Salbulin†; Venteze; Ventodisk†; Ventolin; Volmax; ***Singapore:*** Airomir†; Azmasol; Butahale; Buto Asma†; Buventol; Medolin; Respolin†; Sabutol†; Salamol†; Salbuair; Salmol; Venderol; Ventolin; Volmax; ***Spain:*** Aldobronquial; Asmasal†; Buto Air; Buto Asma; Emican†; Respiroma; Ventadur; Ventilastin; Ventolin; ***Swed.:*** Airomir; Buventol; Ventoline; ***Switz.:*** Airomir†; Buventol†; Ecovent; Ventodisk; Ventolin; Volmax; ***Thai.:*** Airomir†; Asmasal; Asthmolin†; Butamol; Buto Asma; Butovent; Buventol; Respolin†; Salbusian; Salbutac; Salda; Salmol; Solia; Venterol; Ventolin; Violin; Volmax†; Zebu; ***Turk.:*** Asthavent; Salbulin; Salbutam; Salbutol; Ven-o-sal; Ventodisks; Ventolin; Volmax; ***UAE:*** Butalin; ***UK:*** Airomir; Asmasal; Kentamol†; Pulvinal Salbutamol; Salamol; Salapin; Salbulin; Ventmax; Ventodisks†; Ventolin; Volmax; ***USA:*** Accuneb; ProAir; Proventil; Ventolin; Volmax†; VoSpire; ***Venez.:*** Asthalin; Butahale†; Butoas; Respolin†; Salbulis; Salbumed; Salburol; Salbutan; Ventolin†.

Multi-ingredient: ***Arg.:*** Beclasma; Butocort; Butosol; Combivent; Fatigan Bronquial†; Iprasalb; Salbutol Beclo; Salbutral AC; Salbutrop†; Ventide; Ventolin Compuesto†; ***Austral.:*** Combivent; ***Austria:*** Combivent; Di-Promal; Ventide; ***Belg.:*** Combivent; ***Braz.:*** Aeroflux; Aerotide; Clenil Compositum; Combivent; ***Canad.:*** Combivent; ratio-Ipra Sal UDV; ***Chile:*** Aero-Plus; Aerosoma; Asmavent-B; Beclasma†; Belomet; Broncoterol-B†; Butotal B; Combivent; Herolan Aerosol; Salbutral AC; Ventide; ***Cz.:*** Combivent†; Intal Plus†; ***Denm.:*** Combivent; ***Fin.:*** Atrodual; Redol Comp; ***Fr.:*** Combivent; ***Gr.:*** Berovent; ***Hong Kong:*** Combivent; Ventide; Ventolin Expectorant; ***India:*** Aerocort; Albutamol; Ambrodil-S; Amcof; Asthacrom; Asthalin AX; Asthalin Expectorant; Axalin-AX; Axalin†; Bronchilet†; Budesal†; Deletus A†; Duolin; Kofarest; Mucolinc; Okaril; Pulmo-Rest; Pulmo-Rest Expectorant; Suprivent; Suprivent-A; Theo-Asthalin; Ventorlin; ***Indon.:*** Combivent; Fartolin Expectorant; Lasal Expectorant; Proventol Expectorant; Salbron Expectorant; Salbuven Expectorant; Teosal; Ventide; Ventolin Expectorant; ***Irl.:*** Combivent; Ipramol; ***Ital.:*** Breva; Clenil Compositum; Plenaer; Ventolin Espettorante†; Ventolin Flogo†; Zarent†; ***Malaysia:*** Beatolin Expectorant†; Combivent; Ipramol; Salbutamol Expectorant; Ventamol Expectorant†; Ventolin Expectorant; ***Mex.:*** Aeroflux; Broxol Air; Combivent; Flamebin; Fluvicil; Fluxol; Fultac; Mucoflux; Musaldox; Neumyn-AS; Removil; Salamflux; Sibilex; Ulax-C; Ventide; ***Neth.:*** Combivent; ***NZ:*** Combivent; Duolin; ***Philipp.:*** Asbunyl Plus; Asfrenon GF; Asmalin Broncho; Broncaire Expectorant; Clarituss Plus; Combipul; Combivent; Duavent; Hicaryl; Histaril; Neovent; Pecof; Pulmovent; Salvex XP; SGX; Solmux-Broncho (Reformulated); Ventar EXP; Vento-Broncho G; Ventolin Expectorant; Venzadril; ***Port.:*** Combivent; Propavente; ***Rus.:*** Ascoril Expectorant (Аскорил Экспекторант); Biasten (Биастен); ***S.Afr.:*** Combivent; Duolin; Sabax Combineb; ***Singapore:*** Clenil Compositum†; Combivent; Ventide†; ***Spain:*** Butosol; Combivent; Legis†; ***Swed.:*** Combivent; ***Switz.:*** Dospir; ***Thai.:*** Almasal; Asmasal Expectorant†; Biovent; Clenil Compositum; Combivent; Royalin; Salmol Expectorant; Ventide†; Ventolin Expectorant; ***Turk.:*** Combivent; Ventide; ***UK:*** Combivent; Ipramol; ***USA:*** Combivent; DuoNeb; ***Venez.:*** Aerocort; Aeroflux; Beclomet Compositum†; Beclosal; Broxodin; Butosol; Combivent; Duolin; Ipralin; Salbomex†; Salbutide†; Venticort; Ventide.

