IMPROVED DETECTION OF UROTHELIAL CARCINOMA IN SITU WITH HEXAMINOLEVULINATE FLUORESCENCE CYSTOSCOPY

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Citation:
Journal of Urology 2004; 171: 135-8.

HEXVIX®
Hexaminolevulinate 85mg

PHOTOCURE®

AIM

To compare Hexvix® blue-light cystoscopy and standard white light cystoscopy for the detection of carcinoma in situ (CIS) in patients suspected of having high-risk bladder cancer

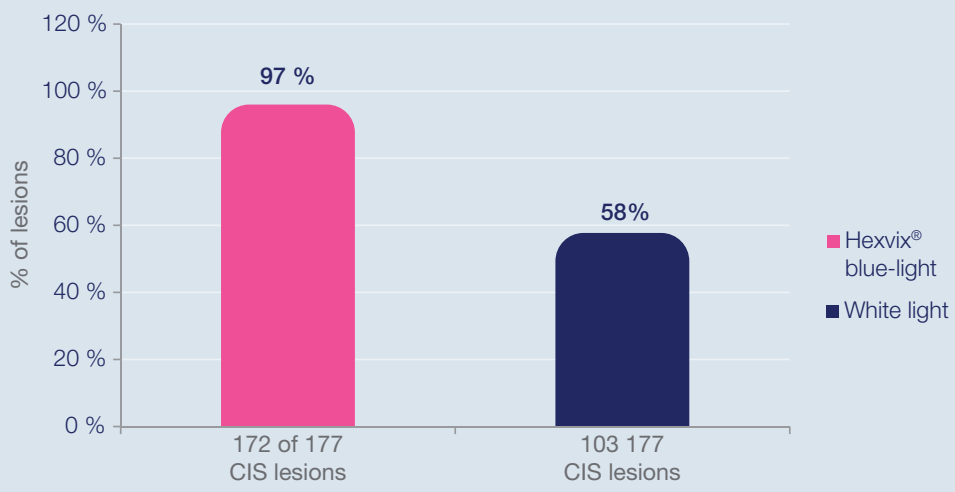
METHODS

- 286 patients entered this European, multi-center, prospective, controlled, within-patient comparison of standard white light and Hexvix® blue-light cystoscopy; 211 were evaluated in the efficacy analysis
- Patients were assessed with standard white light and blue-light cystoscopy 1 hour after Hexvix® instillation
- The number and location of all suspicious areas identified under white light were mapped on a bladder chart. The light was then changed to blue-light mode and all fluorescing areas were identified and documented on the same bladder chart
- All suspicious areas identified under white light were immediately biopsied or resected by transurethral resection. Additional biopsies were then obtained from all suspicious fluorescing lesions not previously identified by white light
- One biopsy was taken from normal appearing urothelium as a reference for the pathologist
- Assessment was by an independent central pathologist blinded to the identity of the lesion

RESULTS

- Hexvix® blue-light cystoscopy significantly improved the detection of CIS lesions

SIGNIFICANTLY IMPROVED CIS LESION DETECTION RATE



- All 11 cytology negative CIS cases were detected by Hexvix® blue-light cystoscopy but only 7 were detected by standard white light cystoscopy
- Overall, Hexvix® blue-light cystoscopy detected 97% of all lesions compared with 78% identified by standard white light cystoscopy. In addition to CIS, Hexvix® blue-light cystoscopy significantly improved the detection of pTa (97% vs 88%) and dysplasia (94% vs 53%)
- Hexvix® blue-light cystoscopy was well tolerated; of the 279 patients who received Hexvix® instillation, only 3 reactions in 2 patients were considered to be related to Hexvix®

CONCLUSION

Hexvix® blue-light cystoscopy significantly improves the detection of bladder CIS, which has consequences for clinical management and may improve patient prognosis. The procedure is easily implemented as an adjunct to standard white light cystoscopy and it adds no significant risk of complications

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 considerable shorter than one hour, examination should start no earlier than after 60 minutes. No minimum retention time has been identified making examination non-informative. For optimal visualisation it is recommended to examine and map the entire bladder under both white and blue light before any surgical measures are initiated. Biopsies of all mapped lesions should normally be taken under white light and complete resection should be verified by switching to blue light. Only CE marked cystoscopic equipment should be used, equipped with necessary filters to allow both standard white light cystoscopy and blue light (wavelength 380–450 nm) fluorescence cystoscopy. Children and adolescents: There is no experience of treating patients below the age of 18 years.

CONTRAINDICATIONS Hypersensitivity to the active substance or to any of the excipients of the solvent. Porphyria.

WARNINGS AND PRECAUTIONS The possibility of hypersensitivity including serious anaphylactic/ anaphylactoid reactions should always be considered. Advanced life support facilities should be readily available. Repeated use of Hexvix as part of follow-up in patients with bladder cancer has not been studied. Hexaminolevulinate should not be used in patients at high risk of bladder inflammation, e.g. after BCG therapy, or in moderate to severe leucocyturia. Widespread inflammation of the bladder should be excluded by cystoscopy before the product is administered. Inflammation may lead to increased porphyrin build up and increased risk of local toxicity upon illumination, and false fluorescence. If a wide-spread inflammation in the bladder becomes evident during white light inspection, the blue light inspection should be avoided. There is an increased risk of false fluorescence in the resection area in patients who recently have undergone surgical procedures of the bladder.

INTERACTIONS No specific interaction studies have been performed with hexaminolevulinate.

FERTILITY, PREGNANCY AND LACTATION No clinical data on exposed pregnancies are available Animal studies do not indicate direct or indirect harmful effects with respect to the reproductive toxicity. As a precautionary measure, it is preferable to avoid the use of Hexvix during pregnancy.

UNDESIRABLE EFFECTS Most of the reported 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
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PRICE Denmark DKK 4 718.50 Finland EUR 464.20 Norway NOK 4 234.50 Sweden SEK 4 222,00

DATE OF REVISION OF TEXT February 2013.

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Date of preparation: June 2012 Job code: 1207-29IL