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References:

1 Lindgren S. Bake B. Larsson S. Eur J Respir Dis 1987;**70**:93-98
2 Crompton G.K. Eur J Respir Dis 1982;**63**(Suppl. 119):101-104
3 Goodman D.E. et al. Am J Respir Crit Care Med 1994;**150**:1256-1261
4 MIMS, February 1995
5 Data on file, Baker Norton

Lung & Asthma Information Agency

Lung & Asthma Information Agency, Department of Public Health Sciences, St George's Hospital Medical School, Cranmer Terrace, London SW17 ORE

Influenza

Introduction

Influenza is an acute infectious disease and one of the most important viral infections of the respiratory tract. It affects all age groups and is characterised by the sudden onset of fever, chills, headache and muscle pain. For most people it is an unpleasant, but not serious disease. However, in those with underlying chronic disease, especially the elderly, complications such as acute bronchitis and pneumonia are common. These can lead to hospitalisation and, in some cases, death. There are three influenza viruses, A, B and C. The influenza A virus changes its surface antigens each year, thus regularly exposing the population to different strains. Approximately once every decade, there is a major antigen change, resulting in a world-wide epidemic. Influenza B is more stable than A and influenza C is the most stable.

Epidemiology

Influenza is common and outbreaks of influenza A occur most winters, with epidemics every five to fifteen years. Influenza B also causes epidemics, but less frequently. Influenza C does not appear to cause epidemics, and by the age of 15 most of the population have developed antibodies against it. Infection rates for influenza are highest among school age children and decrease with age. In contrast, influenza deaths and hospitalisations for severe or complicated influenza mostly occur in infants and the elderly.

Deaths certified as due to influenza have fallen since the 1960s. There are now about 250 deaths in non-epidemic years, 80-90% occurring in those aged over 65. Women have a higher mortality rate from influenza than men. The number of hospital admissions for influenza are fairly low, typically less than twenty a week, rising to 70-80 a week during the winter. These are also concentrated among the elderly.

Figure 1: Age-specific influenza mortality rates. Ages 65+, England & Wales, 1958-92.

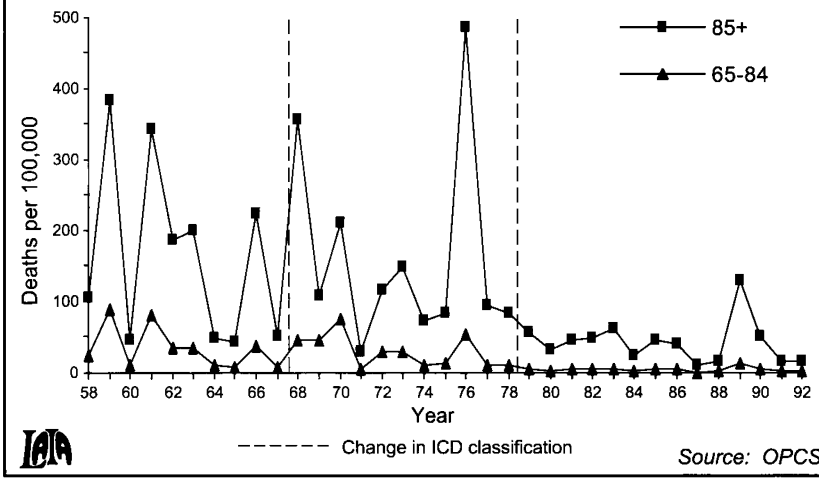
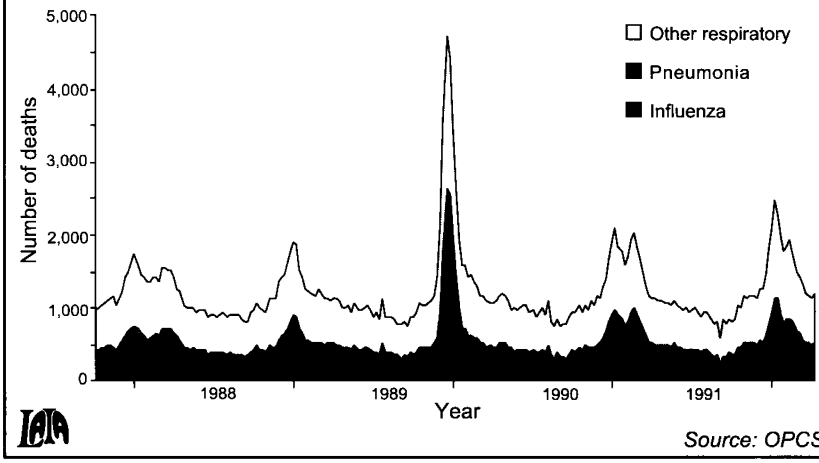


Figure 2: Weekly deaths from respiratory disease. England & Wales, October 1987- March 1992.



Influenza epidemics

Epidemics of influenza occur irregularly - the three most recent in Britain occurred in 1972/3, 1976 and 1989/90. Epidemics give rise to excess influenza mortality, which was most noticeable in 1976 (figure 1). Epidemics also cause considerable morbidity, such as increased hospital admissions, increased visits to General Practitioners, and loss of time from work and school. During epidemics, deaths and hospital admissions for other respiratory diseases and all causes also increase.

The 1989 influenza epidemic

The 1989 influenza epidemic started towards the end of November, the peak in infection rates and hospitalisations occurring during the first two weeks of December.

During the epidemic, deaths from influenza, pneumonia, and other respiratory causes increased markedly (figure 2). All-cause mortality also increased and there was an estimated 30,000 excess deaths. Of these, only 10% were attributed to influenza, 20% being attributed to pneumonia and a further 19% to other respiratory causes. Deaths occurred mostly in those aged 75 and over. Although this excess was followed by a deficit of nearly 11,000 deaths in the following three months, this was only one third of the excess.

