

oralvisc[®] metabolic

ORALVISC[®]
HA Leptin™ 80 mg

RECOMMENDED USE

For improvement of joint discomfort in metabolic osteoarthritis.

DOSAGE

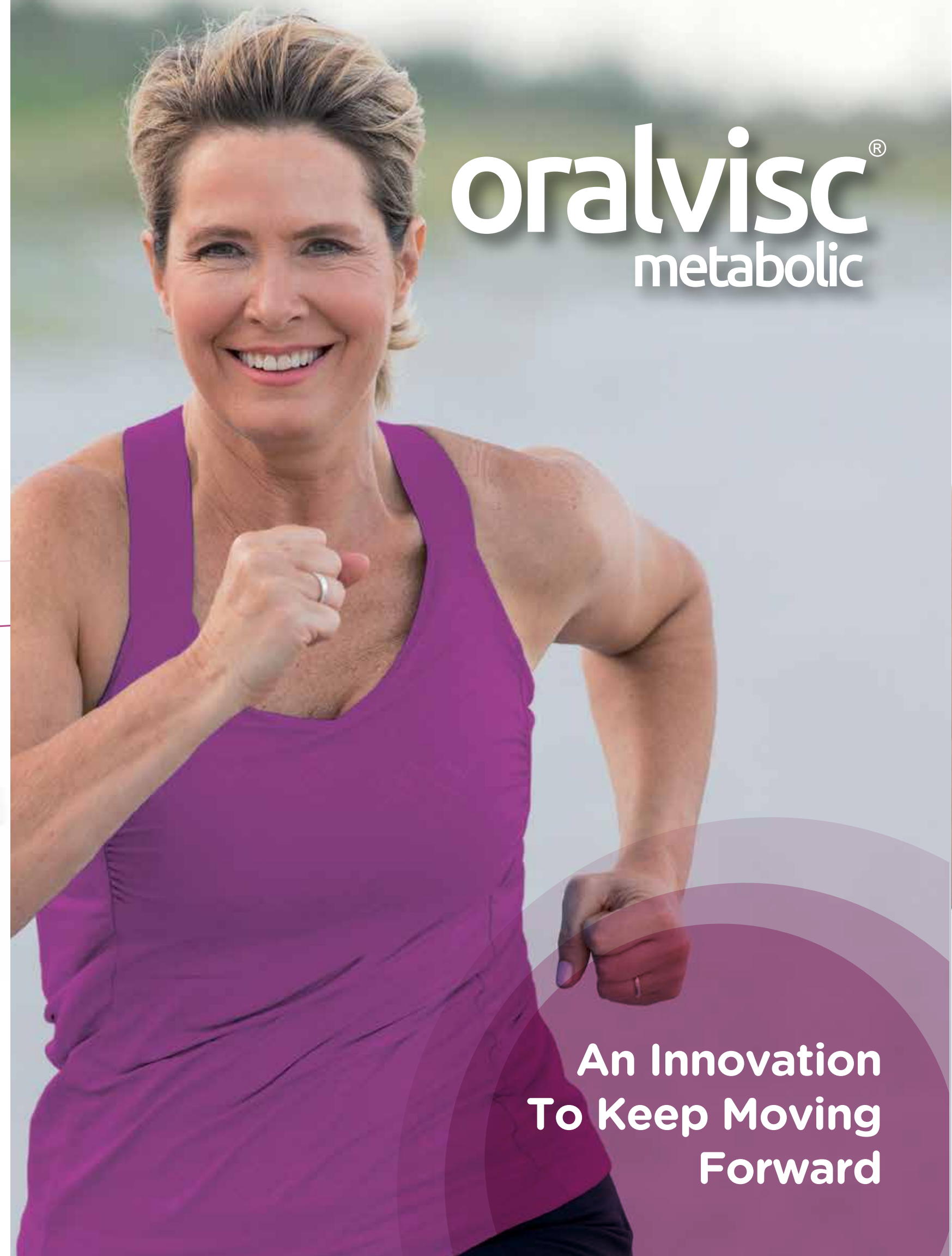
One capsule per day for at least two months.

