Dextropropoxyphene *(BAN, pINN)*

Dekstropropoksifeeni; Dextropropoxifen; Dextropropoxifeno; Dextropropoxyphène; Dextropropoxyphenum; Propoxyphene. (+)-(1*S*,2*R*)-1-Benzyl-3-dimethylamino-2-methyl-1-phenylpropyl propionate.

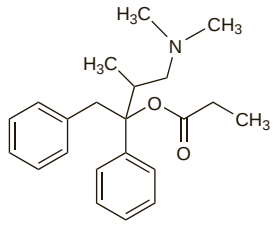
Декстропропоксифен

$C_{22}H_{29}NO_2$ = 339.5.

CAS — 469-62-5.

ATC — N02AC04.

ATC Vet — QN02AC04.



NOTE. The following terms have been used as 'street names' (see p.vi) or slang names for various forms of dextropropoxyphene: Dummies.

Dextropropoxyphene Hydrochloride

(BANM, pINNM)

Dekstropropoksifeenihydrokloridi; Dekstropropoksifeno hidrochloridas; Dextropropoxifén-hidroklorid; Dextropropoxifenhydroklorid; Dextropropoxyfen-hydrochlorid; Dextropropoxyphène, chlorhydrate de; Dextropropoxypheni hydrochloridum; Hidrocloruro de dextropropoxifeno; Propoxyphene Hydrochloride *(USAN)*.

Декстропропоксифена Гидрохлорид

$C_{22}H_{29}NO_2$,HCl = 375.9.

CAS — 1639-60-7.

NOTE. Compounded preparations of dextropropoxyphene hydrochloride may be represented by the following names:

- Co-proxamol (*BAN*)—dextropropoxyphene hydrochloride 1 part and paracetamol 10 parts (w/w).

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

Ph. Eur. 6.2 (Dextropropoxyphene Hydrochloride). A white or almost white crystalline powder. Very soluble in water; freely soluble in alcohol. Protect from light.

USP 31 (Propoxyphene Hydrochloride). A white odourless crystalline powder. Freely soluble in water; soluble in alcohol, in acetone, and in chloroform; practically insoluble in ether and in benzene. Store in airtight containers.

Dextropropoxyphene Napsilate *(BANM, pINNM)*

Dextropropoxyphène, Napsilate de; Dextropropoxyphene Napsylate; Dextropropoxypheni Napsilas; Napsilato de dextropropoxifeno; Propoxyphene Napsylate *(USAN)*. Dextropropoxyphene naphthalene-2-sulphonate monohydrate.

Декстропропоксифена Напсилат

$C_{22}H_{29}NO_2$,$C_{10}H_8O_3S$,H_2O = 565.7.

CAS — 17140-78-2 (anhydrous dextropropoxyphene napsilate); 26570-10-5 (dextropropoxyphene napsilate monohydrate).

NOTE. Compounded preparations of dextropropoxyphene napsilate may be represented by the following names:

- Co-proxAPAP (*PEN*)—dextropropoxyphene napsilate and paracetamol.

Pharmacopoeias. In *Br.* and *US*.

BP 2008 (Dextropropoxyphene Napsilate). An odourless or almost odourless white powder. It exhibits polymorphism. Practically insoluble in water; soluble in alcohol; freely soluble in chloroform.

USP 31 (Propoxyphene Napsylate). A white powder having essentially no odour. Very slightly soluble in water; soluble 1 in 15 of alcohol and 1 in 10 of chloroform; soluble in acetone and in methyl alcohol. Store in airtight containers.

Dependence and Withdrawal

As for Opioid Analgesics, p.101.

Dextropropoxyphene has been subject to abuse (see under Precautions, below).

◊ Reports of dextropropoxyphene dependence and its treatment.

1. Wall R, *et al.* Addiction to Distalgesic (dextropropoxyphene). *BMJ* 1980; **280:** 1213–14.
2. D'Abadie NB, Lenton JD. Propoxyphene dependence: problems in management. *South Med J* 1984; **77:** 299–301.

Adverse Effects

As for Opioid Analgesics in general, p.102.

In the recommended dosage the adverse effects of dextropropoxyphene are less marked than those of morphine. Gastrointestinal effects, dizziness, and drowsiness are the most common. Liver impairment, manifest as abnormal liver function tests and, more rarely, as reversible jaundice, has been reported.

