



FLEXADIN UCI^{II}

Frequently Asked Questions

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Is there a problem with pregnancy or with fertility?

Can I buy FLEXADIN UCI^{II} at my local feed or pet store?

I am a veterinary surgeon and I have not heard of FLEXADIN UCI^{II}, what do I do?

Are there animal products in FLEXADIN UCI^{II}?

How do I know FLEXADIN UCI^{II} contains what is stated on the label?

Vetoquinol advises you to consult your veterinary surgeon concerning any specific health questions about your horse. The information contained in this document is intended for educational purposes only.

FLEXADIN UCI^{II}

Vétoquinol
 *Signe de Passion*

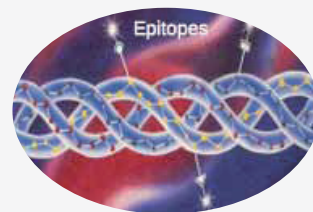
1 What is FLEXADIN UCII?

FLEXADIN UCII is a new and innovative oral joint health supplement developed by Vetoquinol. It contains: a patented¹ natural type II collagen ingredient by the name of UCII (as opposed to the commonly used hydrolysed type II collagen), methylsulfonylmethane (MSM), and a readily assimilated chelated manganese trace element. Each ingredient has been carefully selected according to available scientific supporting evidence for their complementary support of the horse's joint health. Equistro is pleased to be the first in Europe to offer UCII as a means to manage joint health in horses.

2 How does FLEXADIN UCII work?

FLEXADIN UCII reunites 3 different key ingredients that support joint health and mobility. The combination of these ingredients targets the many different aspects necessary for an optimal joint function, rather than simply having an effect on isolated components only.

- UCII is a native biologically active type II collagen that has been extracted from chicken cartilage via a patented¹ process that preserves its molecular form and quality which are key to its unique role in joint nutrition compared to the commonly used hydrolysed type II collagen which is subject to structural modifications following heat and/or chemical intervention. UCII contains specific structural regions called epitopes found on the intact triple helix which enable a privileged and natural interaction with the digestive tract and its closely associated immune system. The consequences for joint health have been demonstrated in equine clinical trials versus the "industry standard", glucosamine and chondroitin sulphate (Gupta 2009).



- Methylsulfonylmethane (MSM) is a naturally occurring sulphur compound and nutritional component of many foods. This sulphur containing element is the stable end product of the methyl-S-methane series of compounds that provide bioavailable sulphur to living organisms. Sulphur is an important component of the cartilage matrix GAG's.

- Chelated manganese is an organic form trace element in a readily assimilated form for optimal absorption and retention in the body compared to the inorganic form. Manganese is a critical cofactor for collagen and Glycosaminoglycan (GAG) synthesis and metabolism which are fundamental components of articular cartilage. Some recent research alludes to an increased role of manganese in synthesis of GAGs.

3 Are there any studies on any of the ingredients in FLEXADIN UCII?

Studies are available on all 3 ingredients in FLEXADIN UCII, and a partial list of those references follows under each categories.

• Undenatured collagen (UCII):

Bagchi M, et al. Beneficial effects of oral administration of undenatured type-II collagen on osteoarthritis: a human clinical trial. Presented at: Journal of the American College of Nutrition 49th Annual Meeting; October 2008

Trentham D, et al. Effects of Oral Administration of Type-II Collagen on Rheumatoid Arthritis. *Science*. 261:1727-1730, 1993.

Barnett, et al. A Pilot Trial of Oral Type-II Collagen in the Treatment of Juvenile Rheumatoid Arthritis. *Arthritis & Rheumatism*. 39:623-628, 1996.

Gupta RC, et al. Pain reduction measured by ground force plate in arthritic dogs treated with type-II collagen. Presented at: Society of Toxicology 48th Annual Meeting; March 2009.

Gupta RC, et al. Therapeutic efficacy of undenatured type-II collagen (UCII) in comparison to glucosamine and chondroitin in arthritic horses. *J Vet Pharmacol Therap*. 32:577-584, 2009.

