3. Krause T, *et al.* Dantrolene—a review of its pharmacology, therapeutic use and new developments. *Anaesthesia* 2004; **59:** 364–73.
4. Wedel DJ, *et al.* Clinical effects of intravenously administered dantrolene. *Mayo Clin Proc* 1995; **70:** 241–6.
5. Litman RS, Rosenberg H. Malignant hyperthermia: update on susceptibility testing. *JAMA* 2005; **293:** 2918–24.
6. Rosenberg H, Gronert GA. Intractable cardiac arrest in children given succinylcholine. *Anesthesiology* 1992; **77:** 1054.

Neuroleptic malignant syndrome. Dantrolene has been used, usually alone or with bromocriptine, in the treatment of neuroleptic malignant syndrome (p.972), although some workers have not found it to be of use,[1] and evidence from controlled trials is lacking.[2] Doses reported for dantrolene have varied greatly.[3,4] For those patients unable to swallow and when rapid control of symptoms is required, doses of 1 mg/kg or more have been given initially by intravenous injection. Up to 600 mg has been given daily by mouth in divided doses.

1. Rosebush PI, *et al.* The treatment of neuroleptic malignant syndrome: are dantrolene and bromocriptine useful adjuncts to supportive care? *Br J Psychiatry* 1991; **159:** 709–12.
2. Krause T, *et al.* Dantrolene—a review of its pharmacology, therapeutic use and new developments. *Anaesthesia* 2004; **59:** 364–73.
3. Ward A, *et al.* Dantrolene: a review of its pharmacodynamic and pharmacokinetic properties and therapeutic use in malignant hyperthermia, the neuroleptic malignant syndrome and an update of its use in muscle spasticity. *Drugs* 1986; **32:** 130–68.
4. Harpe C, Stoudemire A. Aetiology and treatment of neuroleptic malignant syndrome. *Med Toxicol* 1987; **2:** 166–76.

Tetanus. Dantrolene has effectively controlled muscle spasms in the treatment of tetanus (see p.1901). It has also been used as an adjunct[1] to neuromuscular blockade; there are conflicting reports[2,3] of its value in avoiding mechanical ventilation.

1. Tidyman M, *et al.* Adjunctive use of dantrolene in severe tetanus. *Anesth Analg* 1985; **64:** 538–40.
2. Checketts MR, White RJ. Avoidance of intermittent positive pressure ventilation in tetanus with dantrolene therapy. *Anaesthesia* 1993; **48:** 969–71.
3. Possamai C, *et al.* Dantrolene infusion in severe tetanus. *Anaesthesia* 1997; **52:** 610.

Preparations

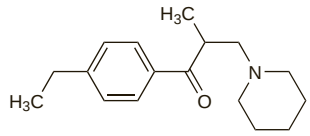
BP 2008: Dantrolene Oral Suspension;
USP 31: Dantrolene Sodium Capsules; Dantrolene Sodium for Injection.

Proprietary Preparations (details are given in Part 3)
Austral.: Dantrium; ***Belg.:*** Dantrium; ***Braz.:*** Dantrolen; ***Canad.:*** Dantrium; ***Chile:*** Dantrium; ***Denm.:*** Dantrium; ***Fr.:*** Dantrium; ***Ger.:*** Dantamacrin; ***Gr.:*** Dantrium; Dantrolen; ***Hong Kong:*** Dantrium†; ***Irl.:*** Dantrium; ***Israel:*** Dantrium; ***Ital.:*** Dantrium; ***Neth.:*** Dantrium; ***NZ:*** Dantrium; ***Port.:*** Dantrium†; ***S.Afr.:*** Dantrium; ***Switz.:*** Dantamacrin; ***UK:*** Dantrium; ***USA:*** Dantrium.

Eperisone Hydrochloride *(rINNM)*

Épérisone, Chlorhydrate d'; Eperisoni Hydrochloridum; Hidrocloruro de eperisona. 4′-Ethyl-2-methyl-3-piperidinopropiophenone hydrochloride.

Эперизона Гидрохлорид
$C_{17}H_{25}NO,HCl$ = 295.8.
CAS — 64840-90-0 (eperisone); 56839-43-1 (eperisone hydrochloride).



(eperisone)

Pharmacopoeias. In *Jpn.*

Profile
Eperisone is a centrally acting skeletal muscle relaxant that has been used in the symptomatic treatment of muscle spasm (p.1887) and spasticity (p.1887). It may also have a vasodilator action. Eperisone hydrochloride has been given by mouth in usual doses of 50 mg three times daily after food.

Effects on the skin. A non-pigmenting fixed drug eruption developed in a 42-year-old woman after taking oral diclofenac sodium and eperisone hydrochloride.[1] There was no residual hyperpigmentation and the rash and accompanying itching and burning sensation resolved within 7 days after stopping both drugs. On rechallenge with eperisone, an erythematous plaque developed at the same site within a couple of hours. The lesion disappeared within 5 days with no sequelae.

