IMPROVED DETECTION AND TREATMENT OF BLADDER CANCER USING HEXAMINOLEVULINATE IMAGING: A PROSPECTIVE, PHASE III MULTICENTER STUDY

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Citation:
AIM
To determine if improved tumor detection using Hexvix® blue-light cystoscopy could lead to improved treatment in patients with bladder cancer

METHODS
- 146 patients with known or suspected bladder cancer were assessed in this open, comparative, within patient, controlled study
- Patients were assessed with standard white light cystoscopy and blue-light cystoscopy 1 hour after Hexvix® instillation
- Lesions were mapped and biopsies taken from suspicious areas for assessment by an independent pathologist
- Treatment plans were recommended by an independent urologist, blinded to the detection method used, based on biopsy results and medical history according to European Association of Urology bladder cancer guidelines
- In order to ensure thorough examination under white light, 2 patients per center were randomized not to undergo further blue light cystoscopy

RESULTS
- Hexvix® blue-light cystoscopy imaging improved overall tumor detection
- 31 patients were found to have no pathologically confirmed tumor

Figure 1

TUMOR DETECTION RATE

<table>
<thead>
<tr>
<th></th>
<th>White light</th>
<th>Hexvix® blue-light</th>
</tr>
</thead>
<tbody>
<tr>
<td>All tumors</td>
<td>77 %</td>
<td>96 %</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>48 %</td>
<td>93 %</td>
</tr>
<tr>
<td>CIS</td>
<td>68 %</td>
<td>95 %</td>
</tr>
<tr>
<td>Superficial papillary tumors</td>
<td>85 %</td>
<td>96 %</td>
</tr>
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</table>
As a result of improved detection, 22% of patients with verified tumors received more appropriate treatment.

**CONCLUSION**

Hexvix® blue-light cystoscopy improves the detection of tumors and lesions in patients with bladder cancer compared with standard white light cystoscopy leading to more appropriate treatment in 1 of 5.
PREScribing INFORMATION HEXVIX (HEXAMINOLEVULINATE)

Please refer to full national Summary of Product Characteristics (SPC) before prescribing. Indications and approvals may vary in different countries. Further information available on request. Hexvix 85 mg; powder and solvent for solution for intravesical use.

PRESENTATION Pack of one 10ml glass vial containing 85mg of hexaminolevulinate as 100mg hexaminolevulinate hydrochloride as a powder and one 50ml polypropylene vial containing solvent. After reconstitution in 50ml of solvent, 1ml of the solution contains 1.7mg hexaminolevulinate which corresponds to a 8mmol/l solution of hexaminolevulinate.

INDICATIONS This medicinal product is for diagnostic use only. Hexvix blue light fluorescence cystoscopy is indicated as adjunct to standard white light cystoscopy to contribute to the diagnosis and management of bladder cancer in patients with known or high suspicion of bladder cancer.

DOSAGE AND METHOD OF ADMINISTRATION Hexvix cystoscopy should only be performed by health care professionals trained specifically in Hexvix cystoscopy. The bladder should be drained before the instillation. Adults (including the elderly): 50 ml of 8 mmol/l reconstituted solution (see section 6.6) is instilled into the bladder through a catheter. The patient should retain the fluid for approximately 60 minutes. Following evacuation of the bladder, the cystoscopic examination in blue light should start within approximately 60 minutes. The cystoscopic examination should not be performed more than 3 hours after Hexvix is instilled in the bladder. Also if the retention time in the bladder is considerably shorter than one hour, examination should start no earlier than after 60 minutes. No minimum retention time has been identified (instillation time), in one case 343 minutes. No adverse events have been reported with prolonged instillation times exceeding 180 minutes (3 times the recommended instillation time), in one case 343 minutes. No adverse events have been reported. No specific interaction studies have been performed with hexaminolevulinate.

INTERACTIONS No specific interaction studies have been performed. No adverse events have been reported. No adverse reactions from clinical studies were transient and mild or moderate in intensity. The most frequently reported adverse reactions from clinical studies were bladder spasm, reported by 2.4% of the patients, dysuria by 1.8%, bladder pain by 1.7% and hematuria by 1.7%, of the patients. Other commonly reported adverse reactions are: headache, nausea, vomiting, constipation, diarrhea, urinary retention, haematuria, pyrexia and post procedural pain. Uncommonly reported adverse reactions are cystitis, sepsis, urinary tract infection, insomnia, urethral pain, pollakuria, micturition urgency, urinary tract disorder, back pain, incontinence, white blood cell count increase, bilirubin and hepatic enzyme increase, post operative fever, anaemia, gout, rash and balanitis. The adverse reactions that were observed were expected, based on previous experience with standard cystoscopy and transurethral resection of the bladder (TURB) procedures.

OVERDose No case of overdose has been reported. No adverse events have been reported with prolonged instillation times exceeding 180 minutes (3 times the recommended instillation time), in one case 343 minutes. No adverse events have been reported in the dose-finding studies using twice the recommended concentration of hexaminolevulinate. There is no experience of higher light intensity than recommended or prolonged light exposure.

INSTRUCTIONS FOR USE AND HANDLING Hexaminolevulinate may cause sensitisation by skin contact. The product should be reconstituted under aseptic conditions using sterile equipment.

MARKETING AUTHORISATION HOLDER Photocure ASA, Hoffsvien 4, N-0275 Oslo, Norway

PRICE Denmark DKK 4 718.50 Finland EUR 464.20 Norway NOK 4 234.50 Sweden SEK 4 222.00

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