PACKAGE

Box of 28 capsules.



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**An Innovation
To Keep Moving
Forward**

MEDEXUS Inc.

Medexus Inc., 35 Nixon Road, Unit 1, Bolton ON, L7E 1K1. Tel. (1) 877 633 3987. www.medexus.ca



75% OF people WITH osteoarthritis are overweight¹

MECHANICAL OVERLOAD BY ITSELF CANNOT EXPLAIN THE CORRELATION BETWEEN OVERWEIGHT AND OSTEOARTHRITIS

OVERWEIGHT AND JOINTS

Beyond the mechanical load

>> OVERWEIGHT IS:

A risk factor for developing osteoarthritis*
It increases 4.2-6.8 times

An accelerator of the osteoarthritis process**
The higher the BMI, the faster the progression

* Coggon, D. et al. *Int. J. Obes. Relat. Metab. Disord. J. Int. Assoc. Study Obes.* 2001 May;25(5):622-7.
Ettinger, W. H. et al. *J. Clin. Epidemiol.* 1994 Jul;47(7):809-15.

** Raynauld J.P. et al. *Arthritis Res. Ther* 2006 Dec;8(1):R21.

>> MECHANICAL OVERLOAD:

It is associated with an increased wear and tear of weight-bearing joints (knees and hips), but cannot by itself explain **the close correlation between overweight and osteoarthritis.**

Hand osteoarthritis is twice as common in overweight persons***

*** Calvet J, et al. *Scand J Rheumatol.* 2016 Jan;45(1):41-4.



Metabolic factors produced by fat tissue play a key role in the development of osteoarthritis

THE METABOLIC FACTOR - A new perspective

>> THE RELATIONSHIP BETWEEN OVERWEIGHT AND OSTEOARTHRITIS WAS TRADITIONALLY BELIEVED TO BE SOLELY CAUSED BY MECHANICAL LOAD FACTORS.