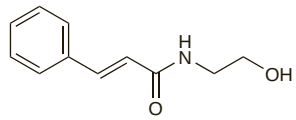
1. Choonhakarn C. Non-pigmenting fixed drug eruption: a new case due to eperisone hydrochloride. *Br J Dermatol* 2001; **144:** 1288–9.

Preparations
Proprietary Preparations (details are given in Part 3)
Indon.: Eprinoc; Epsonal; Forelax; Forres; Myonal; Myonep; Myori; Permyo; Rizonax; Zonal; ***Jpn:*** Myonal; ***Malaysia:*** Myonal; ***Philipp.:*** Myonal; ***Singapore:*** Myonal; ***Thai.:*** Myonal.

Idrocilamide *(rINN)*

Idrocilamida; Idrocilamidum; LCB-29. *N*-(2-Hydroxyethyl)cinnamamide.

Идроциламид
$C_{11}H_{13}NO_2$ = 191.2.
CAS — 6961-46-2.



Adverse Effects
When given by mouth idrocilamide was reported to produce abdominal pain, nausea, and drowsiness. Excitement, euphoria and hallucinations, and depression may occur.

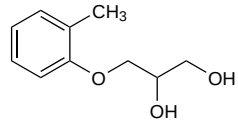
Uses and Administration
Idrocilamide is a centrally acting muscle relaxant. It is reported to have local muscle relaxant and anti-inflammatory effects and is now mainly used topically.

Preparations
Proprietary Preparations (details are given in Part 3)
Belg.: Srilane; ***Fr.:*** Srilane; ***Hong Kong:*** Srilane†; ***Switz.:*** Talval.

Mephenesin *(BAN, rINN)*

Cresoxydiol; Glykresin; Mefenesiini; Mefenesin; Mefenesina; Méphénésine; Mephenesinum. 3-(*o*-Tolyloxy)propane-1,2-diol.

Мефенезин
$C_{10}H_{14}O_3$ = 182.2.
CAS — 59-47-2.
ATC — M03BX06.
ATC Vet — QM03BX06.



NOTE. The name tolynol has been applied to both mephenesin and *p*,α-dimethylbenzyl alcohol (p.2294).

Pharmacopoeias. In *It.*

Profile
Mephenesin is a centrally acting skeletal muscle relaxant used for the symptomatic treatment of painful muscle spasm (p.1887) associated with musculoskeletal conditions. Its clinical usefulness is considered to be limited by its brief duration of action. It is given orally in doses of 1.5 to 3 g daily in divided doses. It is also applied topically, usually with rubefacients.

Porphyria. Mephenesin is considered to be unsafe in patients with porphyria because it has been shown to be porphyrinogenic in *in-vitro* systems.

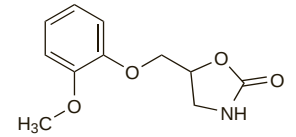
Preparations
Proprietary Preparations (details are given in Part 3)
Fr.: Decontractyl; ***Ger.:*** DoloVisano M.

Multi-ingredient: ***Belg.:*** Algipan; ***Fr.:*** Algipan; Decontractyl; Traumalgyl; ***India:*** Acks; Flamar; Inflazone; Medicreme; Relaxyl; ***Ital.:*** Relaxar; ***S.Afr.:*** Spasmend.

Mephenoxalone *(rINN)*

AHR-233; Mefenoksalon; Mefenoxalona; Méphénoxalone; Mephenoxalonum; Methoxadone; OM-518. 5-(2-Methoxyphenoxymethyl)oxazolidin-2-one.

Мефеноксалон
$C_{11}H_{13}NO_4$ = 223.2.
CAS — 70-07-5.
ATC — N05BX01.
ATC Vet — QN05BX01.



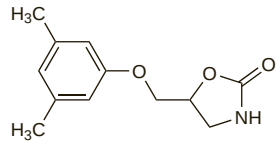
Profile
Mephenoxalone has actions similar to those of meprobamate (p.1006). It has been given orally in a dose of 200 to 400 mg three times daily as a muscle relaxant in the treatment of muscle spasm (p.1887). It has also been given for the treatment of anxiety.

Preparations
Proprietary Preparations (details are given in Part 3)
Cz.: Dimexol; Dorsiflex; ***Neth.:*** Dorsiflex; ***Turk.:*** Dorsiflex.
Multi-ingredient: ***Turk.:*** Dorsilon.

Metaxalone *(BAN, USAN, rINN)*

AHR-438; Metaxalona; Métaxalone; Metaxalonum. 5-(3,5-Xylyloxymethyl)oxazolidin-2-one.

