- Götrick B, et al. Oral pilocarpine for treatment of opioid-in-duced oral dryness in healthy adults. J Dent Res 2004; 83: 393-7.
- Nelson JD, et al. Oral pilocarpine for symptomatic relief of keratoconjunctivitis sicca in patients with Sjögren's syndrome. Adv Exp Med Biol 1998; 438: 979–83.
- Nino FB, et al. Pilocarpine tablets for the treatment of dry mouth and dry eye symptoms in patients with Sjögren syndrome: a randomized, placebo-controlled, fixed-dose, multi-center trial. Arch Intern Med 1999; 159: 174–81.
- center trial. Areh Intern Med 1999; 159: 174–81.

  9. Tsifetaki N, et al. Oral pilocarpine for the treatment of ocular symptoms in patients with Sjögren's syndrome: a randomised 12 week controlled study. Ann Rheum Dis 2003; 62: 1204–7.

  10. Baudouin C, et al. Traitements actuels de la xérophtalmie dans
- le syndrome de Gougerot-Sjögren. Rev Med Interne 2004; 25: 376-82.

Reversal of mydriasis. Pilocarpine has been used to reverse the effects of mydriatics after surgery or ophthalmoscopic examination but other miotics may be preferred (see p.1874). It counteracts the mydriatic effects of sympathomimetics, such as phenylephrine and hydroxyamfetamine,1 but is ineffective against mydriasis produced by antimuscarinics, such as homatropine, <sup>1</sup> and may impair vision further when used with tropicamide. <sup>2</sup> Furthermore, there is also the risk of pilocarpine precipitating angleclosure glaucoma in susceptible patients (see Glaucoma, under Precautions, above and also Glaucoma, in Tropicamide, p.1886).

- Anastasi LM, et al. Effect of pilocarpine in counteracting my-driasis. Arch Ophthalmol 1968; 79: 710–15.
- Nelson ME, Orton HP. Counteracting the effects of mydriatics: does it benefit the patient? Arch Ophthalmol 1987; 105: 486–9.

## **Preparations**

BP 2008: Pilocarpine Hydrochloride Eye Drops; Pilocarpine Nitrate Eye

USP 31: Pilocarpine Hydrochloride Ophthalmic Solution: Pilocarpine Nitrate Ophthalmic Solution; Pilocarpine Ocular System

Proprietary Preparations (details are given in Part 3)

Proprietary Preparations (details are given in Part 3)
Arg.: Alvis†, Gel Carpina†, Isopto Carpina; Klonocarpina†, Omaclopi!, Pilocarpin; Alvis†, Gel Carpina†, Isopto Carpina; Klonocarpina†, Omaclopi!, Pilocarpin; Pilomet, Sonadry!, Tensicacay. Weto!, Xao Pil; Austrad.: Isopto Carpine; Pilopt; PV Carpine; Austrad: Pilocarpin Puroptal; Salagen; Belg.: Isopto Carpine; Pilo; Salagen; Brazz.: Isopto Carpine; Pilocarpi. Pilocarpin; Pilocarpine; Pilocarpis; Piloca sert†; Pilocar; Pilopine HS; Piloptic; Pilopto-Carpine; Pilostat; Salagen; **Venez.:** Isopto Carpina†; Pilocar.

ez.: Isopto Carpina†; Pilocar:

