Methocarbamol may cause drowsiness; patients affected should not drive or operate machinery.

Preparations for injection may contain, as a solvent, a macrogol which could increase existing acidosis and urea retention in patients with renal impairment; such preparations should not be used in patients with known or suspected renal disease.

Abnormal coloration. Methocarbamol has been reported to cause brown to black or green discoloration of the urine on standing.[1]

1. Baran RB, Rowles B. Factors affecting coloration of urine and feces. *J Am Pharm Assoc* 1973; **NS13:** 139–42.

Interactions

The CNS effects of methocarbamol may be potentiated by alcohol or other CNS depressants. Methocarbamol has also been reported to potentiate the effects of anorectics and antimuscarinics, and to inhibit the effect of pyridostigmine.

Pharmacokinetics

Methocarbamol is rapidly and almost completely absorbed from the gastrointestinal tract after oral doses. Its plasma half-life is reported to be about 1 to 2 hours. It is metabolised by dealkylation and hydroxylation and is excreted in urine primarily as the glucuronide and sulfate conjugates of its metabolites. A small amount is excreted in faeces.

Uses and Administration

Methocarbamol is a centrally acting skeletal muscle relaxant whose action may be due to general depressant effects on the CNS.

Methocarbamol is used as an adjunct in the short-term symptomatic treatment of painful muscle spasm (p.1887) associated with musculoskeletal conditions. It is sometimes given with analgesics in compound preparations for the treatment of musculoskeletal pain.

The usual initial oral dose for muscle spasm is 1.5 g four times daily, reduced to a maintenance dose of about 4 g daily after 2 to 3 days. A dose of 750 mg three times daily may be sufficient for a therapeutic effect. Half the maximum daily dose or less may be sufficient for elderly patients.

Methocarbamol has also been given intravenously at a rate of not more than 300 mg/minute, by slow injection or by infusion in sodium chloride 0.9% or glucose 5% injection. The parenteral route should not be used for more than 3 consecutive days and the dose should not exceed 3 g daily. The patient should remain lying down during, and for 10 to 15 minutes after, intravenous doses. The US manufacturers state that the injection is hypertonic and extravasation should be avoided. However, it may also be given by intramuscular injection in a dose of up to 500 mg into each gluteal region at intervals of 8 hours.

Preparations

USP 31: Methocarbamol Injection; Methocarbamol Tablets.

Proprietary Preparations (details are given in Part 3)
Canad.: Robaxin; ***Fr.:*** Lumirelax; ***Ger.:*** Ortoton; ***Hong Kong:*** Robaxin†; ***India:*** Robinax; ***Mex.:*** Remisol; Rexivin; ***S.Afr.:*** Robaxin; ***Spain:*** Robaxin; ***Thai.:*** Laxan; Manobaxine; Musxan; Myocin†; Myomethol; Robaxin†; ***UK:*** Robaxin; ***USA:*** Robaxin.

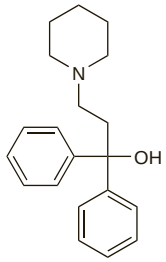
Multi-ingredient: ***Canad.:*** Aspirin Backache; Dodds Back Ease; Methoxacet; Methoxacet-C; Methoxisal; Methoxisal-C; Muscle & Back Pain Relief; Muscle & Back Pain Relief Extra Strength; Muscle & Back Pain Relief-8; Muscle Relaxant and Analgesic†; Obusforme†; Relaxophen; Robax Platinum; Robaxacet; Robaxacet-8; Robaxisal; Robaxisal-C; Spasmhalt; Spasmhalt-ASA; ***Ger.:*** Ortoton Plus; ***India:*** Flexinol; Ibugesic-M; Robiflam; Robinaxol; ***Mex.:*** Artridol; Carbafen; Carbager-Plus; Carbamox; Dolocam Plus; Flexamol; Malival Compuesto; Morlan; Remisol-Plus; Retoflam F; Reupat; Robaxifen; Robaxisal; Vengesic†; ***S.Afr.:*** Robaxisal; ***Spain:*** Robaxisal Compuesto; Robaxisal†; ***Turk.:*** Miyorel; ***Venez.:*** Beseroldos; Robaxifen; Robaxisal.

Pridinol Mesilate *(rINNM)*

C-238 (pridinol); Mesilato de pridinol; Pridinol, Mésilate de; Pridinol Mesylate; Pridinoli Mesilas. 1,1-Diphenyl-3-piperidinopropan-1-ol methanesulphonate.

Придинола Мезилат

$C_{20}H_{25}NO,CH_3SO_3H$ = 391.5.
CAS — 511-45-5 (pridinol); 968-58-1 (pridinol hydrochloride); 6856-31-1 (pridinol mesilate).
ATC — M03BX03.
ATC Vet — QM03BX03.