There have been a large number of fatalities from either accidental or intentional overdosage with dextropropoxyphene. Many reports emphasise the rapidity with which death ensues; death within an hour of overdosage is not uncommon, and it can occur within 15 minutes. Overdosage is often complicated by patients also taking other CNS depressants such as alcohol and using mixed preparations such as dextropropoxyphene with paracetamol or aspirin.

Symptoms of overdosage are similar to those of opioid poisoning in general, but in addition patients may experience psychotic reactions. There may be cardiac conduction abnormalities and arrhythmias.

Dextropropoxyphene injections are painful and have a very destructive effect on soft tissues and veins when abused in this way.

Anorectal reactions have followed the prolonged use of suppositories containing dextropropoxyphene; the reactions appear to be dose dependent.

Effects on the blood. A 12-year history of haemolysis and subsequent significant haemolytic anaemia in an elderly woman[1] was associated with chronic, periodic, and occasionally excessive intake of co-proxamol.

1. Fulton JD, McGonigal G. Steroid responsive haemolytic anaemia due to dextropropoxyphene paracetamol combination. *J R Soc Med* 1989; **82:** 228.

Effects on the ears. A report of complete nerve deafness associated with chronic abuse of co-proxamol was made to the UK CSM.[1] The CSM had received 2 other reports of permanent hearing loss attributed to co-proxamol abuse; transient hearing loss had also been reported in 2 patients taking usual doses; 7 further reports described tinnitus.

1. Ramsay BC. Complete nerve deafness after abuse of co-proxamol. *Lancet* 1991; **338:** 446–7.

Effects on the liver. There have been occasional reports of jaundice in patients taking dextropropoxyphene alone but many of the 49 suspected hepatic reactions with dextropropoxyphene reported to the UK CSM by 1985[1] had involved use with paracetamol; clinical features including malaise, jaundice, raised serum transaminases, and sometimes fever, were however generally characteristic of dextropropoxyphene alone. Relapsing jaundice mimicking biliary disease was attributable to the dextropropoxyphene component of co-proxamol in 3 patients,[2] whereas there was no abnormality of liver function in 11 patients on long-term co-proxamol analgesia.[3] Another report of 9 cases found that the hepatotoxicity of dextropropoxyphene mimicked symptoms of large bile duct obstruction, and suggested that such toxicity might be misdiagnosed.[4] A more recent review[5] also concluded that hepatotoxicity with dextropropoxyphene might mimic a biliary tract disease, sometimes with few or no symptoms.

1. CSM. Hepatotoxicity with dextropropoxyphene. *Current Problems 17* 1986. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2024424&RevisionSelectionMethod=LatestReleased (accessed 26/06/08)
2. Bassendine MF, *et al.* Dextropropoxyphene induced hepatotoxicity mimicking biliary tract disease. *Gut* 1986; **27:** 444–9.
3. Hutchinson DR, *et al.* Liver function in patients on long-term paracetamol (co-proxamol) analgesia. *J Pharm Pharmacol* 1986; **38:** 242–3.
4. Rosenberg WMC, *et al.* Dextropropoxyphene induced hepatotoxicity: a report of nine cases. *J Hepatol* 1993; **19:** 470–4.
5. Bergeron L, *et al.* Dextropropoxyphène et atteintes hépatiques: à propos de 4 cas et revue de littèrature. *Therapie* 2002; **57:** 464–72.

Effects on the lungs. Hypersensitivity pneumonitis and skin rash has been reported in a patient taking co-proxamol.[1] No such reaction occurred when the patient was subsequently given paracetamol alone.

1. Matusiewicz SP, *et al.* Hypersensitivity pneumonitis associated with co-proxamol (paracetamol + dextropropoxyphene) therapy. *Postgrad Med J* 1999; **75:** 475–6.

