elmiron®

pentosan polysulfate sodium

A REVIEW of evidence and guidelines

elmiron® is indicated for bladder pain syndrome with glomerulations and/or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition [1]

For more information on **elmiron®** visit the website

Prescribing information and adverse event reporting can be found on page 6

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Consilient Health

Efficacy of pentosan polysulfate for the treatment of interstitial cystitis/bladder pain syndrome: results of a systematic review of randomized controlled trials [2]

Arndt van Ophoven, Kirsten Vonde, Winfried Koch, Günter Auerbach and Klaus P. Maag
Current Medical Research and Opinion 2019;35(9):1495–1503.

Aims: To compare and critically evaluate all data available from randomized, placebo-controlled trials testing pentosan polysulfate sodium (PPS) for the treatment of interstitial cystitis (IC)/bladder pain syndrome (BPS).

Search strategy: A systematic review of PubMed/Medline, the Cochrane Library and a search for additional potentially unpublished studies on PPS on ClinicalTrials.gov as provided by the US National Library of Medicine and the European Union Clinical Trials Register.

Eligibility criteria:

To be included in the meta-analyses, studies had to:

(a) evaluate the therapeutic effect of oral PPS on treating IC

(b) be randomised placebo-controlled clinical trials

(c) involve patients with a clinical and cystoscopically verified diagnosis of IC

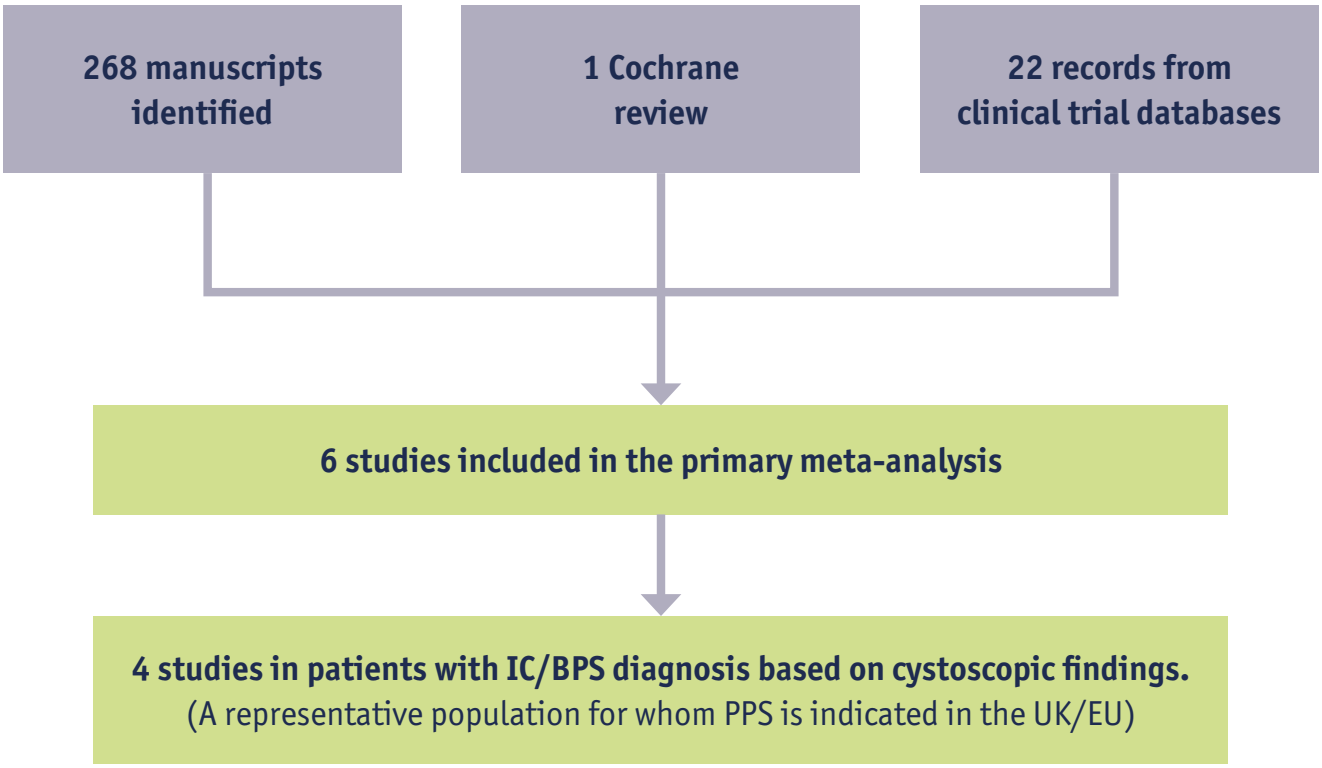
(d) provide sufficient information to estimate at least one relevant effect size measure to compare the efficacy of PPS versus placebo

Exclusion criteria:

- reviews
- studies in animals
- no intervention
- comments / letters
- open label trials
- intravesical treatments
- editorials/summaries
- re-analyses
- not IC/BPS
- case reports

PPS: pentosan polysulfate sodium; IC: interstitial cystitis; BPS: bladder pain syndrome

Treatments: 3x100mg **elmiron®** capsules per day or a comparable dosing regimen were evaluated in the six studies. Furthermore, the treatment periods of the studies covered 3–6 months and were considered comparable.