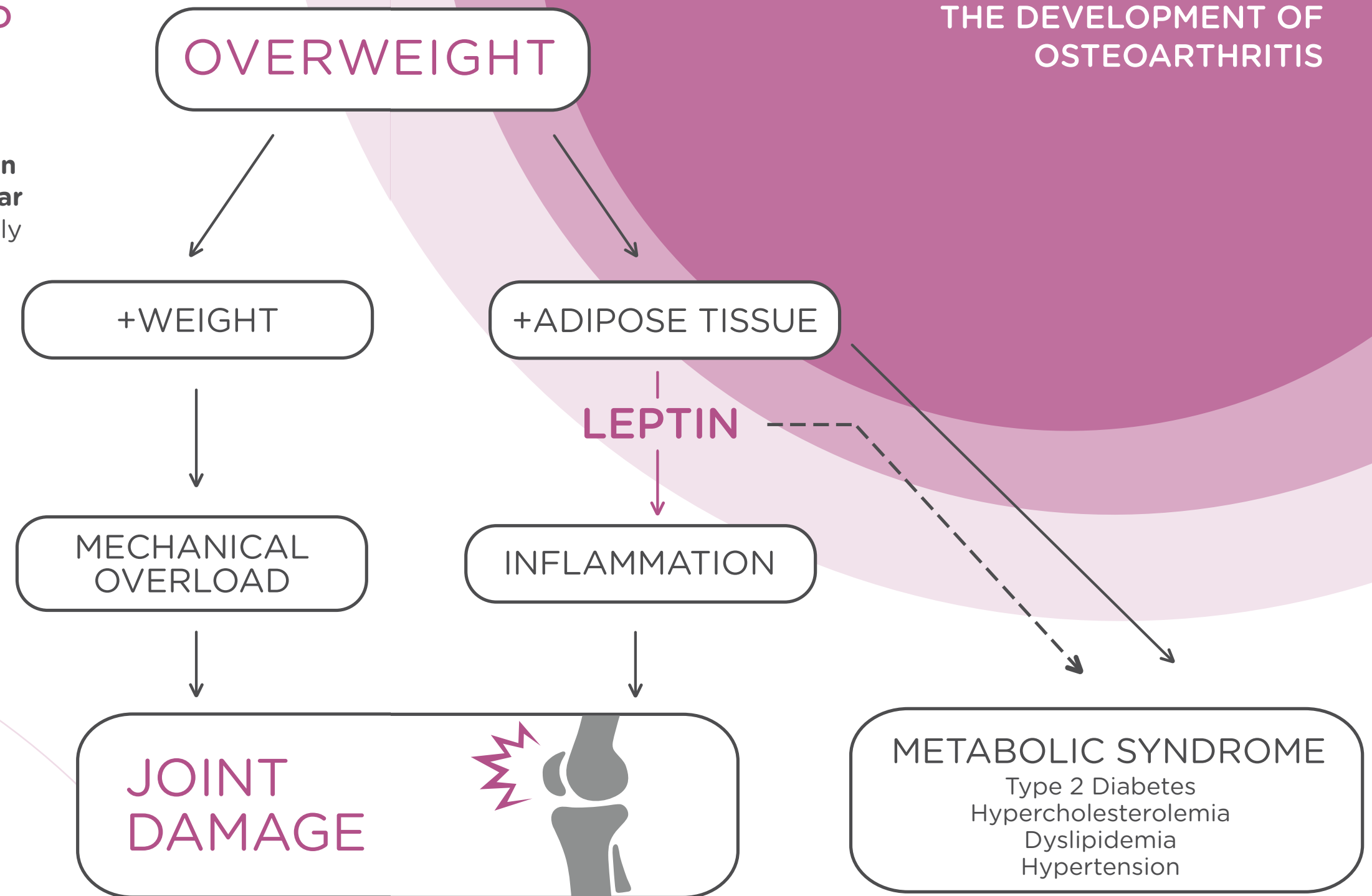
With overweight, **the increased weight on the joint results in an increased joint wear and tear**, and joint deterioration eventually causes osteoarthritis.

However, this cannot explain why hand and elbow osteoarthritis is more common in obese persons.

Excess adipose tissue associated with overweight increases the **release of leptin**, which induces **proinflammatory factors** contributing to **joint deterioration** and causing further joint damage. Overweight and excess body fat are the main causes of the metabolic syndrome.

Patients treated with ORALVISC® for three months showed significant improvement in joint function as measured by the WOMAC index.