Multi-Ingredient: Arg.: Amplus; Glaucocin†; Glaucotensil; Ofal P†; Pilotim; Timpilo†; Austral: Timpilo; Austrai: Betacarpin; Fotil; Normastigmin mit Pilocarpin; Pilotigmin Puroptal; Thiloadren; Timpilo†; Belg.: Carteopil; Normoglaucon; Canad.: Timpilo†; Ez.: Fotil; Glauko Biciron†; Ipecarin†; Timpilo†; Denm.: Fotil; Timpilo†; Fin.: Fotil; Timpilo†; Fin.: Fotil; Timpilo†; Fin.: Fotil; Timpilo†; Fin.: Fotil; Glauko Biciron; Normoglaucon; Syncarpin-N+†riloadren N; Timpilo†; TP-Ophtal; Gr.: Dropiltim; Fotil†; Ripsk; Ryvina†; T+P, Thilocombin†; Timpilo†, Yano; Hong Kong: Timpilo; Hung.: Fotil; Ndai: Bi-Hilotic; Israel: Timpilo; Nano; Hong Kong: Timpilo; Hung.: Fotil; Ndai: Bi-Hilotic; Israel: Timpilo†; Timpilo†; Neth.: Fotil; Normoglaucon; Norw.: Fotil; Timpilo†; Timpilo†; Neth.: Fotil; Normoglaucon; Port.: Fotil; Normoglaucon; Timpilo†; Swed.: Fotil; Tim

## Travoprost (BAN, USAN, rINN)

AL-6221; Travoprosti; Travoprostum. Isopropyl (Z)-7-fluoro-m-tolyl)oxy]-I-butenyl}cyclopentyl)-5-heptenoate.

Травопрост

 $C_{26}H_{35}F_3O_6 = 500.5.$ CAS — 157283-68-6. ATC — S01EE04. ATC Vet - QS01EE04.

## Adverse Effects and Precautions

As for Latanoprost, p.1882.

**Effects on the eyes.** Severe iritis and corneal oedema developed in an elderly woman 3 weeks after restarting travoprost after eye surgery; rechallenge was positive. The authors commented that the UK MHRA was aware of one other case of uveitis associated with travoprost.

Kumarasamy M, Desai SP. Anterior uveitis is associated with travoprost. BMJ 2004; 329: 205.

#### **Uses and Administration**

Travoprost is a synthetic analogue of dinoprost (prostaglandin  $F_2$ ). It is used in the treatment of open-angle glaucoma and ocular hypertension (p.1873), as a 0.004% ophthalmic solution once daily, preferably in the evening. The reduction in pressure starts about 2 hours after instillation and is maximal after 12 hours; the effect is maintained for at least 24 hours.

#### **Preparations**

Proprietary Preparations (details are given in Part 3)
Arg.: Arvo, Glaucoprost, Travatan, Austral.: Iravatan, Austria: Travatan, Belg.: Iravatan, Braz.: Travatan, Canad.: Travatan, Chile: Travatan, Canad.: Travatan, Chile: Travatan, Canad.: Travatan, Gr.: Travatan, Gr.: Travatan, Hong Kong: Travatan, Hung.: Travatan, Hong. Travatan, Hong. Travatan, Hong.: Travatan, Hong.: Travatan, Soad: Travatan, Mex.: Travatan, Not.: Travatan, Not.: Travatan, Philipp.: Travatan, Phil: Travatan, Port.: Travatan, Rus.: Travatan (Tpasaran), S.Afr.: Travatan, Sapopore: Travatan, Spain: Travatan, Gravatan, Surv.: Travatan, Surv.: Travatan, Thai:: Travatan, Turk.: Travatan, UK: Travatan, USA: Travatan, Thai:: Travatan, Turk.: Travatan, UK: Travatan, USA: Travatan, US

Multi-ingredient: Cz.: DuoTrav; Gr.: DuoTrav; Hung.: DuoTrav; NZ: DuoTrav; Pol.: DuoTrav; Port.: DuoTrav; UK: DuoTrav.

## **Tropicamide** (BAN, USAN, rINN)

Bistropamide; Ro-1-7683; Tropicamida; Tropicamidum; Tropika-Tropikamidas; Tropikamidi. N-Ethyl-N-(4-pyridylmethyl)tropamide; (2RS)-N-Ethyl-3-hydroxy-2-phenyl-N-(pyridin-4ylmethyl)propanamide.

Тропикамид

 $C_{17}H_{20}N_2O_2 = 284.4.$ CAS — 1508-75-4.