Метаксалон
$C_{12}H_{15}NO_3$ = 221.3.
CAS — 1665-48-1.



Adverse Effects, Treatment, and Precautions
As for Chlorzoxazone, p.1895.

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

Patients taking metaxalone excrete in the urine a metabolite which gives a false positive reaction to copper sulfate-based tests for glycosuria.

Interactions
The CNS effects of metaxalone may be enhanced by alcohol and other CNS depressants.

Pharmacokinetics
Metaxalone is absorbed from the gastrointestinal tract, metabolised in the liver, and excreted in urine as metabolites. The plasma elimination half-life is about 2 to 3 hours.

Uses and Administration
Metaxalone is a centrally acting skeletal muscle relaxant. Its mode of action may be related to its sedative properties.

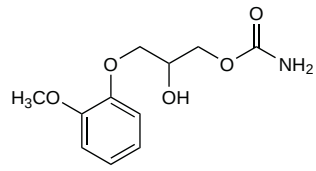
It is used as an adjunct in the symptomatic treatment of painful muscle spasm (p.1887) associated with musculoskeletal conditions. The usual oral dose is 800 mg three or four times daily.

Preparations
Proprietary Preparations (details are given in Part 3)
USA: Skelaxin.

Methocarbamol *(BAN, rINN)*

Guaiphenesin Carbamate; Méthocarbamol; Methocarbamolum; Metocarbamol; Metokarbamol; Metokarbamoli. 2-Hydroxy-3-(2-methoxyphenoxy)propyl carbamate.

Метокарбамол
$C_{11}H_{15}NO_5$ = 241.2.
CAS — 532-03-6.
ATC — M03BA03.
ATC Vet — QM03BA03.



Pharmacopoeias. In *US.*

USP 31 (Methocarbamol). A white powder, odourless or having a slight characteristic odour. M.p. about 94° or, if previously ground to a fine powder, about 90°. Soluble 1 in 40 of water at 20°; sparingly soluble in chloroform; soluble in alcohol only with heating; insoluble in *n*-hexane and in benzene. Store in airtight containers.

Adverse Effects
Adverse effects reported with methocarbamol include nausea, vomiting, anorexia, lightheadedness, dizziness, lassitude, drowsiness, restlessness, anxiety, confusion, tremor, vertigo, blurred vision, fever, headache, convulsions, and hypersensitivity reactions including rashes, pruritus, urticaria, angioedema, and conjunctivitis with nasal congestion.

After injection patients may experience flushing and a metallic taste; incoordination, diplopia, nystagmus, vertigo, syncope, hypotension, bradycardia, and anaphylaxis have been reported. There may be sloughing and thrombophlebitis at the site of injection.

Precautions
Methocarbamol is contra-indicated in coma or pre-coma states, brain damage, myasthenia gravis, or in patients with a history of epilepsy. Caution is advisable in renal or hepatic impairment.

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.

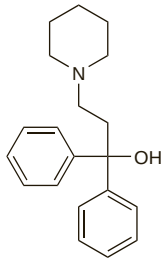
Multi-ingredient: ***Canad.:*** Aspirin Backache; Dodds Back Ease; Methoxacet; Methoxacet-C; Methoxisal; Methoxisal-C; Muscle & Back Pain Relief; Muscle & Back Pain Relief Extra Strength; Muscle & Back Pain Relief-8; Muscle Relaxant and Analgesic†; Obusforme†; Relaxophen; Robax Platinum; Robaxacet; Robaxacet-8; 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.

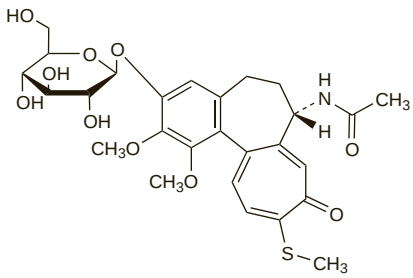
Multi-ingredient: ***Arg.:*** Blokium Flex; Curinflam Plus; Diclogesic Relax; Diclomar Flex; Diclonex Relax; Dioxaflex Plus; Dolvan Flex; Doxtran Flex; Flexidol Relax; Iglodine Flex; Metaflex Plus NF; Mextran Flex; Mio Aldoron NF; Mio-Virobron NF; Nalgiflex Relax; Oxa Sport; Oxadisten; Pancloflex; Rodinac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

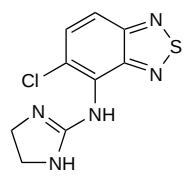
Multi-ingredient: ***Ital.:*** Muscoril Trauma; ***Mex.:*** Neuroflax; ***Port.:*** Adalgur N; Relmus Compositum†; ***Spain:*** Adalgur; ***Venez.:*** Colfene.

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.