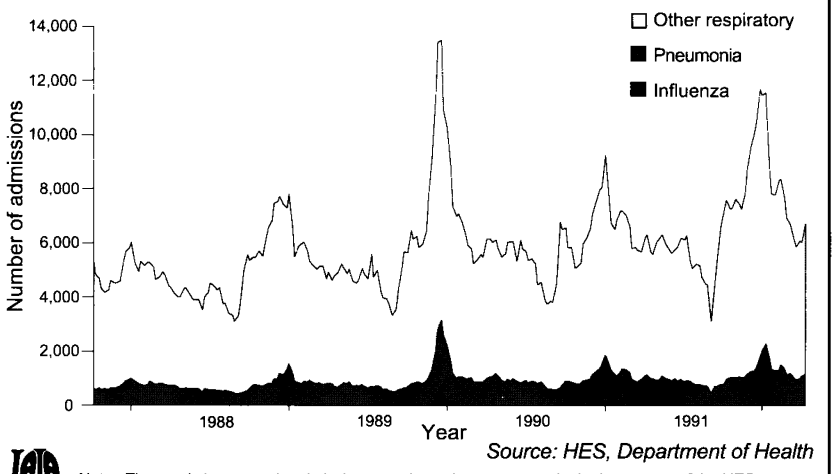
Hospital admissions for influenza and other respiratory diseases also increased (figure 3). As with mortality, only a small percentage of the excess admissions were attributed to influenza. At the peak of the epidemic, influenza accounted for only 4% of all respiratory admissions and pneumonia for a further 20%.

New episodes of influenza and influenza-like illness seen by General Practitioners increased sharply through December, peaking at 272 and 311 per 100,000 respectively (figure 4). Consultations for all respiratory diseases also increased. In the last six weeks of 1989, approximately 8% of the population visited their GP for respiratory diseases - twice the number normally expected.

Influenza vaccine

The influenza vaccine is effective in reducing the severity of the disease, and the chances of developing complications such as pneumonia. It protects primarily against influenza A, and as this virus regularly changes its surface antigens, new vaccine is produced each year. Thus, protection only lasts for one season, and re-immunisation each year is needed. It is particularly recommended for the elderly, those with chronic underlying disease such as asthma, chronic heart disease or diabetes mellitus, and people living in long-stay or residential homes. In Great Britain, uptake of the vaccine is low, even among those for whom it is recommended - special studies have found vaccination coverage among the elderly ranging from 20% to 50%. This low uptake may be explained in part by patients not being offered the vaccine.

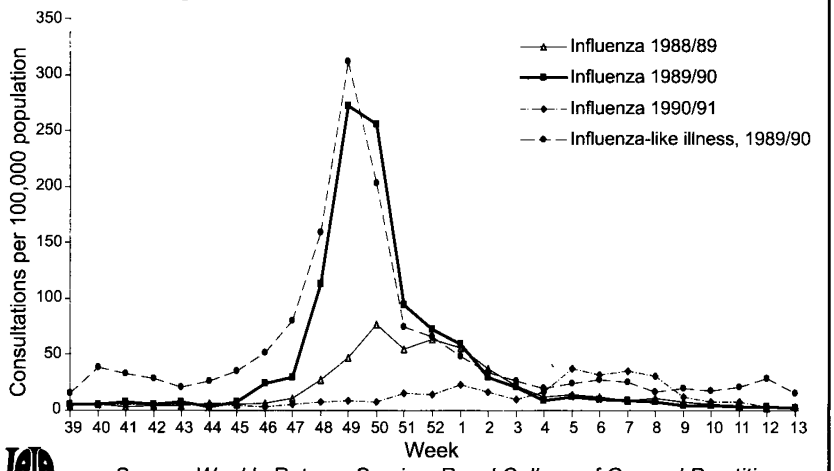
Figure 3: Weekly hospital admissions for respiratory diseases, England, October 1987 - March 1992.



Source: HES, Department of Health

Note: The yearly increases in admissions are due to improvements in the later years of the HES system.

Figure 4: New episodes of influenza seen by GPs. England & Wales, October-March 1988-91.



Source: Weekly Returns Service, Royal College of General Practitioners

Summary

- **Influenza is one of the most important viral infections of the respiratory tract. It is usually not a serious disease, but in some people can lead to complications such as pneumonia.**
- **Epidemics of influenza occur irregularly. They lead to an increase in visits to general practitioners, hospitalisations for influenza, pneumonia, and other respiratory diseases and all cause mortality. Few of the excess deaths are certified as due to influenza; many are attributed to non-respiratory causes**
- **Infection rates are highest amongst children, but hospitalisations and mortality are higher among the elderly.**
- **The influenza vaccine is effective and recommended especially for the elderly or those with chronic underlying disease.**

Footnote

An epidemic is defined as the occurrence of a disease in excess of what would be expected.

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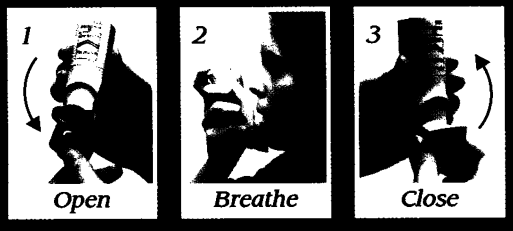

