**HIGHLIGHTS OF PRESCRIBING INFORMATION**
**These highlights do not include all the information needed to use CYSVIEW safely and effectively. See full prescribing information for CYSVIEW.**

**CYSVIEW (hexaminolevulinate hydrochloride) for intravesical solution**
**Initial U.S. Approval: 2010**

**----------RECENT MAJOR CHANGES----------**

| | |
|---|---|
| Dosage and Administration, Blue Light Imaging Devices (2.4) | 6/2026 |
| Contraindications, gross hematuria (4) - Removed | 6/2026 |

**----------INDICATIONS AND USAGE----------**

CYSVIEW is an optical imaging agent indicated for the cystoscopic detection of carcinoma of the bladder, including carcinoma in situ (CIS), in adult patients:

- With suspected or known lesion(s) on the basis of a prior cystoscopy
- Undergoing surveillance cystoscopy for bladder cancer

Limitations of Use

CYSVIEW is not a replacement for random bladder biopsies or other procedures used in the detection of bladder cancer. (1, 5.2)

**----------DOSAGE AND ADMINISTRATION----------**

- The recommended adult dose is 100 mg reconstituted in 50 mL of the supplied diluent instilled into the bladder via a urinary catheter and retained for 1 hour to 3 hours before evacuation. (2.1)
- Use an FDA-authorized blue light imaging device intended to perform blue light cystoscopy with hexaminolevulinate hydrochloride. (2.4)
- Perform cystosopic examination of the entire bladder first under white light and then under blue light. (2.5)
- For reconstitution, administration, and cystoscopic examination see full prescribing information. (2.2, 2.3, 2.5)

**----------DOSAGE FORMS AND STRENGTHS----------**

For intravesical solution: 100 mg of hexaminolevulinate hydrochloride for reconstitution with the supplied diluent

**----------CONTRAINDICATIONS----------**

- Porphyria
- Known hypersensitivity to hexaminolevulinate or aminolevulinate derivatives (4)

**---------- WARNINGS AND PRECAUTIONS----------**

- Anaphylaxis: Have trained personnel and therapies available. (5.1).
- Failed Detection: CYSVIEW may not detect all malignant lesions. Always perform white light cystoscopy followed by blue light cystoscopy. Do not biopsy with blue light only. (5.2)
- False fluorescence may occur due to inflammation, cystoscopic trauma, scar tissue, previous bladder biopsy, recent BCG therapy, or chemotherapy. (5.3)

**----------ADVERSE REACTIONS----------**

The most common adverse reaction was bladder spasm followed by dysuria, hematuria, and bladder pain. (6.1)

**To report SUSPECTED ADVERSE REACTIONS, contact Photocure Inc. at 1-855-297-8439 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**See 17 for PATIENT COUNSELING INFORMATION.**

**Revised: 6/2026**

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**FULL PRESCRIBING INFORMATION: CONTENTS***



*Sections or subsections omitted from the full prescribing information are not listed.

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**FULL PRESCRIBING INFORMATION**

## 1 INDICATIONS AND USAGE

CYSVIEW is indicated for the cystoscopic detection of carcinoma of the bladder, including carcinoma in situ (CIS), in adult patients:

- With suspected or known lesion(s) based on a prior cystoscopy
- Undergoing surveillance cystoscopy for bladder cancer

Limitations of Use

CYSVIEW is not a replacement for random bladder biopsies or other procedures used in the detection of bladder cancer *[see Warnings and Precautions (5.2)]*.

## 2 DOSAGE AND ADMINISTRATION

### 2.1 Recommended Dose

The recommended dose for adults is 100 mg of CYSVIEW administered by bladder instillation.

Reconstitute the CYSVIEW 100 mg powder in the vial with the supplied diluent to a final volume of 50 mL. Administer the entire 50 mL dose via a urinary catheter. The solution should be retained in the bladder for 1 hour to 3 hours following instillation. *[see Dosage and Administration (2.2, 2.3)]*.

### 2.2 Reconstitution of CYSVIEW

General Instructions

- CYSVIEW is supplied as a kit with diluent for reconstitution, with or without a vial adapter for use during reconstitution *[see How Supplied/Storage and Handling (16)]*.
- Perform all steps using aseptic technique.
- Wear gloves during the reconstitution procedure; skin exposure to CYSVIEW may increase the risk of sensitization to the drug.
- Reconstituted CYSVIEW has a concentration of 2 mg/mL hexaminolevulinate hydrochloride and appears as a colorless to pale yellow, clear to slightly opalescent solution free from visible particles.
- If not immediately used, store the reconstituted solution in the labeled syringe under refrigeration at 2°C to 8°C (36°F to 46°F) for up to 2 hours. The solution should be discarded if not used within 2 hours.