(pridinol)

Profile

Pridinol mesilate is a centrally acting muscle relaxant used in the symptomatic treatment of muscle spasm (p.1887). The usual initial oral dose is 2 to 8 mg three times daily, reduced to 4 to 8 mg daily for maintenance treatment. It is also given by intramuscular injection or rectally, and has been applied in compound topical preparations.

Pridinol has been used as the hydrochloride for its antimuscarinic properties in the management of parkinsonism (p.791).

Preparations

Proprietary Preparations (details are given in Part 3)
Ger.: Myoson; Parks†; ***Hong Kong:*** Konlax†; ***Ital.:*** Lyseen; ***Pol.:*** Polmesilat.

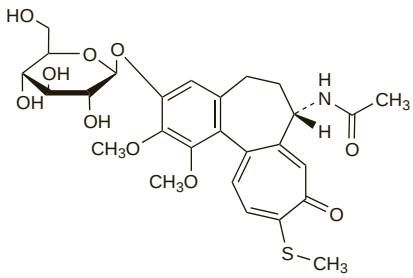
Multi-ingredient: ***Arg.:*** Blokium Flex; Curinflam Plus; Diclogesic Relax; Diclomar Flex; Diclonex Relax; Dioxaflex Plus; Dolvan Flex; Doxtran Flex; Flexidol Relax; Iglodine Flex; Metaflex Plus NF; Mextran Flex; Mio Aldoron NF; Mio-Virobron NF; Nalgiflex Relax; Oxa Sport; Oxadisten; Pancloflex; Rodinac Flex; Silfox Flex; Tomanil Flex; Vesalion Flex; Viartril Flex; Voltaren Flex; Xedenol Flex; ***Ital.:*** Algolisina†.

Thiocolchicoside *(rINN)*

Thiocolchicosidum; Tiocolchicósido; Tiyokolşikozid. 3,10-Di(demethoxy)-3-glucopyranosyloxy-10-methylthiocolchicine.

Тиокольхикозид

$C_{27}H_{33}NO_{10}S$ = 563.6.
CAS — 602-41-5.
ATC — M03BX05.
ATC Vet — QM03BX05.



Pharmacopoeias. In *Fr.*

Profile

Thiocolchicoside is a muscle relaxant that has been claimed to possess GABA-mimetic and glycinergic actions. It is used in the symptomatic treatment of painful muscle spasm (p.1887). The usual initial oral dose is 16 mg daily given in 2 divided doses. It has also been given intramuscularly, in doses up to 8 mg daily, or applied as cream or ointment. Photosensitivity reactions may occur.

Preparations

Proprietary Preparations (details are given in Part 3)
Braz.: Coltrax; Muscoril; ***Cz.:*** Muscoril; ***Fr.:*** Coltramyl; Miorel; Myoplege; ***Gr.:*** Disintryl; Haliver; Klesidren; Musco-ril; Thiacomin†; ***India:*** Myoril; ***Ital.:*** Decontril; Miotens; Muscoflex; Muscoril; Sciomir; Strialisin; Teraside; Ticathion; Tiorilene; Tioside; ***Pol.:*** Muscoril; ***Port.:*** Coltramyl; Relmus; ***Turk.:*** Muscoflex; Muscoril; ***Venez.:*** Biocolchid; Coltrax; Colval; Cosiden†; Eusilen; Lampral; Tiochax; Tractil†.

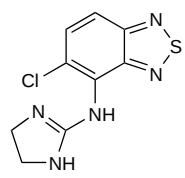
Multi-ingredient: ***Ital.:*** Muscoril Trauma; ***Mex.:*** Neuroflax; ***Port.:*** Adalgur N; Relmus Compositum†; ***Spain:*** Adalgur; ***Venez.:*** Colfene.

Tizanidine Hydrochloride *(BANM, USAN, rINNM)*

AN-021; DS-103-282; DS-103-282-ch; Hidrocloruro de tizanidina; Tizanidine, Chlorhydrate de; Tizanidini Hydrochloridum. 5-Chloro-*N*-(2-imidazolin-2-yl)-2,1,3-benzothiadiazol-4-ylamine hydrochloride.

Тизанидина Гидрохлорид

$C_9H_8ClN_5S,HCl$ = 290.2.
CAS — 51322-75-9 (tizanidine); 64461-82-1 (tizanidine hydrochloride).
ATC — M03BX02.
ATC Vet — QM03BX02.



(tizanidine)

Pharmacopoeias. In *Jpn* and *US.*
USP 31 (Tizanidine Hydrochloride). Store in airtight containers.

Adverse Effects and Precautions

Tizanidine hydrochloride may cause drowsiness; patients affected should not drive or operate machinery. Other adverse effects include dry mouth, fatigue, dizziness or vertigo, muscle pain and weakness, insomnia, anxiety, headache, bradycardia, nausea, and gastrointestinal disturbances. Hallucinations have occurred on rare occasions. Many adverse effects have been found to be dose related and slow titration of doses appears to reduce the frequency of occurrence. Hypotension may occur.