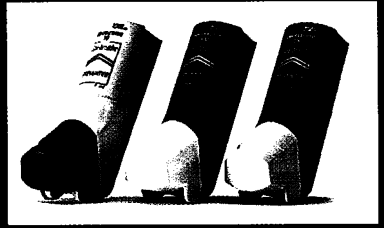

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Presentations: Pulmicort Respules. (2ml single dose unit ampoules) containing 0.25mg/ml or 0.5mg/ml budesonide in a suspension for nebulisation. **Uses**: Bronchial asthma where use of a pressurised inhaler or dry powder formulation is unsatisfactory or inappropriate. **Dosage and administration:** Dosage schedules: Administer from suitable nebulisers. Dose delivered to the patient varies depending on the nebulising equipment used (see data sheet). Adjust dosage individually. Initially during periods of severe asthma and while reducing or discontinuing oral glucocorticosteroids the recommended dose in adults (including elderly and children 12 years and older) is usually 1-2mg twice daily. In very severe cases the dosage may be further increased. Children 3 months to 12 years: 0.5-1mg twice daily. The maintenance dose should be the lowest dose which keeps the patient symptom-free. Recommended doses are: Adults (including elderly and children 12 years and older): 0.5-1mg twice daily. Children (3 months to 12 years): 0.25-0.5mg twice daily. For an increased therapeutic effect increase dose of Pulmicort rather than combine treatment with oral corticosteroids because of the lower risk of systemic effects. **Contra-indications, warnings, etc.:** Contra-indications: Hypersensitivity to any of the constituents. Special warnings and precautions: Care is needed in patients with pulmonary tuberculosis and viral infections in the airways. A short course of oral steroids in addition to Pulmicort may be required in patients with excessive mucus in the bronchi. Transfer of patients dependent on oral steroids to Pulmicort demands special care; see data sheet for further details. The nebuliser chamber should be cleaned and dried after every administration. Pulmicort does not affect the ability to drive and use machines. Pulmicort Respules can be mixed with 0.9% saline and with solutions of terbutaline, salbutamol, sodium cromoglycate or ipratropium bromide. **Side-effects:** Mild irritation in the throat, coughing and hoarseness and oral candidiasis have been reported. In rare cases inhaled drugs may provoke bronchoconstriction in hyperreactive patients. Facial skin should be washed after use of the face mask as irritation can occur. Coughing can usually be prevented by inhaling a β_2-agonist (e.g. terbutaline) 5-10 minutes before inhalation of Pulmicort Respules. Avoid in pregnancy. **Pharmaceutical precautions:** Store below 30°C. Use within 3 months of opening the foil envelope. Protect opened ampoule from light. Use within 12 hours of opening. **Legal status:** POM. **Basic NHS price:** Pulmicort Respules 0.25mg/ml (20 single dose units) £32.00. Pulmicort Respules 0.5mg/ml (20 single dose units) £44.64. **Product licence nos.:** Pulmicort Respules 0.25mg/ml PL 0017/0309. Pulmicort Respules 0.5mg/ml PL 0017/0310. **Name and address of product licence holder:** Astra Pharmaceuticals Ltd., Home Park, Kings Langley, Herts WD4 8DH.

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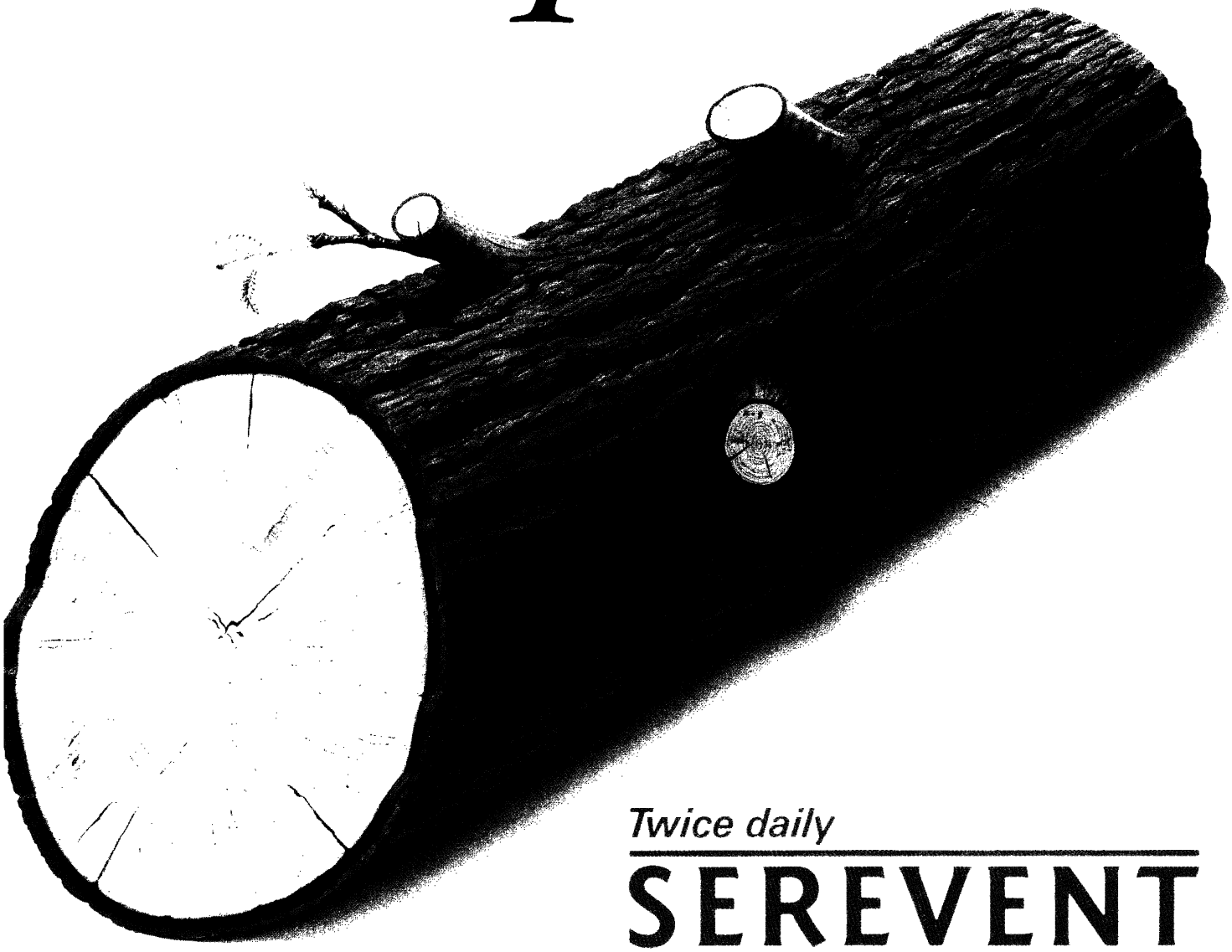

