Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Chondromel 400 mg Capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each hard capsule contains chondroitin sulfate 400mg as chondroitin sulfate sodium.

Excipient with known effects: sodium.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Hard capsule.
Transparent green and blue gelatin capsule.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Chondromelis indicated for the symptomatic treatment of osteoarthritis.

4.2 Posology and method of administration

Adults (including the elderly):
The recommended dose of Chondromel is 800 mg/day as a single-dose (2 capsules at a time) for 3 months at least.

For symptoms of severe inflammation, the recommend starting dose is 1200 mg/day as a single (3 capsules at a time) or divided dose (1 capsule 3 times a day) for 4-6 weeks, followed by 800 mg for up to 3 months. Therapy comprises repeatable courses of treatment; each course comprises 3 months intake at least, followed by a 2 month treatment-free interval.

The clinical effect will usually be seen in 4 weeks.
Clinical trials have only assessed the efficacy of the product over a two year treatment period.

Children:
The use of Chondromel is not recommended for children.

Kidney failure:
There is little experience available on the use of Chondromel by patients suffering from kidney failure. Therefore, these patients must be treated with special attention (see section 4.4).

Liver failure:
There is no experience available on the use of Chondromel by patients suffering from liver failure. Therefore, it is not recommended for use in this group (see section 4.4).

Chondromel can be taken before, during or after a meal. Patients with a history of gastric intolerance to medicines are recommended to take it after a meal.
The capsules must be swallowed, not chewed, with sufficient liquid.

4.3 Contraindications

Chondromel is contraindicated in individuals with known or suspected hypersensitivity to chondroitin sulfate or any of its excipients.

4.4 Special warnings and precautions for use

Heart and/or kidney failure:
In very rare occasions (<1/10,000) such patients have experienced cases of edema and/or water retention. This can be attributed to the osmotic effect of Chrondoitin sulfate.

Liver failure:
There is no experience available on the use of Chondromel by patients suffering from liver failure. Therefore, is not recommended for use in this group.

No effect at platelet level has been observed within the recommended dose rates. However, with rats and doses greatly in excess of the recommended 50 mg/kg/day (which would correspond to 4,000 mg in humans/day), a slight platelet antiaggregant activity has been observed. This reaction will have to be taken into account when Chondromel is used in conjunction with platelet antiaggregants (acetylsalicylic acid, dipyridamole, clopidogrel, ditazole, triflusal or ticlopidine).

This medicinal product contains 36.5 mg sodium per capsule, equivalent to 1.8% of the WHO recommended maximum daily intake of 2 g sodium for an adult.

4.5 Interaction with other medicinal products and other forms of interactions

For use in conjunction with platelet antiaggregants see section 4.4.

4.6 Fertility, pregnancy and lactation

There is no research on the use of Chondromel by pregnant or lactating women. Therefore, its use should be avoided during these periods.

4.7 Effects on ability to drive and use machines

There is no evidence thatChondromelinterferes with the ability to drive vehicles or operate machinery.

4.8 Undesirable effects

In the following table adverse reactions observed in clinical trials* (on a total of 1826 patients, out of which 1264 were treated with Chondromel) and during post marketing surveillance are listed. Adverse reactions are grouped by System Organ Class. Within each System Organ Class, the adverse reactions are classified according to frequency of observation, using the following convention: very common (>1/10); common (>1/100, <1/10), uncommon (>1/1,.000, <1/100); rare (>1/10,000, <1/1,000); very rare (<1/10,000).

Gastro-intestinal disorders	Rare	Gastrointestinal disorder* Epigastralgia* Nausea* Diarrhoea*
Skin and subcutaneous tissue disorders	Rare	Erythema Rash* Rash maculo-papular
	Very rare	Urticaria Eczema Pruritus Allergic reaction**

General disorders and administration site conditions	Very rare	Oedema

* adverse reactions observed in clinical trials
** Cases of allergic reactions (such as angioneurotic edema) have rarely been reported

4.9 Overdose

During post marketing surveillance one case of intentioned overdose to commit suicide was observed. After a dose of 64g, the patient did not experience any adverse reactions and laboratory data showed electrolyte values in the normal range.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

M01AX: Other non-steroidal anti-inflammatories and anti-rheumatics.