Hypoglycaemia. Hypoglycaemia has occasionally been reported with the use of dextropropoxyphene.[1-6]

1. Wiederholt IC, *et al.* Recurrent episodes of hypoglycemia induced by propoxyphene. *Neurology* 1967; **17:** 703–4.
2. Almirall J, *et al.* Propoxyphene-induced hypoglycemia in a patient with chronic renal failure. *Nephron* 1989; **53:** 273–5.
3. Laurent M, *et al.* Hypoglycémie sous dextropropoxyphène chez des grands vieillards: 7 cas. *Presse Med* 1991; **20:** 1628.
4. Lowenstein W, *et al.* Hypoglycémie au dextropropoxyphène: une urgence chez le toxicomane. *Presse Med* 1993; **22:** 133.
5. Santos Gil I, *et al.* Hipoglucemia secundaria a ingestión de dextropropoxifeno en un paciente adicto a drogas. *Med Clin (Barc)* 1998; **110:** 475–6.
6. Shah P, *et al.* Propoxyphene-induced hypoglycemia in renal failure. *Endocr Pract* 2006; **12:** 170–3.

Overdosage. There have been several reviews or retrospective studies of acute self-poisoning with dextropropoxyphene.[1-4] At a symposium on the safety and efficacy of dextropropoxyphene[5] many of the participants dealt with the problems of dextropropoxyphene overdosage, often in conjunction with paracetamol and sometimes with alcohol. Profound and even fatal CNS depression can develop rapidly as a result of the dextropropoxyphene content and in many cases death has occurred within an hour;[6] it was suggested that as few as 15 to 20 tablets of co-proxamol may be fatal.[7,8] Analysis of suicides involving drugs in England and Wales between 1997 and 1999 revealed that the odds of dying after overdose with co-proxamol were 2.3 times that for tricyclic antidepressant overdose, and 28.1 times greater than for paracetamol.[9] Another analysis of suicides due to poisoning in 3 areas of the UK between 2000 and 2001 identified 123 cases of fatal overdose with co-proxamol;[10] those who also consumed alcohol had generally taken fewer co-proxamol tablets than those who had not, emphasising the increased toxicity of the combination.

An analysis of overdosage involving combination analgesic preparations prescribed in Scotland between 2000 and 2002 also found that overdoses with co-proxamol were 10 times more likely to be fatal when compared with co-dydramol or co-codamol.[11] In the USA[12] the incidence of dextropropoxyphene-associated deaths reached a peak in 1977 and then fell at a rate that was not matched by a decline in prescribing.

It is not clear whether the metabolite, nordextropropoxyphene, plays an important role in fatalities.[12] However, nordextropropoxyphene, like dextropropoxyphene, is considered to have local anaesthetic activity and the membrane stabilising activity of dextropropoxyphene has been implicated as a major factor responsible for its severe cardiac depressant effect.[13]

In January 2005, the UK CSM found the risk of toxicity of co-proxamol in overdose to be unacceptable;[14] consequently, co-proxamol has been gradually withdrawn from the UK market. Fixed-dose combinations of dextropropoxyphene and paracetamol have also been withdrawn in several other countries including Sweden and Switzerland.

1. Young RJ. Dextropropoxyphene overdosage: pharmacological considerations and clinical management. *Drugs* 1983; **26:** 70–9.
2. Madsen PS, *et al.* Acute propoxyphene self-poisoning in 222 consecutive patients. *Acta Anaesthesiol Scand* 1984; **28:** 661–5.
3. Segest E. Poisoning with dextropropoxyphene in Denmark. *Hum Toxicol* 1987; **6:** 203–7.
4. Jonasson U, *et al.* Correlation between prescription of various dextropropoxyphene preparations and their involvement in fatal poisonings. *Forensic Sci Int* 1999; **103:** 125–32.
5. Bowen D, *et al.* (ed). Distalgesic; safety and efficacy. *Hum Toxicol* 1984; **3** (suppl): 1S–238S.
6. Proudfoot AT. Clinical features and management of Distalgesic overdose. *Hum Toxicol* 1984; **3** (suppl): 85S–94S.
7. Whittington RM. Dextropropoxyphene deaths: coroner's report. *Hum Toxicol* 1984; **3** (suppl): 175S–185S.
8. Young RJ, Lawson AAH. Distalgesic poisoning—cause for concern. *BMJ* 1980; **280:** 1045–7.
9. Hawton K, *et al.* Co-proxamol and suicide: a study of national mortality statistics and local non-fatal self-poisonings. *BMJ* 2003; **326:** 1006–8.
10. Hawton K, *et al.* A multicentre study of coproxamol poisoning suicides based on coroners' records in England. *Br J Clin Pharmacol* 2005; **59:** 207–12.
11. Afshari R, *et al.* Co-proxamol overdose is associated with a 10-fold excess mortality compared with other paracetamol combination analgesics. *Br J Clin Pharmacol* 2005; **60:** 444–7.
12. Finkle BS. Self-poisoning with dextropropoxyphene and dextropropoxyphene compounds: the USA experience. *Hum Toxicol* 1984; **3** (suppl): 115S–34S.
13. Henry JA, Cassidy SL. Membrane stabilising activity: a major cause of fatal poisoning. *Lancet* 1986; **i:** 1414–17.
14. MHRA. Withdrawal of co-proxamol products and interim updated prescribing information. Message from Professor G Duff, Chairman of CSM (issued 31st January, 2005). Available at: http://www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con019461.pdf (accessed 28/08/08)