Twice daily

SEREVENT

salmeterol xinafoate

FOR ACTIVE DAYS AND RESTFUL NIGHTS

Serevent (salmeterol xinafoate)
Abridged Prescribing Information
(Please refer to the full data sheet before prescribing) **Uses** Treatment of asthma (including nocturnal and exercise-induced) in patients requiring long-term regular bronchodilator therapy. Patients should normally also be receiving regular and adequate doses of inhaled anti-inflammatory agents, or oral corticosteroids. **Dosage and administration** For inhalation only. *Adults and children 4 years and over:* 50 micrograms twice daily. *Adults only:* More severe cases 100 micrograms twice daily. *Children below 4 years:* Not recommended at present. **Contra-indication** Hypersensitivity. **Precautions** *Steroid therapy:* Serevent is not a replacement for corticosteroids and/or, in children, sodium cromoglycate. Warn patients not to stop or reduce such therapy. *Severe or unstable asthma:* Bronchodilators should not be the only or main treatment. Consider using oral steroids and/or maximum doses of inhaled corticosteroids. Warn patients to seek medical advice if short-acting bronchodilator use increases or becomes less effective. Treat severe exacerbations in the normal way. *Acute symptoms:* Serevent is not for relief of acute symptoms. A short-acting inhaled bronchodilator is required. *Thyrotoxicosis:* Use with caution. *Drug interactions:* Avoid beta-blockers. *Hypokalaemia:* May occur, particularly in acute severe asthma. It may be potentiated by xanthine derivatives, steroids, diuretics and hypoxia. Monitor serum potassium levels in these situations. *Pregnancy and lactation:* Experience is limited. Balance risks against benefits. **Side effects** Tremor, subjective palpitations and headaches have been reported, but are usually mild and transient. Skin reactions, muscle cramps, non-specific chest pain, local irritation and arthralgia have been reported. Potentially serious hypokalaemia may result from β_2-agonist therapy. *Paradoxical bronchospasm:* Substitute alternative therapy. **Presentation and Basic NHS cost** *Serevent Diskhaler:* Pack of 14 four-place disk foils, together with a Serevent Diskhaler. 50 micrograms – £29·97. *Serevent Diskhaler refill pack:* Pack of 14 four-place disk foils only – £29·40. *Serevent Inhaler:* 120 actuations per inhaler. 25 micrograms – £28·60. Hospital packs are also available. **Product licence numbers** 0045/0158, 0045/0157.

POM

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Further information is available on request from:
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Uxbridge, Middlesex UB11 1BT

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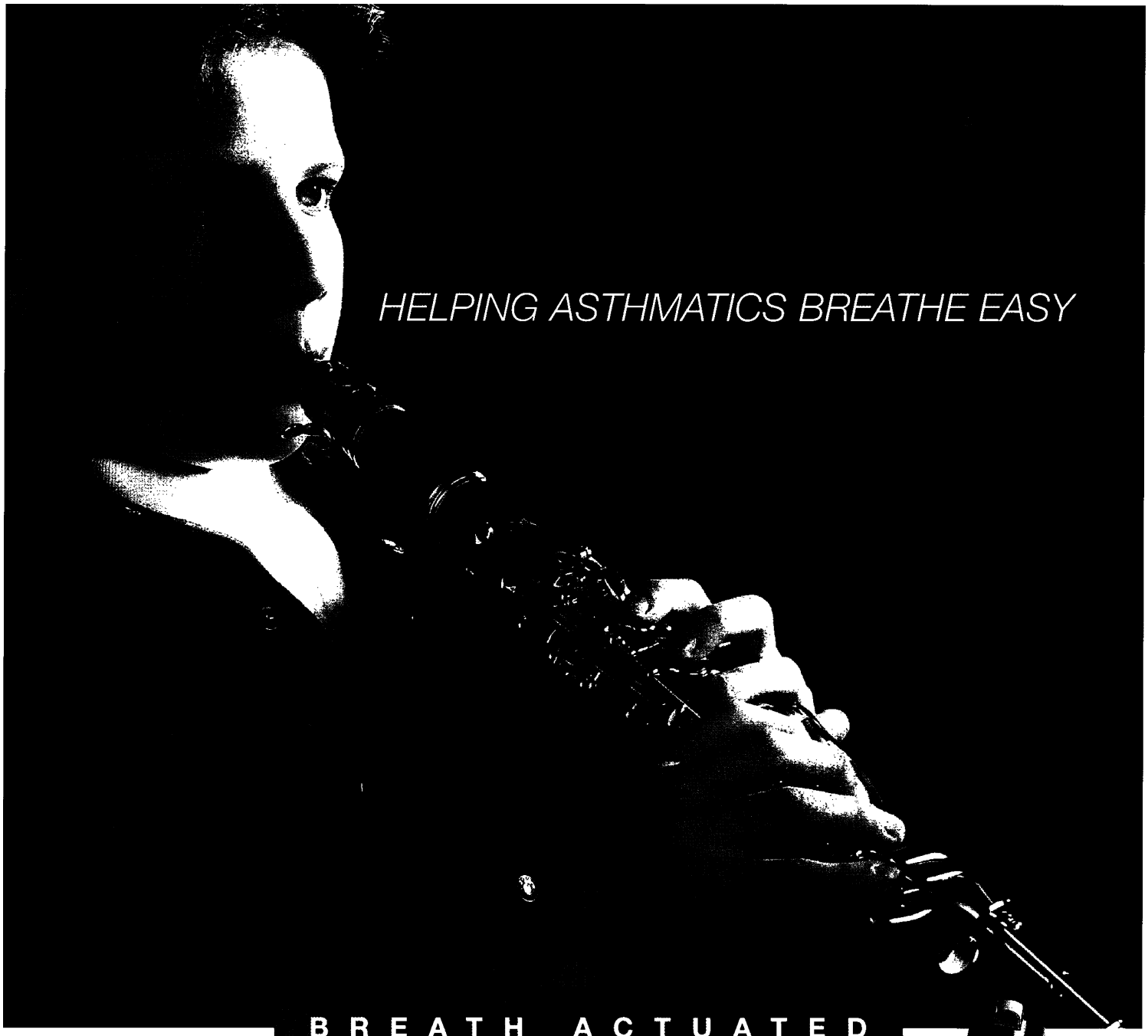
September 1993

