Summary of Product Characteristics SPC

1. Product Information: COMFORA (Pentosan Polysulfate Sodium Capsules 100mg)

2. Qualitative and quantitative composition:

Each hard gelatin capsule contains:
Pentosan Polysulfate Sodium 100mg
Excipients q.s.
Approved colours are added in empty capsule shell

Pharmaceutical dosage form:

Hard gelatin capsules

Off white/blue colour hard gelatin capsule containing white powder.

3.Clinical Particulars:

3.1 Therapeutic Indications

Pentosan Polysulfate Sodium is indicated for the relief of bladder pain or discomfort associated with interstitial cystitis.

3.2 Posology and method of administration

Adults:

The recommended dose of pentosan polysulfate sodium is 300 mg/day taken as one 100mg capsule orally three times daily.

Response to treatment with pentosan polysulfate sodium should be reassessed every 6 months. In case no improvement is reached 6 months after treatment initiation, treatment with pentosan polysulfate sodium should be stopped. In responders pentosan polysulfate sodium treatment should be continued chronically as long as the response is maintained.

Special populations:

Pentosan polysulfate sodium has not been specifically studied in special patient populations like elderly or patients with renal or hepatic impairment. No dose adjustment is recommended for these patients.

Paediatric population:

The safety and efficacy of pentosan polysulfate sodium in children and adolescent below 18 years has not been established.

No data are available.

Method of administration:

The capsules should be taken with water at least 1 hour before meals or 2 hours after meals.

3.3 Contraindications:

Hypersensitivity to the active substance or to any of the excipients.

Due to the weak anticoagulant effect of pentosan polysulfate sodium, pentosan polysulfate capsule must not be used in patients who actively bleed. Menstruation is no contraindication.

3.4 Special warnings and precautions for use:

Bladder pain syndrome is a diagnosis of exclusion and other urologic disorders should be eliminated by the prescriber, such as urinary tract infection or bladder cancer.

Pentosan polysulfate sodium is a weak anticoagulant. Patients undergoing invasive procedures or having signs/symptoms of underlying coagulopathy or other increased risk of bleeding (due to treatment with other medicinal products influencing coagulation such as anticoagulants, heparin derivatives, thrombolytic or antiplatelet agents including acetylsalicylic acid, or nonsteroidal anti-inflammatory medicinal products should be evaluated for haemorrhagic events. Patients who have a history of heparin or pentosan polysulfate sodium induced thrombocytopenia should be carefully monitored when treated with pentosan polysulfate sodium.

<u>Hepatic or renal insufficiency</u>

Pentosan polysulfate sodium capsules has not been studied in patients with hepatic or renal insufficiency. Because there is evidence of hepatic and renal contribution to the elimination of pentosan polysulfate sodium, hepatic or renal impairment may have an impact on the pharmacokinetics of pentosan polysulfate sodium. Patients with relevant hepatic or renal insufficiency should be carefully monitored when treated with pentosan polysulfate sodium.

3.5 Interaction with other medicinal products and other forms of interaction:

A study in healthy subjects revealed no pharmacokinetic or pharmacodynamic interactions between therapeutic doses of warfarin and pentosan polysulfate sodium. No further interaction studies have been performed.

Due to the weak anticoagulant effect of pentosan polysulfate sodium, patients, who are concomitantly treated with anticoagulants, heparin derivatives, thrombolytic or antiplatelet agents including acetylsalicylic acid, or nonsteroidal anti-inflammatory medicinal products should be evaluated for any haemorrhagic event in order to adapt the dose if needed.

3.6 Fertility, Pregnancy and lactation:

There are no data from the use of pentosan polysulfate sodium in pregnant women. Animal studies with respect to reproductive toxicity were not conducted.

Pentosan polysulfate sodium capsules is not recommended during pregnancy.

Breast-feeding:

It is unknown whether pentosane polysulfate sodium or metabolites are excreted in human milk.

A risk to the newborns/infants cannot be excluded.

Therefore, pentosan polysulfate sodium should not be used during breast-feeding.

Fertility:

No information on a potential impact of pentosane polysulfate sodium on fertility is available.

3.7 Effects on ability to drive and use machines:

Pentosan polysulfate sodium has no or negligible influence on the ability to drive and use machines.

3.8 Undesirable effects:

Summary of the safety profile:

The following section lists adverse events reported in the literature from clinical studies with pentosan polysulfate sodium. The potential relatedness between these adverse events and the treatment with pentosan polysulfate sodium was not discussed in the respective publications.

The most common adverse events reported from the clinical studies are headache, dizziness and gastro-intestinal events like diarrhoea, nausea, abdominal pain and rectal bleeding.

The adverse events reported under treatment with pentosan polysulfate sodium were comparable to those reported under treatment with placebo in regards to quality and quantity.

<u>Tabulated summary of adverse events:</u>

Adverse events are listed below by MedDRA body system organ class and by frequency. Very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000); not known (cannot be estimated from available data).