Treatment of Adverse Effects

As for Opioid Analgesics in general, p.102.

Rapid treatment of overdosage with naloxone and assisted respiration is essential. Cardiac effects may not be reversed by naloxone. Gastric lavage and activated charcoal may be of value within 1 hour of ingestion, but dialysis is of little use.

Convulsions may require control with an anticonvulsant, bearing in mind that the CNS depressant effects of dextropropoxyphene can be exacerbated (see also Interactions, below). Stimulants should not be used because of the risk of inducing convulsions.

Patients taking overdoses of dextropropoxyphene with paracetamol will also require treatment for paracetamol poisoning (p.108). Mixtures of dextropropoxyphene and aspirin may be involved; the treatment of aspirin poisoning is described on p.20.

Precautions

As for Opioid Analgesics in general, p.103.

Abuse. There have been reports[1] of the abuse of dextropropoxyphene, and some[2] considered that the ready availability of dextropropoxyphene made it liable to abuse although it was a relatively weak opioid analgesic. However, others[3] thought there was no evidence that dextropropoxyphene was frequently associated with abuse, or concluded that, although there was abuse potential, it was of relatively low importance in terms of the community as a whole.[4]

A severe withdrawal syndrome has been reported[5] in an elderly patient who covertly consumed a daily dose of dextropropoxyphene of 1 to 3 g for at least 12 months. The patient was treated by a gradually decreasing dosage schedule of dextropropoxyphene over 9 weeks.

1. Tennant FS. Complications of propoxyphene abuse. *Arch Intern Med* 1973; **132:** 191–4.
2. Lader M. Abuse of weak opioid analgesics. *Hum Toxicol* 1984; **3** (suppl): 229S–36S.
3. Finkle BS. Self-poisoning with dextropropoxyphene and dextropropoxyphene compounds: the USA experience. *Hum Toxicol* 1984; **3** (suppl): 115S–34S.
4. Turner P. Final remarks. *Hum Toxicol* 1984; **3** (suppl): 237S–8S.
5. Hedenmalm K. A case of severe withdrawal syndrome due to dextropropoxyphene. *Ann Intern Med* 1995; **123:** 473.

Breast feeding. No adverse effects have been seen in breast-fed infants whose mothers were receiving dextropropoxyphene, and the American Academy of Pediatrics considers[1] that it is therefore usually compatible with breast feeding. The *BNF* also considers that the amount of dextropropoxyphene in breast milk is too small to be harmful.

1. American Academy of Pediatrics. The transfer of drugs and other chemicals into human milk. *Pediatrics* 2001; **108:** 776–89. Correction. *ibid.*; 1029. Also available at: http://aappolicy.aappublications.org/cgi/content/full/pediatrics%3b108/3/776 (accessed 26/06/08)

Porphyria. Dextropropoxyphene has been associated with acute attacks of porphyria and is considered unsafe in porphyric patients.

Interactions

For interactions associated with opioid analgesics, see p.103.

Plasma concentrations of dextropropoxyphene are increased by ritonavir, with a resultant risk of toxicity; they should not be given together.

CNS depressants, including alcohol, may contribute to the hazards of dextropropoxyphene, see also Overdosage, above. The convulsant action of high doses of dextropropoxyphene may be enhanced by CNS stimulants.