Deparle L, Gupta R, Canerdy T: Efficacy and safety of glycosylated undenatured type-II collagen (UCII) in therapy of arthritic dogs. *J Vet Pharmacol Therap* 2005; 28: 385-390

• MSM:

Kim L et al. Efficacy of methylsulfonylmethane (MSM) in osteoarthritis pain of the knee: a pilot clinical trial. *Osteoarthritis and Cartilage* 2006; 14: 286-294

Usha P, Naidu M. Randomised double blind, parallel, placebo controlled study of oral glucosamine, methylsulfonylmethane and their combination in osteoarthritis. *Clin. Drug Investig*. 2004 ;24 (6): 353-363.

Maranon G et al. The effect of methyl sulphonyl methane supplementation on biomarkers of oxidative stress in sport horses following jumping exercise. *Acta Veterinaria Scandinavica* 2008, 50:45

• Manganese:

Leach RM. Role of manganese in mucopolysaccharide metabolism. *Fed Proc* 1971; 30:99

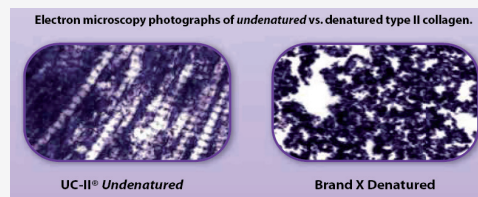
4 Denatured collagen (hydrolysed) vs. Undenatured (native UCII) – Why the Difference is important?

Denatured (hydrolysed). Most of the type II chicken collagen found in dietary supplements is denatured or hydrolysed, which means that high heat and/or chemicals have been used to process it. These processes fundamentally alter the molecular structure of the protein, rendering the collagen ineffective as an immunomodulator.

Undenatured (native). Undenatured type II collagen is made using little or no heat and very limited processing - just enough to concentrate the collagen and make it soluble. The UC-II® patented manufacturing process ensures that the collagen remains biologically active in its most native, triple helix form, with its privileged immunomodulating ability intact.

Undenatured vs. Denatured

Other forms of type II collagen sold as dietary supplements are *denatured* (hydrolyzed) by chemical or high-temperature processing, altering their molecular structure and rendering them inactive.



5 What kind of cases benefit most from FLEXADIN UCII?

FLEXADIN UCII is recommended for athletic horses whose joints are heavily solicited. However, it also can play a major role when given to young, active athletes to ensure continued joint health. Given early on in a horse's athletic career whilst its articulations are still healthy may reduce or eliminate the need for intervention with conventional medicines that may have negative side effects.

6 Is FLEXADIN UCII safe in horses?

At this moment in time, no known safety issues to this product when taken in line with the recommendations have been identified. Furthermore, substantial safety and tolerance data exists for the 3 components of FLEXADIN UCII not only in laboratory animals but also humans and horses. Manganese, while being recognised as the safest of the trace elements for horses (Schwyer 1990) is subject to European legislation as an additive which means that a maximum permitted level per day must be adhered to and hence for a 500 kg horse, it must not consume more than 900 g of FLEXADIN UCII per day. That is to say the entire 600g pot can be consumed in one go and the horse remains well inside the safety limits.

Deichman, WB, Gerarde, HW. (eds.) Toxicology of Drugs and Chemicals, (the ed.) New York Academic Press, 1969.

Horvath K, Noker PE, Somfai-Relle S, et al. Toxicity of methylsulfonylmethane in rats. Food Chem Toxicol 2002;40: 1459-1462.

Gupta RC et al. Therapeutic efficacy of undenatured type-II collagen (UCII) in comparison to glucosamine and chondroitin in arthritic horses. J. vet. Pharmacol. Therap. 2009

Bagchi M. Efficacy and Safety of Undenatured Type II Collagen (UCII) in Arthritic Horses. Volume 172S (2007) S1-S240

Schwyer HF. Mineral and vitamin intoxication in horses. Vet. Clin. North Am. Equine Pract. 6:295-318 (2009)

7 Why has banana flavour been chosen for FLEXADIN UCII when horses do not naturally eat bananas?

The reason behind this choice of flavouring lies again on the scientific findings resulting from a panel of flavours presented to horses (Goodwin 2005) where banana flavour was the most preferred fruit coming ahead of the classic flavourings such as cherry and apple.