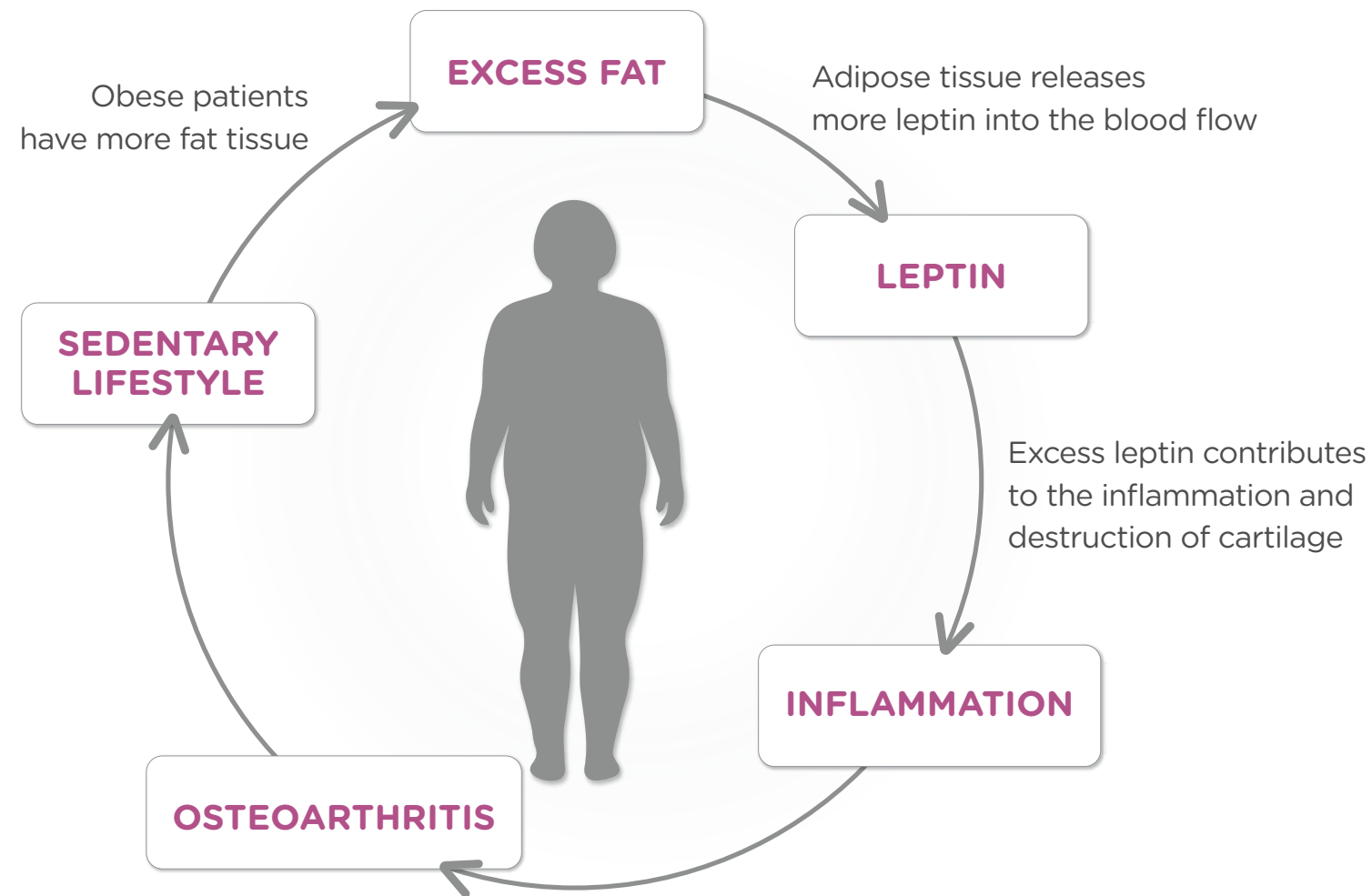
>> METABOLIC FACTORS ASSOCIATED WITH OVERWEIGHT INFLUENCE THE DEVELOPMENT OF OSTEOARTHRITIS



LEPTIN

A key role in joints*

Leptin is a hormone produced by fat cells that regulates the body's energy metabolism.



- **Leptin in human physiology and pathophysiology.**
Mantzoros, C. S. et al. Am. J. Physiol. Endocrinol. Metab. 2001 Oct;301(4):E567-84.
- **Evidence for a key role of leptin in osteoarthritis.**
Dumond, H. et al. Arthritis Rheum. 2003 Nov;48(11):3118-29.
- **Correlation of synovial fluid leptin concentrations with the severity of osteoarthritis.**
Ku, J.H. et al. Clin Rheumatol. 2009 Dec;28(12):1431-5.
- **Cross-sectional and longitudinal associations between circulating leptin and knee cartilage thickness in older adults.**
Stannus, O.P. et al. Ann Rheum Dis. 2015 Jan;74(1):82-8.
- **Leptin - a link between obesity and osteoarthritis. Applications for prevention and treatment.**
Vuolteenaho, K. et al. Basic Clin Pharmacol Toxicol. 2014 Jan;114(1):103-8.

ORALVISC®

An innovation to keep moving forward

>> WHAT IS ORALVISC®?

