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.

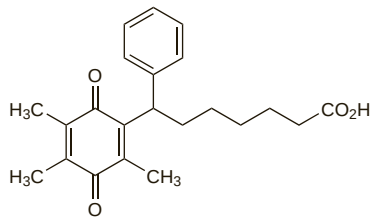
Сератродаст

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

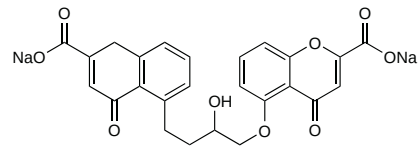
Натрий Кромоглициат

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