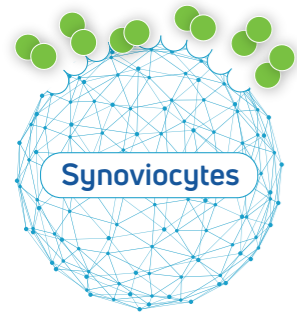
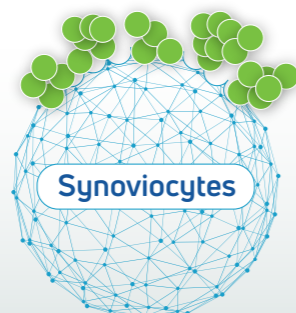


### Optimal high molecular weight HA

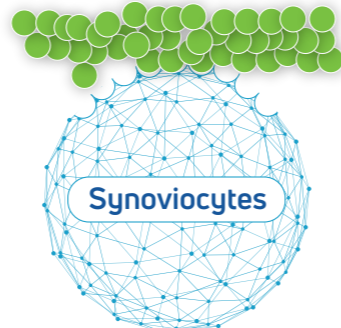
Results in greater pain reduction and longer duration of effect than low molecular weight or excessively high molecular weight HA.<sup>10</sup>



**MW ≤ 500,000**  
**Low Binding Affinity**  
 Limited stimulation of biosynthesis of HA



**500,000 < MW < 4,000,000**  
**Optimal Binding Affinity**  
 Stimulation of biosynthesis of HA<sup>11</sup>



**MW ≥ 4,000,000**  
**Steric Hindrance**  
 Limited stimulation of biosynthesis of HA

1,000,000 Da < 2,900,000 Da

**CINGAL**

### Indications

Cingal® is indicated as a viscoelastic supplement or a replacement for synovial fluid in human knee joints. Cingal® is well suited for rapid and long-term relief of the symptoms of human knee joint dysfunctions such as osteoarthritis. The actions of Cingal® are long-term relief of symptoms by lubrication and mechanical support supplemented by short-term pain relief provided by triamcinolone hexacetonide.

<sup>1</sup> Hangody L, et al. Intraarticular injection of a cross-linked sodium hyaluronate combined with triamcinolone hexacetonide (Cingal) to provide symptomatic relief of osteoarthritis of the knee: a randomized, double-blind, placebo-controlled multicenter clinical trial. *Cartilage*. 2018 Jul;9(3):276-283. doi: 10.1177/1947603517703732. Epub 2017 May 23. PMID: 28535076; PMCID: PMC6042027. <sup>2</sup> Data on File. <sup>3</sup> Internal Anika Sales Data. <sup>4</sup> Cingal IFU. <sup>5</sup> 16-02 Data on File. <sup>6</sup> 19-01 Data on File. <sup>7</sup> Rezende MU, Constantino de Campos G. Viscosupplementation updating article. [www.rbo.org.br](http://www.rbo.org.br) and [www.scielo.br/rbort](http://www.scielo.br/rbort) <sup>8</sup> Stephens M, et al. Musculoskeletal injections: a review of the evidence. *Am Fam Physician*. 2008 Oct 15;78(8):971-976. <sup>9</sup> Bauer C, Moser LB, Jeyakumar V, et al. Increased chondroprotective effect of combining hyaluronic acid with a glucocorticoid compared to separate administration on cytokine-treated osteoarthritic chondrocytes in a 2D culture. *Biomedicines* 2022, 10, 1733. <https://doi.org/10.3390/biomedicines10071733>. <sup>10</sup> Altman RD et al. The mechanism of action for hyaluronic acid treatment in the osteoarthritic knee: a systematic review. *BMC Musculoskelet Discord*. 2015 Oct;16(321). <sup>11</sup> Smith MM, Ghosh P. The synthesis of hyaluronic acid by human synovial fibroblasts is influenced by the nature of the hyaluronate in the extracellular environment. *Rheumatol Int*. 1987; 7(3):113-122.

