Colforsin Daropate Hydrochloride *(rINNM)*

Colforsin Dapropate Hydrochloride; Colforsine, Chlorhydrate de Daropate de; Colforsini Daropatis Hydrochloridum; Hidrocloruro del daropato de colforsina; NKH-477.

Колфорсина Даропата Гидрохлорид

$C_{27}H_{43}NO_8$,HCl = 546.1.

CAS — 138605-00-2.

Profile

Colforsin is an adenylate cyclase stimulator derived from the plant *Plectranthus barbatus* (*Coleus forskohlii*) (Labiatae). It has been investigated for a number of conditions, including glaucoma and impotence. It is reported to have positive inotropic and bronchodilator effects. It has been used in the form of colforsin daropate hydrochloride.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Adehl.

Collagen

Colágeno.

ATC — B02BC07; G04BX11.

ATC Vet — QB02BC07; QG04BX11.

Pharmacopoeias. *US* includes Bovine Acellular Dermal Matrix.

USP 31 (Bovine Acellular Dermal Matrix). A remodelable collagen scaffold derived from fetal or neonatal bovine skin. It is presented as a flat white sheet that is cut to size and hydrated in sterile saline solution prior to implantation. It is utilised as a structural scaffold in orthopaedic, neurosurgical, urogynaecological, dermatological, plastic, and other reconstructive procedures. The source fetal or neonatal bovine skin is mechanically and chemically processed to isolate the dermis and remove cells and cellular components. To prevent the transmission of infectious disease, the manufacturing process is validated to inactivate viruses potentially present in the source material. To prevent the spread of transmissible spongiform encephalopathies, the source material is acquired from appropriate geographic locations. Store at 15° to 30°.

Profile

Collagen is a fibrous protein component of mammalian connective tissue making up almost one third of the total body protein.

Collagen, processed in a variety of ways, has been used in surgery as a haemostatic and as a repair and suture material. For cosmetic purposes it has been injected into the dermis to correct scars and other contour deformities of the skin. Collagen implants have been used to block tear outflow in the management of dry eye (p.2140).

Intraurethral administration of collagen has been used in the treatment of stress incontinence (p.2180). There has also been interest in the use of collagen by mouth to suppress the inflammatory process in rheumatoid arthritis (p.11), osteoarthritis (p.11), and scleroderma (p.1817).

Elastin, another component of connective tissue, is an ingredient, often with collagen, of various topical preparations promoted for skin disorders.

◊ References.

1. Herschorn S, *et al.* Early experience with intraurethral collagen injections for urinary incontinence. *J Urol (Baltimore)* 1992; **148:** 1797–1800.
2. Sieper J, *et al.* Oral type II collagen treatment in early rheumatoid arthritis: a double-blind, placebo-controlled, randomized trial. *Arthritis Rheum* 1996; **39:** 41–51.
3. Stanton SL, Monga AK. Incontinence in elderly women: is periurethral collagen an advance? *Br J Obstet Gynaecol* 1997; **104:** 154–7.
4. Anonymous. GAX collagen for genuine stress incontinence. *Drug Ther Bull* 1997; **35:** 86–7.
5. Moskowitz RW. Role of collagen hydrolysate in bone and joint disease. *Semin Arthritis Rheum* 2000; **30:** 87–99.
6. Hamraoui K, *et al.* Efficacy and safety of percutaneous treatment of iatrogenic femoral artery pseudoaneurysm by biodegradable collagen injection. *J Am Coll Cardiol* 2002; **39:** 1297–1304.
7. Corcos J, *et al.* Multicenter randomized clinical trial comparing surgery and collagen injections for treatment of female stress urinary incontinence. *Urology* 2005; **65:** 898–904.
8. Bello AE, Oesser S. Collagen hydrolysate for the treatment of osteoarthritis and other joint disorders: a review of the literature. *Curr Med Res Opin* 2006; **22:** 2221–32.
9. Poon CI, Zimmern PE. Is there a role for periurethral collagen injection in the management of urodynamically proven mixed urinary incontinence? *Urology* 2006; **67:** 725–9.
10. Sakamoto K, *et al.* Long-term subjective continence status and use of alternative treatments by women with stress urinary incontinence after collagen injection therapy. *World J Urol* 2007; **25:** 431–3.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Covadenyl; Eurohair; Hidroplus CL; Medic-S†; Membracel†; Proteita†; Skinderm CL; Zyplast†; ***Austral.:*** Ionil Rinse; Zyderm; Zyplast; ***Canad.:*** Dermatix Catrix†; ***Chile:*** Artrimax; ***Fr.:*** Pangen; ***Ger.:*** Catrix; Colloss; Hemocol; Matricur; Medifome; Pangen†; Porcoll†; Promogran†; Surgicoll†; Tachotop N†; TissuCone; TissuFleece; TissuFoil; Tutoplast Dura; Tutoplast Fascia lata; Zyderm†; Zyplast†; ***Gr.:*** Gelfix; ***Hong Kong:*** Avitene†; Zyderm†; Zyplast†; ***Ital.:*** Alfagen†; Condress; Idroskin; Neopelle†; Skinat; Stimtes†; ***Mex.:*** Fibroquel; ***Neth.:*** Willospon Forte†; ***NZ:*** Contigen; Ionil Rinse†; ***Port.:*** Catrix†; ***Singapore:*** Articolase†; CosmoDerm; CosmoPlast; Zyderm†; Zyplast†; ***UK:*** Catrix†; Contigen; ***USA:*** Avitene; Hemotene†.

