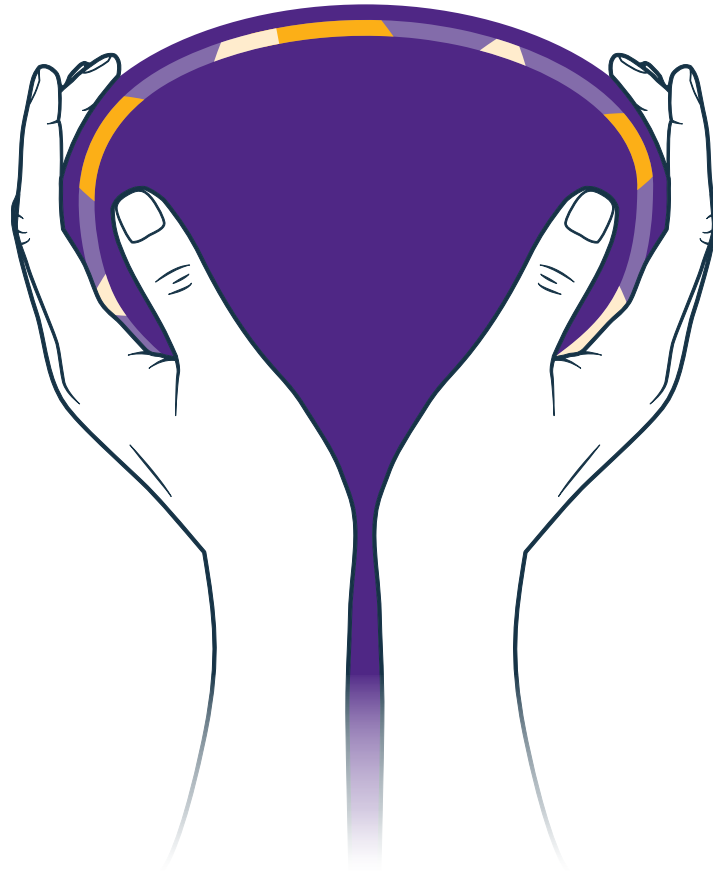


Dual protection for the bladder.

Proven instillation therapy with hyaluronic acid and chondroitin sulfate for treatment of interstitial cystitis, recurrent urinary tract infections, and radiation cystitis.

