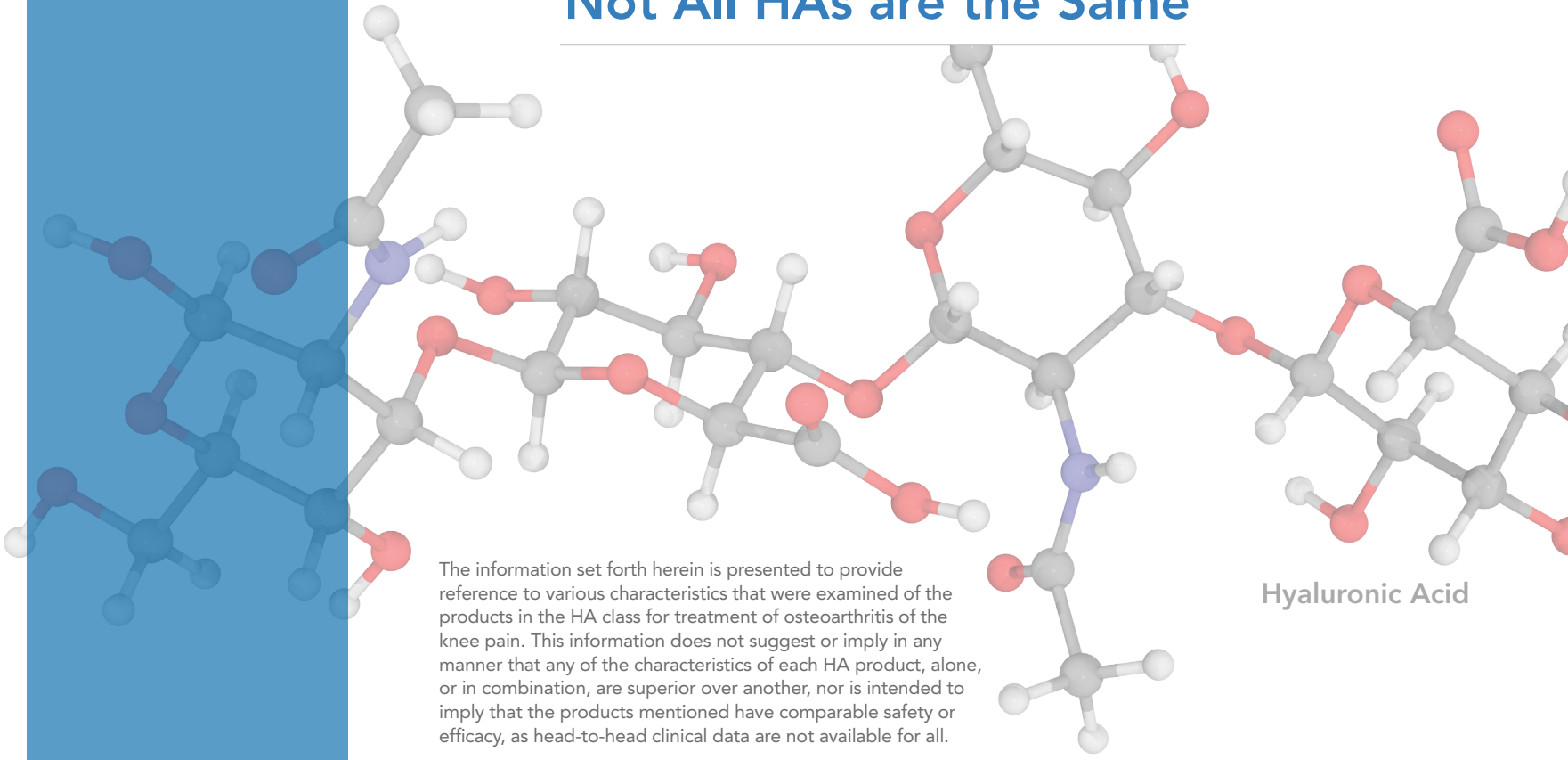
Hyaluronic Acid Product Attributes:

Not All HAs are the Same



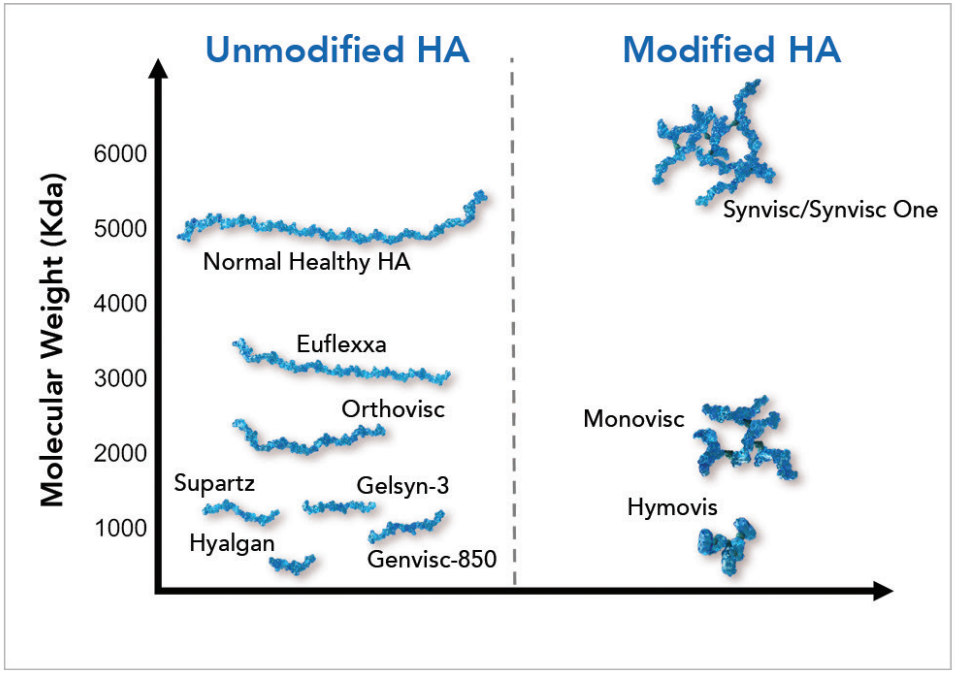
Hyaluronic Acid

The information set forth herein is presented to provide reference to various characteristics that were examined of the products in the HA class for treatment of osteoarthritis of the knee pain. This information does not suggest or imply in any manner that any of the characteristics of each HA product, alone, or in combination, are superior over another, nor is intended to imply that the products mentioned have comparable safety or efficacy, as head-to-head clinical data are not available for all.

EUFLEXXA® (1% sodium hyaluronate) Closely Resembles Normal Healthy HA

- **EUFLEXXA average molecular weight of 3000 kDa**
- **EUFLEXXA unmodified, linear, non-crosslinked**

HA Product Attributes



Gel-One: Modified, cross-linked HA. Molecular Weight not reported
Durolane: Modified, cross-linked HA. Molecular Weight not reported

HAs Available in the US

Endogenous HA	EUFLEXXA® (1% Sodium Hyaluronate)	HYMOVIS® High MW Viscoelastic Hyaluronan	ORTHOVISC® High MW Hyaluronan	MONOVISC® High MW Hyaluronan	GELSYN-3® Sodium Hyaluronate	GENVISC-850® Sodium Hyaluronate	DUROLANE® Hyaluronic Acid, stabilized	SUPARTZ® Sodium Hyaluronate	HYALGAN® Sodium Hyaluronate	SYNVISC® Hylan G-F 20	SYNVISC-ONE® Hylan G-F 20	GEL-ONE® Crosslinked Hyaluronate
Human	Bacteria	Bacteria	Bacteria	Bacteria	Bacteria	Bacteria	Bacteria	Avian	Avian	Avian	Avian	Avian
Single-chain	Single-chain	Single-chain	Single-chain	Crosslinked • Proprietary agent	Single-chain	Single-chain	Crosslinked • NASHA Technology*	Single-chain	Single-chain	Crosslinked • Formaldehyde • Vinyl sulfone	Crosslinked • Formaldehyde • Vinyl sulfone	Crosslinked • Cinnamic acid
~5000 kDa	2400–3600 kDa	500–730 kDa	1000–2900 kDa	1000–2900 kDa	~1100 kDa	620–1170 kDa	Not Reported	620–1170 kDa	500–730 kDa	6000 kDa	6000 kDa	Not Reported

*DUROLANE contains non-animal stabilized hyaluronic acid (NASHA) in buffered physiological sodium chloride solution pH 7.