Reconstitution Using a Vial Adapter

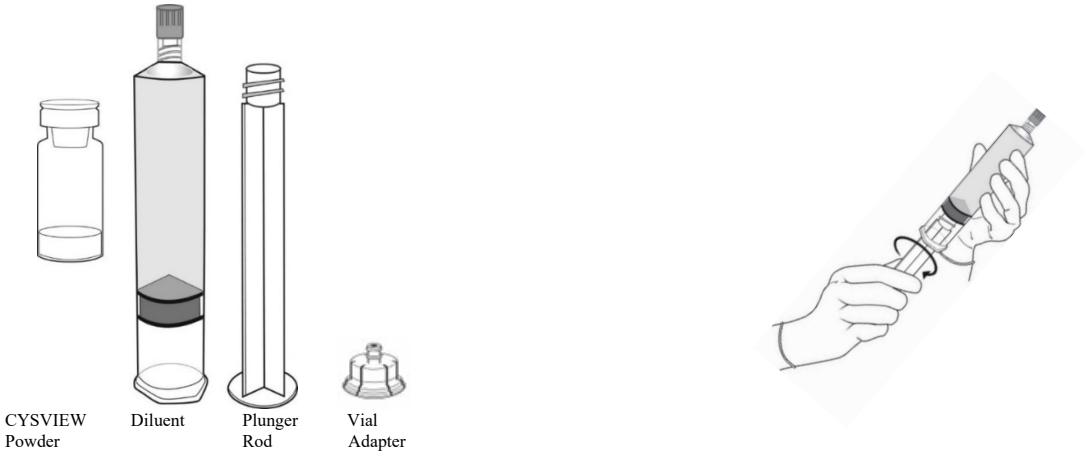



**Figure A. Components of CYSVIEW and Attachment of Plunger Rod to Diluent Syringe**

1. Fasten the plunger rod into the rubber stopper of the prefilled syringe by turning the plunger rod clockwise until it stops (see **Figure A**).

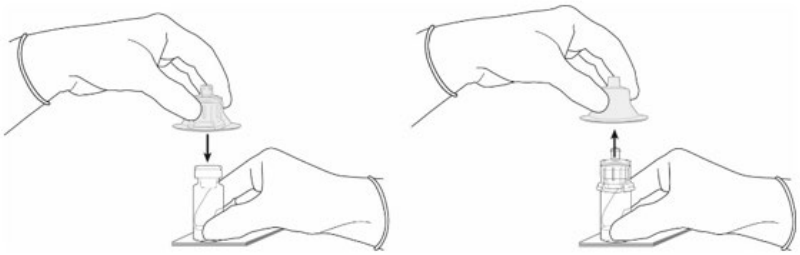


**Figure B. Connection of Vial Adapter to CYSVIEW Vial**

2. Remove the plastic cap from the vial. Remove the TyveK® cover from the vial adapter blister package. Do not remove the vial adapter from the package. Place the CYSVIEW vial on a flat surface. Using the blister package to hold the vial adapter, connect to the vial with a downward vertical motion. The vial adapter snaps onto the vial as the spike penetrates the rubber stopper of the vial. Remove the plastic blister package and discard it. Take care not to touch the exposed end of the vial adapter (see **Figure B**).

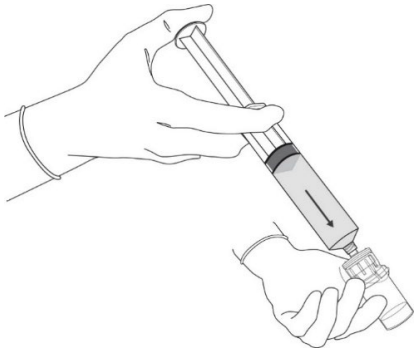


**Figure C. Injection of Diluent into CYSVIEW Vial**

3. Remove the cap from the prefilled syringe and carefully retain it for subsequent reattachment to the syringe. Hold the prefilled syringe upright and carefully press the plunger rod upward to remove air. Connect the syringe to the vial adapter. Inject about 10 mL of the diluent from the prefilled syringe down into the vial. The vial should be about ¾ full (see **Figure C**).

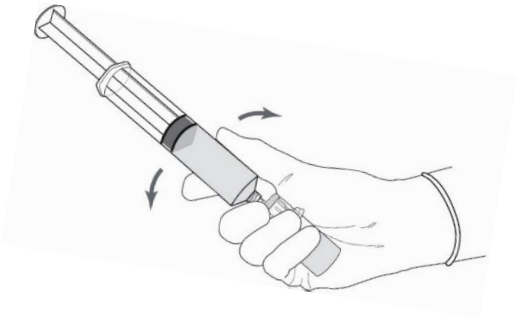
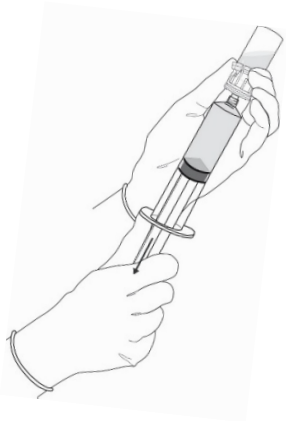


**Figure D. Dissolution of CYSVIEW Powder in Diluent**

4. Without disconnecting the vial adapter from the vial, hold the vial and syringe in a firm grip and gently shake to dissolve the powder in the diluent. The powder normally dissolves almost immediately (see **Figure D**).