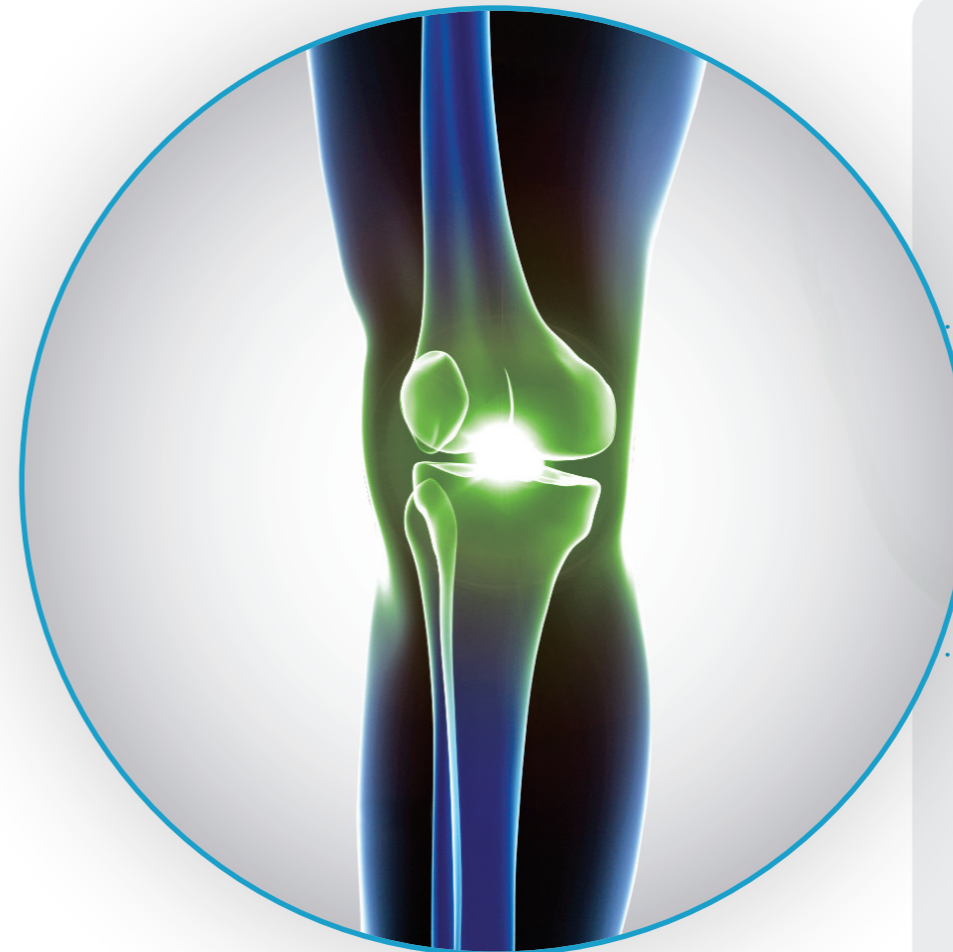
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 AML-900-656 REV 01



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 tel. 02 309 52 27



**FASTER**  
**59%**  
 Pain Reduction  
 at Week 1<sup>1</sup>

**LONGER**  
**72%**  
 Pain Reduction  
 at Week 26<sup>1</sup>

**CONSISTENT**  
**92%**  
 Responder Rate at  
 Week 26<sup>1</sup>

The most powerful next-generation OA pain management treatment available<sup>1,2</sup>

For chronic pain associated with osteoarthritis of the knee

# Cingal®

One-Injection Combination Hyaluronic Acid and Triamcinolone Hexacetonide

## Fast-acting, long-lasting pain relief

For patients who demand rapid and long-lasting relief from chronic knee pain associated with OA, there is one treatment that surpasses all others.<sup>2</sup>

### Anika's Market-Leading Hyaluronic Acid (HA)



### Safe and Proven Triamcinolone Hexacetonide (TH) Steroid



Micronised TH steroid uniformly suspended within a high-dose, ultra-pure and lightly cross-linked HA<sup>4</sup>

### Unmatched clinical data proving Cingal's efficacy

Cingal is supported by robust clinical data, consistently proving efficacy and safety, and stronger in terms of pain relief than any other OA pain management injection with published data on the market.

