

## DEVICE DESCRIPTION

ViziLite Plus consists of ViziLite and TBlue<sup>630</sup>™ (Zila Tolonium Chloride (ZTC™)) Oral Lesion Marking System. Following the conventional manual and visual examination, ViziLite is used for the identification, evaluation, and monitoring of oral mucosal abnormalities in a patient population at increased risk for oral cancer. TBlue<sup>630</sup>™ (Zila Tolonium Chloride (ZTC™)) Oral Lesion Marking System, is used to further assist with the evaluation and monitoring of lesions identified during the ViziLite exam.

ViziLite Plus with TBlue<sup>630</sup> is a visualization system that is intended as an adjunct to conventional visual examination with incandescent light of oral mucosa. ViziLite Plus utilizes the same components and mechanism of action as the previously cleared ViziLite Test Kit (a.k.a. ViziLite Comprehensive Exam Tray and the OralLite Test Kit and Acetic Acid Rinse) and is indicated for the same patient population and intended use. Neither the ViziLite examination light source, nor the 1% Acetic Acid Rinse, have been changed or significantly modified for production of ViziLite Plus.

The TBlue<sup>630</sup> Oral Lesion Marking System consists of three swab components: two swabs of Acetic Acid solution, and one swab with TBlue<sup>630</sup> (ZTC) solution, which is similar to the metachromatic vital dye known as toluidine blue. The application of the dye to lesions identified during the ViziLite exam during clinical trials was able to assist with evaluation, monitoring, and tissue sampling, physically marking 51% of the lesions and enabling the health care provider to further evaluate those lesions identified during the ViziLite exam.

The TBlue<sup>630</sup> Oral Lesion Marking System contains 1% Acetic Acid Rinse (with the inactive ingredients: Purified Water, USP; Sodium Benzoate, NF; and Raspberry Flavor) and the 0.5% Zila Tolonium Chloride solution (with the inactive ingredients Purified Water, USP; Acetic Acid, USP; Sodium Acetate, NF; Hydrogen Peroxide, 30%, USP; SD 18 Ethyl Alcohol; and Raspberry Flavor).

## DEVICE ACCESSORY

ViziLite Plus, as described above, may be used with or without ViziLite Plus accessory eyewear, depending on the operatory environment. ViziLite Plus accessory eyewear consists of lenses that filter ambient light outside the wavelength transmission range of the chemiluminescent light. Hence, there is no need to reduce or darken ambient lighting by extinguishing room light (other than patient light) or by other means (hood, drapes, or dedicated examination suite).

## PRINCIPLE OF ACTION — ViziLite

Following the application of a cytoplasmic dehydration agent such as an acetic acid solution, oral mucosal abnormalities are better visualized due to changes in their refractile properties. This occurs in atypical non-keratinized squamous epithelium due to an increase in the nuclear:cytoplasmic ratio of the cells.

Adding diffuse chemiluminescent light (Speculite) to a conventional projected incandescent light examination of the cervical squamous epithelium has been clinically shown to increase the detection of biopsy proven squamous cell dysplasia (pre-malignant lesions) and malignancies when compared with detection by the unaided eye and detection with magnified visualization with incandescent light.

## CLINICAL STUDIES

A clinical study was conducted with patients presenting with known oral leukoplakia or erythroleukoplakia as well as patients who previously had oral cancer and were at risk for recurrence. ViziLite identified 102 lesions. Ninety two of the 102 lesions found in 85 patients were stained with TBlue<sup>630</sup>, biopsied, then sent for pathology diagnosis and the results are listed in TABLE 1. Ten lesions were not biopsied because they had been biopsied within a one-year period of the time of the current study examination, and because there had been no change in the appearance of these lesions.

TABLE 1

Biopsy Diagnoses of ViziLite Identified Lesions	
PATHOLOGY DIAGNOSIS	QUANTITY
Normal tissue	2
Benign Leukoplakia	1
Inflammatory Abnormality	17
Hyperkeratosis/atypia	21
Lichen Planus	6
Mild Dysplasia	14
Moderate Dysplasia	13
Severe Dysplasia (carcinoma-in-situ)	10
Squamous cell cancer	8

Forty-five of the 92 lesions were determined to be atypical, i.e. mild dysplasia, moderate dysplasia, severe dysplasia (carcinoma-in-situ) or squamous cell carcinoma. The remaining 47 biopsies were considered not to have pathology. The correlations between the TBlue<sup>630</sup> staining results and the biopsy results of the 92 lesions identified by ViziLite are presented in TABLE 2.

