renal impairment (see below). It is unsuitable for the relief of acute bronchospasm or in patients with unstable respiratory disease.

Effects on the heart. A prescription event monitoring study found an excess risk of non-fatal heart failure in elderly patients receiving bambuterol, particularly in the first month of treatment.[1] See also under Salbutamol, p.1131.

1. Martin RM, *et al.* Risk of non-fatal cardiac failure and ischaemic heart disease with long acting β agonists. *Thorax* 1998; **53:** 558–62.

Interactions

As for Salbutamol, p.1132. Bambuterol inhibits plasma cholinesterases and can prolong the action of drugs such as suxamethonium (see Sympathomimetics, under Suxamethonium, p.1912) that are inactivated by these enzymes.

Pharmacokinetics

Nearly 20% of a dose of bambuterol is absorbed from the gastrointestinal tract after oral doses. It is slowly metabolised in the body to its active metabolite, terbutaline; peak terbutaline concentrations are reported to occur about 4 to 7 hours after a dose of bambuterol as tablets. The slow rate at which metabolism occurs determines the prolonged duration of action of bambuterol of at least 24 hours. Hydrolysis of bambuterol is catalysed by plasma cholinesterase; however, bambuterol also inhibits plasma cholinesterase and therefore partly inhibits its own metabolism. For the metabolism and excretion of terbutaline, see p.1139.

◊ References.

1. Sitar DS. Clinical pharmacokinetics of bambuterol. *Clin Pharmacokinet* 1996; **31:** 246–56.
2. Nyberg L, *et al.* Pharmacokinetics of bambuterol in healthy subjects. *Br J Clin Pharmacol* 1998; **45:** 471–8.
3. Bang U, *et al.* Pharmacokinetics of bambuterol in subjects homozygous for the atypical gene for plasma cholinesterase. *Br J Clin Pharmacol* 1998; **45:** 479–84.
4. Ahlström H, *et al.* Pharmacokinetics of bambuterol during oral administration to asthmatic children. *Br J Clin Pharmacol* 1999; **48:** 299–308.
5. Rosenborg J, *et al.* Pharmacokinetics of bambuterol during oral administration of plain tablets and solution to healthy adults. *Br J Clin Pharmacol* 2000; **49:** 199–206.

Uses and Administration

Bambuterol is an inactive prodrug of terbutaline (p.1138), a direct-acting sympathomimetic with mainly beta-adrenergic activity and a selective action on $beta_2$ receptors (a $beta_2$ agonist). It has similar actions to those of salbutamol (p.1133) except that it has a more prolonged duration of action (at least 24 hours). Bambuterol hydrochloride is used as a long-acting bronchodilator for persistent reversible airways obstruction in conditions such as asthma (p.1108). The usual dose is 10 to 20 mg orally once daily at bedtime. Doses may need to be reduced in renal impairment (see below).

Administration in renal impairment. Licensed product information recommends that the initial dose of bambuterol hydrochloride should be halved in patients with renal impairment (glomerular filtration rate less than 50 mL/minute). Further doses should be adjusted according to response.

Asthma. References.

1. Fugleholm AM, *et al.* Therapeutic equivalence between bambuterol, 10 mg once daily, and terbutaline controlled release, 5 mg twice daily, in mild to moderate asthma. *Eur Respir J* 1993; **6:** 1474–8.
2. Gunn SD, *et al.* Comparison of the efficacy, tolerability and patient acceptability of once-daily bambuterol tablets against twice-daily controlled release salbutamol in nocturnal asthma. *Eur J Clin Pharmacol* 1995; **48:** 23–8.
3. Zarkovic JP, *et al.* The Bambuterol Multicentre Study Group. One-year safety study with bambuterol once daily and terbutaline three times daily in 2-12-year-old children with asthma. *Pediatr Pulmonol* 2000; **29:** 424–9.