Dextropropoxyphene interacts with several other drugs through inhibition of liver metabolism. Drugs reported to be affected include antidepressants (see p.379), benzodiazepines (see p.989), beta blockers (see p.1229), carbamazepine (see p.474), phenobarbital (see p.493), phenytoin (see p.497), and warfarin (see p.1427).

Antimuscarinics. A suggested interaction between *orphenadrine* and dextropropoxyphene has been questioned (see p.812).

Pharmacokinetics

Dextropropoxyphene is readily absorbed from the gastrointestinal tract, the napsilate tending to be more slowly absorbed than the hydrochloride, but both are subject to considerable first-pass metabolism. Peak plasma concentrations occur about 2 to 2.5 hours after ingestion. It is rapidly distributed and concentrated in the liver, lungs, and brain. About 80% of dextropropoxyphene and its metabolites are reported to be bound to plasma proteins. Dextropropoxyphene crosses the placenta. It has been detected in breast milk.

Dextropropoxyphene is *N*-demethylated to nordextropropoxyphene (norpropoxyphene) in the liver. It is excreted in the urine mainly as metabolites. It is now recognised that dextropropoxyphene and nordextropropoxyphene have prolonged elimination half-lives; values of 6 to 12 hours and 30 to 36 hours, respectively, have been reported. Accumulation of dextropropoxyphene and its metabolites may occur with repeated doses and nordextropropoxyphene may contribute to the toxicity seen with overdosage.

◊ Reviews.

1. Pearson RM. Pharmacokinetics of propoxyphene. *Hum Toxicol* 1984; **3** (suppl): 37S–40S.

The elderly. The elimination half-lives of dextropropoxyphene and its metabolite nordextropropoxyphene were prolonged in healthy elderly subjects when compared with young controls.[1] After multiple dosing median half-lives of dextropropoxyphene and nordextropropoxyphene were 36.8 and 41.8 hours, respectively in the elderly compared with 22.0 and 22.1 hours in the young subjects. In this study[1] there was a strong correlation between half-life of nordextropropoxyphene and estimated creatinine clearance.

1. Flanagan RJ, *et al.* Pharmacokinetics of dextropropoxyphene and nordextropropoxyphene in young and elderly volunteers after single and multiple dextropropoxyphene dosage. *Br J Clin Pharmacol* 1989; **28:** 463–9.

Hepatic impairment. Plasma concentrations of dextropropoxyphene were higher in patients with cirrhosis given the drug than in healthy subjects whereas concentrations of nordextropropoxyphene were lower.[1]

1. Giacomini KM, *et al.* Propoxyphene and norpropoxyphene plasma concentrations after oral propoxyphene in cirrhotic patients with and without surgically constructed portacaval shunt. *Clin Pharmacol Ther* 1980; **28:** 417–24.

Renal impairment. Higher and more persistent plasma concentrations of dextropropoxyphene and nordextropropoxyphene in anephric patients when compared with healthy subjects[1] were attributed to decreased first-pass metabolism of dextropropoxyphene and decreased renal excretion of nordextropropoxyphene in the anephric patients.

1. Gibson TP, *et al.* Propoxyphene and norpropoxyphene plasma concentrations in the anephric patient. *Clin Pharmacol Ther* 1980; **27:** 665–70.

Uses and Administration

Dextropropoxyphene is an opioid analgesic (p.104) structurally related to methadone (p.82). It has mild analgesic activity and is given orally as the hydrochloride or napsilate to alleviate mild to moderate pain. Unlike the laevo-isomer (levopropoxyphene), dextropropoxyphene has little antitussive activity.

Dextropropoxyphene is mainly used with other analgesics that have anti-inflammatory and antipyretic effects, such as aspirin or paracetamol. In the USA the usual dose is 65 mg of the hydrochloride or 100 mg of the napsilate given every 4 hours up to a maximum total daily dose of 390 mg or 600 mg, respectively. In the UK similar doses have been given three or four times daily.

The combination preparation co-proxamol (dextropropoxyphene with paracetamol) has been gradually withdrawn from the UK market (see also Pain, below) although such combinations may remain available in a number of countries.