In TABLE 1, since all clinically suspicious lesions were biopsied, it can be seen that ViziLite identified all lesions containing any pathology with no false negatives (Sensitivity 100%).

In TABLE 2, 45 lesions were determined to be dysplastic on biopsy (exam positive or negative), the TBlue<sup>630</sup> Oral Lesion Marking System identified 32 of them (71% PPV). It should be noted that all 10 cases of severe dysplasia (carcinoma-in-situ) and all 8 cases of squamous cell cancer were ViziLite positive and TBlue<sup>630</sup> positive (NPV of 100% for serious pathology).

The 13 ViziLite positive cases that were TBlue<sup>630</sup> negative but biopsy positive consisted of 8 mildly dysplastic and 5 moderately dysplastic lesions.

TABLE 2

Correlation of Biopsy Results with the TBlue <sup>630</sup> Examination Results			
TBLUE <sup>630</sup> EXAM RESULT	MUCOSAL BIOPSY RESULTS (FOR ANY DYSPLASIA) OF VIZILITE POSITIVE LESIONS		
	Biopsy Positive	Biopsy Negative	Total
Positive	32	15	47
Negative	13	32	45
<b>Total</b>	<b>45</b>	<b>47</b>	

## INDICATIONS FOR USE

The ViziLite Blue Oral Exam product consists of ViziLite and ViziLite Blue Oral Lesion Marking System and is intended to be used only as an adjunct to the conventional oral mucosal examination.

The ViziLite (OralLite) is a chemiluminescent light source system indicated for use as an adjunct to conventional oral cancer screening by trained health care providers for the identification, evaluation, and monitoring of abnormalities in a patient population at increased risk for oral cancer. These include precancerous as well as cancerous lesions. ViziLite is also indicated for the identification of occult lesions not previously identified during conventional examination under incandescent illumination.

The ViziLite TBlue<sup>630</sup> Oral Lesion Identification and Marking System is a three-component swab system which is indicated as an adjunct to the ViziLite examination for oral mucosa lesions for further evaluation and monitoring of lesions by physically marking lesions suspicious for cancer or precancer already differentially identified with ViziLite in a population at increased risk for oral cancer.

The ViziLite TBlue<sup>630</sup> Oral Lesion Identification and Marking System is not being proposed for use in the initial oral mucosal examination without initial differential identification with ViziLite. The retention of the dye by a suspicious lesion may or may not indicate the need for further study, including biopsy.

## CONTRAINDICATIONS

The ViziLite Plus with TBlue<sup>630</sup> Oral Lesion Marking System is contraindicated in patients with a known history of hypersensitivity to any of the ingredients or their analogs.

The TBlue<sup>630</sup> Oral Lesion Marking System is contraindicated in patients who are pregnant or lactating.

Due to the lack of safety data, the TBlue<sup>630</sup> Oral Lesion Marking System should not be used in children, patients with liver or renal insufficiency, or patients with difficulty swallowing.

The TBlue<sup>630</sup> Oral Lesion Marking System should be used with caution in patients who may have difficulty following directions during the lesion staining procedure (e.g. patients with severe physical or mental disabilities).

## WARNING PRECAUTIONS — ViziLite Rinse

Removable oral prostheses should be removed and any associated trauma or inflammation given time to heal prior to use of the product. Have the patient remove any acrylic-based prosthesis. In the event of an acrylic permanent crown, re-polish (if necessary) with regular prophylaxis paste and cup.

- Patients may experience a slight burning sensation of the oral mucosa due to the acetic acid.
- Do not swallow.
- ViziLite Rinse is intended for oral use only. Keep out of reach of children.
- Do not refrigerate ViziLite Rinse.

## WARNING/PRECAUTIONS — ViziLite

The activated ViziLite should be firmly inserted into the provided ViziLite retractor before placing it into the patient's mouth in order to prevent accidental swallowing or choking.

The health care provider should hold the ViziLite retractor firmly while it is placed inside the patient's mouth.

Inspect the ViziLite for any evidence of chemical leakage prior to and after capsule activation in order to prevent potential leakage of

ViziLite chemicals into the mouth. Discard any capsule that does not appear to be intact.

Refer to the Material Safety Data Sheet (MSDS) for ViziLite Plus for accidental exposure.

## WARNINGS/PRECAUTIONS — TBlue<sup>630</sup> Oral Lesion Marking System

Removable oral prostheses should be removed and any associated trauma or inflammation given time to heal prior to use of the product.

Patients should be informed prior to the TBlue<sup>630</sup> procedure that there may be a residual bluish discoloration on the vermilion border, dorsum of the tongue, and dental plaque, which usually wears off in 2-6 hours. Staining in these areas with the Zila Tolonium Chloride is normal and should not be considered a positive result in the absence of clinical suspicion.