Salmeterol Xinafoate *(BANM, USAN, rINNM)* ⊗

GR-33343G; Salmaterol Xinafoate; Salmeterol 1-Hydroxy-2-naphthoate; Salmeterol Ksinafoat; Salmétérol, xinafoate de; Salmeteroli xinafoas; Salmeteroliksinafoaatti; Salmeterolio ksinafoatas; Salmeterol-xinafoát; Sameterolxinafoat; Xinafoato de Salmeterol. (*RS*)-5-{1-Hydroxy-2-[6-(4-phenylbutoxy)hexylamino]ethyl}-salicyl alcohol 1-hydroxy-2-naphthoate.

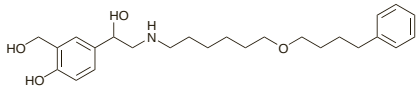
Салметерола Ксинафоат

$C_{25}H_{37}NO_4,C_{11}H_8O_3$ = 603.7.

CAS — 89365-50-4 (salmeterol); 94749-08-3 (salmeterol xinafoate).

ATC — R03AC12.

ATC Vet — QR03AC12.



(salmeterol)

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

Ph. Eur. 6.2 (Salmeterol Xinafoate). A white or almost white powder. Practically insoluble in water; slightly soluble in dehydrated alcohol; soluble in methyl alcohol. Protect from light.

Adverse Effects and Precautions

As for Salbutamol, p.1131. Inhalation of salmeterol may be associated with paradoxical bronchospasm, and it should not be used in patients who are not also receiving an inhaled corticosteroid.

Salmeterol is not appropriate for the treatment of acute bronchospasm or for patients whose asthma is deteriorating.

Effects on the cardiovascular system. A pooled analysis[1] of safety data from 7 studies of salmeterol in chronic obstructive pulmonary disease found no evidence of an increased risk of cardiovascular adverse effects. The duration of these studies had ranged from 12 weeks to 1 year.

1. Ferguson GT, *et al.* Cardiovascular safety of salmeterol in COPD. *Chest* 2003; **123:** 1817–24.

Effects on the respiratory system. Transient paradoxical bronchoconstriction with breathlessness, wheeze, or cough has been reported in 6 asthmatic patients after inhalation of salmeterol from a metered-dose aerosol but not after inhalation of the dry powder formulation by diskhaler.[1] The fluorocarbon propellants in the metered-dose aerosol were suspected as the irritants causing bronchoconstriction.

1. Wilkinson JRW, *et al.* Paradoxical bronchoconstriction in asthmatic patients after salmeterol by metered dose inhaler. *BMJ* 1992; **305:** 931–2.

Effects on the skin. Urticarial rash associated with inhaled salmeterol, of which the propellant was not the cause, has been reported. Although many urticarial reactions and a variety of rashes had been attributed to beta-agonist therapy their reproducibility had not always been documented.[1]

1. Hatton MQF, *et al.* Salmeterol rash. *Lancet* 1991; **337:** 1169–70.

Increased mortality. Interim results from a large controlled study (SMART)[1] designed to evaluate the safety of salmeterol compared with placebo, found a small but statistically significant increase in respiratory-related and asthma-related deaths or life-threatening episodes in the total population receiving salmeterol compared with placebo. This imbalance occurred mainly in the African-American subpopulation, and combined with difficulties in enrolment, led to early termination of the study. Various factors may have influenced the differences in outcomes seen with salmeterol; greater disease severity was noted at baseline in the African-American subgroup compared to Caucasian subjects, and nearly half of all participants were not receiving inhaled corticosteroids.

