ELMIRON®-100 MG
(PENTOSAN POLYSULFATE SODIUM)
CAPSULES
PRESCRIBING INFORMATION
DESCRIPTION
Pentosan polysulfate is a semi-synthetically produced heparin-like macromolecular carbohydrate derivative, which chemically and structurally resembles glycosaminoglycans. It is a white odorless powder, slightly hygroscopic and soluble in water.

Pharmacodynamics
In a clinical pharmacology study in which healthy female volunteers received a single oral 300 or 450 mg dose of pentosan polysulfate sodium containing radiolabeled drug and a double radiolabeled drug dose both of which were radiolabeled with 125I-based tracer, about 30% of the orally administered dose of IC-based tracer was seen approximately at a median of 2 hours (range 0.6-120 hours) after dosing. Based on urinary excretion of radioactivity, a mean of approximately 6% of a radiolabeled oral dose of pentosan polysulfate sodium was excreted and reaches the systemic circulation.

Food Effects: In clinical trials, ELMIRON® was administered with water 1 hour before or 2 hours after meals; the effect of food on absorption of pentosan polysulfate sodium is not known.

Distribution:
Preclinical studies with parenterally administered radiolabeled pentosan polysulfate sodium showed distribution to the uroepithelium of the genitourinary tract with lesser amounts found in the liver, lung, skin, peritoneum, and bone marrow.

Pharmacokinetics
The pharmacokinetics of pentosan polysulfate sodium has not been studied in geriatric patients. In a study of patients with hepatic or renal impairment, see also PRECAUTIONS."
ELMIRON® was evaluated in clinical trials in a total of 2627 patients (2343 women, 262 men, 22 unknown) with a mean age of 47 [range 18 to 88 with 581 (22%) over 60 years of age]. Of the 2627 patients, 128 patients were in a 3-month trial and the remaining 2499 patients were in a long-term, unblinded trial. Deaths occurred in 6/2627 (0.2%) patients who received the drug over a period of 3 to 76 months. The deaths appear to be related to other concurrent illnesses or procedures, except in one patient for whom the cause was not known.

Serious adverse events occurred in 33/2627 (1.3%) patients. Two patients had severe abdominal pain or diarrhea and dehydration that required hospitalization. Because there was not a control group of patients with interstitial cystitis who were concurrently evaluated, it is difficult to determine which events are associated with ELMIRON® and which events are associated with concurrent illness, medicine, or other factors.

Adverse Reaction in Placebo-Controlled Clinical Trials of ELMIRON® 100 mg

<table>
<thead>
<tr>
<th>Body System/Adverse Experience</th>
<th>ELMIRON® n = 128</th>
<th>Placebo n = 140</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS Overall Number of Patients*</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>Insomnia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Headache</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Severe Emotional Lability/Depression</td>
<td>1 (1%)</td>
<td>0</td>
</tr>
<tr>
<td>Angiitis</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Hyperkinesia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>GI Overall Number of Patients*</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>Nausea</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Diarrhea</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Dyspepsia</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Jaundice</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vomiting</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Skin/Allergic Overall Number of Patients*</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Rash</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Pruritus</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Laceration</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Rhinitis</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Increased Sweating</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Other Overall Number of Patients*</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Vaginitis</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total Events</td>
<td>12</td>
<td>22</td>
</tr>
<tr>
<td>Total Number of Patients*</td>
<td>13</td>
<td>19</td>
</tr>
</tbody>
</table>

* Within a body system, the individual events do not sum to equal overall number of patients because a patient may have more than one event.

The adverse events below were reported in an unblinded clinical trial of 2409 interstitial cystitis patients treated with ELMIRON®. Of the original 2499 patients, 1192 (48%) received ELMIRON® for 3 months; 892 (36%) received ELMIRON® for 6 months; and 598 (24%) received ELMIRON® for one year; 355 (14%) received ELMIRON® for 2 years, and 145 (6%) for 4 years.

Frequency (1 to 4%): Alopexia (4%), diarrhea (4%), nausea (4%), headache (5%), rash (3%), dyspepsia (2%), abdominal pain (2%), liver function abnormalities (1%), diarrhea (1%).

Frequency (c: 1%):
- Digestive: Vomiting, mouth ulcer, colitis, esophagitis, gastritis, flatulence, constipation, anorexia, gum hemorrhage.
- Hematologic: Anemia, ecchymosis, increased prothrombin time, increased partial thromboplastin time, leukopenia, thrombocytopenia.
- Hypersensitivity Reactions: Allergic reaction, photosensitivity.
- Respiratory System: Pharyngitis, rhinitis, epistaxis, dyspnea.
- Skin and Appendages: Pruritus, urticaria.
- Special Senses: Conjunctivitis, trinitis, optic neuritis, amblyopia, retinal hemorrhage.