.

**Figure E. Withdrawal of Reconstituted CYSVIEW from Vial**

5. Turn the vial upside down and withdraw all of the dissolved solution from the vial back into the syringe (see **Figure E**).

   Do not inject large amounts of air or diluent when vial is inverted as it may block the venting action of the vial adapter. If this occurs, turn the vial upright and pull back on the plunger rod in the syringe.

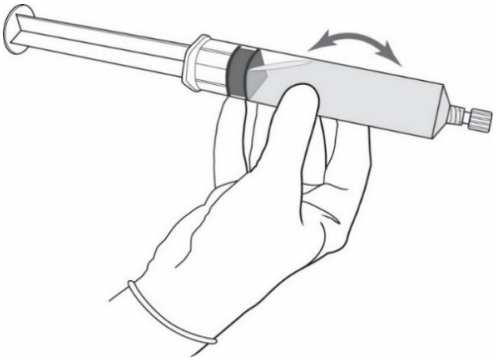


**Figure F. Final Preparation of Reconstituted CYSVIEW Solution**

6. Disconnect the empty vial with the vial adapter from the syringe tip and discard it. Plug the syringe with the syringe cap. Gently mix the contents of the syringe (see **Figure F**).

7. Peel off the detachable portion of the syringe label. On the syringe label, add 2 hours to the present time and write the resulting expiration time and date.

Reconstitution Without Using a Vial Adapter


**Figure G. Components of CYSVIEW and Attachment of Plunger Rod to Diluent Syringe**

1. Fasten the plunger rod into the rubber stopper of the prefilled syringe by turning the plunger rod clockwise until it stops (see **Figure G**).

**Figure H. Injection of Diluent into CYSVIEW Vial**

2. Remove the plastic cap from the vial. Remove the cap from the prefilled syringe and carefully retain it for subsequent reattachment to the syringe. Attach a needle to the prefilled syringe. Hold the prefilled syringe upright and carefully press the plunger rod upward to remove air. Penetrate the stopper of the CYSVIEW vial with the needle and inject about 10 mL of the diluent from the prefilled syringe down into the vial. The vial should be about ¾ full (see **Figure H**).

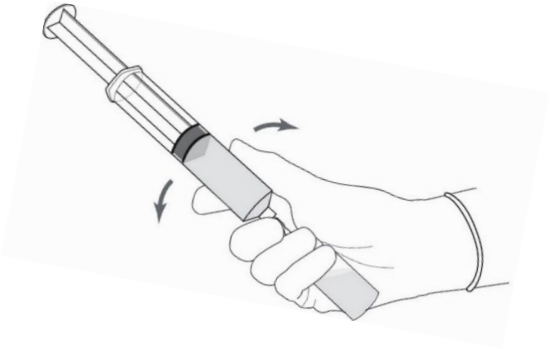


**Figure I. Dissolution of CYSVIEW Powder in Diluent**

3. Without withdrawing the needle from the vial, hold the vial and syringe in a firm grip and gently shake to dissolve of the powder in the diluent. The powder normally dissolves almost immediately (see **Figure I**).

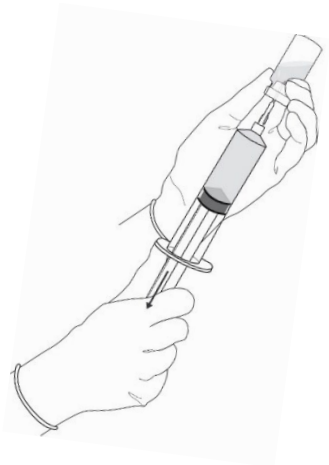


**Figure J. Withdrawal of Reconstituted CYSVIEW from Vial**

4. Turn the vial upside down and withdraw all of the dissolved solution from the vial back into the syringe (see **Figure J**).

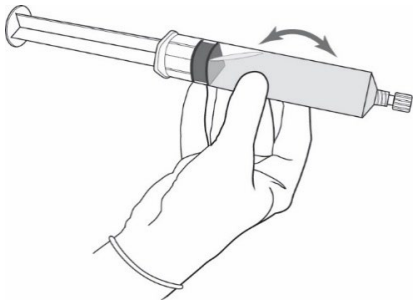


**Figure K. Final Preparation of Reconstituted CYSVIEW Solution**

5. Remove the needle from the vial, disconnect the needle from the syringe tip and discard it. Plug the syringe with the syringe cap. Gently mix the contents of the syringe (see **Figure K**).