Chondroitin sulfate, the active ingredient of Chondromel, belongs to the polysaccharide subgroup of glycosaminoglycans.

Chondroitin sulfate is one of the main elements of the cartilage, which joins a central protein, forming what we know as proteoglycan, which is what gives the cartilage its mechanical and elastic properties.
The therapeutic effect of chondroitin sulfate in patients suffering from arthritis, is due to an anti-inflammatory activity at the level of the cellular components of the inflammation *(invivo*), to the stimulation of the synthesis of endogen proteoglycans (*in vitro*) and hyaluronic acid (*in vivo*), and to a decrease in the catabolic activity of chondrocytes (*in vivo*), inhibiting some proteolytic enzymes (collagenase, elastase, proteoglycanase, phospholipase A_2, N-acetylglucosaminidase, etc.) (*in vitro, in vivo*) and the formation of other substances that damage the cartilage (*in vitro*).

Clinical studies carried out on arthritis patients have shown that chondroitin sulfate treatment improves symptoms such as pain and functional impotence, or causes such symptoms to disappear altogether. Movement in the affected joints is improved. The effects of chondroitin sulfate treatment are sustained, lasting 2 to 3 months after treatment has stopped.

5.2 Pharmacokinetic properties

Absorption:
Several studies indicate that the bioavailability of chondroitin sulfate fluctuates between 15 and 24% of the dose by oral administration. 10% of the absorbed portion of chondroitin sulfate appears in the form of chondroitin sulfate and 90% in the form of depolymerase derivatives of inferior molecular weight, which suggests that it goes through a first pass effect. After oral administration of chondroitin sulfate, maximum blood levels are reached in about 4 hours.

Distribution:
In the blood, 85% of the concentration of chondroitin sulfate and the depolymerase derivatives is bound to plasma proteins. The volume of distribution of chondroitin sulfate is relatively small, around 0.3 l/kg. In humans, chondroitin sulfate shows an affinity for joint tissue. In rats, as well as joint tissue, chondroitin sulfate shows an affinity for the wall of the small intestine, liver, brain and kidneys.

Metabolism:
At least 90% of the dose of chondroitin sulfate is metabolised firstly by lysosomal sulfatases, and then is depolymerased by hyaluronidases, beta-glucuronidases and beta-N-acetylhexosaminidases. The liver, the kidneys and other organs take part in the depolymerisation of chondroitin sulfate. There have been no observation interactions with other medicines at metabolisation level. Chondroitin sulfate is not metabolised by cytochrome enzyme P450.

Elimination:
The systematic clearance of chondroitin sulfate is 30.5 ml/min or 0.43 ml/min/kg. The average lifetime fluctuates between 5 and 15 hours, depending on the experimental protocol. Elimination of chondroitin sulfate and its depolymerased derivatives is chiefly through the kidneys.

Linearity:
The kinetics of chondroitin sulfate are of first order up to single doses of 3,000 mg. Multiple doses of 800 mg in patients suffering from arthritis do not alter the order of the kinetics of chondroitin sulfate.

5.3 Preclinical safety data

Toxicity (severe, sub severe and chronic), mutagenicity, genotoxicity, carcinogenicity and reproductive toxicity studies, have given negative results in all cases.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Magnesium stearate.
The capsule shells contain:
Gelatin,
Quinoline yellow (E104),
Indigo carmine (E132).

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Store in the original package in order to protect from moisture.

6.5 Nature and contents of container

PVC/Al blister strips in an outer carton: each pack contains either 60 or 180 capsules.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product

No special requirements

7 MARKETING AUTHORISATION HOLDER

IBSA Farmaceutici Italia S.r.l
Via Martiri di Cefalonia 2,
26900 Lodi (LO)
Italy

8 MARKETING AUTHORISATION NUMBER

PA1104/003/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 22 December 2005

Date of last renewal: 22 December 2010

10 DATE OF REVISION OF THE TEXT

September 2021