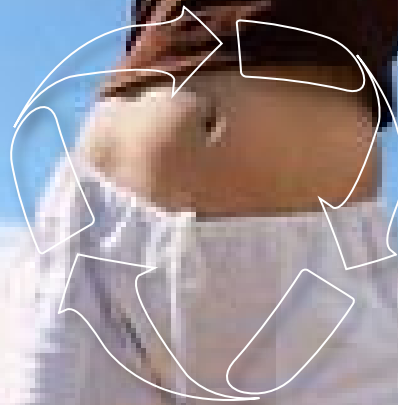


cystistat[®]

Get on with life.

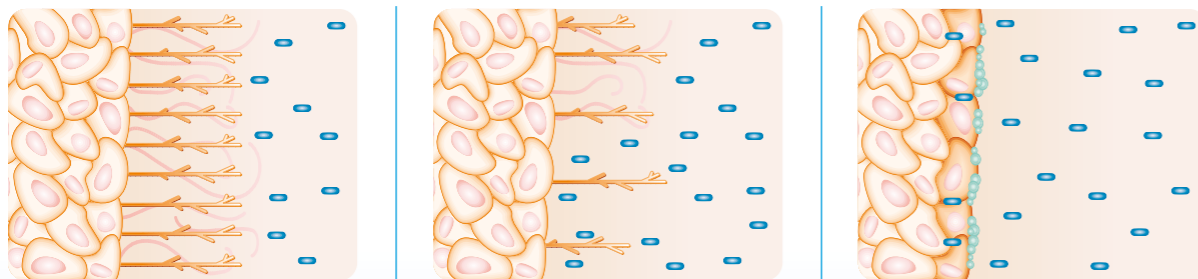
Cystistat[®]
**restores the
urine-tissue
barrier**



BIONICHE
PHARMA GROUP LIMITED

A Solution to a Real Problem

Bladder Pain Syndrome/Interstitial Cystitis (BPS/IC) is a debilitating chronic disorder of the bladder. Without adequate therapy it can lead to a state of unremitting Pain and Urinary Frequency, Urgency and Nocturia.



The bladder wall is protected by a thick layer of Proteoglycans and Glycoproteins (Glycosaminoglycans, GAGs). This layer protects the epithelium against toxic agents and bacteria.

Sodium Hyaluronate (Na-HA) is the structural backbone of the extracellular protective layer: Na-HA can help to rebuild the bladder wall structure.

Cystistat® biochemical rationale^(6, 26)

Biochemistry of Sulphated GAGs

Do not appear to penetrate the wall of the bladder
Short molecule (approx. 250 repeats)
Are covalently linked to proteins
Not electrostatic
Appear to bind to CD44 at a significantly lower affinity than hyaluronan
Cannot form new structures because of the energy required for synthesis

Biochemistry of Sodium Hyaluronate (the "only" not sulphated GAG)

Penetrates at the sub-epithelial level
Long molecule (approx. 50,000 repeats)
Na-HA is not linked to protein
Is electrostatic
Binds to CD44 as a natural ligand
Interaction with GAG containing proteoglycans allows formation of extracellular and potentially pericellular matrices

Cystistat® Therapeutic Objectives

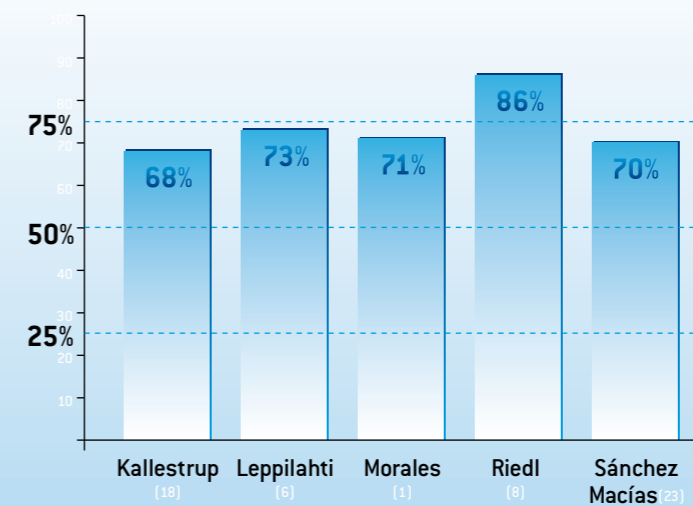
REPAIRING
THE GAG
DEFICIENCY

RECONSTRUCTING
THE URINE-TISSUE
BARRIER

AVOIDING THE
PASSAGE OF
POTENTIALLY
INFLAMMATORY
SOLUTES

Cystistat® Efficacy

The results of some clinical experiences have shown that Cystistat® can give a high response rate



Up to date, in the region of 300.000 doses of Cystistat® have been administered worldwide.



Around 40.000 patients may have been treated by Cystistat® instillations.



The product has been proven to be well tolerated as reported in numerous clinical studies involving over 750 patients.

cystistat®

Get on with life.

For temporary replacement of the glycosaminoglycan (GAG) layer in the bladder.

DESCRIPTION:

The glycosaminoglycan (GAG) layer on the luminal surface of the bladder wall is believed to provide a protective barrier against microorganisms, carcinogens, crystals and other agents present in the urine and has been identified as the primary defense mechanism in protecting the transitional epithelium from urinary irritants¹. Deficiencies in this GAG layer of the bladder epithelium may destroy its barrier function and allow the adherence of bacteria, microcrystals, proteins and ions, or the movement of ionic and nonionic solute residues (i.e. urea) across the epithelium². CYSTISTAT® has been developed to temporarily replenish the deficient GAG layer on the bladder epithelium. The active substance is a highly purified sodium salt of hyaluronic acid.



Each CYSTISTAT® vial contains:

40 mg sodium hyaluronate.

DIRECTIONS:

Instill the entire volume of this solution into the bladder after any residual urine has been removed. Discard any unused portion. For best results, CYSTISTAT® should be retained in the bladder for as long as possible (a minimum of 30 minutes). There is evidence that the GAG layer of the bladder is deficient in cystitis. This deficiency contributes to the clinical symptoms² in the diseases such as interstitial cystitis³, cystitis caused by infections, trauma, urolithiasis, urinary retention, neoplasia and radiation induced cystitis⁴. To alleviate cystitis associated with these conditions, it is recommended that CYSTISTAT® be instilled into the bladder each week for four treatments and then monthly until symptoms resolve. The attending physician, urologist or radiologist should direct any prophylactic use of CYSTISTAT®.

PRECAUTION: Do not administer to patients with known hypersensitivity reactions. Discontinue use if adverse reactions are experienced.

WARNING: KEEP OUT OF THE REACH OF CHILDREN.

STORAGE: Store at room temperature (15-30°C). Do not freeze.

SUPPLIED: 1 x 50 mL vial of CYSTISTAT® 40 mg.

For single use only. Discard after use. Manufactured by: Bioniche Teo. Inverin, Co. Galway. Ireland.

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