 21-119 provide valid scientific evidence and reasonable assurance that the Coherent Opal Photoactivator Laser Console and the LaserLink Adapter are safe and effective when used in accordance with the drug and device labeling.

Please refer to the conclusions presented in the VISUDYNE™ NDA (NDA 21-119) in regard to the safety and effectiveness of verteporfin under the conditions of use described in the labeling. The VISUDYNE Package Insert contains a summary of the clinical trials with the appropriate warnings, contraindications, and precautions.

IX. PANEL RECOMMENDATIONS

The Dermatologic and Ophthalmic Drug Advisory Committee reviewed this application on November 17, 1999 and recommended approval of the Coherent Opal Photoactivator Laser Console and the LaserLink Adapter as part of the combination device drug system which includes the drug VISUDYNE. The recommendation of approval was for the combination product for use in the treatment of age-related macular degeneration (AMD) in patients with predominantly classic subfoveal choroidal neovascularization (CNV).

X. FDA DECISION

FDA concurred with the above recommendation of the Dermatologic and Ophthalmic Drug Advisory Committee regarding the combination drug device product which includes the drug VISUDYNE submitted in NDA 21-119.

XI. APPROVAL SPECIFICATIONS

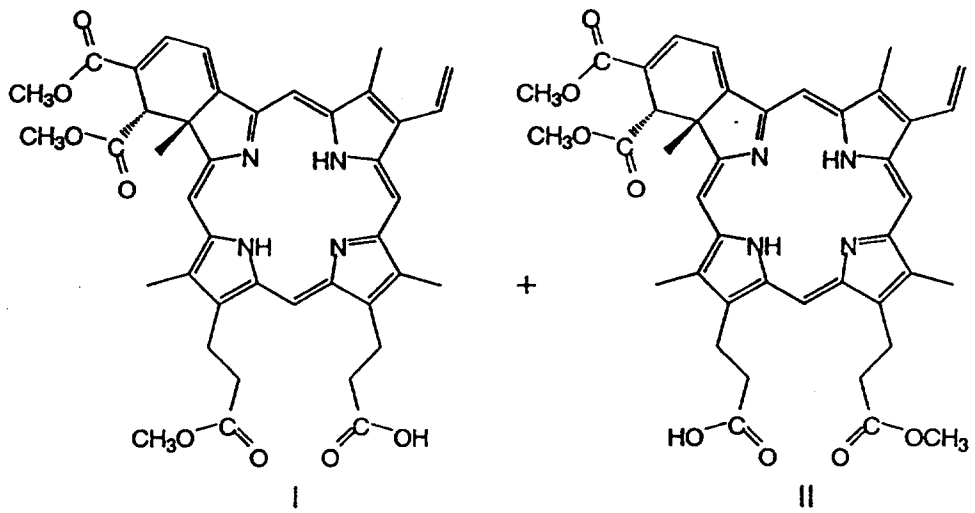
Information on the use of the Coherent Opal Photoactivator Laser Console and the LaserLink Adapter can be found in the Coherent Opal Photoactivator and LaserLink Adapter Operator Manuals. Instructions for use of these devices for the photoactivation of the drug VISUDYNE can be found in the drug Package Insert and in the Operator Manuals.

Basis for Approval
4/7/00

VISUDYNE™
(verteporfin for injection)

DESCRIPTION

VISUDYNE™ (verteporfin for injection) is a light activated drug used in photodynamic therapy. The finished drug product is a lyophilized dark green cake. Verteporfin is a 1:1 mixture of two regioisomers (I and II), represented by the following structures:



I + II

The chemical names for the verteporfin regioisomers are:

9-methyl (I) and 13-methyl (II) *trans*-(±)-18-ethenyl-4,4a-dihydro-3,4-bis(methoxycarbonyl)-4a,8,14,19-tetramethyl-23*H*, 25*H*-benzo[*b*]porphine-9,13-dipropanoate

The molecular formula is $C_{41}H_{42}N_4O_8$ with a molecular weight of approximately 718.8.

Each mL of reconstituted VISUDYNE contains:

ACTIVE: Verteporfin, 2 mg

INACTIVES: Lactose, egg phosphatidylglycerol, dimyristoyl phosphatidylcholine, ascorbyl palmitate and butylated hydroxytoluene

CLINICAL PHARMACOLOGY

Mechanism of Action

VISUDYNE therapy is a two-stage process requiring administration of both verteporfin for injection and nonthermal red light.