ATC — SOIFA06.

ATC Vet - QS01FA06.

NOTE. TRO is a code approved by the BP 2008 for use on single unit doses of eye drops containing tropicamide where the indi-vidual container may be too small to bear all the appropriate labelling information.

Pharmacopoeias. In Chin., Eur. (see p.vii), Int., Jpn, and US. Ph. Eur. 6.2 (Tropicamide). A white or almost white, crystalline powder. M.p. 95° to 98°. Slightly soluble in water; freely soluble in alcohol and in dichloromethane. Protect from light.

USP 31 (Tropicamide). A white or practically white crystalline powder, odourless or having not more than a slight odour. M.p. 96° to 100°. Slightly soluble in water; freely soluble in chloroform and in solutions of strong acids. Store in airtight containers. Protect from light.

# Adverse Effects, Treatment, and Precau-

As for Atropine Sulfate, p.1219.

1. Vuori M-L, et al. Systemic absorption and anticholinergic activity of topically applied tropicamide. J Ocul Pharmacol 1994; 10: 431–7.

Glaucoma. The use of mydriatics is considered liable to provoke an acute attack in patients with glaucoma or a tendency to glaucoma; licensed product information generally contra-indicates their use in such patients. However, a systematic review concluded that in fact a history of open-angle glaucoma did not predispose to acute angle closure under mydriasis, and that mydriasis with tropicamide in particular appeared to be safe and should be recommended in all patients when thorough retinal examination was indicated.1 In contrast, the use of pilocarpine to reverse mydriatics was potentially harmful.

Pandit RJ, Taylor R. Mydriasis and glaucoma: exploding the myth. A systematic review. *Diabet Med* 2000; 17: 693–9.

## Interactions

As for antimuscarinics in general (see Atropine Sulfate, p.1220).

## **Uses and Administration**

Tropicamide is a tertiary amine antimuscarinic with actions similar to those of atropine (p.1219). It is used as eye drops to produce mydriasis and cycloplegia (p.1874). It has a more rapid onset and a shorter duration of effect than atropine: mydriasis is produced within 20 to 40 minutes of use and usually lasts for

about 6 hours; cycloplegia is maximal within about 30 minutes and is short-lasting, with complete recovery of accommodation normally within 6 hours. Tropicamide has been reported to be inadequate for cycloplegia in

To produce **mydriasis**, a 0.5% solution is instilled 15 to 20 minutes before examination of the eve. To produce cycloplegia a 1% solution is used and repeated after 5 minutes; a further instillation may be necessary to prolong the effect after 20 to 30 minutes.

Dementia. Tropicamide has been studied for use in the differential diagnosis of Alzheimer's disease (see Dementia, p.362). Excessive pupil dilatation in response to tropicamide eye drops occurred in patients with signs and symptoms of Alzheimer's disease. However, a double-blind placebo-controlled study in similar patients and healthy subjects indicated that this was not a reliable diagnostic test for Alzheimer's disease.

- 1. Gómez-Tortosa E, et al. Pupil response to tropicamide in Alzheimer's disease and other neurodegenerative disorders. Acta Neu-
- inite s usease and other leadune generative disorders. *Acta Neurol Scand* 1996; **94**: 104–9.

  2. Graff-Radford NR, *et al.* Tropicamide eyedrops cannot be used for reliable diagnosis of Alzheimer's disease. *Mayo Clin Proc* 1997; **72**: 495–504.

## **Preparations**

BP 2008: Tropicamide Eye Drops USP 31: Tropicamide Ophthalmic Solution.

USP 31: Tropicamide Ophthalmic Solution.