A proprietary, naturally occurring source of glycosaminoglycans formulated for the management of osteoarthritis.

>> WHAT IS ORALVISC® RECOMMENDED FOR?

For improvement of joint discomfort in metabolic osteoarthritis.

>> MECHANISM ACTION OF ORALVISC®

ORALVISC® regulates leptin levels.

Thus, helping to reduce inflammation and improve joint discomfort



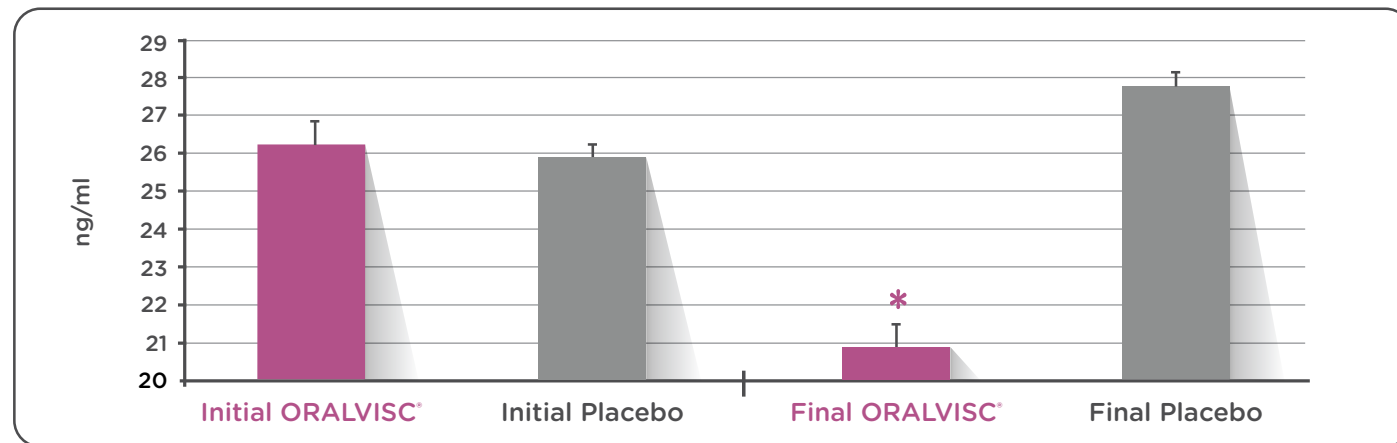
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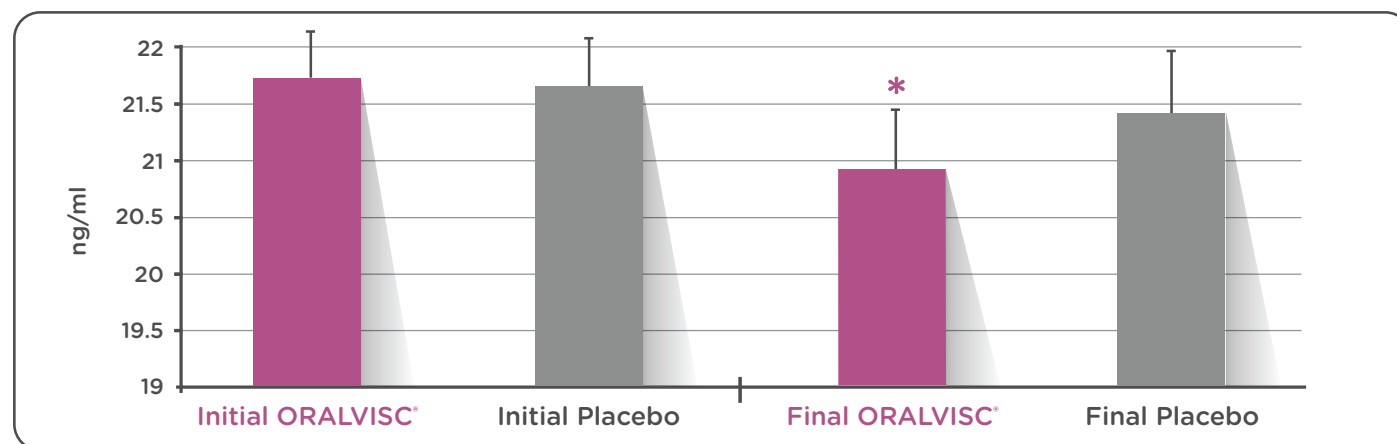
>> REDUCED PRODUCTION OF LEPTIN*

