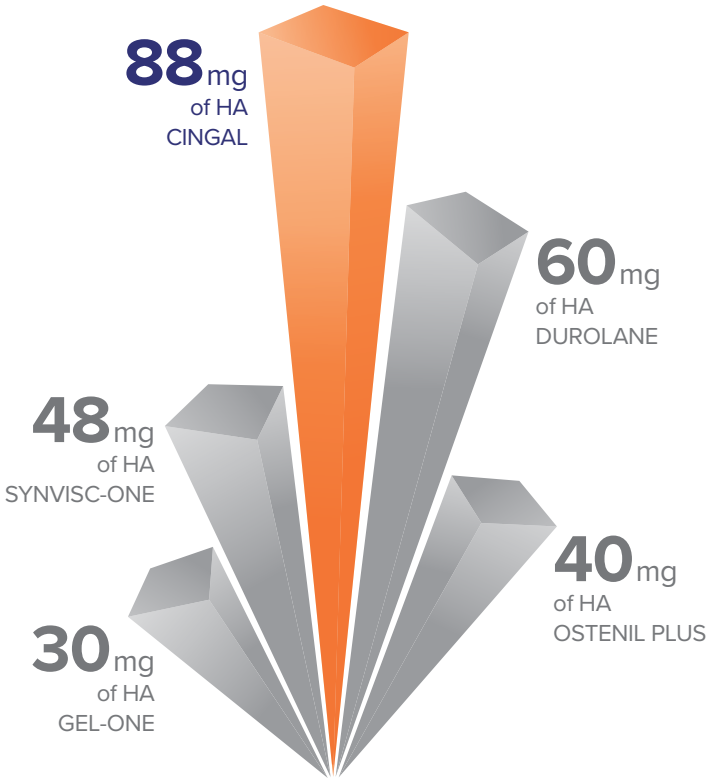
CINGAL®

FAST ACTING. LONG LASTING.

CINGAL®

is the first and only approved hyaluronic acid (HA) plus corticosteroid combination therapy for the pain of OA*

CINGAL DELIVERS A HIGHER DOSE OF HA[2]



LIGHTLY CROSS-LINKED HA

CINGAL contains sodium hyaluronate that is lightly cross-linked to increase residence time in the joint[1,3]

NON-AVIAN HA

CINGAL is made from ultra pure, high molecular weight sodium hyaluronate produced by bacterial fermentation[1]

NO PSEUDOSEPTIC REACTIONS

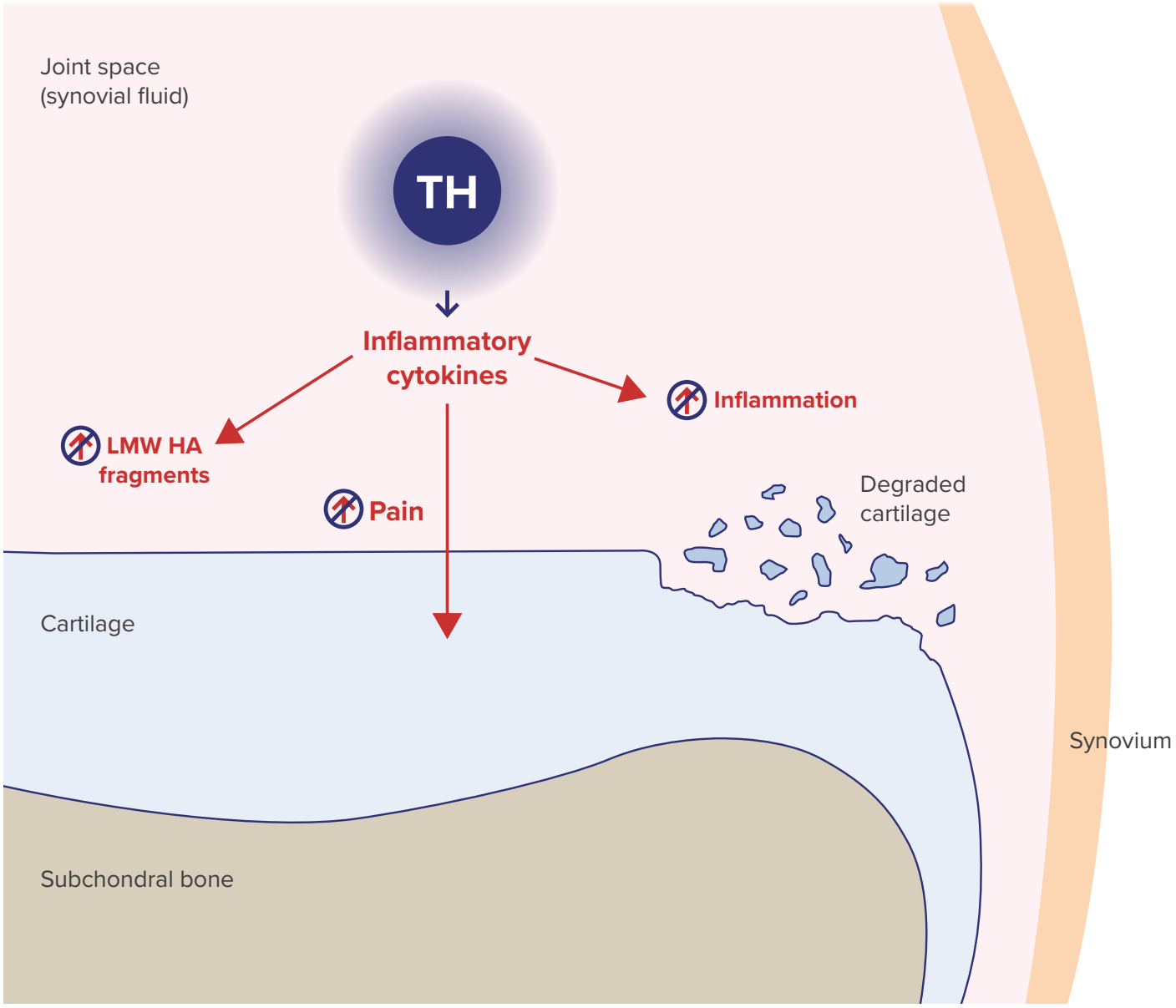
No pseudoseptic reactions associated with CINGAL have been reported worldwide[4]