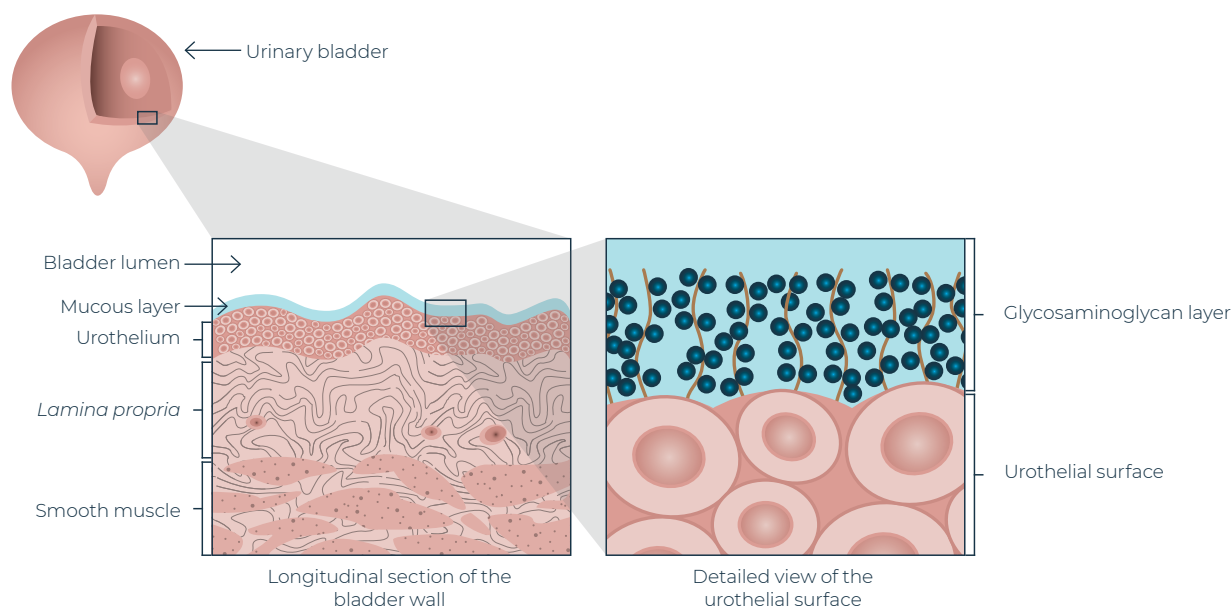


Instillamed® —
The dual component protection



Damage to the GAG layer – chronic distress for the patient.

The healthy bladder is coated with a protective glycosaminoglycan (GAG) layer that shields it against toxic and irritating substances in the urine. **Hyaluronic acid** and **chondroitin sulfate** are key components of this protective layer.



Structure of the bladder wall and GAG layer.

With chronic bladder disorders, the GAG layer is often damaged and no longer able to provide full protection. The consequences:



Frequent urination



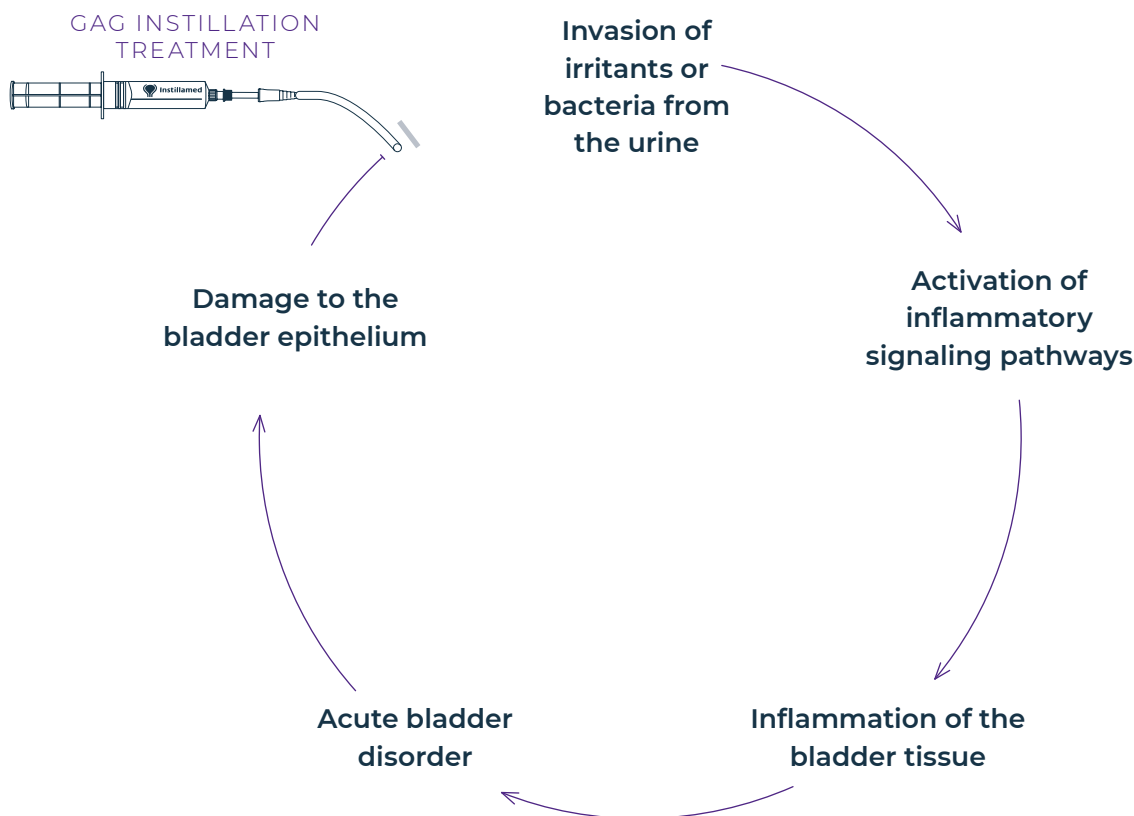
Strong urge to urinate



Burning pain

Instillation treatment – considerable improvement in quality of life.