Verteporfin is transported in the plasma primarily by lipoproteins. Once verteporfin is activated by light in the presence of oxygen, highly reactive, short-lived singlet oxygen and reactive oxygen radicals are generated. Light activation of verteporfin results in local damage to neovascular endothelium, resulting in vessel occlusion. Damaged endothelium is known to release procoagulant and vasoactive factors through the lipo-oxygenase (leukotriene) and cyclo-oxygenase (eicosanoids such as thromboxane) pathways, resulting in platelet aggregation, fibrin clot formation and vasoconstriction. Verteporfin appears to somewhat preferentially accumulate in neovasculature, including choroidal neovasculature. However, animal models indicate that the drug is also present in the retina. Therefore, there may be collateral damage to retinal structures following photoactivation including the retinal pigmented epithelium and outer nuclear layer of the retina. The temporary occlusion of choroidal neovascularization (CNV) following VISUDYNE therapy has been confirmed in humans by fluorescein angiography.

Pharmacokinetics

Following intravenous infusion, verteporfin exhibits a bi-exponential elimination with a terminal elimination half-life of approximately 5-6 hours. The extent of exposure and the maximal plasma concentration are proportional to the dose between 6 and 20 mg/m^2. At the intended dose, pharmacokinetic parameters are not significantly affected by gender.

Verteporfin is metabolized to a small extent to its diacid metabolite by liver and plasma esterases. NADPH-dependent liver enzyme systems (including the cytochrome P450 isozymes) do not appear to play a role in the metabolism of verteporfin. Elimination is by the fecal route, with less than 0.01% of the dose recovered in urine.

In a study of patients with mild hepatic insufficiency (defined as having two abnormal hepatic function tests at enrollment), AUC and C_{max} were not significantly different from the control group, half-life however was significantly increased by approximately 20%.

Clinical Studies

Two adequate and well-controlled, double-masked, placebo-controlled, randomized studies were conducted in patients with classic-containing subfoveal CNV secondary to age-related macular degeneration. A total of 609 patients (VISUDYNE 402, placebo 207) were enrolled in these two studies. A planned analysis of safety and efficacy was conducted at 1 year, with 94% of patients completing that portion of the study. During these studies, retreatment was allowed every 3 months if fluorescein angiograms showed any recurrence or persistence of leakage. The placebo control (sham treatment) consisted of intravenous administration of Dextrose 5% in Water, followed by light application identical to that used for VISUDYNE therapy.

The difference between treatment groups statistically favored VISUDYNE at the 1-year analysis for visual acuity endpoints.

The subgroup of patients with predominantly classic CNV lesions was more likely to exhibit a treatment benefit (N=243; VISUDYNE 159, placebo 84). Predominantly classic CNV lesions were defined as those in which the classic component comprised 50% or more of the area of the entire lesion. For the primary efficacy endpoint (percentage of patients who lost less than 3 lines of visual acuity), these patients showed a difference of 28% between treatment groups (67% for VISUDYNE patients compared to 39% for placebo patients, $P<.001$). Severe vision loss (≥6 lines of visual acuity from baseline) was experienced by only 12% of VISUDYNE-treated patients compared to 33% of placebo-treated patients.

Patients with predominantly classic CNV lesions that did not contain occult CNV exhibited the greatest benefit (N=134; VISUDYNE 90, placebo 44). These patients demonstrated a 49% difference between treatment groups when assessed by the <3 lines-lost definition (77% vs. 27%). Severe vision loss (≥6 lines of visual acuity from baseline) was experienced by only 10% of VISUDYNE-treated patients compared to 41% of placebo-treated patients.

Older patients (≥75 years), patients with dark irides, patients with occult lesions or patients with less than 50% classic CNV were less likely to benefit from VISUDYNE therapy.

The safety and efficacy of VISUDYNE beyond 2 years have not been demonstrated.

INDICATIONS AND USAGE

VISUDYNE therapy is indicated for the treatment of age-related macular degeneration in patients with predominantly classic subfoveal choroidal neovascularization.

CONTRAINDICATIONS

VISUDYNE is contraindicated for patients with porphyria or a known hypersensitivity to any component of this preparation.

WARNINGS

Following injection with VISUDYNE, care should be taken to avoid exposure of skin or eyes to direct sunlight or bright indoor light for 5 days. In the event of extravasation during infusion, the extravasation area must be thoroughly protected from direct light until the swelling and discoloration have faded in order to prevent the occurrence of a local burn which could be severe. If emergency surgery is necessary within 48 hours after treatment, as much of the internal tissue as possible should be protected from intense light.