Multi-ingredient: ***Arg.:*** Amenite E†; Amenite Plus†; Aristaloe; Aspergun†; Celuvital†; Colageno + C; Collagen T2-Gag†; E-devit; Estri-Atlas; Fibracol Plus; Galenic Restaurador Capilar; Hidroplus Nieve†; Hidrosam; Hidrosam T; Lociherp Liposomas Antiage; Lociherp Liposomas Vitaminado; Medicreme; Puraloe Nutritivo; Rep-Cartil; Skinderm R; Totalos Plus; Turgent Colageno; ***Austral.:*** John Plunketts Protective Day Cream; John Plunketts Super Wrinkle Cream; ***Austria:*** TachoComb; ***Belg.:*** Duracoll; ***Chile:*** Acnoxyl Gel Humectante; ***Cz.:*** TachoComb†; ***Fr.:*** Collatamp G†; Promogran; Taido; ***Ger.:*** Collapat II; Integra†; Septocoll; TachoComb†; Targobone; ***Hong Kong:*** TachoComb; ***Hung.:*** TachoComb†; ***Indon.:*** Biolastin; Jointfit; Legreskin; OA Plus; ***Ital.:*** Artrodue; Biomineral 5-Alfa Shampoo; Emofix; Osteoclar; Promogran; Reumilase SD; Secril; Unidermo; ***Malaysia:*** Balance Elastin E†; ***Rus.:*** TachoComb (ТахоКомб); ***Singapore:*** Articolase (w/glucosamine); Seven Seas JointCare Max; ***Switz.:*** Gorgonium; ***Thai.:*** TachoComb†; ***UK:*** Collatamp EG; Jointace; JointCare Max; ***USA:*** PDP Liquid Protein; ***Venez.:*** Artrosamin.

Collagenase

Clostridiopeptidas; Clostridiopeptidase A; Clostridiopeptidasum A; Colagenasa; Klostridiopeptidaasi A.

CAS — 9001-12-1.

ATC Vet — QD03BA02.

Profile

Collagenase is a proteolytic enzyme derived from the fermentation of *Clostridium histolyticum* and has the ability to break down collagen. Preparations containing collagenase are used topically for the debridement of dermal ulcers and burns, and possibly other necrotic lesions, to facilitate granulation and epithelialisation. It has also been given by injection into the intervertebral disc for chemonucleolysis in the treatment of lumbar disc herniation (see low Back Pain, p.7). Collagenase is under investigation for use in Dupuytren's disease and Peyronie's disease.

Hypersensitivity reactions may occur. Local burning, erythema, and pain have been reported at the site of application. It has been suggested that debridement of infected wounds may increase the risk of bacteraemia and that patients should be watched for signs of systemic bacterial infection. The activity of collagenase may be reduced by antiseptics containing detergents, hexachlorophene, and heavy metal ions.

Collagenase potency is expressed in units based on the amount of enzyme required to degrade a standard preparation of undenatured collagen.