When introducing Serevent in adults we strongly recommend that you do not stop or reduce the dose of corticosteroids. Similarly, in children, do not stop or reduce corticosteroids or sodium cromoglycate.



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beclomethasone dipropionate breath-actuated inhaler

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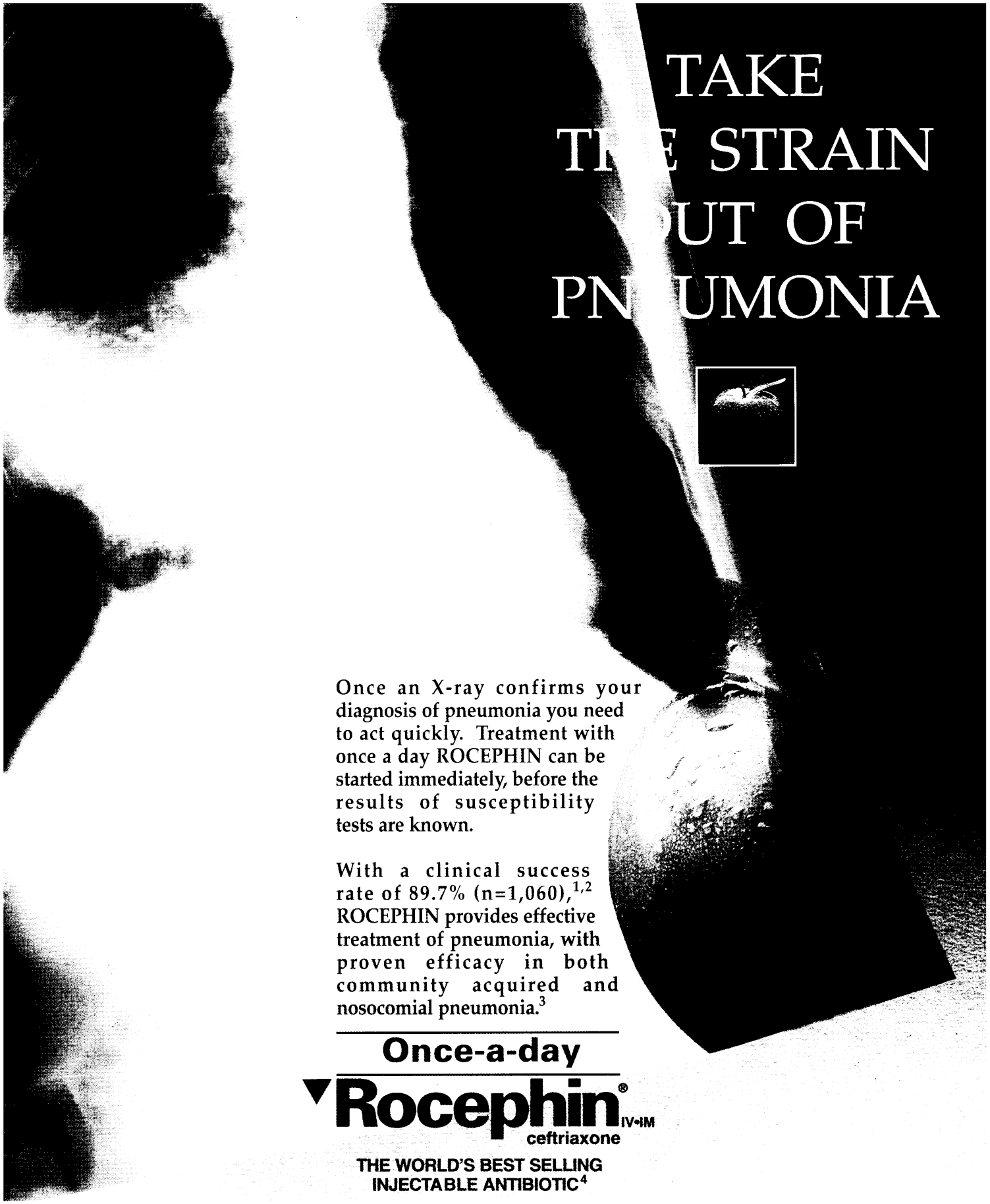
3M Health Care



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References
1. Brown, R.B. and Sands, M., Curr. Ther. Res.(1989),**46** (2), 285-91.
2. Data On File, (GCR B-116 232). 3. Niebuhr, H. *et al.* Chemotherapie Journal (1993), **2**, 28-35. 4. Estimated current cash annual sales worldwide - Data on File. Roche Products Ltd.

