

nSTRIDE[®] Autologous Protein Solution (APS) Kit

Once OA Pain Starts, It's Hard to Stop.



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Do more than just treat knee pain

Intra-Articular Injection for the Treatment of Knee Osteoarthritis

Once OA pain starts it is hard to stop. The nSTRIDE APS Kit is designed to produce a groundbreaking autologous therapy to treat pain and slow the progression of cartilage degradation and destruction in the knee. The nSTRIDE APS Kit is a cell-concentration system which concentrates anti-inflammatory cytokines and anabolic growth factors to significantly decrease pain and promote cartilage health.

Pre-Clinical & Clinical

- Significantly Reduces Pain Associated with Knee OA¹⁻³
- Significantly Improves Function in the Knee Joint associated with OA¹⁻³
- Stimulates Cartilage Cell Proliferation⁴^
- Blocks Cartilage Destruction^{4^}
- Slows Cartilage Degradation^{4^}
- Point-of-Care
- Single Injection



How does nSTRIDE APS work?

The nSTRIDE APS Kit is a cell-concentration system designed to concentrate anti-inflammatory cytokines and anabolic growth factors to significantly decrease pain and promote cartilage health.









Pre-Clinical

The nSTRIDE APS Kit produces APS via density-based separation and filtration-based concentration. In pre-clinical studies, nSTRIDE APS has been shown to:

- inhibit catabolic enzyme production from chondrocytes stimulated with IL-1ß and $TNF\alpha^{8^{\wedge}}$
- inhibit inflammatory cytokine production from IL-1B-stimulated macrophages^{9[^]}
- inhibit catabolic destruction of cartilage tissue^{4^}
- protect cartilage in a meniscal-tear model (Figure 4)^{10*}
- reduce pain in large animals with naturally occurring OA (Figure 5)^{11*}



Figure 4. Thirty male athymic rats underwent surgery to induce OA by a complete tear of the medial meniscus of the right knee.^{10*} Seven days later, rats were administered 50 µl intra-articular (IA) APS from a human donor or phosphate buffered saline (PBS) control. Rats were euthanized 3 weeks following treatment, and knee joints were processed for histological analysis. Treatment with a single IA injection of APS reduced the cartilage degeneration that characterizes the progression of OA. A) Single injection of Saline. B) Single injection of APS (50X).



Figure 5. Forty horses (20 injected with APS and 20 injected with saline control) were enrolled into a randomized, investigator-blinded study.^{11*} Following the two-week primary endpoint, all control horses were offered a cross-over APS injection. A) Mean lameness score evaluated by the veterinarian was significantly improved compared to saline at two weeks. B) Owner surveys at baseline, 3 months, and 12 months after a single injection of APS. Horses demonstrated significant improvement in lameness and comfort.

Clinical

The nSTRIDE APS Kit has improved pain and function with patients with knee OA.

- Significant pain reduction using leukocyte–containing APS compared to baseline (Figure 6a)^{1,2}
- IL-1ra concentration correlated to white blood cell content in APS (Figure 6b)¹
- IL-18 concentration did not increase with white blood cell content (Figure 6b)¹
- The ratio of IL-1ra to IL-1ß in APS was significantly correlated with improved WOMAC pain scores at six months post-injection¹
- 72.7% of subjects were OMERACT-OARSI high responders six months post-injection¹
- Significant percent improvement in pain over saline injection in double blinded study (Figure 7)³



Figure 6a. Eleven subjects with knee osteoarthritis were enrolled in a Safety study of a single intra-articular injection of APS.² White blood cell (WBC) and cytokine concentrations were measured from the output. WOMAC surveys were completed at baseline and at follow-up visits.



Figure 6b. The WBC concentration in APS was significantly (p < 0.05) and strongly ($R^2 > 0.7$) correlated with IL-1ra in APS (Panel A) but not significantly correlated with IL-1ß (Panel B).¹



Figure 7. 46 patients with unilateral OA (Kellgren-Lawrence 2 or 3) knee pain were randomized at three institutions into two groups.³ Group 1 (31 patients) received a single ultrasound-guided injection of this novel treatment, and Group 2 (15 patients) received a single saline injection. The change from baseline to 12 months in WOMAC pain score was 65% in Group 1 and 41% in Group 2 (p = 0.02). The safety profile was also positive, with no significant differences in frequency, severity, or relatedness of adverse events between groups.

What is the nSTRIDE APS Kit?

The nSTRIDE APS Kit is a self-contained, sterile-packaged, single-use device system. It is designed to separate anti-inflammatory cytokines and growth factors from whole blood. The device system is to be used at the point of care to create an autologous solution.

How does the nSTRIDE APS Kit work?

The nSTRIDE APS Kit uses a small sample of the patient's own blood to create an autologous solution. This device system consists of two parts: the nSTRIDE Cell Separator and the nSTRIDE Concentrator. The nSTRIDE Cell Separator utilizes centrifugal force to process the blood sample and separate the cellular components from plasma and red blood cells. The cell suspension is then loaded into the nSTRIDE Concentrator, which uses centrifugal filtration through polyacrylamide beads to concentrate the injectable output.

What is Autologous Protein Solution made of?

Autologous Protein Solution contains concentrated white blood cells, platelets, and plasma proteins in a small volume of plasma. The output is approximately a 2 to 3 cc anti-inflammatory solution.

How does APS work and why?

The proposed APS mechanism of action is a process of reducing OA-related upregulated inflammatory cytokines by introducing antagonistic cytokines which inhibit the inflammatory cytokine activity. APS has been shown to reduce production of proteins associated with osteoarthritic inflammation and pain responses in vitro.^{8^}

How is Autologous Protein Solution administered?

2-3 cc of final output and will be injected directly in the knee joint. The treatment is designed to be a single injection therapy in clinic.

Are there side effects?

Side effects may occur (e.g., bruising, local pain or swelling) associated with the blood draw and/or knee injection. For product information, including indications, contraindications, warnings, precautions, and potential adverse effects, see the package insert and www.zimmerbiomet.com.

Will nSTRIDE Autologous Protein Solution Cure OA?

There is no cure for OA, but successful treatment using nSTRIDE APS may reduce or relieve pain.¹⁻³

What are the main benefits of nSTRIDE Autologous Protein Solution?

nSTRIDE APS may significantly decrease pain, reduce stiffness and help restore function.¹⁻³

When will the treatment start to work?

Pain relief can be expected after one to two weeks.^{2;3}

Is nSTRIDE Autologous Protein Solution safe?

Yes. Clinical studies have demonstrated the safety of nSTRIDE APS.¹⁻³

Will I be able to be active as usual during the course of my treatment?

It is recommended that you minimize your activity level for 14 days (not to exceed pre-injection levels) after the injection.

How long will the benefits last?

Based on clinical results, patients may expect to see benefits for at least 12 months.¹⁻³

Who can be treated with nSTRIDE APS?

Patients with knee osteoarthritis can receive nSTRIDE APS.

How many injections of nSTRIDE Autologous Protein Solution are required?

Clinical studies have demonstrated the effectiveness of one injection. Studies suggest one injection can last at least 12 months.¹⁻³

References

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- ^ Cell culture assays are not necessarily indicative of clinical outcomes.
- * Animal studies are not necessarily indicative of clinical outcomes.

Results may vary. Not all patiens are candidates for this product and/or procedure.

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