Infections and infestations	Common	Infections, influenza
Blood and lymphatic system disorders	Uncommon	Anaemia, ecchymosis, haemorrhage, leukopenia, thrombocytopenia
	Not known	Coagulation disorders
Immune system disorder	Uncommon	Photosensitivity
	Not known	Allergic reactions
Metabolism and nutrition disorders	Uncommon	Anorexia, weight gain, weight loss
Psychiatric disorders	Uncommon	Severe Emotional Lability/Depression
Nervous system disorders	Common	Headache, dizziness
	Uncommon	Increased sweating, insomnia, hyperkinesia, paraesthesia
Eye disorders	Uncommon	Lacrimation, amblyopia
Ear disorders	Uncommon	Tinnitus
Respiratory, thoracic and mediastinal disorders	Uncommon	Dyspnoea
Gastrointestinal disorders	Common	Nausea, diarrhoea, dyspepsia, abdominal pain, abdomen enlarged, rectal haemorrhage
	Uncommon	Indigestion, vomiting, mouth ulcer, flatulence, constipation

Skin and subcutaneous tissue disorders	Common	Peripheral oedema, alopecia
	Uncommon	Rash, increased mole size
Musculoskeletal and connective tissue disorders	Common	Back pain
	Uncommon	Myalgia, Arthralgia
Renal and urinary disorders	Common	Urinary frequency
General disorders and administration site conditions	Common	Asthenia, pelvic pain
Investigation	Not known	Liver function abnormalities

3.9 Overdose

In the case of an accidental overdose, patients should be evaluated for potential adverse effects of pentosan polysulfate sodium like gastrointestinal symptoms or bleeding. In case of adverse reactions, treatment might be paused until the symptoms abate and treatment should be continued at the recommended dose after a critical balancing of the risks thereafter.

4. Pharmacological properties:

Pharmacodynamic properties

Pharmacotherapeutic group: Urologicals, other urologicals, ATC code: G04BX15.

Mechanism of action:

The hypothetic mechanism of action of pentosan polysulfate sodium includes a local effect in the bladder after systemic administration and excretion into the urine by binding

of glycosaminoglycans to the deficient mucous of the bladder. This binding of glycosaminoglycans to the bladder mucous reduces bacterial adherence to the inner surface of the bladder and in consequence the incidence of infections is reduced as well. It is hypothesized, that a potential barrier function of pentosan polysulfate sodium instead of the damaged urothelial mucus might play a role as well the anti-inflammatory activity of pentosan polysulfate sodium.

Clinical efficacy and safety:

A total of four randomised placebo-controlled, double-blind clinical studies prospectively enrolling patients with bladder pain syndrome diagnosed via cystoscopic examination with or without bladder hydrodistension evaluating the efficacy of oral treatment with pentosan polysulfate sodium were published in scientific literature. In all of these studies, patients reported a better subjective improvement of bladder pain syndrome under treatment with pentosan polysulfate sodium compared to placebo. In three studies, the observed difference was clearly statistically significant.

The first study was a double-blind, randomized, placebo-controlled study with a planned cross-over design evaluating pentosan polysulfate sodium versus placebo. Depending on which institution the patients attended they were treated with either 3x100 mg or 2x200 mg PPS per day. 75 patients were randomised into the study and 62 of those completed the study. Efficacy of treatment was evaluated based on the patient reported improvement on four typical symptoms of bladder pain syndrome: pain, urgency, frequency, and nocturia, no primary endpoint was defined. A patient was counted as a responder to treatment in case a 50% improvement compared to baseline was reported for a specific symptom after 3 months of treatment.

PRECLINICAL SAFETY DATA

No information available

5.Pharmaceutical particulars

LIST OF EXCIPIENTS

Microcrystalline Cellulose BP

Croscarmellose Sodium EP
Magnesium Stearate BP

6. Incompatibilities

The excipients have no deleterious effect on the chemical stability of the active ingredient. This has been demonstrated by the stability studies carried out on the finished product.

7. Shelf-Life

36 months

8.Special precautions for storage

Store below 30°C, in a dry and dark place. Keep out of reach of children.

9.Nature and contents of the container

The presentation of 100 mg is packed as 90 capsules in HDPE bottle with child lock cap.

10.Instructions for use/handling

Pentosan Polysulfate sodium capsules is for oral administration and is supplied HDPE bottle with childlock cap. The contents of the bottle are must be keep out of reach of children.

11. Marketing Authorization holder

Marketed By:

Swati Spentose Pvt. Ltd.
114, Marine Chambers,
11, New Marine Lines.
Mumbai – 400012

Manufactured By:

M/S. STERIL -GENE LIFE SCIENCES (P) LTD
(J V of Lloyds Lab & Madras Pharma)
No: 45, Mangalam Main Road, Mangalam Village,
Villianur Commune, Puducherry – 605 110,
India.

12. Marketing Authorization Numbers:

TAN 21 HM 0349

13. Date of renewal of Authorization:

Not applicable

14. Date of revision of the text:

April, 2022