Regardless of the underlying disease, all recurrent bladder infections may damage the protective lining of the bladder (GAG layer). Instillation treatment with hyaluronic acid and chondroitin sulfate supports the repair of the GAG layer and restores this barrier protecting against irritants and bacteria.¹ The pathogens and inflammatory processes causing chronic disease may thus be effectively inhibited.



Instillation treatment with exogenous glycosaminoglycans (GAG) may interrupt the pathogenic cycle in chronic bladder disorders and greatly improve patient quality of life.

Dual component protection – with endogenous active substances.

Instillamed® combines hyaluronic acid and chondroitin sulfate in a single formulation. Such a combination provides effective GAG replacement in the urinary bladder.



Instillamed® is particularly suitable for the treatment of

- Interstitial cystitis (IC)
- recurrent urinary tract infections (rUTI)
- Radiation cystitis

As a result of intensive regeneration of the GAG layer

- ✓ considerable reduction in pain and urgency symptoms ^{2,3,*}
- ✓ 77% fewer UTIs after 12 months compared to placebo (p=0.0002) ^{4,*}
- ✓ improvement in the quality of life ^{2,5,*}

Case study data support the efficacy of combination formulations such as Instillamed®.

“With its few side effects, intravesical instillation of hyaluronic acid combined with chondroitin sulfate has become an established effective alternative to drug treatment. And with its good tolerability it can provide long-term improvement in symptomatic chronic cystitis.”



PROF. DANIELA SCHULTZ-LAMPEL, M.D.
Board certified in Urology and Special Urological Surgery,
Director, South-West Continence Center, Schwarzwald-Baar Hospital, Germany

Safe application – with ready-to-use sterile syringe.

Depending on the symptoms, treatment should be initiated with one instillation per week over a treatment period of 4–6 weeks. This should then be followed by monthly instillations for up to 6 months.

Recommended treatment intervals



Depending on the severity, one instillation per week over a period of 4–6 weeks

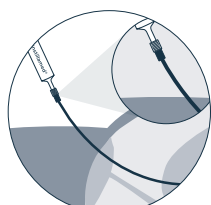


One instillation per month

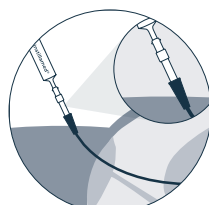
The Instillamed® dual component protection comes in a ready-to-use sterile, disposable syringe. The included safety adapter ensures firm connection of the Luer lock with all standard catheters.

Application

- First empty the bladder completely.
- Then instill the entire contents of the Instillamed® ready-to-use syringe into the bladder through the disposable catheter.
- For this purpose, connect the syringe **A** to an appropriate catheter via the Luer lock connector. **B** using the included adapter to a catheter without a Luer lock connector.



A



B



SAFETY ADAPTER



After instillation, Instillamed® should be retained in the bladder until the next urination, for at least 30 minutes or longer if possible.

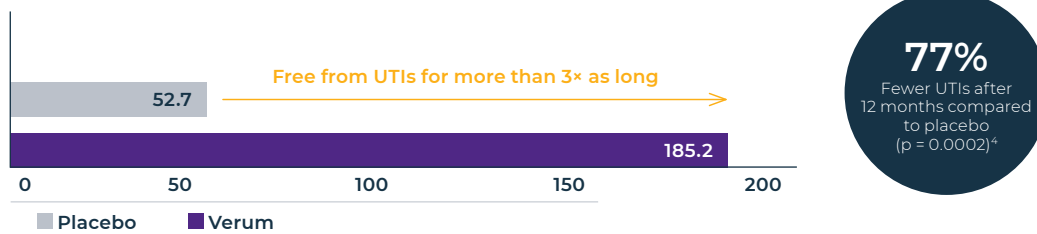
Instillation therapy with HA/CS: Study verified efficacy in rUTI.