Data extraction: The main focus of the meta-analysis was patient global response assessment (GRA), which was assessed in most of the identified studies. For studies that did not evaluate any form of global improvement versus baseline, data was imputed based on the closest information provided in the respective publication.

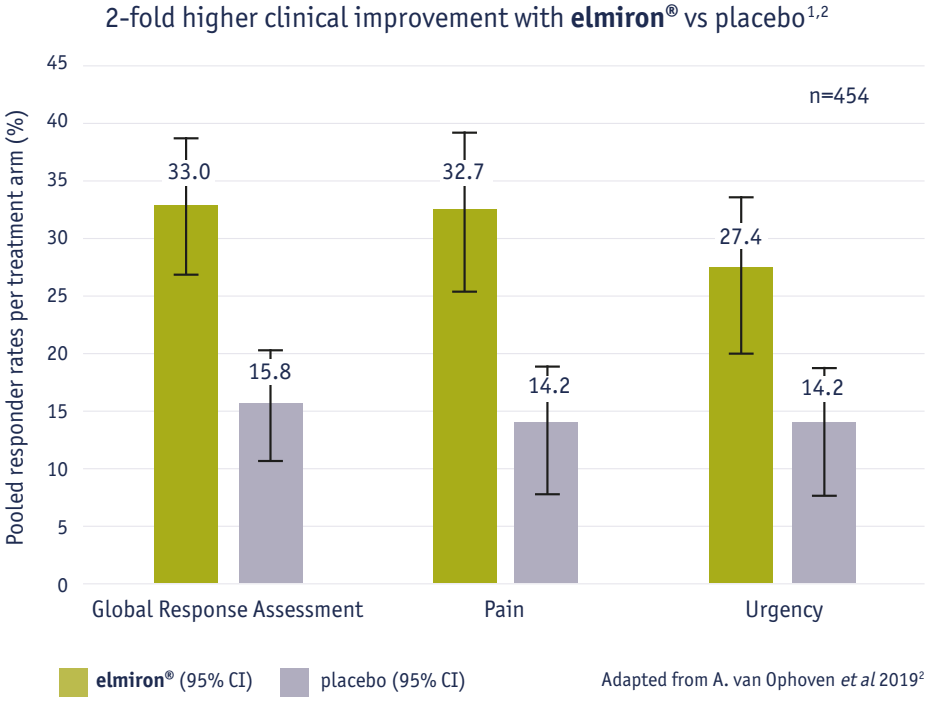
Effect size data for the meta-analyses was extracted from the original publications as well as from the meta-analyses identified in the literature search.

Statistical analysis: As the individual studies mostly analysed and compared success rate differences, this approach was also followed for the meta-analyses. Success rate was defined as the proportion of responders per group, defined as at least a moderate or 50% improvement in patient GRA. Differences in success rates (PPS - placebo) were denoted as benefit differences, as a greater difference in rates indicated higher benefit with PPS.

The intent-to-treat (ITT) principle including all randomized patients was used for the meta-analysis. Patients with missing data were considered as failure. To assess the treatment effect on symptom scores, mean changes from baseline and standard deviations were used.

Results of meta-analysis: Focusing on the four studies that limited enrolment to those patients diagnosed based on cystoscopic examinations,[3-6] the meta-analysis showed a benefit difference of 17.0% (95% CI: 9.3–24.7%) in favour of PPS. The difference was highly statistically significant (p<.001) without any indication of heterogeneity (Q=0.470, p=.925, I^2=0).

A pooled analysis of results per treatment group (PPS treatment versus no PPS treatment) allowed a comparison between the magnitudes of treatment effects in each treatment group. Results of this analysis revealed an approximate duplication of response rates between PPS and placebo for GRA, pain and urgency, shown below.



The GRA assessment was evaluated via a 7-point centred scale, in which the patients can assess their global response compared to baseline as markedly worse, moderately worse, slightly worse, no change, slightly improved, moderately improved or markedly improved. Participants who reported either of the latter two categories were defined as treatment responders. A patient reaching a 50% improvement compared to baseline was considered a responder for the specific symptoms of pain and urgency.

The duplication of the treatment effect was confirmed by an adequate meta-analysis which resulted in a benefit ratio of GRA of 2.085 (95% CI: 1.464–2.967). Additionally, there was no indication of heterogeneity for this meta-analysis (Q=0.245, p=.970, I^2=0). This confirms that the benefit ratio is an appropriate measure to describe the superiority of PPS over placebo.

Limitations: Publication bias was an identified risk. High drop-out rate and response rate in the placebo group in the latest studies are to be considered.