Care should be taken to protect clothing, as well as equipment and environmental surfaces from being stained.

Should any of the material be accidentally swallowed, the urine and and/or stools may be colored temporarily blue-green or blue, respectively. The patient should be advised of the possibility of this effect, and assured that the color change is temporary.

Common restorative materials including porcelain, composites, and acrylics and margins of dental restorations may stain transiently; dental materials are not known to stain permanently.

## INTERACTIONS

Interactions of the TBlue<sup>630</sup> Oral Lesion Marking System components with other medications have not been studied, but are unlikely.

## PREGNANCY AND LACTATION

The TBlue<sup>630</sup> Oral Lesion Marking System is contraindicated for use in pregnant women. There have been no well controlled studies in pregnant women to know the safety of use in this population.

The TBlue<sup>630</sup> Oral Lesion Marking System is contraindicated for lactating women. It is not known whether Zila Tolonium Chloride is excreted in human breast milk.

## ADVERSE EVENTS

Patients may experience a slight burning sensation of the oral mucosa due to the acetic acid in the ViziLite Rinse and the TBlue<sup>630</sup> Oral Lesion Marking System.

No severe adverse reactions are expected when the TBlue<sup>630</sup> Oral Lesion Marking System is used according to package instructions. Some patients may find the taste of the product unappealing and may gag.

## OVERDOSAGE

No adverse events have been reported in the published literature concerning the use of Tolonium Chloride in the mouth for staining oral lesions. The TBlue<sup>630</sup> Oral Lesion Marking System contains a Zila Tolonium Chloride dye swab with 7mg of Zila Tolonium Chloride, which conservatively yields an exposure of approximately 0.1mg/kg (based on a 60kg person). Reports from published studies indicate physiological alterations are not observed at dose levels below 5 mg/kg administered intravenously. Some patients, receiving 100 mg commercially available toluidine blue orally in capsule form three times daily, reported nausea. The NOAEL (No-Observable-Adverse-Effect Level) determined in toxicology studies on orally administered toluidine chloride was 20mg/kg in rats and was 15 mg/kg in rabbits. Data regarding Zila Tolonium Chloride and toluidine blue toxicity are available upon request.

## GENERAL PROCEDURE for ViziLite Plus

The ViziLite examination consists of visualization of leukoplakic areas using a diffuse chemiluminescent light source. Following conventional oral examination with incandescent light, there is a pre-exam rinse with the ViziLite rinse, activation of the ViziLite with placement in the ViziLite retractor, dimming of the ambient light and re-examination with ViziLite. Under ViziLite, atypical or dysplastic mucosal abnormalities will appear as bright white, distinctly demarcated, and sharply marginated areas that contrast with the surrounding non-involved epithelium. Any lesion identified with ViziLite is further evaluated using the adjunctive TBlue<sup>630</sup> Oral Lesion Marking System (pre- and post-acetic acid swabs and Zila Tolonium Chloride stain swab).

The TBlue<sup>630</sup> Oral Lesion Marking System should only be used in conjunction with a complete oral screening exam using the ViziLite. This includes:

1. Conventional oral examination with overhead exam light
2. A 30-60 second oral rinse with ViziLite pre-rinse solution (1% acetic acid)
3. Examination with the ViziLite in a dim exam room
4. Application of the pre-dye 1% Acetic Acid solution swab
5. Application of the TBlue<sup>630</sup> (ZTC) to any mucosal abnormalities observed
6. Application of the post-dye 1% Acetic Acid solution swab

**All lesions seen using ViziLite illumination are potentially important. The absence of marking by the TBlue<sup>630</sup> Oral Lesion Marking System of a lesion seen with ViziLite should not preclude further analysis of the lesion, including biopsy. Any lesion seen with ViziLite may harbor pathology, and clinical judgment should always prevail when deciding the further analysis and management of these lesions.**

The ViziLite oral screening exam and, if indicated, application of the TBlue<sup>630</sup> Oral Lesion Marking System to any mucosal abnormalities should be done before the application of any instrumentation to soft tissues. The observation, measurement and documentation of the pre-staining appearance of the oral soft tissue lesions must be completed *before* any observed lesions are stained with the TBlue<sup>630</sup> Oral Lesion Marking System.

Instruments used in the mouth can cause minor abrasions that can retain the dye solution. In addition, areas of oral trauma (e.g. cheek bites) may show up as white lesions on the ViziLite exam and may retain the dye solution.