A subsequent meta-analysis[2] of 19 placebo-controlled studies of patients with asthma who were taking the long-acting beta$_2$ agonists salmeterol or formoterol (see p.1122), reported an increased risk of hospitalisation for an asthma exacerbation, life-threatening asthma attacks, and asthma-related deaths compared with placebo. A sub-group analysis that examined studies in which more than 75% of patients were also receiving inhaled corticosteroids also found an increased risk of hospital admission. The applicability of this review to therapy as recommended by current guidelines has been questioned,[3] as many of the studies included in the primary analysis did not require inhaled corticosteroids to be used, and studies which compared different asthma maintenance regimens were excluded because they were not placebo-controlled. Concomitant asthma treatments and adherence to treatment,[4,5] differences in baseline disease severity,[1,4] racial or genetic factors,[1] polymorphism,[6] tolerance,[6,7] and masking of underlying airway inflammation by long-acting beta$_2$ agonists[6] have all been proposed as possible explanations for the increased risk of adverse outcomes reported with long-acting beta$_2$ agonists.

In contrast to the above studies, a case-control study[8] that included 532 patients under age 65 who had died from asthma, matched with 532 controls with a hospital admission for asthma, found no evidence of adverse effects on mortality with medium to long-term use of inhaled long-acting beta$_2$ agonists. An earlier observational cohort study also found no evidence that salmeterol contributed to deaths reported from asthma.[9]

Current guidelines advocate use of a long-acting beta$_2$ agonist in addition to inhaled corticosteroids, and not as monotherapy, see Management of Asthma, p.1108

A recent review[10] by the UK MHRA concluded that:

- epidemiological data indicated that since the introduction of long-acting beta-agonists there had been a reduction in asthma-related hospitalisations in adolescents and a decrease in asthma related-mortality in all ages.
- data from controlled clinical study did not reflect the safety concern from postmarketing studies, possibly due to more consistent use of corticosteroids in controlled settings
- the data supported the use of long-acting beta-agonists with inhaled corticosteroids consistent with the UK guidelines on the management of asthma and that to aid compliance in the concomitant use of a corticosteroid, a combination inhaler should be used when appropriate

1. Nelson HS, *et al.* The salmeterol multicenter asthma research trial: a comparison of usual pharmacotherapy for asthma or usual pharmacotherapy plus salmeterol. *Chest* 2006; **129:** 15–26.
2. Salpeter SR, *et al.* Meta-analysis: effect of long-acting β-agonists on severe asthma exacerbations and asthma-related deaths. *Ann Intern Med* 2006; **144:** 904–12.
3. Ernst P, *et al.* Safety and effectiveness of long-acting inhaled β-agonist bronchodilators when taken with inhaled corticosteroids. *Ann Intern Med* 2006; **145:** 692–4.
4. Glassroth J. The role of long-acting β-agonists in the management of asthma: analysis, meta-analysis, and more analysis. *Ann Intern Med* 2006; **144:** 936–7.
5. Nelson HS, Dorinsky PM. Safety of long-acting β-agonists. *Ann Intern Med* 2006; **145:** 706.
6. Currie GP, *et al.* Long-acting β -agonists in asthma: not so SMART? *Drug Safety* 2006; **29:** 647–56.
7. Weinberger M, Abu-Hasan M. Life-threatening asthma during treatment with salmeterol. *N Engl J Med* 2006; **355:** 852–3.
8. Anderson HR, *et al.* Bronchodilator treatment and deaths from asthma: case-control study. Abridged version: *BMJ* 2005; **330:** 117. Full version: http://www.bmj.com/cgi/content/full/330/7483/117 (accessed 15/01/08)
9. Mann RD, *et al.* Salmeterol: a study by prescription-event monitoring in a UK cohort of 15,407 patients. *J Clin Epidemiol* 1996; **49:** 247–50.
10. MHRA/CHM. Long-acting β agonists for asthma: review. *Drug Safety Update* 2008: **1** (6): 9. Available at: http://www.mhra.gov.uk/home/idcplg?IdcService=GET_FILE&dDocName=CON2033510&RevisionSelectionMethod=LatestReleased (accessed 22/05/08)