Proprietary Preparations (details are given in Part 3)

Arg.: Midriaticum; Mydril; Austral: Mydriacyl; Austria: Mydral; Mydral; Mydriaticum; Belg:: Mydriacyl; Tropicol; Braz.: Ciclomidrin; Mydriacyl; Tropicon; Canda: Diotrope; Mydriacyl; Car.: Mydriacyl; Try, Mydram; Monm.: Mydriacyl; Fr.: Mydriaticum; Ger.: Mydriaticum; Mydrum; Gr.: Tropical; Hong Kong; Mydriaticum; Ger.: Mydriacyl; Mydram; Mydrum; India: Tropimi; Visumidratic, Malaysic: Mydriacyl; Mex.: Myriacyl; Norw.: Mydriary; Mydriaticum; Millipp.: Mydriacyl; Mex.: Mydriacyl; Norw.: Mydriacyl; Mydriaticum; Tropimi; Visumidratic, Malaysic: Mydriacyl; Mex.: Mydriacyl; Mydriaticum; Tropimi; Mydriam; NZ: Mydriacyl; Mydriam; NZ: Mydriacyl; Mydriam; NZ: Mydriacyl; Mydriaticum; Tropic: Mydriacyl; Mydriaticum; Tropic. Mydriacyl; Turk.: Tropamid; UK: Mydriacyl; USA: Mydriak; Mydriacyl; Ocu-Tropic Opticyl; Tropicacyl; Memz.: Mydriacyl; Mydriacyl; Dionhe-Multi-ingredient: Are; Fotometin; Sensu: Tropical F; Canda; Dionhe-

Multi-ingredient: Arg.: Fotorretin; Sensu; Tropioftal F; Canad.: Diophenyl-T; Fr.: Mydriasert; Hong Kong: Mydrin-P; India: Itrop Plus; Tropico Plus; Ital.: Visumidriatic Fenilefrina; Philipp.: Sanmyd-P; Port.: Mydriasert; USA: Paremyd; Venez.: Dyfrin†; Fotorretin.

## Unoprostone Isopropyl (dNNM)

Isopropyl Lunoprostone; Isopropyl Unoprostone; UF-021; Unoprostona de isopropilo; Unoprostone, Isopropyle d'; Unoprostoni Isopropylas. Isopropyl (+)-(Z)-7-[(1R,2R,3R,5S)-3,5-Dihydroxy-2-(3-oxodecyl)cyclopentyl]-5-heptenoate.

Унопростона Изопропил

 $C_{25}H_{44}O_5 = 424.6$ . CAS — 120373-36-6 (unoprostone); 120373-24-2 (unoprostone isopropyl). ATC — SOIĖEÖŹ

ATC Vet — QS01EE02.

## **Profile**

Unoprostone, like latanoprost (p.1882), is a synthetic analogue of dinoprost (prostaglandin  $F_2$  ). It is used as the isopropyl ester for the treatment of glaucoma and ocular hypertension (p.1873). An ophthalmic solution containing unoprostone isopropyl 0.12 or 0.15% is instilled twice daily.

- 1. Yamamoto T, et al. Clinical evaluation of UF-021 (Rescula; isopropyl unoprostone). Surv Ophthalmol 1997; 41 (suppl 2): S99-S103.
- S99-S103.
   Eisenberg DL, Camras CB. A preliminary risk-benefit assessment of latanoprost and unoprostone in open-angle glaucoma and ocular hypertension. *Drng Safety* 1999; 20: 505-14.
   de Arruda Mello PA, et al. Safety of unoprostone isopropyl as mono- or adjunctive therapy in patients with primary open-angle glaucoma or ocular hypertension. *Drng Safety* 2002; 25: 583-97.
   Chiba T, et al. Comparison of iridial pigmentation between latanoprost and isopropyl unoprostone: a long term properties.
- Linua 1, et al. Comparison of iridial pigmentation between latanoprost and isopropyl unoprostone: a long term prospective comparative study. Br J Ophthalmol 2003; 87: 956–9.
   Stewart WC, et al. The safety and efficacy of unoprostone 0.15% versus brimonidine 0.2%. Acta Ophthalmol Scand 2004; 82: 161–5.