Markedly fewer recurrent urinary tract infections

In the urological practice rUTI is a disorder commonly seen in female patients. The therapeutic approach is often limited to repeated administration of antibiotics. This carries the risk of antibiotic resistance developing in the bacteria triggering the inflammation. Antibiotics may also have a negative effect on the structure of the natural protective layer of the bladder.⁶ This weakens the natural defence of the bladder against pathogens and increases the risk of interstitial cystitis developing as a consequence.⁷

Instillation therapy with hyaluronic acid and chondroitin sulfate restores the natural protection against bacteria and irritants. Numerous studies have shown that such a treatment may significantly reduce the number of rUTIs.^{4,8}

Days to recurrence of UTI (mean)

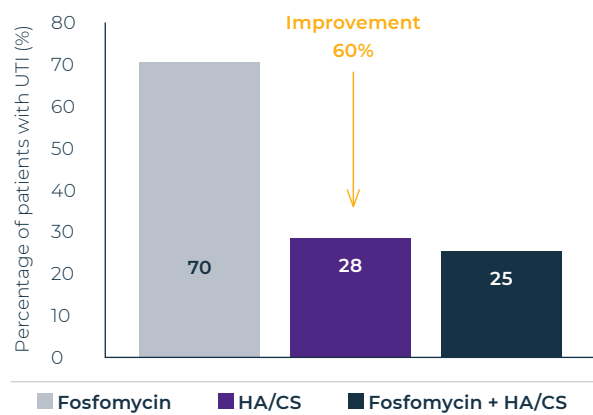


Using a chondroitin sulfate/hyaluronic acid solution, it was possible to significantly prolong the mean time until occurrence of the next UTI by 133 days. After 12 months the occurrence of UTIs per year in the verum group was significantly reduced by a mean of 77% (p = 0.0002).⁴

Effective alternative to antibiotics

Instillation therapy with hyaluronic acid and chondroitin sulfate is a promising and effective alternative to antibiotic prophylaxis. The number of newly occurring UTIs may be significantly reduced compared to an antibiotic-based treatment.^{9,10}

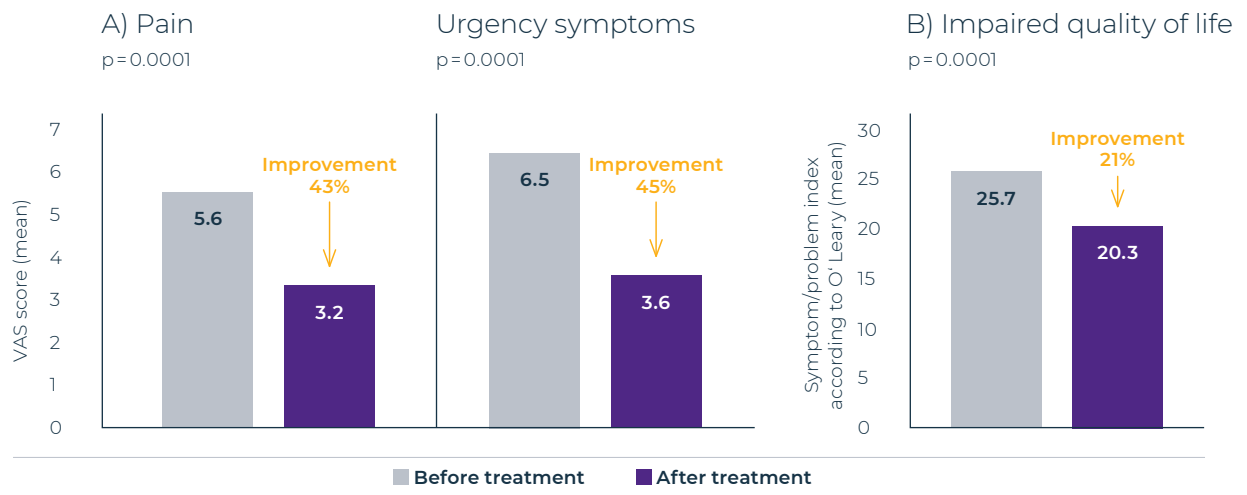
Considerably fewer recurrent urinary tract infections after 6 months



Alone or in combination with the antibiotic fosfomycin, hyaluronic acid/chondroitin sulfate (HA/CS) demonstrated a markedly superior efficacy compared to antibiotic alone: more than twice as many patients remained free of UTIs over 6 months.⁹

Instillation therapy with HA/CS: Study verified efficacy in IC.

