Cystoscope

A cystoscope is a specialised endoscope allowing for direct visual inspection of the urothelium. The cystoscope is inserted through the urethra into the bladder. The cystoscopy can be performed immediately after the cystoscope has been introduced into the bladder and the pictures generated by the integrated camera are transmitted onto a nearby video screen. Cystoscopy can be performed with a local anaesthetic - usually for outpatients - and under general anaesthesia. Most cystoscopes have extra tubes to guide other instruments for taking a biopsy of a bladder tumour or removal of superficial bladder tumours.

There are two different types of cystoscope; the standard rigid cystoscope and the flexible cystoscope. The three major manufacturers of cystoscopes and cystoscopy equipment are Karl Storz, Richard Wolf and Olympus. All three provide the necessary equipment for both standard white light cystoscopy and fluorescence cystoscopy.

Standard white light cystoscopy

Standard white light cystoscopy is used in the diagnosis and monitoring of bladder cancer. Illumination for standard white light cystoscopy is provided by special light sources integrated with the cystoscope, which emit bright, white light. Cystoscopy-guided biopsy of suspicious lesions and areas, remains the standard procedure for verification of bladder cancer - including carcinoma in situ (CIS). Visual inspection using standard white light cystoscopy is particularly good at detecting three-dimensional, i.e. papillary, lesions. However, detection of flat lesions - such as CIS -, which may be diffuse and indistinguishable from normal or nonspecific inflammatory-appearing mucosa, is limited when conventional standard white light cystoscopy is being used.

Hexvix® (hexaminolevulinate) cystoscopy

In order to assist the early and accurate diagnosis of bladder cancer, methods to improve cystoscopy such as fluorescence cystoscopy have been investigated. Intravesical porphyrin-based fluorescence cystoscopy involves instilling a photosensitizing agent - such as Hexvix - into the bladder. Hexvix induces preferential accumulation of fluorescent - photoactive - endogenous porphyrins in malignant cells as opposed to non-malignant cells of urothelial origin. Under subsequent blue-light illumination, neoplastic lesions fluoresce red enabling visualisation of tumours. Significant improvements in detection of malignant lesions with Hexvix cystoscopy compared to standard white light cystoscopy have been observed. In addition, the capabilities of Hexvix in identifying CIS, which is very difficult to recognize under standard white light, have also been noted. Overall, Hexvix cystoscopy shows a statistically significant superiority over white light cystoscopy regarding sensitivity for the detection of bladder lesions, which has been demonstrated in published studies.