Brief Prescribing Information

Indications: Pneumonia, septicaemia; meningitis; bone, skin and soft tissue infections; infections in neutropenic patients; gonorrhoea; peri-operative prophylaxis of infections associated with surgery. Treatment may be started before the results of susceptibility tests are known. **Dosage and Administration:** Rocephin should be administered by deep intramuscular injection, slow intravenous injection, or as a slow intravenous infusion, after reconstitution of the solution. **Adults and children 12 years and over:** Standard dosage -1g once daily. Severe infections - 2-4g normally once daily. Duration of therapy varies according to course of disease. Gonorrhoea - single dose of 250mg i.m. Peri-operative prophylaxis - usually single dose of 1g, colorectal surgery 2g in conjunction with a suitable agent against anaerobic bacteria. **Children under 12 years:** Standard dosage - 20-50mg/kg once daily. Severe infections - maximum 80mg/kg once daily. Doses of 50mg/kg or over should be given by slow intravenous infusion over at least 30 minutes. **Renal and hepatic impairment:** In the absence of hepatic impairment dose reduction is required only in severe renal failure (creatinine clearance <10ml/min), when the daily dose should be 2g or less. No dose reduction is required in liver damage provided renal function is intact. In severe renal impairment accompanied by hepatic insufficiency the plasma concentration should be determined at regular intervals and dosage adjusted. Serum concentrations should be monitored in dialysis. **Contra-indications, Warnings etc.** Cephalosporin hypersensitivity. Premature infants. Full-term infants during first six weeks of life. Safety in pregnancy has not been established. **Precautions:** Stated dose should not be exceeded. Caution in patients with a history of hypersensitivity (especially anaphylactic reaction) to penicillins or other non-cephalosporin beta-lactam antibiotics. Anaphylactic shock requires immediate countermeasures. Severe renal impairment accompanied by hepatic insufficiency (see Dosage). **Side-effects and Adverse Reactions:** Gastro-intestinal side-effects including loose stools, diarrhoea, nausea, vomiting, stomatitis and glossitis. Cutaneous reactions including maculopapular rash, pruritus, urticaria, oedema and erythema multiforme. Haematological reactions including anaemia (all grades), leucopenia, neutropenia, thrombocytopenia, eosinophilia, agranulocytosis, positive Coombs' test and prolongation of prothrombin time. Regular blood counts should be carried out during treatment. Other reactions include headache, dizziness, drug fever and transient elevations in liver function tests. Rarely: glycosuria, oliguria, haematuria, anaphylaxis and bronchospasm. Very rarely, precipitation of ceftriaxone calcium salt in urine in patients on higher than recommended dose. Reversible precipitates of calcium ceftriaxone have been detected by gallbladder sonograms. In symptomatic cases (which are rare), conservative non-surgical management is recommended. Superinfections with yeasts, fungi or other resistant organisms. Rare instances of pseudomembranous colitis. Injection site pain and local phlebitis. **Legal Category:** POM. **Presentations and Basic NHS Cost:** 250mg vials i.m. and i.v. (containing 250mg ceftriaxone) - £2.87. 1g vials i.m. and i.v. (containing 1g ceftriaxone) - £11.46. 2g vials for infusion (containing 2g ceftriaxone) - £22.92. **Product Licence Numbers:** PL 0031/0169 (250mg vials), PL 0031/0171 (1g vials), PL 0031/0172 (2g vials) **Product Licence Holder:** Roche Products Limited, PO Box 8, Welwyn Garden City, Hertfordshire, AL7 3AY. Full prescribing information is available on request.