## **Preparations**

Proprietary Preparations (details are given in Part 3)
Arg.: Rescula; Austria: Rescula: Braz.: Rescula: Chile: Rescula: Cz.: Rescula; Hung.: Rescula: Chile: Rescula: Philipp.: Philipp.: Rescula: Philipp.: Rescula: Philipp.: Rescula: Philipp. cula†; Venez.: Rescula.

## Muscle Relaxants

The muscle relaxants included in this chapter are used in the management of musculoskeletal and neuromuscular disorders. There are 2 main types:

- · centrally acting relaxants—these generally have a selective action on the CNS and are principally used for relieving painful muscle spasms or spasticity occurring in musculoskeletal and neuromuscular disorders. Their mechanism of action may be due to their CNS-depressant activity. Baclofen and tizanidine are two examples.
- directly acting relaxants—dantrolene is a drug that has a direct action on skeletal muscle and is used for the relief of spasticity associated with a variety of conditions.

Also included in this chapter are botulinum toxins A and B, which inhibit the release of acetylcholine at the motor nerve terminals.

Some benzodiazepines are also used in the treatment of muscle spasms; further details may be found under Diazepam, p.986.

Other drugs that block transmission at the neuromuscular junction and are used as adjuncts to general anaesthesia are discussed in the chapter on Neuromuscular Blockers, p.1900.

Drugs used to relax *smooth muscle* include the various antispasmodics (p.1692) used for their antimuscarinic or direct smooth-muscle relaxant effects in the management of gastrointestinal disorders, as well as some other drugs such as papaverine (p.2191).

### Muscle spasm

Spasm is a painful involuntary contraction of muscle that can cause involuntary movement, interfere with function, and cause distortion. It is a symptom of many muscular and other types of disorders and treatment should primarily be aimed at the underlying cause. Centrally acting muscle relaxants and benzodiazepines are used to treat muscle spasms such as splinting that occur in response to local trauma or musculoskeletal and joint disorders. Splinting is a reflex muscular spasm that produces muscular rigidity and acts as a protective mechanism to prevent movement and further damage of the affected part. Short courses of muscle relaxants may be considered in the management of acute low back pain (p.7).

Cramps are muscle spasms of abrupt onset that occur at rest and usually last for a few seconds or minutes. They are often precipitated by dehydration and hyponatraemia produced by vigorous exercise, excessive sweating, diarrhoea, and vomiting, or may be associated with drug therapy or haemodialysis (see Haemodialysis-induced Cramp, p.1671). Pregnant women, the elderly, and those with peripheral vascular disease, appear to be particularly susceptible to night cramps of the feet or legs, the cause of which is not well understood.

The management of muscle cramps has been reviewed.<sup>1,2</sup> Quinine has traditionally been used for *nocturnal cramps* but there has been concern over its efficacy and potential for adverse effects, especially in the elderly. Metaanalyses<sup>3,4</sup> have indicated that although quinine was modestly effective in the treatment of nocturnal cramps in ambulatory patients the risk of serious adverse effects should be borne in mind; patients should be closely monitored over a period of at least 4 weeks while the efficacy of quinine was assessed. In the UK, it is recommended that treatment should be stopped every 3 months to see whether it is still needed.<sup>5</sup> In the USA, the FDA has ruled that quinine products should no longer be used for the management of nocturnal cramps.<sup>6,7</sup> There is little convincing evidence to support the use of other drugs. 1,2,6

A systematic review<sup>8</sup> concluded that magnesium (as the lactate and citrate) is modestly effective in the treatment of leg cramps in pregnancy; calcium salts were ineffective, and although early evidence suggested benefit with sodium chloride, high doses were required with their attendant cardiovascular risks.