6. Peel off the detachable portion of the syringe label. On the syringe label, add two hours to the present time and write the resulting expiration time and date.

### 2.3 Administration Instructions

Catheter Requirements

For bladder instillation of the solution of CYSVIEW, use straight or intermittent, urethral catheters with a proximal funnel opening that will accommodate the Luer Lock adapter. Use only catheters made of vinyl (uncoated or coated with hydrogel), latex (amber or red), and silicone to instill the reconstituted CYSVIEW. Do not use catheters coated or embedded with silver or antibiotics. In-dwelling bladder catheters (Foley catheters) may be used if the catheters are inserted shortly prior to CYSVIEW administration and are removed following the CYSVIEW instillation.

Instructions for Bladder Instillation of CYSVIEW

1. Using standard sterile catheterization technique, first insert the urethral catheter into the bladder of the patient and use the catheter to completely empty the patient's bladder before instillation of CYSVIEW.

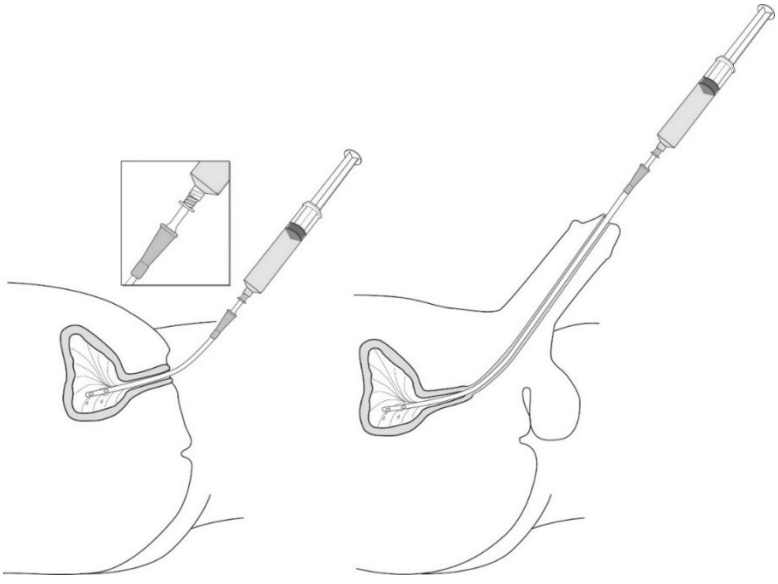


**Figure L. Connection of Catheter Adapter and Instillation of CYSVIEW**

2. To attach the syringe containing the solution of CYSVIEW to the catheter, do the following:
    - Remove the syringe cap from the syringe that contains the reconstituted solution of CYSVIEW.

- Attach the Luer Lock end of the (provided) catheter adapter to the syringe.
- Insert the tapered end of the catheter adapter into the funnel opening of the catheter (see **Figure L**).

3. Slowly instill the solution of CYSVIEW into the bladder through the catheter, ensuring that the complete volume of the syringe (50 mL) is administered (see **Figure L**).

4. After the solution is instilled, remove the catheter and instruct the patient to retain the solution within the bladder for at least 1 hour; do not exceed 3 hours *[see Dosage and Administration (2.5)]*. Patients may stand, sit and move about during the time period between instillation and start of the cystoscopic procedure.

5. Evacuate the solution of CYSVIEW from the bladder as part of routine emptying of the bladder immediately prior to the initiation of the cystoscopic procedure. Also, the patient may void and completely empty the bladder prior to the procedure.

6. Avoid skin contact with CYSVIEW. If skin does come in contact with CYSVIEW, wash immediately with soap and water and dry off. After voiding the bladder of CYSVIEW, routinely wash the patient's perineal skin region with soap and water and dry.

### 2.4 Blue Light Imaging Devices

Use CYSVIEW with the KARL STORZ D-Light C Photodynamic Diagnostic (PDD) System or other FDA-authorized imaging device intended to perform blue light cystoscopy (BLC) with hexaminolevulinate hydrochloride in the indicated population. The light source enables both white light cystoscopy and blue light (wavelength between 360 nm and 450 nm) fluorescence cystoscopy.

For system set-up and general information for the safe use of a blue light imaging device, refer to the instruction manual for each of the system components.

Certain blue light imaging devices may not be suitable for use by healthcare providers with green-red color blindness. See the instruction manual from the device manufacturer before use.

### 2.5 Cystoscopic Examination

User Training

Training and proficiency in cystoscopic procedures are essential prior to the use of CYSVIEW. Carefully review the instruction manual provided with the blue light imaging device. For additional training in the use of a blue light imaging device, contact the manufacturer's representative.

CYSVIEW Administration and Cystoscopic Timing

- Instill CYSVIEW into the bladder and retain in the bladder for a minimum of 1 hour and a maximum of 3 hours *[see Dosage and Administration (2.3)]*.