Tolerance. As with short-acting beta$_2$ agonists (see Salbutamol, p.1132), there is evidence that regular use of long-acting beta$_2$ agonists such as salmeterol produces tachyphylaxis to their protective effect against bronchoconstriction, as provoked by stimuli such as allergen, methacholine, or exercise.[1-4] The authors of a study of the long-term effect of salmeterol on exercise-induced asthma concluded that the decreased bronchoprotective effect over time was due to a decrease in duration of action (to less than 9 hours) rather than tachyphylaxis,[5] but this interpretation was criticised.[6,7]

There is also some evidence to suggest that symptomatic relief by short-acting beta$_2$ agonists is significantly reduced by regular use of long-acting beta$_2$ agonists.[8,9] Receptor downregulation, induced by regular use of a long-acting beta$_2$ agonist, has been suggested as the mechanism for this reduction in response and may lead to patients requiring higher doses of beta$_2$ agonists to attain relief from an acute asthma attack.[9,10] One study suggested that the greater tachyphylaxis to short-acting beta$_2$ agonists seen with salmeterol compared with formoterol might represent the expression of partial antagonism by salmeterol at beta$_2$ receptors.[8] Whatever the mechanism, the reduced bronchoprotective effect is perhaps more of a concern with long-acting beta$_2$ agonists, since, unlike the short-acting beta$_2$ agonists, their use on a regular basis is recommended.[11] See also Beta$_2$ Agonists, under Interactions of Salbutamol, p.1132.

1. Cheung D, *et al.* Long-term effects of a long-acting β -adrenoceptor agonist, salmeterol, on airway hyperresponsiveness in patients with mild asthma. *N Engl J Med* 1992; **327:** 1198–1203.
2. Bhagat R, *et al.* Rapid onset of tolerance to the bronchoprotective effect of salmeterol. *Chest* 1995; **108:** 1235–9.
3. Booth H, *et al.* Salmeterol tachyphylaxis in steroid treated asthmatic subjects. *Thorax* 1996; **51:** 1100–4.
4. Simons FER, *et al.* Tolerance to the bronchoprotective effect of salmeterol in adolescents with exercise-induced asthma using concurrent inhaled glucocorticoid treatment. *Pediatrics* 1997; **99:** 655–9.
5. Nelson JA, *et al.* Effect of long-term salmeterol treatment on exercise-induced asthma. *N Engl J Med* 1998; **339:** 141–6.
6. Aziz I, Lipworth BJ. Exercise-induced asthma. *N Engl J Med* 1998; **339:** 1783.
7. Dickey BF, Adachi R. Exercise-induced asthma. *N Engl J Med* 1998; **339:** 1783–4.
8. van Veen A, *et al.* A comparison of salmeterol and formoterol in attenuating airway responses to short-acting β -agonists. *Pulm Pharmacol Ther* 2003; **16:** 153–61.
9. Haney S, Hancox RJ. Tolerance to bronchodilation during treatment with long-acting beta-agonists, a randomised controlled trial. Abridged version: *Respir Res* 2005; **6:** 107. Full version: http://respiratory-research.com/content/6/1/107 (accessed 15/01/08)
10. Lipworth BJ. Airway subsensitivity with long-acting β -agonists: is there cause for concern? *Drug Safety* 1997; **16:** 295–308.
11. Abisheganaden J, Bonshey HA. Long-acting inhaled β -agonists and the loss of "bronchoprotective" efficacy. *Am J Med* 1998; **104:** 494–7.

Interactions

As for Salbutamol, p.1132.

◊ For a study suggesting a decreased effect of salbutamol in patients receiving salmeterol, as well as a report of additive effects, see Beta$_2$ Agonists under Interactions of Salbutamol, p.1132.

Pharmacokinetics

Plasma concentrations of salmeterol are negligible after inhalation of therapeutic doses.

◊ Reviews.