- 1. McGee SR. Muscle cramps. Arch Intern Med 1990; 150: 511-18.
- Butler JV, et al. Nocturnal leg cramps in older people. Postgrad Med J 2002; 78: 596–8.
- 3. Man-Son-Hing M, Wells G. Meta-analysis of efficacy of quinine for treatment of nocturnal leg cramps in elderly people. BMJ 1995: 310: 13-17
- 4. Man-Son-Hing M, et al. Quinine for nocturnal leg cramps: a meta-analysis including unpublished data. J Gen Intern Med 1998; 13: 600-606.
- 5. Anonymous. Quinine for nocturnal leg cramps? Drug Ther Bull 1996; 34: 7-8
- 6. FDA. Drug products for the treatment and/or prevention of nocturnal leg muscle cramps for over-the-counter human use. Fed Regist 1994; **59:** 43234–52.
- 7. Nightingale SL. Quinine for nocturnal leg cramps. ACP J Club 1995; 123: 86.
- 8. Young GL, Jewell D. Interventions for leg cramps in pregnancy. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2002 (accessed 16/06/05).

### Spasticity

The term spasticity has been loosely applied to various disorders of motor control resulting from CNS disease and marked by effects such as increased muscle tone, exaggerated stretch reflexes, impaired voluntary movement, weakness, loss of dexterity, abnormal posture, and often disturbed gait. In some patients muscle spasm and pain may be more distressing than impaired movement. Other complications may include contractures, pressure sores, and infection. Spasticity is a feature of neurological conditions such as multiple sclerosis, cerebral palsy, head injury, and stroke, particularly if there are spinal lesions.

Spasticity is disabling and difficult to treat when severe, but mild or moderate forms may be effectively managed by conservative treatment. Some patients may even use spasticity to provide a means of posture control and care should be taken that treatment does not lead to increased

Various discussions on the management of spasticity have been published.  $^{1-10}$  The mainstay of management is physiotherapy with antispastic drugs, although the evidence for the latter is rather scanty. <sup>9,11,12</sup> Baclofen, dantrolene, diazepam, and tizanidine are the drugs most often used. These 4 drugs act via different mechanisms, which are not fully understood.

Baclofen is thought to act at the spinal cord level but may also have supraspinal sites of action. It is a powerful neuronal depressant and may exert its inhibitory effects by acting as an agonist at GABA (gamma aminobutyric acid) receptors. Diazepam is also thought to act centrally by enhancing the response to GABA. In contrast, dantrolene acts directly on muscles, possibly by interfering with the release of calcium from muscular sarcoplasmic reticulum needed for contraction. Tizanidine is a centrally acting relaxant and α-adrenergic agonist; it is thought to act at spinal and supraspinal levels by inhibiting the presynaptic activity of excitatory interneurones.7 It can produce additive effects with baclofen, allowing a reduction in the dosage of both drugs; use with benzodiazepines is not recommended because of the potential for interactions. All these are usually given by mouth but baclofen may also be given intrathecally in severe chronic spasticity. 10,13,14 Injection directly into the spinal subarachnoid space allows immediate delivery to the site of action in the spinal cord and the use of considerably lower doses than those given orally. It has been reported<sup>15</sup> that some patients receiving long-term intrathecal baclofen treatment have been able to stop their therapy without symptoms of spasticity re-appearing, and that others have been able to reduce the dosage required.

Other drugs that may produce some benefit or are being studied in spasticity include other benzodiazepines, clonidine, gabapentin, and memantine.

Alternative approaches to treatment include nerve blocks using local anaesthetics; they should generally only be used when further muscle relaxation would not increase disability. Chemical neurolysis using alcohol or phenol is only considered when there is intractable continuous pain. Local injections of botulinum A toxin have produced some encouraging results in the management of limb spasticity in post-stroke or spinal injury patients and in children with cerebral palsy;16-18 its temporary effect may be an advantage over chemical neurolysis but the need for regular injections may limit acceptability in children. 16 Systematic reviews<sup>19,20</sup> have found insufficient evidence to support or refute such use in children with cerebral palsy.