Before using the TBlue<sup>630</sup> Oral Lesion Marking System, the patient should be draped with a bib to protect clothing. As expectoration is required, the patient should be positioned near a sink. During administration of the staining solutions, the patient should expectorate into a large (8-10 oz) cup that can be discarded as waste.

Alternatively, the contents of the cup may be poured down the center of the drain while water is running rapidly to avoid staining the sink. If the sink or any other surface becomes discolored, the stain may be removed using a soft cloth and standard hard surface cleaner, concentrated bleach, or vinegar. Environmental surfaces or objects that cannot easily be cleaned should be removed from the area or covered.

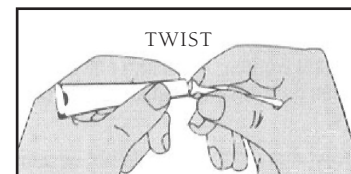
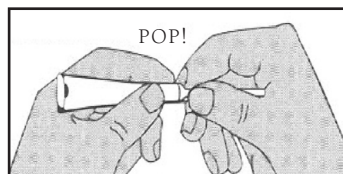
## PROCEDURE for Performing the ViziLite Exam

1. Perform a routine exam of the oral cavity — note the presence of any acetowhite lesion(s) on all oral soft tissue structures.

2. Select one (1) ViziLite acetic acid solution vial, one (1) ViziLite lightstick, and one (1) ViziLite retractor from the tray.
3. Instruct the patient to rinse their mouth with the ViziLite acetic acid solution vial (1% acetic acid solution) for up to one minute and expectorate.
4. Activate the ViziLite lightstick and assemble with the ViziLite retractor:
  - Bend the flexible lightstick, breaking brittle inner vial
  - Shake to mix the contents of the ViziLite lightstick
  - Insert the illuminated lightstick into the open piece (sheath) of the ViziLite retractor
  - Assemble the 2 pieces of the ViziLite retractor
5. Dim ambient room lights.
6. Repeat the exam of the oral cavity using illumination from the ViziLite.
7. Look for acetowhite lesion(s). Document the site(s) of any identified lesions on all oral soft tissue structures.
8. Remove the ViziLite device from the mouth and discard.
9. Take appropriate clinical management action by either:
  - Documenting the absence of acetowhite lesion(s)
  - Documenting the presence of acetowhite lesion(s); and continue with the TBlue<sup>630</sup> procedure

## PROCEDURE for Staining White Oral Mucosal Lesions with the TBlue<sup>630</sup> Oral Lesion Marking System

1. After performing an examination of the oral cavity using conventional dental illumination (incandescent projected illumination), and performing the ViziLite oral exam, any mucosal abnormalities deemed clinically suspicious can be stained with the TBlue<sup>630</sup> Oral Lesion Marking System.
2. Data regarding the location, appearance, and measured size of any oral lesion(s) should be documented in the patient's medical record.
3. Only if a mucosal abnormality is identified during the ViziLite exam can the TBlue<sup>630</sup> Oral Lesion Marking System be used to demarcate the identified lesion(s) for further study or biopsy.
4. To open the swabs, pinch the tube firmly below the applicator handle.
5. With the other hand, grasp applicator handle at base. Bend gently back and forth with a slight twisting motion until the entire seal is broken. Do not excessively bend the applicator.



6. Twist gently and pull swab out slightly to be sure that the swab seal is completely broken. A small amount of solution may remain in the tube; therefore, caution is required to avoid spilling. It is recommended that the open tubes be placed upright in a small cup.
7. Dim the room lights and using the ViziLite (if necessary), visualize the lesion(s). Apply swab #1, the pre-rinse acetic acid solution to the entire area of the white lesion(s). To apply, press firmly in a painting motion. Cover an area extending 2 cm in diameter around the visible lesion(s). Swab for 20 seconds. Direct the patient to expectorate the pre-rinse solution.
8. Direct the patient to rinse and gargle with water and expectorate. This step may be repeated.
9. Lightly dry the ViziLite illuminated area with a gauze sponge or a gentle stream of air to minimize the risk of swallowing excess dye.