"Hexvix cystoscopy is a new diagnostic tool with improved sensitivity for detecting bladder tumours [over standard white light cystoscopy], in particular CIS tumours", explained Professor Patrice Jichlinski, department of urology, CHUV University-Hospital, Lausanne, Switzerland, lead investigator of a recent trial of Hexvix. Elaborating on the clinical results confirmed in several studies, he added: "A statistically significant superiority of fluorescence cystoscopy over standard cystoscopy in the detection of CIS has been established in all published studies to date. Its high sensitivity and negative predictive value improves the diagnosis of malignancies and of CIS tumours in particular. The cases missed by standard white light inspection were typically CIS lesions, confirming the superiority of Hexvix cystoscopy in these cases. Tumour fluorescence is sparkling and well demarcated,
Summary of the product characteristics
Name of the medicinal product
Hexvix 85 mg, powder and solvent for solution for intravesical use
Qualitative and Quantitative Composition
Each vial of powder contains 85 mg of hexaminolevulinate as 100 mg hexaminolevulinate hydrochloride.
After reconstitution in 50 ml of solvent, 1 ml of the solution contains 1.7 mg hexaminolevulinate, which corresponds to a 8 mm2/1 solution of hexaminolevulinate.
For excipients, see below list of excipients
Pharmaceutical Form
Powder and solvent for solution for intravesical use.
For use: white to off-white or pale yellow, Solvent: clear, colourless solution
Clinical Particulars
Indications This medicinal product is for diagnostic use only. Detection of bladder cancer, particularly non-invasive papillary tumours not evident with standard cystoscopy, may help to define the extent of disease and to determine the need for further treatment. After instillation of the reconstituted solution for 1 hour and subsequent illumination with blue light, tumours can be readily visualized by fluorescence. Clinical studies using Hexvix included 665 evaluable patients with known bladder cancer or high suspicion of bladder cancer, who underwent white light, followed by blue light cystoscopy, and biopsies. In the clinical studies, the patients had known or suspected bladder cancer by cystoscopy or positive urine cytology. Significantly more CIS and papillary lesions were detected after blue light cystoscopy, as compared to standard white light cystoscopy. The correction rate for CIS was 49.5% for standard white light cystoscopy and 95.6% for blue light cystoscopy, and the detection rate for papillary lesions produced a production of singlet oxygen at light activation. A local lymph node assay in mice has demonstrated that hexaminolevulinate has a potential to cause skin sensitisation.
Absorption After instillation of the reconstituted solution for 1 hour and subsequent illumination with blue light, 25% for white light cystoscopy and 27.8% for blue light cystoscopy, Mechanism of Action: After intravesical instillation of Hexvix, porphyrins are formed intracellularly in bladder wall lesions. The intracellular porphyrins (including PpIX) are photoactive, fluorescent compounds which emit red light upon blue light excitation. As a result, premalignant and malignant lesions will glow on a blue-white light excitation. Pharmacokinetic Properties In vivo autoradiography studies in rats after intravesical administration have shown high concentrations of hexaminolevulinate in the bladder wall. After intravesical instillation of radioactively labelled hexaminolevulinate in healthy volunteers, the tissue bioavailability of total radioactivity was approximately 5-50%.
Preclinical safety data Studies in rats and dogs have not indicated any risks for systemic toxicity. Seven-day intravesical tolerance studies, without light exposure, were performed in rats and dogs. The study in rats showed lack of leukocytosis, suggesting a proinflammatory activity of hexaminolevulinate. Cases of anemia, coloured urine and weight loss were also seen. In dogs treated with hexaminolevulinate there was a marginally increased incidence and severity of transition cell hyperplasia and basophilic in the urinary epithelium. Potential genotoxicity has been investigated in vitro and in vivo. Micronuclei and aneuploidy were not induced and no aneuploidy was observed. Cytogenetic studies in vitro and in vivo have failed to demonstrate any genotoxic potential.
Special precautions for storage Store below 30°C, protected from light. These instructions apply to the reconstituted solution, the solvent, the powder and the packaging material. Adverse effects and side effects Adverse reactions occurring in >1/100, <1/10 of patients. Only adverse reactions and side effects reported by more than one patient in the clinical studies are included.
Overdose No case of overdose has been reported. No adverse events have been reported with prolonged illumination times exceeding the recommended 18 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 intensities than recommended for use. Unusual, uncommon, infrequent, rare, very rare, undetermined, possible, not known.
Pharmacological Properties Photodynamic therapeutic properties Photodynamic therapy is based on the principle that certain chemicals, when exposed to light of a specific wavelength, can be activated to produce a cytotoxic agent, which destroys cancer cells. The chemical photosensitiser, hexaminolevulinate, is activated by blue light to produce singlet oxygen, a highly reactive species that can cause DNA damage.
Preclinical safety studies The product was found to be non-toxic and non-genotoxic in in vitro and in vivo studies. No significant adverse effects were observed at the recommended dose and duration of exposure. The systemic bioavailability of total radioactivity was approximately 5-50%.
Parenteral administration The product is administered as a single intravesical instillation of the reconstituted solution followed by illumination with blue light. The light doses given during cystoscopy will vary. Typical total light doses (white light) cystoscopy thanks to its higher sensitivity as compared to standard cystoscopy and, included more pTa lesions (20% of the patients), more CIS lesions (2%), and more pT2 lesions (18%) only detected with Hexvix cystoscopy. The rate of false positive biopsies was increased after blue light cystoscopy, 25% for white light cystoscopy and 27.8% for blue light cystoscopy.
Inflammation and infestations, Uncommon, Cystitis, sepsis, urinary tract infection
Renal and urinary bladder disorders, Common, Urolithiasis, renal failure, urinary tract infections, Urinary tract infections
Skin and subcutaneous tissue disorders, Uncommon, Rash
Common adverse reactions: Adverse reactions occurring in >1/1000, <1/10 of patients. Uncommon adverse reactions: Adverse reactions occurring in >1/1000, <1/100 of patients. Rare adverse reactions: Adverse reactions occurring in >1/10000, <1/1000 of patients. Very rare adverse reactions: Adverse reactions occurring in >1/100000, <1/10000 of patients.