Pain. A detailed review[1] of the analgesic effectiveness of dextropropoxyphene suggested that with respect to single oral doses, recommended doses of dextropropoxyphene were no more (and probably less) effective than usual doses of paracetamol, aspirin, or other NSAIDs. However, the comparative effectiveness may vary substantially depending on the cause of the pain.

When it comes to comparative studies involving combinations of dextropropoxyphene with other analgesics, findings are even less clear-cut.[2] The effectiveness of co-proxamol has long been a matter of controversy yet despite this a survey[3] conducted in 30 UK teaching hospitals found that co-proxamol was the most widely used paracetamol-containing analgesic. It was suggested that the popularity of co-proxamol was purely down to prescribing habits passed on to new medical staff, rather than hard evidence regarding efficacy. This view has been refuted by others[4] who say that a large number of studies have shown clear analgesic effects for dextropropoxyphene. However, any assumption that the combination was widely used because it was more effective than paracetamol alone was not supported by a systematic overview of single-dose studies.[5] This concluded that while co-proxamol was indeed an effective analgesic it was no better than paracetamol alone. Although the evidence from this and other systematic reviews indicate that co-proxamol should be replaced by paracetamol alone for acute pain, the position for chronic use is considered to be not so clear (but see below).[6]

In January 2005, the UK CSM found the efficacy of co-proxamol to be poorly established and its risk of toxicity in overdose to be unacceptable;[7] they considered that there was no robust evidence of the superior efficacy of co-proxamol to full-strength paracetamol alone in either acute or chronic pain. Consequently, co-proxamol has been gradually withdrawn from the UK market. Fixed-dose combinations of dextropropoxyphene and paracetamol have also been withdrawn in several other countries including Sweden and Switzerland.

1. Beaver WT. Analgesic efficacy of dextropropoxyphene and dextropropoxyphene-containing combinations: a review. *Hum Toxicol* 1984; **3** (suppl): 191S–220S.
2. Collins SL, *et al.* Single dose dextropropoxyphene, alone and with paracetamol (acetaminophen), for postoperative pain. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 1999 (accessed 26/06/08).
3. Haigh S. 12 Years on: co-proxamol revisited. *Lancet* 1996; **347:** 1840–1. Correction. *ibid.*; **348:** 346.
4. Sykes JV, *et al.* Coproxamol revisited. *Lancet* 1996; **348:** 408.
5. Li Wan Po A, Zhang WY. Systematic overview of co-proxamol to assess analgesic effects of addition of dextropropoxyphene to paracetamol. *BMJ* 1997; **315:** 1565–71. Correction *ibid.* 1998; **316:** 116 and 656.
6. Anonymous. Co-proxamol or paracetamol for acute pain? *Drug Ther Bull* 1998; **36:** 80.
7. MHRA. Withdrawal of co-proxamol products and interim updated prescribing information. Message from Professor G Duff, Chairman of CSM (issued 31st January, 2005). Available at: http://www.mhra.gov.uk/home/groups/pl-a/documents/websiteresources/con019461.pdf (accessed 28/08/08)

Preparations

BP 2008: Co-proxamol Tablets; Dextropropoxyphene Capsules;
USP 31: Propoxyphene Hydrochloride and Acetaminophen Tablets; Propoxyphene Hydrochloride Capsules; Propoxyphene Hydrochloride, Aspirin, and Caffeine Capsules; Propoxyphene Napsylate and Acetaminophen Tablets; Propoxyphene Napsylate and Aspirin Tablets; Propoxyphene Napsylate Oral Suspension; Propoxyphene Napsylate Tablets.

Proprietary Preparations (details are given in Part 3)
Arg.: Gobbigesic; ***Austral.:*** Doloxene; ***Belg.:*** Depronal; ***Canad.:*** 642†; Darvon-N; ***Denm.:*** Abalgin; Doloxene; ***Fin.:*** Abalgin; ***Gr.:*** Romidon; Zideron; ***India:*** Parvodex; ***Irl.:*** Doloxene†; ***Ital.:*** Liberen†; ***Mex.:*** Darvon Simple; ***Neth.:*** Depronal; ***NZ:*** Doloxene†; ***S.Afr.:*** Doloxene; ***Spain:*** Darvon†; Deprancol; ***Swed.:*** Dexofen; Doloxene; ***USA:*** Darvon; Darvon-N.