ANIKA THERAPEUTICS

The corticosteroid triamcinolone hexacetonide (TH) works quickly to reduce inflammation[5,6]

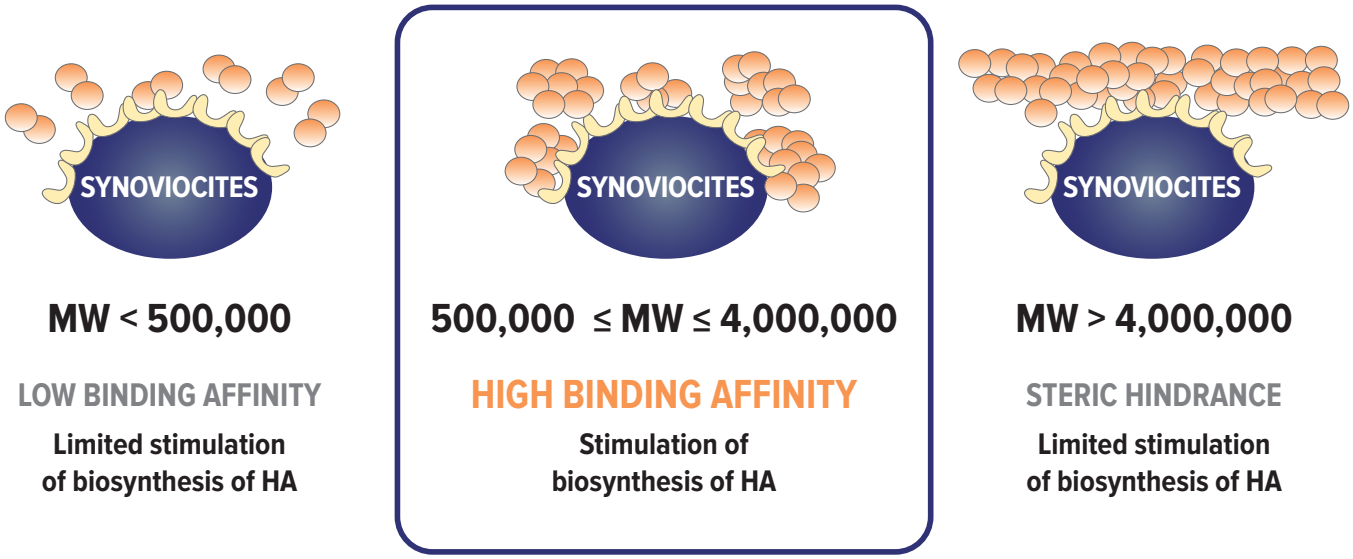
>> *Harmful inflammatory cytokines produce an inflammatory response which causes pain and is destructive to the joint*[5,6]