Conclusion: The meta-analysis and comprehensive review found that PPS is more efficacious than placebo in the treatment of pain, urgency and frequency, and beneficial for symptoms of IC/BPS. In summary, treatment with PPS led to a statistically significant and clinically relevant improvement in patients' overall response assessment (at least moderate or 50% improvement from baseline) in addition to clinically relevant improvements in the main symptoms of IC/BPS, i.e. pain and urgency (50% improvement from baseline). Thus PPS is an evident option for the treatment of IC/BPS symptoms as stipulated in the clinical guidelines of the relevant professional associations.

elmiron®: The first, and only, licensed oral medicine for BPS with bladder lesions (defined as glomerulations and/or Hunner's lesions) [1,7]

- **elmiron®** is indicated for bladder pain syndrome with glomerulations and/or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition [1]
- **elmiron®** offers a convenient and patient-friendly oral treatment option compared with invasive treatments such as bladder instillations [8,9]
- By prescribing **elmiron®** you can:
  - help free the patient from the indignity and the associated risks with bladder instillations
  - avoid time and costs associated with the administration of bladder instillations [8,9]

Using **elmiron®** prior to bladder instillation offers patients a different pathway [8]

Health Technology Appraisals for **elmiron®**

APPROVED NICE[8] APPROVED

APPROVED AWMSG[10] APPROVED

Used as per licensed indication, only if:

- the condition has not responded to an adequate trial of standard oral treatments
- not offered in combination with bladder instillations
- previous treatment with bladder instillations was not stopped due to lack of response
- it is used in secondary care and
- the Patient Access Scheme (PAS) is in place

ACCEPTED SMC[9] ACCEPTED

- Used as per licensed indication
- The Patient Access Scheme (PAS) is in place

elmiron®
pentosan polysulfate sodium

elmiron® (pentosan polysulfate sodium) Prescribing Information. Please refer to the elmiron® Summary of Product Characteristics for full details. Product name: elmiron® 100 mg hard capsules **Composition:** 100mg of pentosan polysulfate sodium **Indication:** Treatment of bladder pain syndrome characterized by either glomerulations or Hunner's lesions in adults with moderate to severe pain, urgency and frequency of micturition. **Dosage and administration: Adults:** One capsule three times daily. Reassess treatment response every 6 months. Discontinue if no improvement in the 6 months after initiation. Continue treatment as long as the response is maintained. **Special populations:** No dose adjustment recommended. **Paediatric population:** Safety and efficacy has not been established. **Method of administration:** Take with water at least 1 hour before or 2 hours after meals. **Contraindications:** Hypersensitivity to active substance(s) or any of the excipients. Patients who actively bleed (menstruation is not a contraindication). **Warnings and precautions (see SmPC for full details):** Diagnosis of other urologic disorders should be eliminated. Evaluate patients for haemorrhagic events if undergoing invasive procedures or having signs/symptoms of underlying coagulopathy or increased risk of bleeding. Monitor patients with a history of heparin or pentosan polysulfate sodium induced thrombocytopenia; or hepatic or renal insufficiency. Rare cases of pigmentary maculopathy have been reported, especially after long term use. Visual symptoms might include difficulty when reading, visual distortions, altered colour vision and/or slow adjustment to low/reduced light. All patients should have an ophthalmologic examination after 6 months, and, if there are no pathologic findings, regularly after 5 years (or earlier, in case of visual complaints). However, in case of relevant ophthalmologic findings, conduct yearly examinations. In such situations, treatment cessation should be considered. **Pregnancy**: Not recommended. **Breast-feeding:** Should not be used. **Fertility:** No information available. **Undesirable effects: Common (≥1/100 to <1/10):** Infections, influenza, headache, dizziness, nausea, diarrhoea, dyspepsia, abdominal pain, abdomen enlarged, rectal haemorrhage, peripheral oedema, alopecia, back pain, urinary frequency, asthenia, pelvic pain. **Uncommon (≥1/1,000 to <1/100)**: Anaemia, ecchymosis, haemorrhage, leukopenia, thrombocytopenia, photosensitivity, anorexia, weight gain, weight loss, severe emotional lability/depression, increased sweating, insomnia, hyperkinesia, paraesthesia, lacrimation, amblyopia, tinnitus, dyspnoea, indigestion, vomiting, mouth ulcer, flatulence, constipation, rash, increased mole size, myalgia, arthralgia. **Not known** Allergic reactions, liver function abnormalities. **NHS Price:** £450.00 per bottle of 90 capsules. **Legal Classification:** POM **MA numbers:** EU/1/17/1189/001, PLGB 12404/0001 **Marketing Authorisation Holder:** bene-Arzneimittel GmbH, Herterichstrasse 1-3, D-81479 Munich, Germany. **Further information is available on request from:** Consilient Health (UK) Ltd, No.1 Church Road, Richmond upon Thames, Surrey TW9 2QE or drugsafety@consilienthealth.com. **Job Code:** UK-ELM-269 **Date of preparation of PI:** May 2021

Adverse events should be reported. Reporting forms and information can be found at www.mhra.gov.uk/yellowcard. Adverse events should also be reported to Consilient Health (UK) Ltd, No. 1 Church Road, Richmond upon Thames, Surrey TW9 2QE UK or drugsafety@consilienthealth.com

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Date of preparation: June 2022 UK-ELM-335b