10. Continuing to use ViziLite illumination in a dim room (if necessary), apply swab #2, the Zila Tolonium Chloride (blue dye) to the suspicious lesion(s) that have had the pre-dye acetic acid solution applied. Press firmly in a painting motion. Cover an area extending 2 cm in diameter around the visible lesion. Swab for 20 seconds. The dye solution should be expectorated.
11. Room lights may now be turned on, the balance of the staining/decolorization procedure and exam is to be done using conventional dental illumination.
12. Using conventional dental illumination, apply swab #3, the post-rinse swab to the stained lesion. Again, press firmly in a painting motion to apply the acetic acid solution using a reasonable mechanical effort to remove the blue stain. Completely cover the area where any blue stain appears. Swab for 20 seconds. This step may be repeated with the remaining post-dye solution (swab #3) to remove any excess dye.
13. Direct the patient to rinse and gargle with water and expectorate. This step may be repeated.
14. Using conventional dental illumination, measure the stained lesion and document the staining pattern. To evaluate a stained area during the exam, a swab saturated with either pre-rinse or post-rinse solution (1% acetic acid) may be used to attempt to remove excess dye
15. Take appropriate clinical management action by either counseling the patient that lesion(s) should be followed and schedule a future appointment; performing a biopsy of identified acetowhite lesion(s); referring the patient to an oral surgeon for further evaluation.

Note: Be aware that the dye will be retained by the irregular papillar crevices on the dorsum of the tongue. Other areas that can retain the TBlue<sup>630</sup> (ZTC) dye include dental plaque, gingival margins around each tooth, diffuse stain of the soft palate transferred from the retained stain on the dorsum of the tongue, and the margins of dental restorations. Acrylic restorations and appliances should be removed prior to application.

TABLE 3

<b>Tolonium Chloride Staining Procedure</b>				
TYPE OF ORAL ILLUMINATION	ROOM LIGHTING	SOLUTION	VOLUME	CONTACT DURATION
ViziLite	dim or off	Swab #1 Pre-rinse 1% acetic acid (Flavored)	swab	20 seconds
		Water	30 ml	20 seconds
ViziLite	dim or off	Swab #2 dye Tolonium Chloride 5 mg/ml	swab	20 seconds
Conventional Dental Illumination	on	Swab #3 Post-rinse 1% acetic acid (Flavored)	swab	20 seconds
		Water	30 ml	20 seconds

## HOW SUPPLIED

ViziLite Plus is supplied with ViziLite Test Kits and TBlue<sup>630</sup> Oral Lesion Marking System Kits in a 20-pack configuration, a 40-pack configuration and a supplemental pack.

### 20-pack ViziLite Plus

- 20 ViziLite acetic acid solution vials, 30 mL (1% Acetic Acid)
- 20 ViziLite lightsticks
- 20 ViziLite retractors
- 2 TBlue<sup>630</sup> Oral Lesion Marking System kits, each containing:
  - 1 Acetic Acid pre-rinse solution swab, 1.3 mL (1% Acetic Acid)
  - 1 Zila Tolonium Chloride solution swab, 1.3 mL (0.5% Zila Tolonium Chloride)
  - 1 Acetic Acid post-rinse solution swab, 1.3 mL (1% Acetic Acid)

### 40-pack ViziLite Plus

- 40 ViziLite acetic acid solution vials, 30 mL (1% Acetic Acid)
- 40 ViziLite lightsticks
- 40 ViziLite retractors
- 4 TBlue<sup>630</sup> Oral Lesion Marking System kits each containing:
  - 1 Acetic Acid pre-rinse solution swab, 1.3 mL (1% Acetic Acid)
  - 1 Zila Tolonium Chloride solution swab, 1.3 mL (0.5% Zila Tolonium Chloride)
  - 1 Acetic Acid post-rinse solution swab, 1.3 mL (1% Acetic Acid)

### ViziLite Plus Supplemental Pack

- 1 ViziLite acetic acid solution vial, 30 mL (1% Acetic Acid)
- 1 ViziLite lightstick
- 1 ViziLite retractor
- 6 TBlue<sup>630</sup> Oral Lesion Marking System kits each containing:
  - 1 Acetic Acid pre-rinse solution swab, 1.3 mL (1% Acetic Acid)
  - 1 Zila Tolonium Chloride solution swab, 1.3 mL (0.5% Zila Tolonium Chloride)
  - 1 Acetic Acid post-rinse solution swab, 1.3 mL (1% Acetic Acid)

## STORAGE

Store between 15° and 30°C (59°–86°F)

ViziLite, when used in combination with conventional visual oral mucosal examination by health care professionals, provides improved identification, evaluation, and monitoring of oral mucosal abnormalities in a population at increased risk for oral cancer.

The TBlue<sup>630</sup> Oral Lesion Marking System can allow the examiner to continue to visualize white oral mucosal lesions using incandescent (conventional projected) light, even after the ViziLite and its holder are removed from the oral cavity. This allows the examiner to measure the lesion size, observe the lesion borders, and obtain an appropriate tissue sample (biopsy) when clinically indicated.