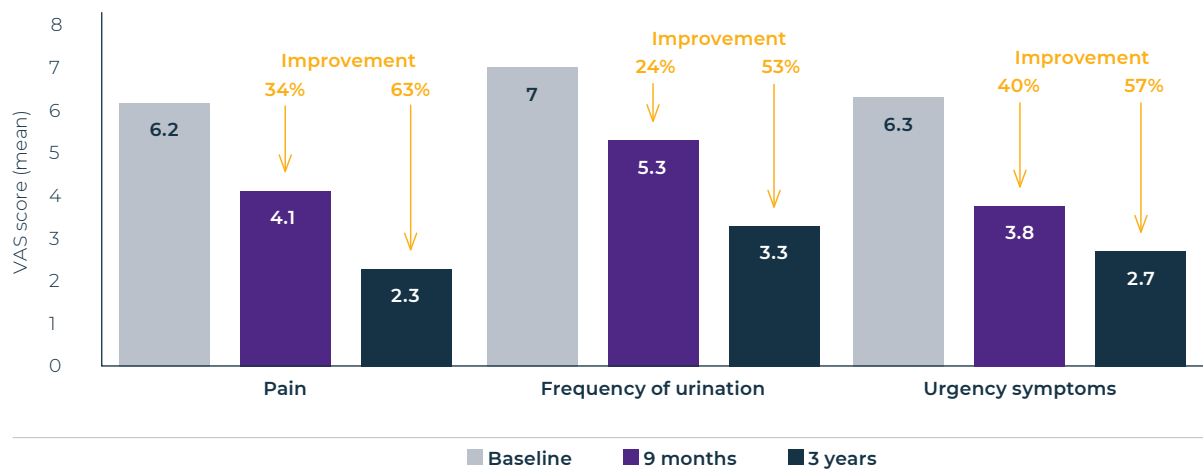
Marked improvement in symptoms



In patients with interstitial cystitis, instillation treatment with a chondroitin sulfate/hyaluronic acid solution was able to achieve A) a highly significant improvement in the pain and urgency symptoms as well as B) a positive effect on the quality of life (measured according to the symptom/problem index of O'Leary).²

Long-term effect

Vesical instillation of hyaluronic acid and chondroitin sulfate verifiably contributes to the restoration of the GAG layer.¹¹ The sustained regeneration results in long-term improvement in bladder function. Urinary urge, pain, and frequency of urination are markedly reduced.³



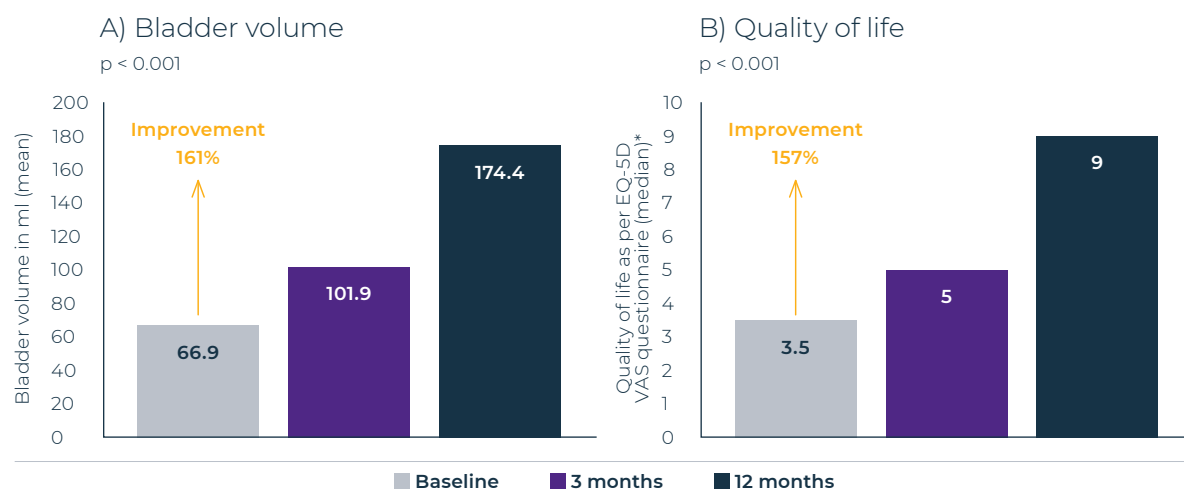
At a three-year follow-up, the pain and urgency symptoms in patients with interstitial cystitis were sustainably reduced under instillation treatment with a chondroitin sulfate/hyaluronic acid solution. Pain, frequency of urination, and urge to urinate had decreased by more than half.³