Preparations

Proprietary Preparations (details are given in Part 3)

Austria: Bambec; ***Braz.:*** Bambec; ***Cz.:*** Bambec†; ***Denm.:*** Bambec; ***Fr.:*** Oxeol; ***Ger.:*** Bambec; ***Hong Kong:*** Bambec†; ***Hung.:*** Bambec†; ***India:*** Bambudil; ***Ital.:*** Bambec†; ***Malaysia:*** Bambec†; ***Norw.:*** Bambec; ***NZ:*** Bambec; ***Philipp.:*** Bambec; ***Singapore:*** Bambec; ***Spain:*** Bambec; ***Swed.:*** Bambec; ***Thai.:*** Bambec; ***UK:*** Bambec.

Multi-ingredient: ***India:*** Montair Plus.

Bamifylline Hydrochloride *(BANM, USAN, rINNM)*

AC-3810; Bamifylline, Chlorhydrate de; Bamifyllini Hydrochloridum; BAX-2739Z; 8102-CB; CB-8102; Hidrocloruro de bamifilina. 8-Benzyl-7-[2-(*N*-ethyl-*N*-2-hydroxyethylamino)ethyl]theophylline hydrochloride.

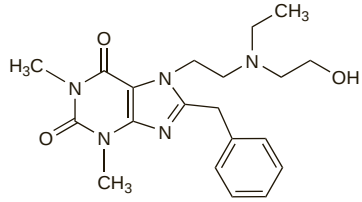
Бамифиллина Гидрохлорид

$C_{20}H_{27}N_5O_3,HCl$ = 421.9.

CAS — 2016-63-9 (bamifylline); 20684-06-4 (bamifylline hydrochloride).

ATC — R03DA08.

ATC Vet — QR03DA08.



(bamifylline)

Profile

Bamifylline hydrochloride is a theophylline derivative (p.1140) that is used for its bronchodilator properties in reversible airways obstruction. It is not converted to theophylline in the body. It is given in usual oral doses of 600 or 900 mg daily in 2 or 3 divided doses. It is also given rectally as suppositories, and by slow intravenous infusion.

Preparations

Proprietary Preparations (details are given in Part 3)

Belg.: Trentadil; ***Braz.:*** Bamifix; ***Fr.:*** Trentadil; ***Ital.:*** Airest†; Bamifix; Bamixol†; Briofil.

Bitolterol Mesilate *(BANM, rINNM)* ⊗

Bitoltérol, Mésilate de; Bitolterol Mesylate *(USAN)*; Bitolteroli Mesilas; Mesilato de bitolterol; Win-32784. 4-[2-(*tert*-Butylamino)-1-hydroxyethyl]-*o*-phenylene di-*p*-toluate methanesulphonate.

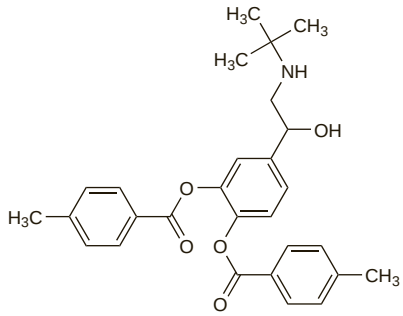
Битолтерола Мезилат

$C_{28}H_{31}NO_5,CH_4O_3S$ = 557.7.

CAS — 30392-40-6 (bitolterol); 30392-41-7 (bitolterol mesilate).

ATC — R03AC17.

ATC Vet — QR03AC17.



(bitolterol)

Profile

Bitolterol is an inactive prodrug that is hydrolysed in the body to colterol, a direct-acting sympathomimetic with mainly beta-adrenergic activity and a selective action on $beta_2$ receptors (a $beta_2$ agonist). It has similar properties to those of salbutamol (p.1131).

It has been used as a bronchodilator in the management of diseases with reversible airways obstruction such as asthma (p.1108) or in some patients with chronic obstructive pulmonary disease (p.1112); inhalation results in the rapid onset of bronchodilatation (2 to 4 minutes) with a duration of action of 5 or more hours.