Treatment with **ORALVISC[®]** for three months resulted in significantly reduced (P < 0.05) serum and synovial fluid leptin levels.

· REDUCED synovial fluid leptin levels*



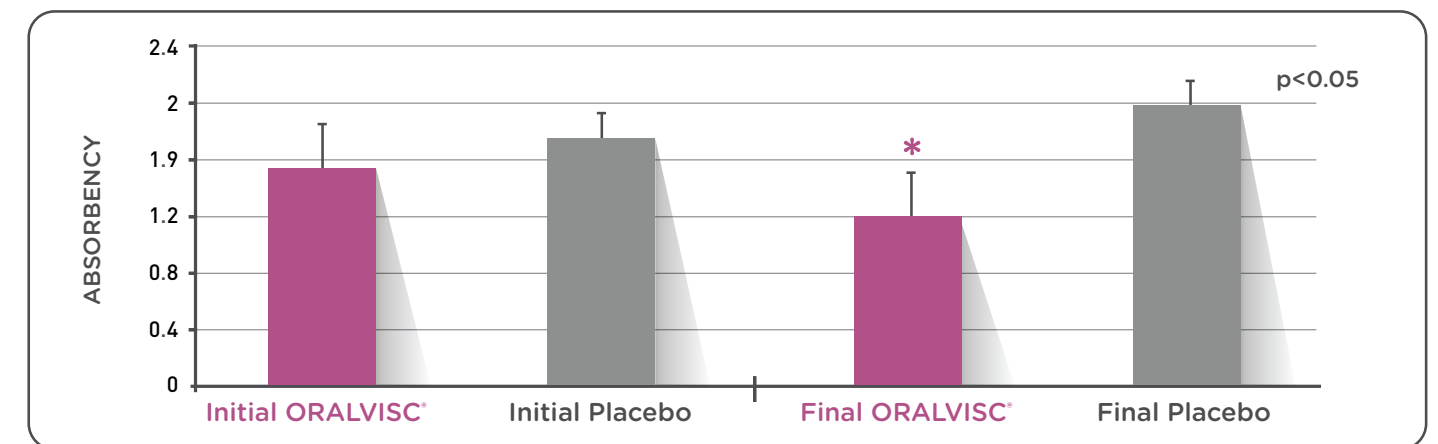
· REDUCED SERUM leptin levels*



>> REDUCED INFLAMMATION AT THE SYSTEMIC AND JOINT LEVELS*

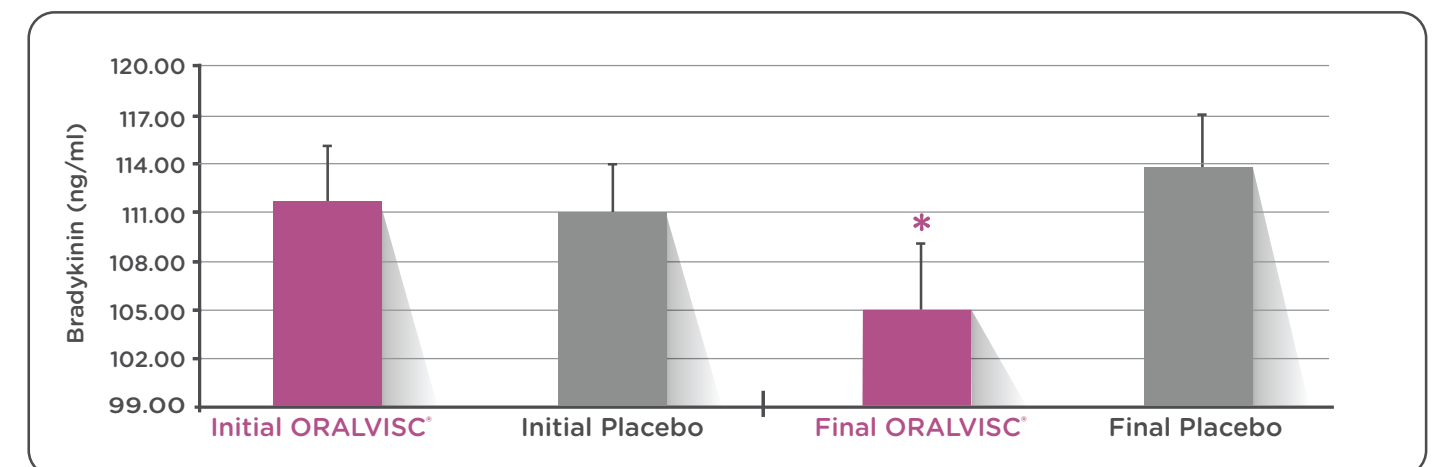