INDICATION

EUFLEXXA (1% sodium hyaluronate) is indicated for the treatment of pain in osteoarthritis (OA) of the knee in patients who have failed to respond adequately to conservative nonpharmacologic therapy and simple analgesics (eg, acetaminophen).

IMPORTANT SAFETY INFORMATION

EUFLEXXA is contraindicated in patients who have a known hypersensitivity to hyaluronate preparations or who have knee joint infections, infections, or skin disease in the area of the injection site.

EUFLEXXA should not be administered through a needle previously used with medical solutions containing benzalkonium chloride. Do not use skin disinfectants for skin preparation that contain quaternary ammonium salts. Do not inject intravascularly due to potential for systemic adverse events. The safety and effectiveness of injection in conjunction with other intra-articular injectables, or into joints other than the knee have not been studied. Remove any joint effusion prior to injecting. Transient pain or swelling of the injected joint may occur after intra-articular injection with EUFLEXXA.

The most common adverse events related to EUFLEXXA injections reported in 12- and 26-week clinical studies were arthralgia, back pain, pain in extremity, musculoskeletal pain, and joint swelling. In an open-label extension of the 26-week clinical study with repeat series of injections, the most common adverse events related to EUFLEXXA at Week 52 were arthralgia and joint swelling.

PLEASE SEE ACCOMPANYING FULL PRESCRIBING INFORMATION

REFERENCES:

1. Temple-Wong MM, Ren S, Quach P, et al. Hyaluronan concentration and size distribution in human knee synovial fluid: variations with age and cartilage degeneration. *Arthritis Res Ther.* 2016;18:18.
2. EUFLEXXA® [package insert]. Parsippany, NJ: Ferring Pharmaceuticals Inc.
3. Orthovisc® [package insert]. Woburn, MA: Anika Therapeutics, Inc.; 2005.
4. MONOVISC™ Summary of Safety and Effectiveness Data. MONOVISC Injectable Intra-articular Device– P090031. http://www.accessdata.fda.gov/cdrh_docs/pdf9/P090031b.pdf. Accessed December 28, 2016.
5. Supartz® [package insert]. Durham, NC: Bioventus; 2012.
6. Hyalgan® [package insert]. Parsippany, NJ: Fidia Pharma USA Inc; 2011.
7. Synvisc® [package insert]. Cambridge, MA: Genzyme Corp.; 2010.
8. Synvisc-One® [package insert]. Cambridge, MA: Genzyme Corp.; 2010.
9. Gel-One® [package insert]. Warsaw, IN: Zimmer; 2011.
10. Weissmann B, Meyer K. The structure of hyalobiuronic acid and of hyaluronic acid from umbilical cord. *J Am Chem Soc.* 1954;76:1753-1757.
11. Gelsyn-3® [package insert]. Durham, NC: Bioventus; 2016.
12. Genvisc-850® [package insert]. Doylestown, PA: OrthogenRx; 2016.
13. Hymovis® (Hyadd-4®) [package insert]. Parsippany, NJ: Fidia Pharma USA Inc, 2016.
14. Mainil-Varlet P, Schiavinato A, Ganster MM. Efficacy Evaluation of a New Hyaluronan Derivative HYADD 4-G to Maintain Cartilage Integrity in a Rabbit Model of Osteoarthritis. *Cartilage.* Jan 2013;4(1):28-41.
15. US FDA. DUROLANE®. Prescribing Information. https://www.accessdata.fda.gov/cdrh_docs/pdf17/P170007D.pdf. Accessed November 28, 2017.

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