- Initiate the cystoscopic examination within 30 minutes after evacuation of CYSVIEW from the bladder, but no less than 1 hour or more than 3 hours after CYSVIEW instillation.

- If the patient did not retain CYSVIEW in the bladder for 1 hour, allow 1 hour to pass from the instillation of Cysview into the bladder to the start of the cystoscopic examination.

Cystoscopic Examination with White and Blue Light

- Empty the patient's bladder and then fill the bladder with a clear fluid (standard bladder irrigation fluid) to distend the bladder wall. Ensure adequate irrigation during examination of the bladder; blood, urine or floating particles in the bladder can interfere with visualization under both white and blue light cystoscopy.

- First, perform a complete cystoscopic examination of the entire bladder using white light. If this initial examination does not reveal widespread mucosal inflammation, proceed to repeat the full examination using blue light.

- Under blue light, abnormal lesions typically demonstrate homogenous and intense red fluorescence with well-demarcated margins, contrasting with the blue appearance of normal urothelium. Register and map the location and appearance of any suspicious lesions or other abnormalities identified under either white or blue light.

- For accurate interpretation, consider the following:

- Less intense, more diffuse red fluorescence is expected in normal tissue at the bladder outlet and the prostatic urethra and should be distinguished from malignant lesions.
- To avoid false fluorescence from tangential light, hold the endoscope perpendicular and close to the bladder wall with the bladder distended.
- False positive fluorescence can result from scope trauma from a previous cystoscopic examination or bladder inflammation *[see Warnings and Precautions (5.3)]*.
- Malignant lesions may not fluoresce, particularly if they are coated with necrotic tissue. Necrotic cells generally do not fluoresce *[see Warnings and Precautions (5.2)]*.

- Avoid prolonged blue light exposure, as potential adverse effects have not been studied. In clinical trials, the cumulative blue light exposure time for evaluation, mapping, and resection did not exceed 32 minutes for any procedure *[see Clinical Studies (14)]*.
- Only after completing white and blue light examinations and mapping should you proceed with biopsy and/or resection of suspicious lesions by transurethral resection of the bladder (TURB). Before finalizing the TURB procedure, confirm the completeness of the resections under both white and blue light.

## 3 DOSAGE FORMS AND STRENGTHS

For intravesical solution: 100 mg of hexaminolevulinate hydrochloride as a white to off-white or pale yellow freeze-dried powder for reconstitution with the supplied diluent.

## 4 CONTRAINDICATIONS

CYSVIEW is contraindicated in patients with:

- Porphyria
- Known hypersensitivity to hexaminolevulinate or any derivative of aminolevulinic acid

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Anaphylaxis

Anaphylaxis, including anaphylactic shock, has been reported following administration of CYSVIEW *[see Adverse Reactions (6.2)]*. Prior to and during use of CYSVIEW, have trained personnel and therapies available for the treatment of anaphylaxis.

### 5.2 Failed Detection

CYSVIEW may fail to detect some bladder tumors, including malignant lesions. CYSVIEW is not a replacement for random biopsies or any other procedure usually performed in the cystoscopic evaluation for cancer. Do not perform cystoscopy with blue light alone as malignant lesions can be missed unless the bladder is initially examined under white light *[see Dosage and Administration (2.5)* and *Clinical Studies (14)]*.

The presence of urine and/or blood within the bladder may interfere with the detection of tissue fluorescence. To enhance the diagnostic utility of CYSVIEW:

- Ensure the bladder is emptied of urine prior to the instillation of fluids at cystoscopy.
- Rinse the bladder as needed during cystoscopy to optimize visualisation.
- Biopsy/resect bladder mucosal lesions only following completion of both white light and blue light rigid cystoscopy.

### 5.3 False Positive Fluorescence

Fluorescent areas detected during blue light cystoscopy may not indicate a bladder mucosal lesion. In clinical studies, approximately 20% of the lesions detected only by blue light cystoscopy showed neither dysplasia nor carcinoma *[see Clinical Studies (14)]*. False positive fluorescence may result from inflammation, cystoscopic trauma, and scar tissue from bladder mucosal biopsy from a previous cystoscopic examination, or following intravesical treatment such as recent BCG immunotherapy or intravesical chemotherapy. In a study of patients treated with recent BCG immunotherapy or intravesical chemotherapy, the rate of false positives with blue light was

55% between 6 weeks to 90 days and 41% after 90 days; the false positive rate was 53% and 33% at the respective time intervals with white light.

## 6 ADVERSE REACTIONS

The following clinically significant adverse reaction is discussed elsewhere in the Prescribing Information:

- Anaphylaxis *[see Warnings and Precautions (5.1)]*.

### 6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.

The safety of CYSVIEW was evaluated in 1,628 patients in seven clinical trials. Patients were aged 32 to 96 years with a median age of 70 years, 77% male, 88% White, 3% Black or African American, and 9% of unspecified racial group. All patients were evaluated after a single instillation of 100 mg of CYSVIEW, and 103 patients received a repeat administration of CYSVIEW *[see Clinical Studies (14)]*.