1. Cazzola M, *et al.* Clinical pharmacokinetics of salmeterol. *Clin Pharmacokinet* 2002; **41:** 19–30.

Uses and Administration

Salmeterol is a direct-acting sympathomimetic with beta-adrenoceptor stimulant activity and a selective action on beta$_2$ receptors (a beta$_2$ agonist). When given by inhalation, salmeterol acts as a bronchodilator. The onset of action is about 10 to 20 minutes but the full effect may not be apparent until after several doses. Unlike short-acting beta$_2$ agonists (see Salbutamol, p.1133), salmeterol is therefore not suitable for the symptomatic relief of an acute attack of bronchospasm. However, it is long-acting with a duration of action of about 12 hours and is indicated where the regular use of a long-acting beta$_2$ agonist is required for persistent reversible airways obstruction, as in chronic asthma or in some patients with chronic obstructive pulmonary disease. It may be useful in protecting against nocturnal and exercise-induced asthma attacks. Short-acting

beta$_2$ agonists (on an as-required basis) and regular anti-inflammatory therapy should continue to be used.

Salmeterol is used in the form of the xinafoate; doses are expressed in terms of the equivalent amount of salmeterol; salmeterol xinafoate 1.45 micrograms is equivalent to about 1 microgram of salmeterol.

The usual dose is 50 micrograms of salmeterol twice daily from a metered-dose aerosol or dry powder inhaler; if necessary, up to 100 micrograms may be inhaled twice daily. For doses of salmeterol used in children, see Administration in Children, below.

◊ Reviews.

1. Meyer JM, *et al.* Salmeterol: a novel, long-acting beta -agonist. *Ann Pharmacother* 1993; **27:** 1478–87.
2. Bennett J, Tattersfield A. Drugs in focus: 15. Salmeterol. *Prescribers' J* 1995; **35:** 84–8.
3. Adkins JC, McTavish D. Salmeterol: a review of its pharmacological properties and clinical efficacy in the management of children with asthma. *Drugs* 1997; **54:** 331–54.
4. Jackson CM, Lipworth B. Benefit-risk assessment of long-acting β -agonists in asthma. *Drug Safety* 2004; **27:** 243–70.
5. Sovani MP, *et al.* A benefit-risk assessment of inhaled long-acting β -agonists in the management of obstructive pulmonary disease. *Drug Safety* 2004; **27:** 689–715.

Administration in children. For persistent reversible airways obstruction which requires regular bronchodilatation, including nocturnal asthma and prevention of exercise-induced asthma, children aged 4 to 12 years may be given 50 micrograms of salmeterol twice daily by inhalation.

Asthma. Salmeterol is a long-acting beta$_2$ agonist (duration of action about 12 hours). Guidelines on the management of asthma, see p.1108, generally recommend that salmeterol should be reserved for use in patients with chronic asthma who have already progressed to inhaled corticosteroids; it is not a substitute for corticosteroids. Evidence suggests that, apart from in severe exacerbations, adding a long-acting beta$_2$ agonist to standard dose inhaled corticosteroid therapy may be more effective than increasing the dose of corticosteroid, or than combining a corticosteroid and an anti-leukotriene drug. Salmeterol may also be useful in controlling persistent nocturnal asthma or preventing exercise-induced attacks. There is some evidence that after prolonged use, duration of protection against exercise-induced bronchoconstriction is reduced (see Tolerance, above).

References.