Increases in liver enzymes and rarely acute hepatitis have been associated with tizanidine and it is contra-indicated in patients with severe hepatic dysfunction. In the UK it is recommended that liver function should be monitored monthly in all patients for the first 4 months and in those who develop symptoms suggestive of hepatic dysfunction; similarly, in the USA baseline assessment and monitoring at 1, 3, and 6 months is advised. Treatment should be stopped if liver enzymes are persistently raised.

Caution is required in the elderly and in patients with renal insufficiency.

Interactions

Tizanidine is metabolised by the cytochrome P450 isoenzyme CYP1A2 and use with ciprofloxacin or fluvoxamine, both potent inhibitors of this isoenzyme, is contra-indicated. Use with other more moderate inhibitors of CYP1A2 (such as other quinolone antibacterials, cimetidine, and antiarrhythmics such as amiodarone, mexiletine, propafenone, and verapamil) should be avoided unless clinically necessary. The CNS effects of tizanidine may be enhanced by alcohol or other CNS depressants. There may be an additive hypotensive effect when tizanidine is used in patients receiving antihypertensive therapy; bradycardia may also be enhanced if given with beta blockers or digoxin. Caution should be exercised when tizanidine is given with drugs known to increase the QT interval. The clearance of tizanidine has been reported to be lower in women receiving hormonal contraceptives.

Antibacterials. In a study of healthy subjects,[1] *ciprofloxacin*, an inhibitor of the cytochrome P450 isoenzyme CYP1A2, was reported to elevate the plasma concentrations of tizanidine thereby potentiating its hypotensive and sedative effects.

1. Granfors MT, *et al.* Ciprofloxacin greatly increases concentrations and hypotensive effect of tizanidine by inhibiting its cytochrome P450 1A2-mediated presystemic metabolism. *Clin Pharmacol Ther* 2004; **76:** 598–606.

Antidepressants. In a study[1] in 10 healthy subjects, *fluvoxamine*, a potent inhibitor of the cytochrome P450 isoenzyme CYP1A2, was reported to increase tizanidine's peak plasma concentrations and elimination half-life 12-fold and 3-fold, respectively. An increased incidence of adverse effects associated with tizanidine such as hypotension, bradycardia, drowsiness, and dizziness was noted in these subjects.

A 70-year-old woman receiving fluvoxamine 150 mg daily and other medications developed bradycardia, dry mouth, urinary retention, and a low body temperature when given tizanidine 3 mg daily;[2] the patient improved when tizanidine was stopped. In a retrospective survey of medical records, the authors reported adverse effects associated with tizanidine in 6 of 23 patients also receiving fluvoxamine.

1. Granfors MT, *et al.* Fluvoxamine drastically increases concentrations and effects of tizanidine: a potentially hazardous interaction. *Clin Pharmacol Ther* 2004; **75:** 331–41.
2. Momo K, *et al.* Drug interaction of tizanidine and fluvoxamine. *Clin Pharmacol Ther* 2004; **76:** 509–10.

Antiepileptics. For reference to an interaction between tizanidine and *phenytoin*, see p.500.

Cardiovascular drugs. Severe hypotension, occurring 2 hours after treatment with tizanidine, has been reported in a patient receiving antihypertensives, including *lisinopril*, and other medications.[1] The patient improved after tizanidine and antihypertensives were stopped; they were later resumed without lisinopril, and caused no problems.

1. Kao C-D, *et al.* Hypotension due to interaction between lisinopril and tizanidine. *Ann Pharmacother* 2004; **38:** 1840–3.

Oral contraceptives. Mean peak plasma concentrations after a single 4-mg dose of tizanidine were 3 times greater in 15 women using an oral contraceptive containing *ethinylestradiol* and *gestodene* than in controls;[1] the elimination half-life was not, however, significantly different. The effect appeared to be due to inhibition of the cytochrome P450 isoenzyme CYP1A2 by the contraceptive, resulting in reduced presystemic metabolism of tizanidine. Because the therapeutic range of tizanidine is narrow, care should be exercised if it is given to patients taking oral contraceptives.

1. Granfors MT, *et al.* Oral contraceptives containing ethinyl estradiol and gestodene markedly increase plasma concentrations and effects of tizanidine by inhibiting cytochrome P450 1A2. *Clin Pharmacol Ther* 2005; **78:** 400–11.

Pharmacokinetics

Tizanidine is well absorbed from the gastrointestinal tract and peak plasma concentrations occur about 1 to 2 hours after oral doses. It is about 30% bound to plasma proteins. Tizanidine undergoes extensive first-pass metabolism in the liver mainly via the cytochrome P450 isoenzyme CYP1A2 and is excreted mainly in the urine as inactive metabolites. Elimination half-lives of 2 to 4 hours have been reported.