Patients who experience severe decrease of vision of 4 lines or more within 1 week after treatment should not be retreated, at least until their vision completely recovers to pretreatment levels and the potential benefits and risks of subsequent treatment are carefully considered by the treating physician.

Use of incompatible lasers that do not provide the required characteristics of light for the photoactivation of VISUDYNE could result in incomplete treatment due to partial photoactivation of VISUDYNE, overtreatment due to overactivation of VISUDYNE, or damage to surrounding normal tissue.

PRECAUTIONS

General

Standard precautions should be taken during infusion of VISUDYNE to avoid extravasation. Examples of standard precautions include, but are not limited to:

- A free-flowing intravenous (IV) line should be established before starting VISUDYNE infusion and the line should be carefully monitored.
- Due to the possible fragility of vein walls of some elderly patients, it is strongly recommended that the largest arm vein possible, preferably antecubital, be used for injection.
- Small veins in the back of the hand should be avoided.

If extravasation does occur, the infusion should be stopped immediately and cold compresses applied (see Warnings).

VISUDYNE therapy should be considered carefully in patients with moderate to severe hepatic impairment since there is no clinical experience with verteporfin in such patients.

There is no clinical data related to the use of VISUDYNE in anesthetized patients. At a >10-fold higher dose given by bolus injection to anesthetized pigs, verteporfin caused severe hemodynamic effects, including death, probably as a result of complement activation. These effects were diminished or abolished by pretreatment with antihistamine and they were not seen in conscious pigs or in any other species, whether conscious or under general anesthesia.

Information for Patients

Patients who receive VISUDYNE will become temporarily photosensitive after the infusion. Patients should wear a wrist band to remind them to avoid direct sunlight for 5 days. During that period, patients should avoid exposure of unprotected skin, eyes or other body organs to direct sunlight or bright indoor light. Sources of bright light include, but are not limited to, tanning salons, bright halogen lighting and high power lighting used in surgical operating rooms or dental offices.

If treated patients must go outdoors in daylight during the first 5 days after treatment, they should protect all parts of their skin and their eyes by wearing protective clothing and dark sunglasses. UV sunscreens are not effective in protecting against photosensitivity reactions because photoactivation of the residual drug in the skin can be caused by visible light.

Patients should not stay in the dark and should be encouraged to expose their skin to ambient indoor light, as it will help inactivate the drug in the skin through a process called photobleaching.

Drug Interactions

Drug interaction studies in humans have not been conducted with VISUDYNE.

Verteporfin is rapidly eliminated by the liver, mainly as unchanged drug. Metabolism is limited and occurs by liver and plasma esterases. Microsomal cytochrome P450 does not appear to play a role in verteporfin metabolism.

Based on the mechanism of action of verteporfin, many drugs used concomitantly could influence the effect of VISUDYNE therapy. Possible examples include the following:

Calcium channel blockers, polymyxin B or radiation therapy could enhance the rate of VISUDYNE uptake by the vascular endothelium. Other photosensitizing agents (e.g., tetracyclines, sulfonamides, phenothiazines, sulfonylurea hypoglycemic agents, thiazide, diuretics and griseofulvin) could increase the potential for skin photosensitivity reactions. Compounds that quench active oxygen species or scavenge radicals, such as dimethyl sulfoxide, β-carotene, ethanol, formate and mannitol, would be expected to decrease VISUDYNE activity. Drugs that decrease clotting, vasoconstriction or platelet aggregation, e.g., thromboxane A_2 inhibitors, could also decrease the efficacy of VISUDYNE therapy.

Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies have been conducted to evaluate the carcinogenic potential of verteporfin.

Photodynamic therapy (PDT) as a class has been reported to result in DNA damage including DNA strand breaks, alkali-labile sites, DNA degradation, and DNA-protein cross links which may result in chromosomal aberrations, sister chromatid exchanges (SCE), and mutations. In addition, other photodynamic therapeutic agents have been shown to increase the incidence of SCE in Chinese hamster ovary (CHO) cells irradiated with visible light and in Chinese hamster lung fibroblasts irradiated with near UV light, increase mutations and DNA-protein cross-linking in mouse L5178 cells, and increase DNA-strand breaks in malignant human cervical carcinoma cells, but not in normal cells. Verteporfin was not evaluated in these latter systems. It is not known how the potential for DNA damage with PDT agents translates into human risk.

No effect on male or female fertility has been observed in rats following intravenous administration of verteporfin for injection up to 10 mg/kg/day (approximately 60 and 40 fold human exposure at 6 mg/m^2 based on AUC_{inf} in male and female rats, respectively).