The most common adverse reaction was bladder spasm (reported in 2% of the patients) followed by dysuria, hematuria, and bladder pain.

### 6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of CYSVIEW. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure:

Anaphylactic shock, hypersensitivity reactions, bladder pain, cystitis, and abnormal urinalysis.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Risk Summary

There are no available data on CYSVIEW use in pregnant women to inform a drug associated risk of adverse developmental outcomes. Adequate reproductive and developmental toxicity studies in animals have not been performed. Systemic absorption following administration of CYSVIEW is expected to be minimal *[see Clinical Pharmacology (12.3)]*.

The background risk of major birth defects and miscarriage for the indicated populations is unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

### 8.2 Lactation

Risk Summary

There are no data on the presence of hexaminolevulinate in human or animal milk, the effects on a breastfed infant, or the effects on milk production. Systemic absorption following administration of CYSVIEW is expected to be minimal *[see Clinical Pharmacology (12.3)]*. The lack of clinical data during lactation precludes a clear determination of the risk of CYSVIEW to an infant during lactation; therefore, the development and health benefits of breastfeeding should be considered along with the mother's clinical need for CYSVIEW and any potential adverse effects on the breastfed infant from CYSVIEW or from the underlying maternal condition.

### 8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

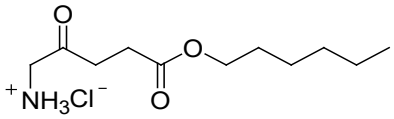
### 8.5 Geriatric Use

Of 2,127 subjects in clinical studies of CYSVIEW, 67% were 65 years and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

## 11 DESCRIPTION

CYSVIEW (hexaminolevulinate hydrochloride) for intravesical solution is an optical imaging agent.

The chemical name of hexaminolevulinate hydrochloride is hexyl 5-amino-4-oxopentanoate hydrochloride, and it has a molecular formula of $C_{11}H_{21}NO_3 \cdot HCl$. Its molecular weight is 251.76, and it has the following structural formula:



CYSVIEW and DILUENT for CYSVIEW are supplied together as a kit:

- CYSVIEW is a sterile, non-pyrogenic, freeze-dried, white to off-white or pale yellow powder provided in a clear glass vial. Each vial contains 100 mg hexaminolevulinate hydrochloride (equivalent to 85 mg hexaminolevulinate).

- The DILUENT for CYSVIEW is a sterile, non-pyrogenic, clear, colorless solution (pH 6) free from visible particles provided in a 50 mL plastic prefilled syringe. Each mL contains 0.61 mg disodium hydrogen phosphate, 0.58 mg potassium dihydrogen phosphate, 7.02 mg sodium chloride, hydrochloric acid and sodium hydroxide for pH adjustment, and water for injection.

The reconstituted solution of CYSVIEW contains 2 mg/mL of hexaminolevulinate hydrochloride and is colorless to pale yellow. It is free from visible particles and has a pH between 5.7 and 6.2.

## 12 CLINICAL PHARMACOLOGY

### 12.1 Mechanism of Action

Hexaminolevulinate is an ester of the heme precursor, aminolevulinic acid. After bladder instillation, hexaminolevulinate enters the bladder mucosa and is proposed to enter the intracellular space of mucosal cells where it is used as a precursor in the formation of the photoactive intermediate protoporphyrin IX (PpIX) and other photoactive porphyrins (PAPs). PpIX and PAPs are reported to accumulate preferentially in neoplastic cells as compared to normal urothelium, partly due to altered enzymatic activity in the neoplastic cells. After excitation with light at wavelengths between 360 nm and 450 nm, PpIX and other PAPs return to a lower energy level by fluorescing, which can be detected and used for cystoscopic detection of lesions. The fluorescence from tumor tissue appears bright red and demarcated, whereas the background normal tissue appears dark blue. Similar processes may occur in inflamed cells.

### 12.2 Pharmacodynamics

*In vitro* studies have shown increased porphyrin fluorescence in normal urothelium after exposure to CYSVIEW. In the human bladder, a greater accumulation of porphyrins is proposed in neoplastic or inflamed cells, compared to normal urothelium. After bladder instillation of CYSVIEW for approximately 1 hour and subsequent illumination with blue light at wavelengths 360 nm – 450nm, the porphyrins will fluoresce red *[see Dosage and Administration (2.5)]*.

### 12.3 Pharmacokinetics

After bladder instillation of [$^{14}$C]-labeled CYSVIEW (100 mg) for approximately 1 hour in healthy volunteers, absolute bioavailability of CYSVIEW was 7% (90% confidence interval [CI]: 5%-10%). The [$^{14}$C]-labeled substance(s) showed biphasic elimination, with an initial elimination half-life of 39 minutes, followed by a terminal half-life of approximately 76 hours. Whole blood analysis showed no evidence of significant binding of CYSVIEW to erythrocytes. An *in vitro* study showed that CYSVIEW underwent rapid metabolism in human blood.