Chemonucleolysis. Collagenase has been studied as an alternative to chymopapain (p.2281) for chemonucleolysis because of the risk of anaphylaxis with the latter. Although early studies with collagenase reported benefit, there were also reports of back pain and muscle spasm.[1] Collagenase was not as effective as chymopapain in a comparative study,[2] and further study may be warranted before a firm recommendation can be made.

1. Brown MD. Update on chemonucleolysis. *Spine* 1996; **21** (24 suppl): 62S–68S.
2. Wittenberg RH, *et al.* Five-year results from chemonucleolysis with chymopapain or collagenase: a prospective randomized study. *Spine* 2001; **26:** 1835–41.

Dupuytren's disease. Collagenase has been reported to be of benefit in the treatment of Dupuytren's contracture.[1]

1. Badalamente MA, Hurst LC. Efficacy and safety of injectable mixed collagenase subtypes in the treatment of Dupuytren's contracture. *J Hand Surg (Am)* 2007; **32:** 767–74.

Peyronie's disease. Beneficial effects have been reported with intralesional collagenase in men with Peyronie's disease.[1-3]

1. Gelbard MK, *et al.* The use of collagenase in the treatment of Peyronie's disease. *J Urol (Baltimore)* 1985; **134:** 280–3.
2. Gelbard MK, *et al.* Collagenase versus placebo in the treatment of Peyronie's disease: a double-blind study. *J Urol (Baltimore)* 1993; **149:** 56–8.
3. Jordan GH. The use of intralesional clostridial collagenase injection therapy for Peyronie's disease: a prospective, single-center, non-placebo-controlled study. *J Sex Med* 2008; **5:** 180–7.

Preparations

Proprietary Preparations (details are given in Part 3)
Belg.: Iruxol Mono; ***Braz.:*** Iruxol Mono; Kollagenase; ***Canad.:*** Santyl†; ***Gr.:*** Iruxol Mono; ***Hong Kong:*** Iruxol Mono; ***Ital.:*** Noruxol; ***Neth.:*** Novuxol; ***Port.:*** Ulcerase; ***Switz.:*** Iruxol Mono; ***Turk.:*** Novuxol; ***USA:*** Santyl; ***Venez.:*** Iruxol Simplex.

Multi-ingredient: ***Arg.:*** Iruxol; ***Braz.:*** Gyno Iruxol; Iruxol; Kollagenase com cloranfenicol; ***Cz.:*** Iruxol Mono; ***Fin.:*** Iruxol; Iruxol Mono; ***Ger.:*** Iruxol N†; ***Hung.:*** Iruxol Mono; ***Irl.:*** Iruxol Mono; ***Ital.:*** Iruxol; ***Malaysia:*** Iruxol Mono; ***Mex.:*** Ulcoderma; ***Rus.:*** Iruxol (Ируксол); ***S.Afr.:*** Iruxol Mono; ***Singapore:*** Iruxol Mono; ***Spain:*** Iruxol Mono; Iruxol Neo.

Colophony

Colofonia; Coloph.; Colophane; Colophonium; Kalafuna; Kanifolija; Kolofoni; Kolofónium; Kolofonium; Resin; Resina Pini; Resina Terebinthinae; Rosin.

Pharmacopoeias. In *Eur.* (see p.vii) and *Jpn.*

Ph. Eur. 6.2 (Colophony). The residue remaining after distillation of the volatile oil from the oleoresin obtained from various species of *Pinus*. Translucent, pale yellow to brownish-yellow, angular, irregularly shaped, brittle, glassy pieces of different sizes the surfaces of which bear conchoidal markings. Do not reduce to a fine powder.

Profile

Colophony is an ingredient of some collodions and plaster-masses. It has been used as an ingredient of ointments and dressings for wounds and minor skin disorders. Skin sensitisation and allergic respiratory symptoms have been reported.

Hypersensitivity. Reviews.

1. Downs AM, Sansom JE. Colophony allergy: a review. *Contact Dermatitis* 1999; **41:** 305–10.

Preparations

BP 2008: Flexible Collodion.

Proprietary Preparations (details are given in Part 3)
Rus.: Biopin (Биопин)†.

Multi-ingredient: ***Austral.:*** Zam-Buk†; ***Austria:*** Ehrenhofer-Salbe; Vulpuran; ***Braz.:*** Basilicao†; ***Ital.:*** Fialetta Odontalgica Dr Knapp; ***Mex.:*** Parche Negro Belladona; ***Switz.:*** Leucen; ***UK:*** Dispello; Herbheal Ointment; Pickles Corn Caps.