Post-Marketing Experience:
The following adverse reactions have been identified during postapproval use of pentosan polysulfate sodium because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure: weight gain and edema.

Rectal Hemorrhage: ELMIRON® was evaluated in a randomized, double-blind, parallel group, Phase 4 study conducted in 380 patients with interstitial cystitis who dosed for 32 weeks. At a daily dose of 300 mg (n = 128), rectal hemorrhage was reported as an adverse event in 6.3% of patients. The severity of these events was described as “mild” in most patients. Patients in that study who were administered ELMIRON® 900 mg daily, a dose higher than the approved dose, experienced a higher incidence of rectal hemorrhage, 15%.

Liver Function Abnormality: A randomized, double-blind, parallel group, Phase 2 study was conducted in 100 men (51 ELMIRON® and 49 placebo) dosed for 16 weeks. At a daily dose of 900 mg, a higher incidence of liver function tests were reported as an adverse event in 11.8% (n = 6) of ELMIRON®-treated patients and 2% (n = 1) of placebo-treated patients.

OVERDOSE:
Overdose has not been reported. Based upon the pharmacodynamics of the drug, toxicity is likely to be reflected as anti-coagulation, bleeding, thrombocytopenia, liver function abnormalities, and gastritis. See CLINICAL PHARMACOLOGY, and PRECAUTIONS sections.) At a daily dose of 900 mg for 32 weeks (n = 127) in a clinical trial, rectal hemorrhage was reported as an adverse event in 15% of patients. At a daily dose of 900 mg for 32 weeks in a clinical trial that enrolled 51 patients in the ELMIRON® group and 49 in the placebo group, elevated liver function tests were reported as an adverse event in 11.8% of patients in the ELMIRON® group and 2% of patients in the placebo group. In the event of acute overdose, the patient should be given gastric lavage if possible, carefully observed and given symptomatic and supportive treatment.

DOSEAGE AND ADMINISTRATION:
The recommended dose of ELMIRON® is 300 mg/day taken as one 100 mg capsule orally three times daily. The capsules should be taken with water at least 1 hour before or 2 hours after meals.

Patients receiving ELMIRON® should be reassessed after 3 months. If improvement has not occurred and if limiting adverse events are not present, ELMIRON® may be continued for another 3 months.

The clinical value and risks of continued treatment in patients whose pain has not improved by 6 months is not known.

HOW SUPPLIED:
ELMIRON® is supplied in white opaque gelatin capsules imprinted “BN 7600” containing 100 mg pentosan polysulfate sodium. Supplied in bottles of 100 capsules.

Storage:
Store at controlled room temperature 15°-30°C (59°-86°F).

Keep out of reach of children.

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Manufactured by: Janssen Ortho LLC Gubaro, Puerto Rico 00778

Manufactured for: Janssen Pharmaceuticals, Inc. Titusville, New Jersey 08560

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PATIENT LEAFLET

ELMIRON® (pronounced EL ma ron) is used to treat the pain or discomfort of interstitial cystitis (IC).

What is the most important information I should know about ELMIRON®?

ELMIRON® is a weak anticoagulant (blood thinner) which may increase bleeding.

Call your doctor if you will be undergoing surgery or will begin taking anticoagulant therapy such as warfarin sodium, heparin, high doses of aspirin, or anti-inflammatory drugs such as ibuprofen.

What is ELMIRON®?

ELMIRON® is used to treat the pain or discomfort of interstitial cystitis (IC). It is not known exactly how ELMIRON® works, but it is not a pain medication like aspirin or acetaminophen and therefore must be taken continuously for relief as prescribed.

What does your doctor need to know?

If you have any liver problems.

If you have any other health problems.

How should I take ELMIRON®?

You should take 1 capsule of ELMIRON® by mouth three times a day, with water at least 1 hour before meals or 2 hours after meals. Each capsule contains 100 mg of ELMIRON®.

What should I avoid while taking ELMIRON®?

Anticoagulant therapy such as warfarin sodium, heparin, high doses of aspirin or anti-inflammatory drugs such as ibuprofen until you speak with your doctor.

What are the most common side effects of ELMIRON®?

The most common side effects are hair loss, diarrhea, nausea, blood in the stool, headache, rash, upper stomach pain, abnormal liver function tests, dizziness and bruising. Weight gain and swelling caused by fluid build up in the body have also been reported in patients taking ELMIRON®.

What do you need to tell your doctor if you will be undergoing surgery or will begin taking anticoagulant therapy such as warfarin sodium, heparin, high doses of aspirin, or anti-inflammatory drugs such as ibuprofen until you speak with your doctor.

Call your doctor if these side effects persist or are bothersome or if there is bleeding in the stool.

If you have any questions or concerns, or want more information about ELMIRON®, contact your doctor or pharmacist. Your pharmacist also has a longer leaflet about ELMIRON® that you can ask to read.

Keep out of reach of children.

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