J 738084 Date of preparation February 1994

Roche

ABBREVIATED PRESCRIBING INFORMATION

Presentation UNIPHYLLIN CONTINUS tablets contain Theophylline BP in a controlled release system. UNIPHYLLIN CONTINUS tablets 400 mg are white, capsule-shaped, scored tablets with the logo NAPP U400 embossed on one side and UNIPHYLLIN on the other. UNIPHYLLIN CONTINUS tablets 300 mg are white, capsule-shaped, scored tablets with U300 embossed on one side. UNIPHYLLIN CONTINUS tablets 200 mg are white, capsule-shaped, scored tablets with U200 embossed on one side. Uses Theophylline is a bronchodilator. In addition it affects the function of a number of cells involved in the inflammatory processes associated with asthma and chronic obstructive airways disease. Of most importance may be enhanced suppressor T-lymphocyte activity and reduction of eosinophil and neutrophil function. These actions may contribute to anti-inflammatory prophylactic activity in asthma and chronic obstructive airways disease. For the treatment and prophylaxis of bronchospasm associated with asthma, emphysema and chronic bronchitis. Also indicated in adults for the treatment of cardiac asthma and left ventricular or congestive cardiac failure. Dosage and administration *NB* Tablets should be swallowed whole and not chewed. *Adults:* The usual maintenance dose for elderly patients or those less than 70 kg body weight is 300 mg, 12-hourly following an initial week of therapy on 200 mg, 12-hourly. The usual maintenance dose for patients of 70 kg body weight or over is 400 mg, 12-hourly following an initial week of therapy on 200 mg or 300 mg, 12-hourly. *Children:* Not recommended for children under seven years of age. The maintenance dose is 9 mg/kg twice daily. Some children with chronic asthma require and tolerate much higher doses (10-16 mg/kg twice daily). Lower dosages (based on usual adult dose) may be required by adolescents. It may be appropriate to administer a larger evening or morning dose in some patients, in order to achieve optimum therapeutic effect when symptoms are quite severe, e.g. at the time of the 'morning dip' in lung function. In patients whose night time or day time symptoms persist despite other therapy and who are not currently receiving theophylline, then the total daily requirement of UNIPHYLLIN CONTINUS tablets (as specified above) may be added to their treatment regimen as either a single evening or morning dose. *Elderly:* The initial dose should be 200 mg, 12-hourly increasing to 300 mg, 12-hourly. Contra-indications Should not be given concomitantly with ephedrine in children. Precautions and warnings The following increase clearance and it may therefore be necessary to increase dosage to ensure a therapeutic effect: phenytoin, carbamazepine, rifampicin, sulphinpyrazone and barbiturates. Smoking and alcohol consumption can also increase clearance of theophylline. The following reduce clearance and a reduced dosage may therefore be necessary to avoid side-effects: allopurinol, cimetidine, ciprofloxacin, erythromycin, thiabendazole, isoprenaline, fluvoxamine, viloxazine hydrochloride and oral contraceptives. Factors such as viral infections, liver disease and heart failure also reduce theophylline clearance. The **hypokalaemia resulting fom beta$_2$ agonist therapy, steroids, diuretics and hypoxia may be potentiated by xanthines. Particular care is advised in patients suffering from severe asthma who require hospitalisation. It is recommended that serum potassium levels are monitored in such circumstances. Safety in human pregnancy has not been established. Side-effects The risk of side-effects usually associated with theophylline and xanthine derivatives such as nausea, gastric irritation,** headache and CNS stimulation is significantly reduced when UNIPHYLLIN CONTINUS tablet preparations are given. Furthermore these side effects can be minimised by dose titration downwards. [illegible] it is not possible to ensure bioequivalence between different sustained release theophylline products. Therefore it should be emphasised that patients once titrated to an effective dose should not be changed from UNIPHYLLIN CONTINUS tablet preparations to other sustained release xanthine preparations without retitration and clinical assessment. Legal category P. Package quantities and basic NHS price UNIPHYLLIN CONTINUS tablets 400 mg - 56s [illegible] UNIPHYLLIN CONTINUS tablets 300 mg - 56s [illegible] UNIPHYLLIN CONTINUS tablets 200 mg - 56s [illegible] Product licence numbers UNIPHYLLIN CONTINUS tablets 400 mg - PL 0337/0074 [illegible] UNIPHYLLIN CONTINUS tablets 300 mg - PL 0337/0108 UNIPHYLLIN CONTINUS tablets 200 mg - PL 0337/0057 Product licence holder Napp Laboratories Limited, Cambridge Science Park, Milton Road, Cambridge CB4 4GW, UK. Tel 01223 424444. Member of Napp Pharmaceutical Group. Further information is available from Napp Laboratories Limited. ® The NAPP device, UNIPHYLLIN and CONTINUS are Registered Trade Marks. © NAPP Laboratories Limited 1995

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NAPP

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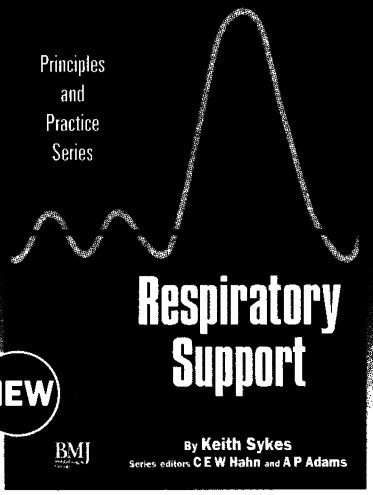

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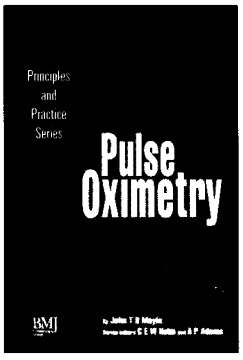