Patients treated with **ORALVISC[®]** showed significant reductions in all tested proinflammatory mediators (IL-1 α , IL-1 β , IL-2, IL-4, IL-6, IL-8, IL-10, IL-12, IL-17 α , IFN, TNF- α y GM-CSF).

· REDUCED SERUM IL-1 β LEVELS*



· REDUCED Bradykinin synovial fluid levels*

Bradykinin is a proinflammatory mediator involved in pain perception.



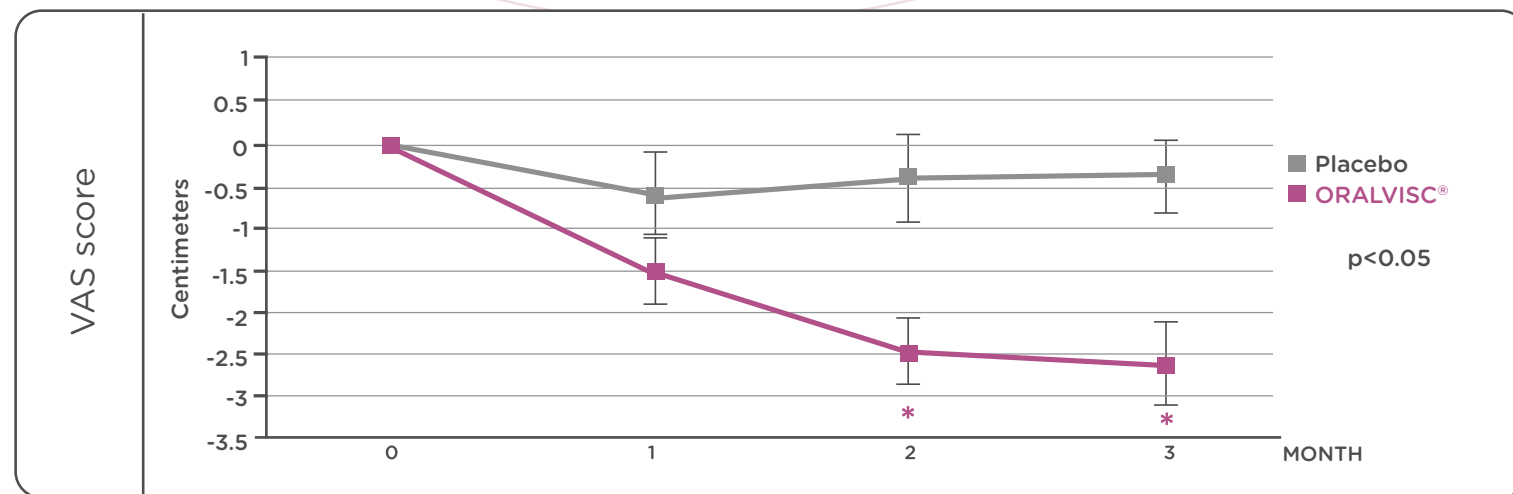
* Nelson FR, et al. Rheumatol Int. 2015 Jan;35(1):43-52.