Bitolterol has been given by inhalation via a metered-dose aerosol supplying 370 micrograms of bitolterol mesilate per inhalation. For the *relief* of bronchospasm the usual adult dose is 2 inhalations (740 micrograms) followed by a third inhalation (370 micrograms) if required. For the *prevention* of bronchospasm the usual adult dose is 2 inhalations (740 micrograms) every 8 hours. Maximum doses have been stated to be 3 inhalations (1110 micrograms) every 6 hours or 2 inhalations (740 micrograms) every 4 hours. In patients with asthma, as-required beta agonist therapy is preferable to regular use. An increased need for, or decreased duration of effect of, bitolterol indicates deterioration of asthma control and the need for review of therapy.

Alternatively, a 0.2% inhalation solution of bitolterol mesilate has been given by nebulisation. Using *continuous flow* nebulisation, the usual adult dose is from 1.5 to 3.5 mg three or four times daily as required, to a maximum daily dose of 14 mg. Using *intermittent flow* nebulisation, the usual adult dose is 0.5 to 2 mg three or four times daily as required, up to a maximum daily dose of 8 mg. In all cases dosage intervals should be greater than or equal to 4 hours.

Preparations

Proprietary Preparations (details are given in Part 3)

USA: Tornalate.

Bufylline *(BAN)*

Ambuphylline *(USAN)*; Bufilina; Theophylline-aminoisobutanol. 2-Amino-2-methylpropan-1-ol theophyllinate.

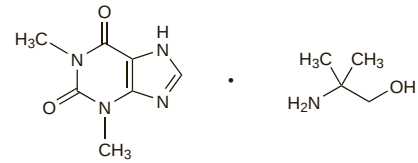
Буфиллин

$C_{11}H_{19}N_5O_3$ = 269.3.

CAS — 5634-34-4.

ATC — R03DA10.

ATC Vet — QR03DA10.



Profile

Bufylline is a theophylline derivative (p.1140) that has been used for its bronchodilator effects as an ingredient of preparations promoted for coughs and other respiratory-tract disorders. The ethiodide has also been used.

Preparations

Proprietary Preparations (details are given in Part 3)

Multi-ingredient: ***Braz.:*** Broncolex†; EMS Expectorante; Revenil; Revenil Dospan; Revenil Expectorante; ***S.Afr.:*** Nethaprin Dospan; Nethaprin Expectorant.

Caffeine *(BAN)*

Anhydrous Caffeine; Cafeína; Caféine; Coffeinum; Guaranine; Kofeiini; Kofein; Kofeina; Kofeinas; Koffein; Methyltheobromine; Théine. 1,3,7-Trimethylpurine-2,6(3*H*,1*H*)-dione; 1,3,7-Trimethylxanthine; 7-Methyltheophylline.

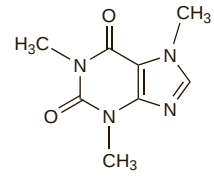
Кофеин

$C_8H_{10}N_4O_2$ = 194.2.

CAS — 58-08-2.

ATC — N06BC01.

ATC Vet — QN06BC01.



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

- Co-bucafAPAP (*PEN*)—butalbital, paracetamol, and caffeine.

Pharmacopoeias. In *Eur.* (see p.vii), *Int.*, *Jpn*, *US*, and *Viet.* Some pharmacopoeias include caffeine and caffeine hydrate under one monograph.

Ph. Eur. 6.2 (Caffeine). A white or almost white, crystalline powder or silky white or almost white crystals. It sublimes readily. Sparingly soluble in water; freely soluble in boiling water; slightly soluble in dehydrated alcohol. It dissolves in concentrated solutions of alkali benzoates or salicylates.

USP 31 (Caffeine). It is anhydrous or contains one molecule of water of hydration. An odourless white powder or white, glistening needles, usually matted together. The hydrate is efflorescent in air. The hydrate is soluble 1 in 50 of water, 1 in 75 of alcohol, 1 in 6 of chloroform, and 1 in 600 of ether. The hydrate should be stored in airtight containers.

Caffeine Citrate *(BANM)*

Cafeína, citrato de; Citrated Caffeine; Coffeinum Citricum.

Кофеина Цитрат

$C_8H_{10}N_4O_2,C_6H_8O_7$ = 386.3.

CAS — 69-22-7.

ATC — N06BC01.

ATC Vet — QN06BC01.