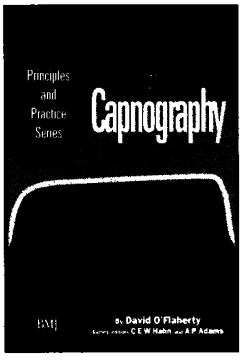

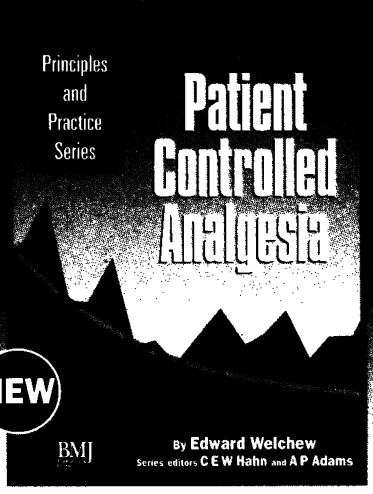

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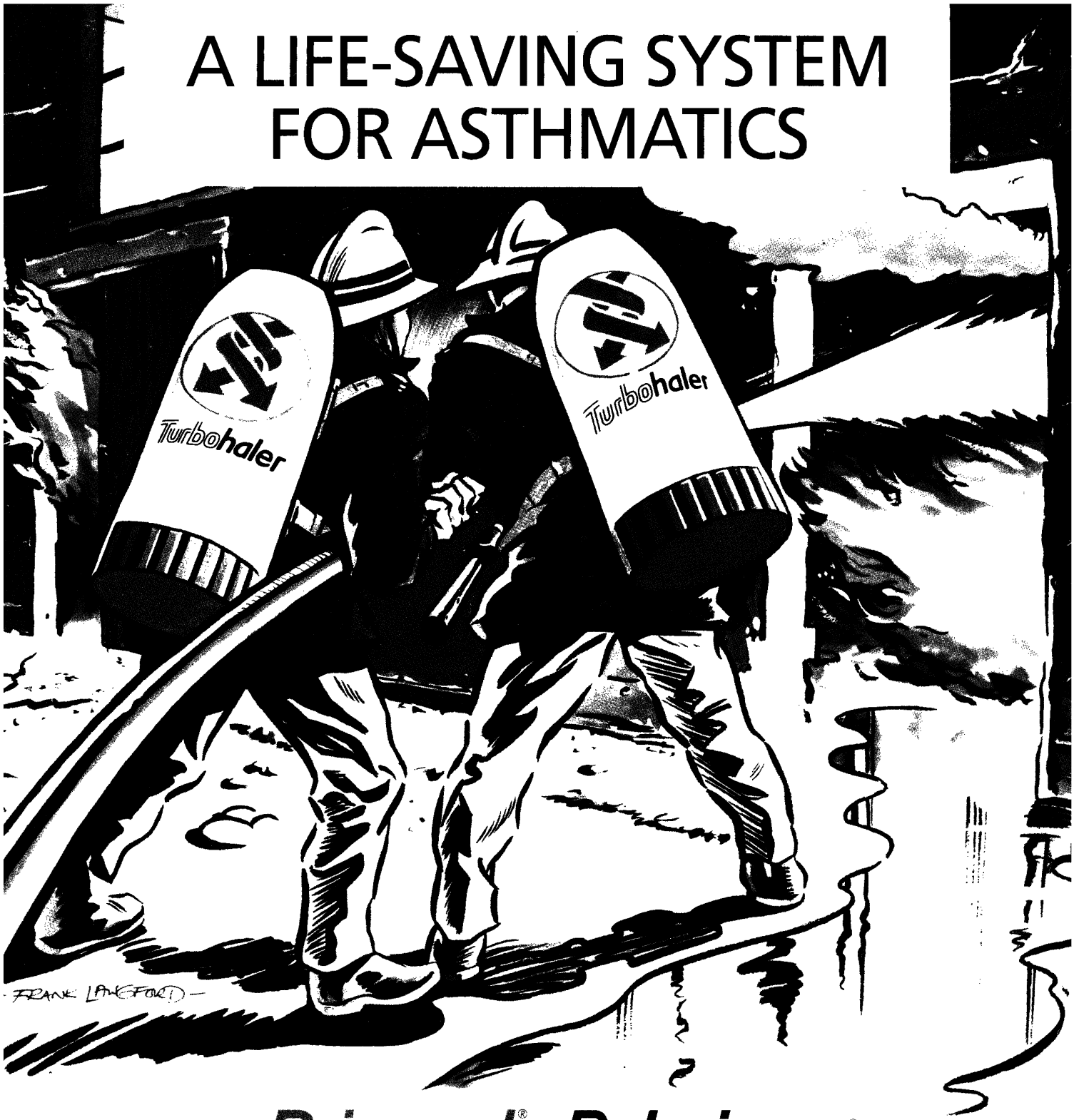

Bricanyl®
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TERBUTALINE SULPHATE

Pulmicort®
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BUDESONIDE

Abridged prescribing information: Presentation: Bricanyl Turbohaler. Dry powder inhaler delivering 0.5 mg terbutaline sulphate per actuation. **Uses** Relief and prevention of bronchospasm in bronchial asthma and bronchopulmonary disorders in which bronchospasm or reversible airways obstruction is a complicating factor. **Dosage and administration:** Adults and children (including elderly): One inhalation (0.5 mg) as required. Not more than 4 inhalations/day. **Contra-indications, warnings, etc:** Sensitivity to terbutaline sulphate. Precautions: Care should be taken in patients with myocardial insufficiency or thyrotoxicosis. Additional blood glucose measurements are initially recommended in diabetic patients. If treatment becomes less effective or shorter acting, the patient's general condition should be reviewed. Do not use in patients with hypertrophic cardiomyopathy. Potentially serious hypokalaemia may result from ß2-agonist therapy. Administer with caution during the first trimester of pregnancy. Do not administer concurrently with non-selective ß-blockers. Use with caution with other sympathomimetics. **Side effects:** Tremor, tonic cramp and palpitations are all characteristic of sympathomimetic amines. A few patients feel tense. **Basic NHS price:** Bricanyl Turbohaler (100 doses) £7.96. **Legal category:** POM. **Product licence number:** PL 0017/0241.

Presentations: Pulmicort Turbohaler 100. 100 µg/puff budesonide dry powder inhaler containing 200 doses. Pulmicort Turbohaler 200. 200 µg/puff budesonide dry powder inhaler containing 100 doses. Pulmicort Turbohaler 400. 400 µg/puff budesonide dry powder inhaler containing 50 doses. **Uses:** Bronchial asthma. **Dosage and administration:** Individualise dose. Adults: 200-1600 µg daily in divided doses. Children: 200-800 µg daily in divided doses. Maintenance: Use lowest possible dose. Brush the teeth and rinse the mouth out with water after each use. **Contra-indications, warnings, etc:** Active pulmonary tuberculosis. Special care is needed in patients with fungal and viral infections in the airways. Avoid administration during pregnancy. A short course of oral steroids in addition to Pulmicort may be required in patients with excessive mucus in the bronchi. Transfer of patients dependent on oral steroids to treatment with Pulmicort demands special care. See data sheet for further details. **Side effects:** Mild irritation in the throat, hoarseness and oral candidiasis occur in some patients. Rare cases of cataract have been reported after prolonged use of corticosteroids. **Legal category:** POM. **Basic NHS price:** Pulmicort Turbohaler 100 (200 doses) £18.50. Pulmicort Turbohaler 200 (100 doses) £18.50. Pulmicort Turbohaler 400 (50 doses) £18.50. **Product licence numbers:** Pulmicort Turbohaler 100 PL 0017/0319 (100 µg/puff). Pulmicort Turbohaler 200 PL 0017/0272 (200 µg/puff). Pulmicort Turbohaler 400 PL 0017/0271 (400 µg/puff). **Further information is available from the product licence holder:** Astra Pharmaceuticals Limited, Home Park, Kings Langley, Herts WD4 8DH. ®Registered trade mark

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