Comfrey

Boneset; Comfrey Root; Consolidae Radix; Consuelda; Symphytum.

NOTE. Boneset is also a common name used for *Eupatorium perfoliatum* (see p.2267).

Pharmacopoeias. *Br.* includes Symphytum Officinale Root for Homoeopathic Preparations and Symphytum Officinale Root, Ethanol. decoctum for Homoeopathic Preparations.

BP 2008 (Symphytum Officinale Root for Homoeopathic Preparations). The fresh root of *Symphytum officinale*.

BP 2008 (Symphytum Officinale Root, Ethanol. decoctum for Homoeopathic Preparations). The fresh root of *Symphytum officinale*.

Profile

Comfrey consists of the dried root and rhizome of *Symphytum officinale* (Boraginaceae); the leaf has also been used. It contains about 0.7% of allantoin, large quantities of mucilage, and some tannin. It may also contain pyrrolizidine alkaloids.

Comfrey was formerly used as an application to wounds and ulcers to stimulate healing and was also given systemically for gastric ulceration. It has been applied topically in the treatment of inflammatory disorders. The healing action of comfrey has been attributed to the presence of allantoin (p.1588).

There are reports of hepatotoxicity attributed to pyrrolizidine alkaloids present in comfrey preparations and such preparations have been withdrawn or banned in a number of countries.

Homoeopathy. Comfrey has been used in homoeopathic medicines under the following names: Symphytum officinale; Symph. of.

◊ References.

1. Stickel F, Seitz HK. The efficacy and safety of comfrey. *Public Health Nutr* 2000; **3:** 501–8.
2. Grube B, *et al.* Efficacy of a comfrey root (Symphyti offic. radix) extract ointment in the treatment of patients with painful osteoarthritis of the knee: results of a double-blind, randomised, bicenter, placebo-controlled trial. *Phytomedicine* 2007; **14:** 2–10.
3. D'Anchise R, *et al.* Comfrey extract ointment in comparison to diclofenac gel in the treatment of acute unilateral ankle sprains (distortions). *Arzneimittelforschung* 2007; **57:** 712–16.

Adverse effects. Toxic pyrrolizidine alkaloids have been isolated from several species of comfrey plants including common comfrey (*Symphytum officinale*), prickly comfrey (*S. asperum*), and Russian comfrey (*S. uplandicum*). Ingestion of plants containing pyrrolizidine alkaloids is a common cause of hepatic veno-occlusive disease in developing countries[1] and pyrrolizidine alkaloid hepatotoxicity presumably due to comfrey has been reported in North America and Europe.[1,2] Pulmonary endothelial hyperplasia and carcinogenic activity have also been reported in *animals*.[1,2]

1. Ridker PM, McDermott WV. Comfrey herb tea and hepatic veno-occlusive disease. *Lancet* 1989; **i:** 657–8.
2. Bach N, *et al.* Comfrey herb tea-induced hepatic veno-occlusive disease. *Am J Med* 1989; **87**: 97–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Austria: Traumaplant; ***Cz.:*** Traumaplant; ***Ger.:*** Kytta-Plasma f; Kytta-Salbe f; Traumaplant; ***Indon.:*** Mediflor; ***Switz.:*** Kytta Pommade; ***UK:*** Comfrelieve; ***Venez.:*** Traumaplant.

Multi-ingredient: ***Cz.:*** Dr Theiss Beinwell Salbe†; Stomatosan†; ***Ger.:*** Kytta-Balsam f; Rhus-Rheuma-Gel N; Syviman N†; ***Israel:*** Comfrey Plus; ***Switz.:*** Gel a la consoude; Keppur; Kytta Baume; Kytta Gel†.

Complement Blockers

Inhibidores del complemento.

Блокаторы Комплемента

Profile

Complement is a group of plasma and cellular proteins contributing to the innate immune system and is so called because it complements the microbicidal action of antibodies. The complement system is activated by the antigen-antibody complex followed by a cascade reaction of complement proteins culminating in microbial cell lysis. Complement also plays a part in many other physiological processes and regulatory mechanisms are in place to prevent inflammatory damage to host tissues through the