>> *TH decreases the production of destructive inflammatory cytokines and reduces their harmful effects*[5,6]



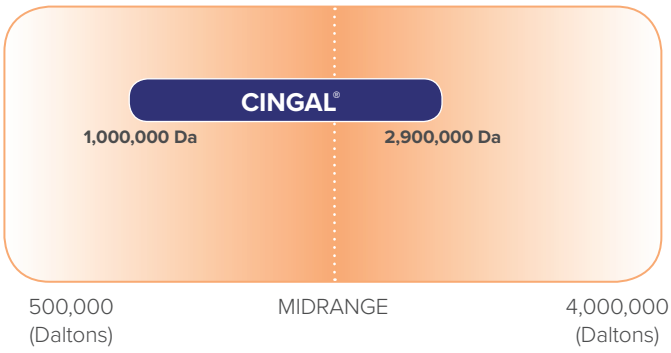
Abbreviations: TH - triamcinolone hexacetonide; HA - hyaluronic acid; LMW - low molecular weight

Preclinical studies suggest that strong binding affinity of hyaluronic acid (HA) stimulates endogenous HA production[7]



Model of hyaluronic acid binding to receptors on the surface of synovial fibroblasts, HA, hyaluronic acid; MW, molecular weight (Adapted from Smith and Ghosh)[7]

MOLECULAR WEIGHT RANGE FOR STIMULATING ENDOGENOUS BIOSYNTHESIS OF HA[7]



>> Low MW (MW < 500,000 Da) molecules of HA appear to bind only weakly to surface receptors, resulting in limited stimulation of endogenous HA biosynthesis by osteoarthritic synoviocyte cells[7]

>> Data suggests that high MW (MW > 4,000,000 Da) molecules of HA cannot bind strongly to synoviocyte surface receptors due to steric hindrance, limiting their ability to stimulate HA biosynthesis[7]

>> Data suggests that HA molecules with MW between 500,000 Da – 4,000,000 Da bind strongly to synoviocyte surface receptors, stimulating endogenous HA biosynthesis[7]

A CINGAL clinical study demonstrated rapid and long-term pain relief[8]

>> CINGAL delivers a **59% improvement** in WOMAC pain at Week 1 relative to baseline (p = 0.008)[8]

>> CINGAL delivers a **72% improvement** in WOMAC pain at Week 26 relative to baseline (p = 0.0027)[8]

>> Cingal delivers an **89% responder rate** in the OMERACT-OARSI Responder Index at 1 Week (p = 0.0161)[8]

>> CINGAL delivers a **92% responder rate** in the OMERACT-OARSI Responder Index through 26 Weeks (p = 0.0100)[9]

Study design: The referenced CINGAL clinical study was a randomized, double-blind, saline-controlled, three-arm, multicenter clinical trial. A total of 368 patients with knee osteoarthritis (KL grades I-III) were treated (149 received CINGAL).[8]

ANIKA THERAPEUTICS

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CINGAL®

CINGAL® is a registered trademark of Anika Therapeutics, Inc., Bedford, MA 01730 U.S.A.

REFERENCES
*CINGAL is CE Mark approved and Health Canada approved. **1.** Cingal Instructions for use. **2.** Instructions for use for Cingal, Durolane, Synvisc-One, Gel-One, Ostenil Plus **3.** Clinical Efficacy and Safety of MONOVISC™: A lightly cross-linked highly concentrated hyaluronan specially formulated for single injection in osteoarthritis. White Paper Study conducted by Michael J. Daley, PhD. 2013 **4.** Anika data on file **5.** Nicholls M.A., et. Al. The Disease-Modifying Effects of Hyaluronan in the Osteoarthritic Disease State. Clin Med Insights Arthritis Musculoskelet Disord. 2017; 10:1179544117723611. **6.** Creamer P. Intra-articular corticosteroid injections in osteoarthritis: do they work and if so, how? Ann Rheum Dis. 1997;56(11):634-636. **7.** 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):113-22. **8.** 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. Cartilage 2017 May; doi: 10.1177/1947603517703732. **9.** CINGAL 13-01, a randomized, double-blind, placebo-controlled, active comparator Phase 3 study

For further information on adverse reactions, precautions and contraindications please refer to the full prescribing information.

AML 900-097/A 11/18