Bananas may initially seem like an odd choice for a horse but in many countries bananas are given as treats as apples and carrots are given in the northern hemisphere.

8 How much does FLEXADIN UCII cost?

Due to the complex and costly extraction that ensures the preservation of the physical integrity of the natural type II collagen (UCII) as well as the other ingredients in FLEXADIN UCII, it will cost more than some supplements, but then again you can expect more... You can obtain prices from your local veterinary surgeon or exclusive distributor according to the country concerned (see www.equistro.com for contact details).

9 My veterinary surgeon has not heard of FLEXADIN UCII, what do I do?

If your veterinary surgeon is not familiar with FLEXADIN UCII, please have him/her call the exclusive distributor in your country. Visit www.equistro.com for contact details. They can also email questions to info@equistro.com.

10 Can I use FLEXADIN UCII with other supplements or pharmaceuticals?

There are no known negative interactions to this product or its 3 ingredients at this time. However, if FLEXADIN UCII is effective in your animal, you may find that other supplements or pharmaceuticals are unnecessary. It is certainly unnecessary to give additional collagen, manganese or MSM to horses on FLEXADIN UCII.

11 Do I need to apply an initial loading protocol?

Vetoquinol recommends that during the initial 12 week period, for a 500 kg horse, 1½ scoops (15 g) once daily of FLEXADIN UCII should be administered which is in accordance with the clinical trial that was conducted on horses (Gupta 2009). After this period, the maintenance administration can be reduced to 1 scoop once daily.

Is FLEXADIN UCII suitable for all breeds of horse and pony?

The answer is clearly yes as the mechanism of action does not change - there is no reason to think otherwise.

12 When should I expect to see results?

As with many complementary feeding stuffs (and this is also the case for medications), individual variation exists. Horses start to show positive results within 4 to 6 weeks. If no positive results have been observed within 16 weeks, FLEXADIN UCII is unlikely to be effective over a longer administration period. Your veterinary surgeon should be contacted.

13 Is FLEXADIN UCII® likely to render a positive doping test?

No. None of the components in FLEXADIN UCII feature in a prohibited substance list (FEI regulations). For the ADMR rules in Germany, nonetheless, MSM requires a 48 hour withdrawal time.

14 Is there a problem with pregnancy or with fertility?

There are no known problems with either pregnancy or with fertility.

15 Can I buy FLEXADIN UCII at my local feed or pet store?

No. FLEXADIN UCII is available through a country selective distribution network, which means that you should contact your veterinary surgeon or exclusive retail outlet according to the country you are based in.

16 I am a veterinary surgeon and I have not heard of FLEXADIN UCII, what do I do?

If you are a veterinary surgeon, you can either contact your local Vétquinol sales representative, or consult the www.equistro.com website for the details of the exclusive Equistro distributor in your country for more information. Alternatively, contact us at info@equistro.com

17 Are there animal products in FLEXADIN UCII?

Yes. The patented native type II collagen (UCII) in FLEXADIN UCII originates from chicken cartilage. This is the same grade UCII that is used in human joint health products.

18 How do I know FLEXADIN UCII contains what is stated on the label?

This is a good question and an all too often concern for horse owners and veterinary surgeons alike who are wanting to use high quality feed supplements. EQUISTRO® is a brand belonging to Vetoquinol, the 10th largest International Veterinary Pharmaceutical company in the world and as such our reputation is based on the quality and transparency of the products and the associated information concerning them. Vetoquinol goes further, the European authorisation as denoted by the production site specific number α FR 69-243-22 (look on the EQUISTRO® range packaging) that authorises the manufacturing of complementary feeding stuffs at its 100% dedicated manufacturing site in France is subject to regular checks and audits from the veterinary authorities with random sampling and analysis controls to ensure that the specific European Directives relating to manufacturing and labelling are conform.

“Be a yardstick of quality. Some people aren’t used to an environment where excellence is expected.”

Steve Jobs quotes (American Entrepreneur Apple co- Founder)