1. Lockey RF, *et al.* Nocturnal asthma: effect of salmeterol on quality of life and clinical outcomes. *Chest* 1999; **115:** 666–73.
2. Shrewsbury S, *et al.* Meta-analysis of increased dose of inhaled steroid or addition of salmeterol in symptomatic asthma (MIASMA). *BMJ* 2000; **320:** 1368–73.
3. Holimon TD, *et al.* Nocturnal asthma uncontrolled by inhaled corticosteroids: theophylline or long-acting beta2 agonists. *Drugs* 2001; **61:** 391–418.
4. Johansson G, *et al.* Comparison of salmeterol/fluticasone propionate combination with budesonide in patients with mild-to-moderate asthma. *Clin Drug Invest* 2001; **21:** 633–42.
5. Heyneman CA, *et al.* Fluticasone versus salmeterol/low-dose fluticasone for long-term asthma control. *Ann Pharmacother* 2002; **36:** 1944–9.
6. Bateman ED, *et al.* Can guideline-defined asthma control be achieved? The gaining optimal asthma control study. *Am J Respir Crit Care Med* 2004; **170:** 836–44.
7. Weiler JM, *et al.* Effect of fluticasone/salmeterol administered via a single device on exercise-induced bronchospasm in patients with persistent asthma. *Ann Allergy Asthma Immunol* 2005; **94:** 65–72.
8. Ni Chroinin M, *et al.* Long-acting beta2-agonists versus placebo in addition to inhaled corticosteroids in children and adults with chronic asthma. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 15/01/08).
9. Gibson PG, *et al.* Long-acting beta2-agonists as an inhaled corticosteroid-sparing agent for chronic asthma in adults and children. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2005 (accessed 15/01/08).
10. Masoli M, *et al.* Moderate dose inhaled corticosteroids plus salmeterol versus higher doses of inhaled corticosteroids in symptomatic asthma. *Thorax* 2005; **60:** 730–4.
11. Ducharme FM, *et al.* Long-acting beta2-agonists versus anti-leukotrienes as add-on therapy to inhaled corticosteroids for chronic asthma. Available in The Cochrane Database of Systematic Reviews; Issue 4. Chichester: John Wiley; 2006 (accessed 15/01/08).
12. Walters EH, *et al.* Long-acting beta2-agonists for chronic asthma in adults and children where background therapy contains varied or no inhaled corticosteroid. Available in The Cochrane Database of Systematic Reviews; Issue 1. Chichester: John Wiley; 2007 (accessed 15/01/08).
13. The American Lung Association Asthma Clinical Research Centers. Randomized comparison of strategies for reducing treatment in mild persistent asthma. *N Engl J Med* 2007; **356:** 2027–39.

Chronic obstructive pulmonary disease. Short-acting beta$_2$ agonists are used as bronchodilators in patients with chronic obstructive pulmonary disease (see p.1112), although there is some evidence to suggest that an antimuscarinic might be preferable. Guidelines indicate that long-acting beta$_2$ agonists such as salmeterol may be used for maintenance therapy in moderate and more severe disease. Improvement in lung function and symptoms has been seen in such patients after regular treatment with inhaled salmeterol;[1-3] a reduction in exacerbations has also been seen.[4] Additional benefit has been reported from the use of salmeterol with inhaled corticosteroids.[5-7]

1. Boyd G, *et al.* An evaluation of salmeterol in the treatment of chronic obstructive pulmonary disease (COPD). *Eur Respir J* 1997; **10:** 815–21.
2. Mahler DA, *et al.* Efficacy of salmeterol xinafoate in the treatment of COPD. *Chest* 1999; **115:** 957–65.
3. Stockley RA, *et al.* Addition of salmeterol to existing treatment in patients with COPD: a 12 month study. *Thorax* 2006; **61:** 122–8.
4. Appleton S, *et al.* Long-acting beta2-agonists for poorly reversible chronic obstructive pulmonary disease. Available in The Cochrane Database of Systematic Reviews; Issue 3. Chichester: John Wiley; 2006 (accessed 15/01/08).
5. Calverley P, *et al.* Combined salmeterol and fluticasone in the treatment of chronic obstructive pulmonary disease: a randomised controlled trial. *Lancet* 2003; **361:** 449–56. Correction. *ibid.*; 1660.
6. Keating GM, McCormack PL. Salmeterol/fluticasone propionate: a review of its use in the treatment of chronic obstructive pulmonary disease. *Drugs* 2007; **67:** 2383–2405.
7. Kardos P, *et al.* Impact of salmeterol/fluticasone propionate versus salmeterol on exacerbations in severe chronic obstructive pulmonary disease. *Am J Respir Crit Care Med* 2007; **175:** 144–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Arg.: Abrilar†; Serevent; ***Austral.:*** Serevent; ***Austria:*** Serevent; ***Belg.:*** Serevent; ***Braz.:*** Serevent; ***Canad.:*** Serevent; ***Chile:*** Kolpovent†; Serevent; Xemos; ***Cz.:*** Serevent; ***Denm.:*** Serevent; ***Fin.:*** Serevent; ***Fr.:*** Serevent; ***Ger.:*** Aeromax; Serevent; ***Gr.:*** Serevent; ***Hong Kong:*** Serevent; ***Hung.:*** Serevent; ***India:*** Salmeter; Serobid; ***Indon.:*** Serevent; ***Irl.:*** Serevent; ***Israel:*** Serevent; ***Ital.:*** Arial; Salmetedur; Serevent; ***Jpn:*** Serevent; ***Malaysia:*** Serevent; ***Mex.:*** Serevent; ***Neth.:*** Serevent; ***Norw.:*** Serevent; ***NZ:*** Serevent; ***Philipp.:*** Serevent; ***Pol.:*** Serevent; ***Port.:*** Dilamax; Serevent; Ultrabeta; ***Rus.:*** Seretide (Серетид); Serevent (Серевент); ***S.Afr.:*** Serevent; ***Singapore:*** Serevent; ***Spain:*** Beglan; Betamican; Inaspir; Serevent; ***Swed.:*** Serevent; ***Switz.:*** Serevent; ***Thai.:*** Serevent; ***Turk.:*** Astmerole; Serevent; ***UK:*** Serevent; ***USA:*** Serevent; ***Venez.:*** Salmeter†; Salspray; Serevent.