Pregnancy

Teratogenic Effects: Pregnancy Category C.

Rat fetuses of dams administered verteporfin for injection intravenously at ≥10 mg/kg/day during organogenesis (approximately 40 fold human exposure at 6 mg/m^2 based on AUC_{inf} in female rats) exhibited an increase in the incidence of anophthalmia/microphthalmia. Rat fetuses of dams administered 25 mg/kg/day (approximately 125 fold the human exposure at 6 mg/m^2 based on AUC_{inf} in female rats) had an increased incidence of wavy ribs and anophthalmia/microphthalmia.

In pregnant rabbits, a decrease in body weight gain and food consumption was observed in animals that received verteporfin for injection intravenously at ≥10 mg/kg/day during organogenesis. The no observed adverse effect level (NOAEL) for maternal toxicity was 3 mg/kg/day (approximately 7 fold human exposure at 6 mg/m^2 based on body surface area). There were no teratogenic effects observed in rabbits at doses up to 10 mg/kg/day.

There are no adequate and well-controlled studies in pregnant women. VISUDYNE should be used during pregnancy only if the benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether verteporfin for injection is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when VISUDYNE is administered to a women who is nursing.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

Approximately 90% of the patients treated with VISUDYNE in the clinical efficacy trials were over the age of 65. A reduced treatment effect was seen with increasing age.

ADVERSE REACTIONS

The most frequently reported adverse events to VISUDYNE are headaches, injection site reactions (including extravasation and rashes) and visual disturbances (including blurred vision, decreased visual acuity and visual field defects). These events occurred in approximately 10-20% of patients. The following events, listed by Body System, were reported more frequently with VISUDYNE therapy than with placebo therapy and occurred in 1-10% of patients:

Ocular Treatment Site:	Cataracts, conjunctivitis/conjunctival injection, dry eyes, ocular itching, severe vision loss, subconjunctival, subretinal or vitreous hemorrhage
Body as a Whole:	Asthenia, back pain (primarily during infusion), fever, flu syndrome, photosensitivity
Cardiovascular:	Atrial fibrillation, hypertension, peripheral vascular disorder, varicose veins
Dermatologic:	Eczema

Digestive:	Constipation, gastrointestinal cancers, nausea
Hemic and Lymphatic:	Anemia, white blood cell count decreased, white blood cell count increased
Hepatic:	Elevated liver function tests
Metabolic/Nutritional:	Albuminuria, creatinine increased
Musculoskeletal:	Arthralgia, arthrosis, myasthenia
Nervous system:	Hypesthesia, sleep disorder, vertigo
Respiratory:	Pharyngitis, pneumonia
Special Senses:	Decreased hearing, diplopia, lacrimation disorder
Urogenital:	Prostatic disorder

Severe vision decrease, equivalent of 4 lines or more, within 7 days after treatment has been reported in 1-4% of patients. Partial recovery of vision was observed in many patients. Photosensitivity reactions occurred in the form of skin sunburn following exposure to sunlight. The higher incidence of back pain in the VISUDYNE group occurred primarily during infusion.

OVERDOSAGE

Overdose of drug and/or light in the treated eye may result in nonperfusion of normal retinal vessels with the possibility of severe decrease in vision that could be permanent. An overdose of drug will also result in the prolongation of the period during which the patient remains photosensitive to bright light. In such cases, it is recommended to extend the photosensitivity precautions for a time proportional to the overdose.

DOSAGE AND ADMINISTRATION

A course of VISUDYNE therapy is a two-step process requiring administration of both drug and light.

The first step is the intravenous infusion of VISUDYNE. The second step is the activation of VISUDYNE with light from a nonthermal diode laser.

The physician should re-evaluate the patient every 3 months and if choroidal neovascular leakage is detected on fluorescein angiography, therapy should be repeated.

Lesion Size Determination

The greatest linear dimension (GLD) of the lesion is estimated by fluorescein angiography and color fundus photography. All classic and occult CNV, blood and/or blocked fluorescence, and any serous detachments of the retinal pigment epithelium should be included for this measurement. Fundus cameras with magnification within the range of 2.4-2.6X are recommended. The GLD of the lesion on the fluorescein angiogram must be corrected for the magnification of the fundus camera to obtain the GLD of the lesion on the retina.

Spot Size Determination

The treatment spot size should be 1000 microns larger than the GLD of the lesion on the retina to allow a 500 micron border, ensuring full coverage of the lesion. The maximum spot size used in the clinical trials was 6400 microns.