Instillation therapy with HA/CS: Study verified efficacy in radiation cystitis.

Marked reduction in pain and urgency symptoms and increase in bladder volume

Persistent pain and a strong urge to urinate severely affect patients with chronic bladder symptoms. The efficacy of instillation treatment with hyaluronic acid and chondroitin sulfate in relieving symptoms and increasing bladder volume has been verified in many studies.^{2,3,5,12,13}

As a result, patients experienced a considerable improvement in their quality of life.^{2,5}



A) A prospective pilot study was able to demonstrate a significant increase in bladder volume after 3 and 12 months ($p < 0.001$) in patients with radiation cystitis. B) The quality of life of the patients (measured with the European Quality of Life 5-Dimensions [EQ-5D] questionnaire, EQ-5D VAS: 0 (very bad) to 10 (best possible health state), also showed a significant improvement after 3 and 12 months compared to baseline ($p < 0.001$) and after 12 months compared to 3 months ($p < 0.001$).⁵

Instillation treatment such as Instillamed® in radiation-induced urocystitis

“We successfully treat patients for post-radiotherapy micturition disorders with dysuria and urgency symptoms using intravesical instillation with chondroitin sulfate/hyaluronic acid. The rationale for this causal, and in our experience successful, treatment is replacement of the bladder’s GAG layer damaged by radiotherapy.”



PROF. ULLRICH OTTO, M.D.
Board Certified Urologist, Medical Director, and Head, Urology Expert Center for Rehabilitation in the Hartenstein Clinics, Germany



OLIVER BROCK, M.D.
Board Certified Urologist, Senior Attending Physician
Urology Expert Center for Rehabilitation in the Hartenstein Clinics, Germany

Internal case study data support the efficacy of Instillamed®

Despite the rather small sample size (n=15; available for complete evaluation: n=14), the present non-interventional study conducted over approximately 6 months provided useful insights into the efficacy and tolerability of this treatment approach for pelvic pain syndrome as well as recurrent and interstitial cystitis.¹³ Treatment efficacy was evaluated based on the documentation of the specific disease symptoms (frequent urination, nocturia, incontinence), patient self-assessment (pain intensity, stress due to the disease symptoms), and final overall assessment by the attending physician.

Indication

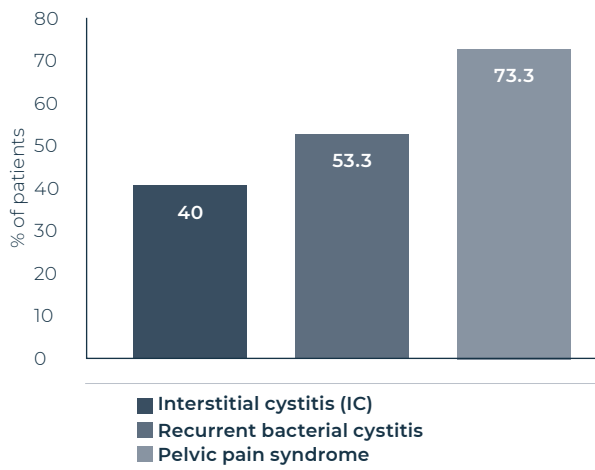


Figure 1 Indications for treatment with Instillamed® for the enrolled 15 patients (multiple entries possible).¹³