## 13 NONCLINICAL TOXICOLOGY

### 13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

No studies in animals have been conducted to evaluate the carcinogenic potential of hexaminolevulinate hydrochloride.

Hexaminolevulinate was not mutagenic in *in vitro* reverse mutation tests in bacteria, or in chromosome aberration tests in human peripheral blood lymphocytes, and was negative in an *in vivo* micronucleus test in mice after intravenous injection of doses up to 45

mg/kg in the absence of light activation. Adequate studies have not been performed to evaluate the genetic toxicity of hexaminolevulinate in the presence of light activation.

Adequate reproductive and developmental toxicity studies in animals have not been performed to evaluate the effects of hexaminolevulinate on fertility.

### 13.2 Animal Toxicology and/or Pharmacology

Dose dependent neurological effects such as tremor, increased motor activity, and increased startle and touch escape responses were observed immediately after dosing at doses ≥ 30 mg/kg (24 times human systemic exposure based on the body surface area, using 10% as the upper level of 90% confidence interval of bioavailability) in a single-dose rat study. The animals recovered to normal status by 60 min after dosing. Adverse neurological effects were also noted in other single- or repeat-dose toxicity studies.

Hexaminolevulinate had moderate to strong potential to cause skin sensitization based on a local lymph node assay in mouse.

## 14 CLINICAL STUDIES

The safety and effectiveness of CYSVIEW to detect bladder carcinoma during cystoscopic examination were studied in two prospective, open-label, controlled clinical trials: Study 1 and Study 2.

Study 1: Patients with Known or Suspected Bladder Cancer

A total of 779 patients with known or suspected bladder cancer were randomized to a control group of 384 patients or a study drug group of 395 patients. Patients in the study drug group received CYSVIEW by bladder instillation. After bladder evacuation of CYSVIEW, lesion mapping was performed using the KARL STORZ PDD system, initially in white light (WL) mode and then in blue light (BL) mode. Patients in the control group underwent lesion mapping using only WL cystoscopy and did not receive CYSVIEW. The average age of the randomized patients was 69 years (range 24 to 96). The study population was 78% male and 94% White. All patients included in the study had a history of previous cystoscopy.

The main diagnostic efficacy outcome was assessed within the study drug group. This assessment compared lesions detected during an initial cystoscopic examination to their centralized histologic findings (the standard of truth). Following the initial diagnostic cystoscopy, patients within both study groups who had histologically confirmed Ta and/or T1 lesions underwent follow-up WL cystoscopy at 3, 6 and 9 months; these histologic evaluations were based upon the site assessments at both the initial and follow-up cystoscopy.

Diagnostic efficacy assessed the number of patients within the study drug group who had at least one additional Ta or T1 bladder cancer detected only by BL; the proportion of these patients was compared to a proposed threshold proportion of 10%. Within the study drug group, 286 patients had at least one Ta and/or T1 lesion, including 47 patients who had at least one of the lesions detected only by BL (see Table 1).

**Table 1: BL Cystoscopic Ta and/or T1 Lesion Detection within the Study Drug Group**

| | |
|---|---|
| Number of patients with any Ta and/or T1 lesion detected with either WL or BL | 286 |
| Number (%) of patients with any Ta and/or T1 lesion detected only with BL | 47 (16%) |
| p-value* | 0.001 |

*Exact test comparison of the proportion to a threshold value of 10%

Some malignant lesions were detected only by WL or BL (see Table 2)

**Table 2: Bladder Tumor Detection within the Study Drug Group by WL and/or BL Cystoscopy**

| Number of lesions | Detected by Both WL & BL | Detected by WL Only | Detected by BL Only |
|---|---|---|---|
| CIS, n = 66 | 33 | 6 | 27 |
| Ta, n = 580 | 472 | 52 | 56 |
| T1, n = 95 | 76 | 10 | 9 |
| T2 – T4, n = 47 | 38 | 8 | 1 |

Among the lesions detected only by BL, 23% were negative for any carcinoma-related pathology, including dysplasia. Among the lesions detected only by WL, 17% were negative for any carcinoma-related pathology, including dysplasia.

Study 2: Patients Undergoing Surveillance Cystoscopy

The study included 304 patients with a history of bladder cancer who were undergoing follow-up surveillance for tumor recurrence. The average patient age was 69 years with a range of 35 to 92 years. The study population was 80% male and 89% White.

For the initial surveillance examination, all 304 patients received CYSVIEW by bladder instillation, which was then evacuated. A surveillance cystoscopy was then performed, first using standard WL and subsequently using BL with the KARL STORZ D-Light C Photodynamic Diagnostic (PDD) System with the Flexible PDD Videoscope System. During this phase, suspected malignant lesions were counted and evaluated.