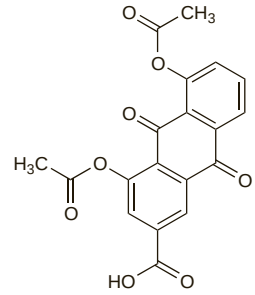
Multi-ingredient: ***Arg.:*** Artifene; Calmopirin; Canovex†; D-P†; Dexprofeno; Dextro + Dipirona; Dextrodip; Dorixina Forte; Gobbicalm; Klosidol; Klosidol B1 B6 B12; Supragesic; Vicefeno; ***Austral.:*** Capadex; Di-Gesic; Paradex; ***Austria:*** APA; Contraforte†; Sigmalin B forte; ***Belg.:*** Algophene; Distalgic†; ***Braz.:*** Doloxene-A; ***Fin.:*** Paraflex comp†; ***Fr.:*** Dextroref; Di Dolko; Di-Antalvic; Diadupsan†; Dialgirex; Dioalgo; Propofan; ***Hong Kong:*** Cosalgesic; Distalgesic†; Dolocin; Dolpocetmol; Medonol; ***Hung.:*** Novopyrin; ***India:*** Buta-Proxyvon; Ibu-Proxyvon; Parvon; Parvon Forte; Parvon-N; Parvon-Spas; Proxytab; Proxyvon; Spasmo-Proxyvon; Spasmocip; Spasmocip Plus; Sudhinol; Walagesic†; Wygesic; ***Irl.:*** Distalgesic†; ***Israel:*** Algolysin; Proxol; Rogaan; ***Mex.:*** Darvon-N Compuesto†; Neo-Percodan; Qual; ***Norw.:*** Aporex; ***NZ:*** Apo-Paradex†; Capadex; Paradex; ***Port.:*** Algifene; ***S.Afr.:*** Distalgesic; Doloxene Co; Doxyfene; Lentogesic; Synap; ***Swed.:*** Distalgesic†; Doleron†; Paraflex comp†; ***Switz.:*** Distalgesic†; ***UK:*** Cosalgesic†; Distalgesic†; ***USA:*** Balacet; Darvocet; Darvocet-N; Darvon Compound†; PC-Cap; Propacet; Trycet; Wygesic†.

Diacerein *(rINN)*

Diacereína; Diacéréine; Diacereinum; Diacerhein; Diacetylrhein; 2,4-dichlorobenzylique, alcool; Rhein Diacetate; SF-277; SF-277. 9,10-Dihydro-4,5-dihydroxy-9,10-dioxo-2-anthroic acid diacetate.

Диацереин

$C_{19}H_{12}O_8$ = 368.3.
CAS — 13739-02-1.
ATC — M01AX21.
ATC Vet — QM01AX21.



Profile

Diacerein is an anthraquinone derivative that is used in osteoarthritis (p.11) in oral doses of 50 mg twice daily. Doses should be halved in patients with creatinine clearance less than 30 mL/minute. Diarrhoea is a common adverse effect with diacerein. Its active metabolite, rhein, a constituent of rhubarb (p.1768), is reported to act as an interleukin-1 inhibitor.

Administration in renal impairment. See above and Pharmacokinetics, below.

Musculoskeletal and joint disorders. Diacerein is thought to act via inhibition of interleukin-1β,[1] which plays a role in inflammatory processes. Systematic reviews[2,3] on the use of diacerein in the treatment of osteoarthritis have indicated that diacerein produces a small, but consistent, improvement in pain. Further research is necessary to confirm its short- and long-term effectiveness and safety but there is some evidence of residual benefit on stopping treatment,[3] which has been postulated to represent an improvement in the disease process.

1. Van den Berg WB. Les mécanismes d'action de la diacerhéine, premier inhibiteur de l'interleukine 1 dans l'arthrose. *Presse Med* 2004; **33:** 10–12.
2. Fidelix TSA, *et al.* Diacerein for osteoarthritis. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2006 (accessed 06/10/06).
3. Rintelen B, *et al.* A meta-analysis of controlled clinical studies with diacerein in the treatment of osteoarthritis. *Arch Intern Med* 2006; **166:** 1899–1906.