#### Consistent responder rates<sup>1,5,6</sup>

Cingal OMERACT-OARSI proportion of responders at 26 weeks over 3 Phase III clinical trials

Cingal 13-01 <sup>1</sup>	Cingal 16-02 <sup>5</sup>	Cingal 19-01 <sup>6</sup>
92%	91%	90%

**Approaching 1 million injections since launch in over 35 countries outside the U.S.<sup>3</sup>**

## Anika's market-leading HA is designed to mimic the molecular properties of endogenous HA<sup>7</sup>

### Mechanical effect

HA binds well to water, producing a viscous, jelly-like consistency that provides lubrication and acts as a shock absorber within the joint.

### Chondroprotective effect

HA has a biomechanical structure that protects cartilage when surrounding chondrocytes.

### Analgesic effect

HA diminishes nerve impulses and the sensitivity of nociceptive nerve endings.

TH directly treats inflammation in the joint, providing **fast-acting** pain relief within days of injection<sup>1</sup>

**FAST ACTING**

**59%**

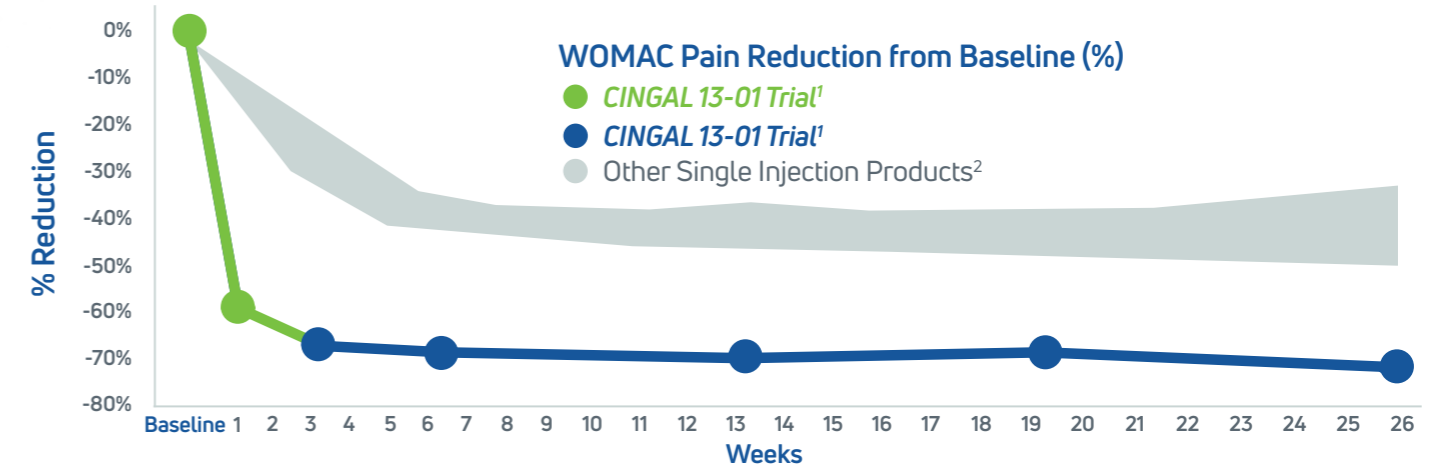
Pain reduction week 1 WOMAC Pain Score

Optimal molecular weight HA in Cingal provides **long-lasting** pain relief<sup>1</sup>

**LONG LASTING**

**72%**

Pain reduction week 26 WOMAC Pain Score



### Cingal: The benefits of a steroid, without the concern

TH is a highly effective, safe, and rapid anti-inflammatory agent of sustained duration.<sup>8</sup>

Cingal (TH+HA) demonstrates an anti-inflammatory and chondroprotective effect, and diminishes side effects associated with steroid supplementation alone.<sup>9</sup>