A total of 103 patients had suspected recurrence and then proceeded to a second examination in an operating room (OR). These patients received another CYSVIEW instillation, followed by WL and BL rigid cystoscopy for lesion mapping using the KARL STORZ D-Light C PDD System with the Rigid PDD Cystoscope System. All suspicious lesions were then biopsied and surgically removed by TURB.

Efficacy was assessed by determining the proportion of patients with a malignancy detected only with BL cystoscopy and not WL cystoscopy during the initial surveillance cystoscopic examination. The assessment was performed at patient-level, and compared malignancy detected during the surveillance cystoscopic examination to the centralized histologic findings (the standard of truth) obtained in the OR examination.

Table 3 shows patient-level detection of malignancy suspected in cystoscopic surveillance stage that was verified in the OR stage (n=103). Among the 103 patients, 63 patients had malignancy confirmed: 49 patients had malignancy detected by both WL and BL; 1 patient had malignancy detected by WL only; and 13 patients had malignancy detected by BL only [12.6% with 95% CI (7%, 21%), p<0.0001*]. Among these 103 patients, 40 patients had false positive detections: 17 patients had false positive detection by both WL and BL; 3 patients had false positive detection by WL only; and 20 patients had false positive detection by BL only.

**Table 3: Patient Level Malignancy Detection Suspected in BL Cystoscopic Surveillance and Verified in the OR**

| | Detected by Both WL and BL | Detected by WL only | Detected by BL only | Total |
|---|---|---|---|---|
| True Positive | 49 | 1 | 13 | 63 |
| False Positive | 17 | 3 | 20 | 40 |
| Total | 66 | 4 | 33 | 103 |

* Exact test comparison of the proportion to a threshold value of 0.5%

Among 26 patients with confirmed CIS malignancy, 9 patients had CIS malignancy detected by BL only and 17 patients had CIS malignancy detected by both WL and BL.

In the same study, there were 315 lesions detected during the cystoscopy in the OR. Table 4 shows the detection of lesions by type of malignancy.

**Table 4: Lesion Detection by Type of Malignancy as Verified in the OR**

| Malignancy Type | Detected by Both WL & BL | Detected by WL Only | Detected by BL Only |
|---|---|---|---|
| CIS, n = 43 | 24 | 3 | 16 |
| Ta, n = 94 | 61 | 9 | 24 |
| T1, n = 10 | 7 | 0 | 3 |
| T2 – T4, n = 5 | 5 | 0 | 0 |
| PUNLMP** n=3 | 2 | 0 | 1 |
| False positive n=160 | 65 | 22 | 73 |
| Total number of lesions | 164 | 34 | 117 |

** papillary urothelial neoplasm of low malignant potential

## 16 HOW SUPPLIED/STORAGE AND HANDLING

How Supplied

CYSVIEW (hexaminolevulinate hydrochloride) for intravesical solution is supplied as a kit. It is available in the following two configurations:

- **CYSVIEW Kit with Vial Adapter** (NDC 10511-3001-2): This kit contains:
    - One vial of CYSVIEW: 100 mg of hexaminolevulinate hydrochloride as a white to off-white or pale yellow freeze-dried powder in a 10 mL clear glass vial

- One DILUENT for CYSVIEW: 50 mL as a clear, colorless solution in plastic prefilled syringe
- One Luer Lock catheter adapter
- One vial adapter (either West Vented Vial Adapter or West Mixject Dispensing Pin)

- **CYSVIEW Kit without Vial Adapter** (NDC 10511-3001-3): This kit contains:

  - One vial of CYSVIEW: 100 mg of hexaminolevulinate hydrochloride as a white to off-white or pale yellow freeze-dried powder in a 10 mL clear glass vial
  - One DILUENT for CYSVIEW: 50 mL as a clear, colorless solution in plastic prefilled syringe
  - One Luer Lock catheter adapter

Storage and Handling

Store the CYSVIEW kit at 20°C to 25°C (68°F to 77°F); excursions are permitted to 15°C to 30°C (59°F to 86°F).

After reconstitution, use the CYSVIEW solution immediately. Alternatively, the solution may be stored in the labeled syringe under refrigeration at 2°C to 8°C (36°F to 46°F) for up to 2 hours.

## 17 PATIENT COUNSELING INFORMATION

Anaphylaxis

Inform patients that CYSVIEW may cause severe hypersensitivity reactions including anaphylactic shock. Instruct patients to seek immediate medical attention if they experience any symptoms of hypersensitivity reactions *[see Warnings and Precautions (5.1)]*.

Administration Instructions

Inform patients that CYSVIEW should be retained in the bladder for at least 1 hour from instillation of CYSVIEW to the start of the cystoscopic procedure. If the patient cannot hold CYSVIEW for 1 hour and needs to void and expel CYSVIEW from the bladder, they may void and should then inform a healthcare professional *[see Dosage and Administration (2.5)]*.

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