Multi-ingredient: ***Arg.:*** Flutivent; Neumotide; Seretide; ***Austral.:*** Seretide; ***Austria:*** Seretide; Viani; ***Belg.:*** Seretide; ***Braz.:*** Seretide; ***Canad.:*** Advair; ***Chile:*** Aerometrol Plus; Aurituss; Brexotide; Seretide; ***Cz.:*** Duaspir; Seretide; ***Denm.:*** Seretide; ***Fin.:*** Seretide; ***Fr.:*** Seretide; ***Ger.:*** Atmadisc; Viani; ***Gr.:*** Seretide; Viani†; ***Hong Kong:*** Seretide; ***Hung.:*** Seretide; Thoreus; ***India:*** Forair; Seretide; Seroflo; ***Indon.:*** Seretide; ***Irl.:*** Seretide; ***Israel:*** Seretide; ***Ital.:*** Aliflus; Seretide; ***Malaysia:*** Seretide; ***Mex.:*** Seretide; ***Neth.:*** Seretide; Viani; ***Norw.:*** Seretide; ***NZ:*** Seretide; ***Philipp.:*** Seretide; ***Pol.:*** Seretide; ***Port.:*** Brisomax; Maizar; Seretaide; Veraspir; ***S.Afr.:*** Seretide; ***Singapore:*** Seretide; ***Spain:*** Anasma; Brisair; Inaladuo; Plusvent; Seretide; ***Swed.:*** Seretide; ***Switz.:*** Seretide; ***Thai.:*** Seretide; ***Turk.:*** Seretide; ***UK:*** Seretide; ***USA:*** Advair; ***Venez.:*** Seretide.

Seratrodast *(USAN, rINN)*

A-73001; AA-2414; Abbott-73001; ABT-001; Sératrodast; Seratrodastum. (±)-2,4,5-Trimethyl-3,6-dioxo-ζ-phenyl-1,4-cyclohexadiene-1-heptanoic acid.

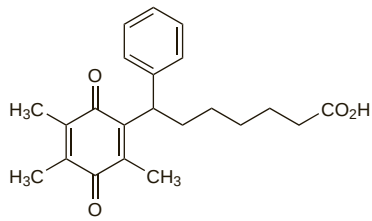
Сератродаст

$C_{22}H_{26}O_4$ = 354.4.

CAS — 112665-43-7; 103186-19-2.

ATC — R03DX06.

ATC Vet — QR03DX06.



Profile

Seratrodast is a thromboxane A_2 antagonist that is reported to reduce airway hyperresponsiveness. It is given orally in the prophylactic management of asthma (p.1108), in single doses of 80 mg in the evening after food.

Adverse effects include gastrointestinal disturbances, drowsiness, headache, palpitations, and hepatitis. Hepatic function should be monitored and the drug should be withdrawn if hypersensitivity reactions such as rashes and pruritus occur, or if there is elevation of liver enzyme values. Seratrodast should be used with care in patients with pre-existing hepatic impairment. It is not suitable for the treatment of an acute asthmatic attack.

◊ References.

1. Tamaoki J, *et al.* Effect of a thromboxane A antagonist on sputum production and its physicochemical properties in patients with mild to moderate asthma. *Chest* 2000; **118:** 73–9.

Preparations

Proprietary Preparations (details are given in Part 3)
Jpn: Bronica.