Nondrug treatments have included electrical stimulation techniques such as transcutaneous nerve stimulation and dorsal column stimulation; vibration applied to agonist spastic muscles to improve voluntary movement; cooling to decrease afferent inputs from peripheral receptors; and orthopaedic surgery or neurosurgery.

- Young RR. Spasticity: a review. Neurology 1994; 44 (suppl 9): \$12-\$20.
   Ko CK, Ward AB. Management of spasticity. Br J Hosp Med
- 1997; **58**: 400–5.

  3. Kita M, Goodkin DE. Drugs used to treat spasticity. *Drugs*
- 2000; **59:** 487–95.
- Anonymous. The management of spasticity. Drug Ther Bull 2000; 38: 44–6.
- 5. Bhakta BB. Management of spasticity in stroke. Br Med Bull 2000; 56: 476-85
- 6. Burchiel KJ, Hsu FPK. Pain and spasticity after spinal cord injury: mechanisms and treatment. *Spine* 2001; **26** (suppl): S146–S160.
- Ward AB. A summary of spasticity management a treatment algorithm. Eur J Neurol 2002; 9 (suppl 1): 48–52.
- Abbruzzese G. The medical management of spasticity. Eur J Neurol 2002; 9 (suppl 1): 30–4.
- Montané E, et al. Oral antispastic drugs in nonprogressive neu-rologic diseases: a systematic review. Neurology 2004; 63: 1357–63.
- Verrotti A, et al. Pharmacotherapy of spasticity in children with cerebral palsy. Pediatr Neurol 2006; 34: 1–6.
- Taricco M, et al. Pharmacological interventions for spasticity following spinal cord injury. Available in The Cochrane Database of Systematic Reviews; Issue 2. Chichester: John Wiley; 2000 (accessed 16/06/05).
- 12. Shakespeare DT, et al. Anti-spasticity agents for multiple sclerosis. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2003 (accessed 16/06/05).
- 13. McLean BN. Intrathecal baclofen in severe spasticity. Br J Hosp Med 1993; 49: 262-7.
- 14. Anonymous. Intrathecal baclofen for spasticity. *Med Lett Drugs*Ther 1994: 36: 21–2.
- 15. Dressnandt J, Conrad B. Lasting reduction of severe spasticity after ending chronic treatment with intrathecal baclofen. J Neurol Neurosurg Psychiatry 1996; 60: 168–73.
- 16. Neville B. Botulinum toxin in the cerebral palsies. BMJ 1994;
- 17. Fried GW, Fried KM. Spinal cord injury and use of botulinum toxin in reducing spasticity. Phys Med Rehabil Clin N Am 2003; 14: 901-10
- 18. Preiss RA. et al. The effects of botulinum toxin (BTX-A) on spasticity of the lower limb and on gait in cerebral palsy. *J Bone Joint Surg Br* 2003; **85:** 943–8.
- Ade-Hall RA, Moore AP. Botulinum toxin type A in the treat-ment of lower limb spasticity in cerebral palsy. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2000 (accessed 07/05/08).
- 20. Wasiak J. et al. Botulinum toxin A as an adjunct to treatment in wastas 3, et al. Doublind with A as a adjunct treatment the management of the upper limb in children with spastic cerebral palsy. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2004 (accessed 07/05/08).

## Afloqualone (rINN)

Aflocualona; Afloqualonum; HQ-495. 6-Amino-2-fluoromethyl-3-o-tolylquinazolin-4(3H)-one.

Афлоквалон

 $C_{16}H_{14}FN_3O = 283.3.$ CAS — 56287-74-2.

## Pharmacopoeias. In Jpn.

## Profile

Afloqualone is a centrally acting skeletal muscle relaxant that has been given orally for the treatment of muscle spasm associated with musculoskeletal conditions. Photosensitivity reactions have been reported.

## ♦ References.

1. Ishikawa T, *et al.* Photoleukomelanodermatitis (Kobori) induced by afloqualone. *J Dermatol* 1994; **21:** 430–3.