The nasal edge of the treatment spot must be positioned at least 200 microns from the temporal edge of the optic disc, even if this will result in lack of photoactivation of CNV within 200 microns of the optic nerve.

VISUDYNE Administration

Reconstitute each vial of VISUDYNE with 7 mL of sterile Water for Injection to provide 7.5 mL containing 2 mg/mL. Reconstituted VISUDYNE must be protected from light and used within 4 hours. It is recommended that reconstituted VISUDYNE be inspected visually for particulate matter and discoloration prior to administration. Reconstituted VISUDYNE is an opaque dark green solution.

The volume of reconstituted VISUDYNE required to achieve the desired dose of 6 mg/m^2 body surface area is withdrawn from the vial and diluted with 5% Dextrose for Injection to a total infusion volume of 30 mL. The full infusion volume is administered intravenously over 10 minutes at a rate of 3 mL/minute, using an appropriate syringe pump and in-line filter.

Precautions should be taken to prevent extravasation at the injection site. If extravasation occurs, protect the site from light (See Precautions).

Light Administration

Initiate 689 nm wavelength laser light delivery to the patient 15 minutes after the start of the 10-minute infusion with VISUDYNE.

Photoactivation of VISUDYNE is controlled by the total light dose delivered. In the treatment of choroidal neovascularization, the recommended light dose is 50 J/cm^2 of neovascular lesion administered at an intensity of 600 mW/cm^2. This dose is administered over 83 seconds.

Light dose, light intensity, ophthalmic lens magnification factor and zoom lens setting are important parameters for the appropriate delivery of light to the predetermined treatment spot. Follow the laser system manuals for procedure set up and operation.

The laser system must deliver a stable power output at a wavelength of 689±3 nm. Light is delivered to the retina as a single circular spot via a fiber optic and a slit lamp, using a suitable ophthalmic magnification lens.

The following laser systems have been tested for compatibility with VISUDYNE and are approved for delivery of a stable power output at a wavelength of 689±3 nm:

Coherent Opal Photoactivator Laser Console and LaserLink Adapter,
Manufactured by Coherent, Inc., Santa Clara, CA

Zeiss VISULAS 690s laser and VISULINK PDT adapter,
Manufactured by Carl Zeiss Inc., Thornwood, NY

Concurrent Bilateral Treatment

The controlled trials only allowed treatment of one eye per patient. In patients who present with eligible lesions in both eyes, physicians should evaluate the potential benefits and risks of treating both eyes concurrently. If the patient has already received previous VISUDYNE therapy in one eye with an acceptable safety profile, both eyes can be treated concurrently after a single administration of VISUDYNE. The more aggressive lesion should be treated first, at 15 minutes after the start of infusion. Immediately at the end of light application to the first eye, the laser settings should be adjusted to introduce the treatment parameters for the second eye, with the same light dose and intensity as for the first eye, starting no later than 20 minutes from the start of infusion.

In patients who present for the first time with eligible lesions in both eyes without prior VISUDYNE therapy, it is prudent to treat only one eye (the most aggressive lesion) at the first course. One week after the first course, if no significant safety issues are identified, the second eye can be treated using the same treatment regimen after a second VISUDYNE infusion. Approximately 3 months later, both eyes can be evaluated and concurrent

treatment following a new VISUDYNE infusion can be started if both lesions still show evidence of leakage.

HOW SUPPLIED

VISUDYNE is supplied in a single use glass vial with a gray bromobutyl stopper and aluminum flip-off cap. It contains a lyophilized cake with 15 mg verteporfin. The product is intended for intravenous injection only.

Spills and Disposal

Spills of VISUDYNE should be wiped up with a damp cloth. Skin and eye contact should be avoided due to the potential for photosensitivity reactions upon exposure to light. Use of rubber gloves and eye protection is recommended. All materials should be disposed of properly.

Accidental Exposure

Because of the potential to induce photosensitivity reactions, it is important to avoid contact with the eyes and skin during preparation and administration of VISUDYNE. Any exposed person must be protected from bright light (See Warnings).

NDC 58768-150-15

Store VISUDYNE between 20°C and 25°C (68°F-77°F).

Rx Only

Manufactured by:

Parkedale Pharmaceuticals, Inc.
Rochester, MI 48307

For:

QLT PhotoTherapeutics, Inc.
Seattle, WA 98101

Co-developed and Distributed by:

CIBA Vision
A Novartis Company
Duluth, GA 30097