Sodium Cromoglicate *(BANM, rINNM)*

Cromoglicate de Sodium; Cromoglicato de sodio; Cromoglicato disódico; Cromolyn Sodium *(USAN)*; Dinatrii Cromoglicas; Dinatrium-chromoglykát; Disodium Cromoglycate; FPL-670; Natrii cromoglicas; Natrio kromoglikatas; Natriumchromoglicat; Natriumkromoglikaatti; Natriumkromoglikat; Nátrium-kromoglikát; Sodium, cromoglicate de; Sodium Cromoglycate; Sodyum Kromoglikat. Disodium 4,4′-dioxo-5,5′-(2-hydroxytrimethylenedioxy)di(4*H*-chromene-2-carboxylate).

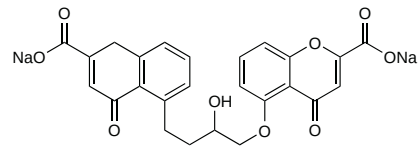
Натрий Кромоглициат

$C_{23}H_{14}Na_2O_{11}$ = 512.3.

CAS — 16110-51-3 (cromoglicic acid); 15826-37-6 (sodium cromoglicate).

ATC — A07EB01; D11AX17; R01AC01; R03BC01; S01GX01.

ATC Vet — QA07EB01; QD11AX17; QR01AC01; QR03BC01; QS01GX01.



Pharmacopoeias. In *Chin.*, *Eur.* (see p.vii), *Int.*, *Jpn*, and *US.*
Ph. Eur. 6.2 (Sodium Cromoglicate). A white or almost white, hygroscopic, crystalline powder. Soluble in water; practically insoluble in alcohol. Store in airtight containers. Protect from light.
USP 31 (Cromolyn Sodium). A white, odourless, hygroscopic, crystalline powder. Soluble in water; insoluble in alcohol and in chloroform. Store in airtight containers.

Adverse Effects

Inhalation of sodium cromoglicate may cause transient bronchospasm, wheezing, cough, nasal congestion, and irritation of the throat. Nausea, headache, dizziness, an unpleasant taste, and joint pain and swelling have been reported. Other reactions include aggravation of existing asthma, urticaria, rashes, pulmonary infiltrates with eosinophilia, dysuria, and urinary frequency. Severe reactions such as marked bronchospasm, laryngeal oedema, angioedema, and anaphylaxis have been reported rarely.

Intranasal use of sodium cromoglicate may cause transient irritation of the nasal mucosa, sneezing, and occasionally epistaxis. Nausea, skin rashes, and joint pains have occurred when it is taken orally. Transient burning and stinging have occasionally been reported after use of sodium cromoglicate eye drops.

Formulation. Some of the adverse effects reported with sodium cromoglicate may be due to its formulation: there is a view that some of the irritant effects reported on inhalation may be due to the use of dry powder inhalers. It has also been suggested that in some patients receiving sodium cromoglicate via a nebuliser, hypotonicity of the nebuliser solution may induce bronchospasm,[1] although others consider this debatable.[2] Nausea, bloating, abdominal cramps, and flatulence developed in a 24-year-old lactase-deficient woman 2 hours after the use of sodium cromoglicate (*Intal*) inhalation capsules via a turbo-haler for exercise-induced asthma.[3] These symptoms recurred on rechallenge and were attributed to ingestion of lactose contained within the capsules.

1. Chin TW, Nussbaum E. Detrimental effect of hypotonic cromolyn sodium. *J Pediatr* 1992; **120:** 641–3.
2. Rachelefsky GS, *et al.* Detrimental effects of hypotonic cromolyn sodium. *J Pediatr* 1992; **121:** 992.
3. Brandstetter RD, *et al.* Lactose intolerance associated with Intal capsules. *N Engl J Med* 1986; **315:** 1613–14.

Precautions

Sodium cromoglicate has no role in the treatment of acute asthmatic attacks. Withdrawal of sodium cromoglicate may lead to recurrence of the symptoms of asthma. Should withdrawal be necessary it has been suggested that the dose be reduced gradually over a period of one week; patients in whom sodium cromoglicate therapy has permitted a reduction of corticosteroid dosage may require restoration of full corticosteroid cover.

Systemic corticosteroid therapy that has been reduced or stopped in asthmatic patients may need to be reinstated if symptoms increase, during periods of stress