Symptoms at baseline

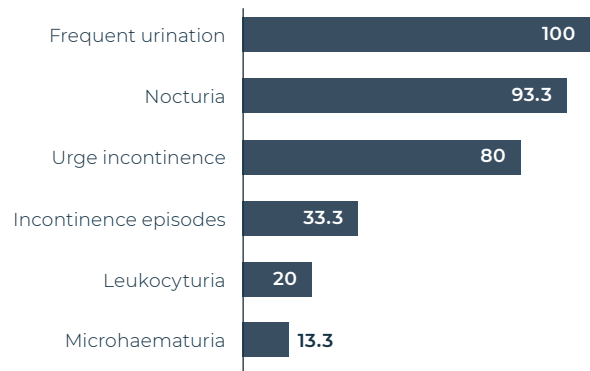


Figure 2 Symptoms of the 15 enrolled patients at baseline (multiple entries possible).¹³

Physician evaluated efficacy and tolerability of Instillamed®

Physician evaluated efficacy and tolerability

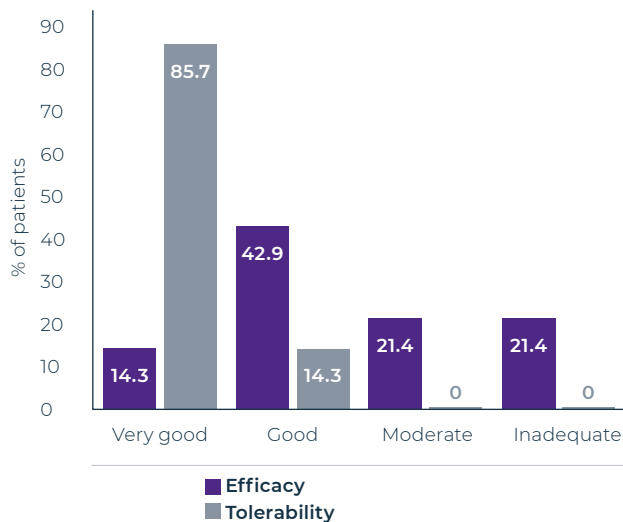


Figure 3 Final evaluation of the efficacy and tolerability of Instillamed® by the attending physician in the patient study population available for evaluation (n=14).¹³

Continuation and repetition of treatment

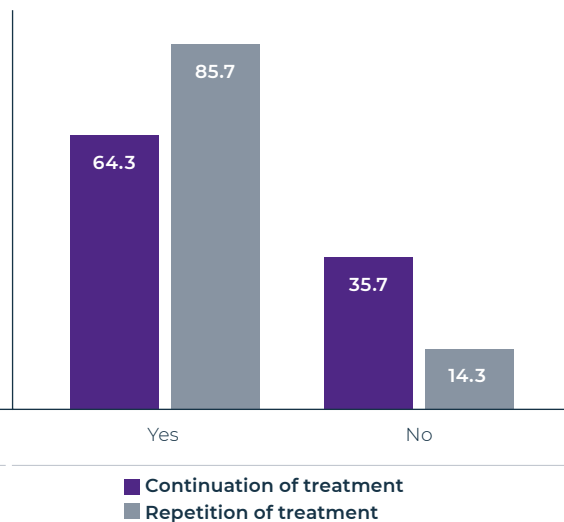


Figure 4 Final statement of intent by the attending physician on the continuation and repetition of treatment with Instillamed® in the patient study population available for evaluation (n=14).¹³

Instillamed® – Dual component protection for intensive regeneration of the GAG layer.



Instillamed®

SIZE	50 ml
NUMBER	1
ARTICLE NO.	351003

EFFECTIVE DATE: 09/2019

Disposable syringe with 50 ml chondroitin sulfate and hyaluronic acid solution. For use with all commercially available catheters.

Composition: 50 ml Instillamed® contains 800 mg sodium hyaluronate, 1000 mg chondroitin sulfate.

Contraindications: Instillamed® should not be administered in children under 12 years of age or pregnant women because there is no treatment experience available. Do not use Instillamed® in macrohaematuria or urethral and/or bladder injury.

LITERATURE

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HA: hyaluronic acid, CS: chondroitin sulfate

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