sterile sodium hyaluronate solution

for temporary replacement of the glycosaminoglycans (GAG) layer in the bladder.

DESCRIPTION:
The GAG layer on the internal surface of the bladder wall provides a protective barrier against microorganisms, carcinogens, crystals and other agents present in the urine. It has been identified as the primary defense mechanism from these urinary irritants. Deficiencies in this GAG layer may affect its barrier function and allow the adherence of bacteria, microcrystals, proteins and ions, or the movement of solute residues (i.e. urea). 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 produced by fermentation.

Each CYSTISTAT vial contains:
40mg 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). The GAG layer of the bladder is deficient in cystitis. This deficiency contributes to the clinical symptoms in diseases such as interstitial cystitis, radiation induced cystitis, cystitis caused by infections, trauma, urolithiasis, urinary retention and neoplasia. To alleviate cystitis associated with these conditions, it is recommended that CYSTISTAT be instilled into the bladder each week for four to twelve treatments and then monthly until symptoms resolve. The attending physician should determine whether and how frequently to use CYSTISTAT.

PRECAUTION:
Do not administer to patients with history of allergy to the components. Discontinue use if adverse reactions are experienced. As no clinical evidence is available on the use of sodium hyaluronate in children, pregnant and lactating women, treatment with CYSTISTAT is not recommended in these patients.

Avoid using CYSTISTAT with instruments sterilized with glutaraldehyde owing to quaternary ammonium salts solutions.

WARNING:
Keep out of reach of children. Do not use if packaging is damaged. To be used by a physician only.

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

CLINICAL REFERENCES:
19. Daha et al. Is a Maximal Bladder Capacity of >400 cc an Automatic Exclusion Criteria for Interstitial Cystitis? 2002 SIU.

For further information:
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A Solution to a Real Problem

UTI is the bacterial invasion of the Urinary Tract, between the urethra and the kidney. It’s the most common infectious outpatient complaint caused by bacteria.

**Recurrent Bacterial Cystitis (RBC):**
3 or more symptomatic episodes within a year

High recurrence rate; 25-35% of initial UTI episodes will be followed by a recurrent infection within 3-6 months.

RBC can be the result of:
- Bacteria remaining in the bladder despite therapy
- Subsequent re-infection

Restoring the GAG layer

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 most relevant component of the extra cellular matrix and constitutes an important proportion of bladder GAG layer.

CLINICAL EXPERIENCE 1

40 women with a history of RBC received Cystistat intravesical instillations.

<table>
<thead>
<tr>
<th>Cystistat administration scheme:</th>
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<tbody>
<tr>
<td>MONTHS</td>
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<thead>
<tr>
<th>BEFORE TREATMENT</th>
<th>TREATED WITH CYSTISTAT</th>
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<tbody>
<tr>
<td>INFECTIONS / PATIENT / YEAR</td>
<td>4,3</td>
</tr>
<tr>
<td>RECURRENCES (in days)</td>
<td>96</td>
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CLINICAL EXPERIENCE 2

20 women with a history of recurrent cystitis received 9 Cystistat instillations over 6 months.

<table>
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<tr>
<td>TIME TO RECURRENCE (days)</td>
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</table>

65% free of recurrences until the end of the study.

Cystistat is effective in preventing Recurrent Bacterial Cystitis