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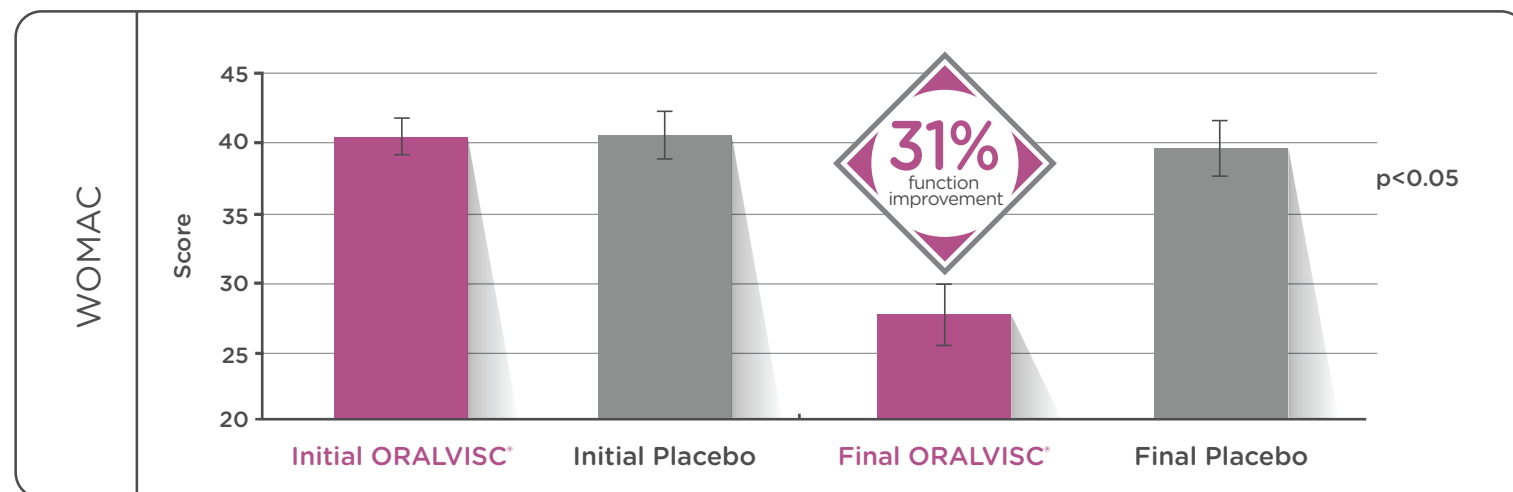
>> REDUCED JOINT PAIN*

Patients treated with **ORALVISC[®]** for three months showed significant improvement in joint pain as measured by the VAS pain scores.



>> IMPROVED JOINT FUNCTION*

Patients treated with **ORALVISC[®]** for three months showed significant improvement in joint function as measured by the WOMAC index.

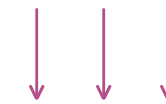


>> MECHANISM ACTION OF ORALVISC[®]

REGULATES LEPTIN LEVELS



REDUCES INFLAMMATION



REDUCES JOINT DISCOMFORT AND IMPROVES MOBILITY

>> A SAFE PRODUCT

ORALVISC[®] has an **excellent safety profile** as shown by **toxicity studies**** and the clinical trial experience, with **no adverse effects being observed**.

* Nelson FR, et al. *Rheumatol Int.* 2015 Jan;35(1):43-52.

** Canut, L. et al. *Regul. Toxicol. Pharmacol.* 2012 Apr;62(3):532-41.

¹ Emaro Study 2015