PULMICORT RESPULES®
(budesonide nebuliser suspension for oral inhalation)
0.25mg/ml & 0.5mg/ml

QUALITATIVE AND QUANTITATIVE COMPOSITION
Each single-dose unit of 2ml contains: 0.5mg or 1mg budesonide.

DESCRIPTION
Budesonide is a white to off-white powder, freely soluble in chloroform, sparingly soluble in ethanol and practically insoluble in water and heptane. Budesonide melts with decomposition between 224°C and 231.5°C.

PULMICORT RESPULES nebuliser suspension for inhalation is a white to off-white suspension in plastic single dose units. PULMICORT RESPULES contain budesonide 0.25mg/ml or 0.5mg/ml as the active ingredient plus, disodium edetate, sodium chloride, polysorbate 80 (E 433) citric acid - anhydrous (E 330), sodium citrate (E 331) and water for injections.

The active ingredient, budesonide, is a non-halogenated glucocorticoid structurally related to 16-α-hydroxyprednisolone. The chemical name is 16α, 17α-22R, S-propylmethylenedioxy-pregna-1, 4-diene-11ß, 21-diol-3, 20-dione; MW 430.5.

PHARMACOLOGY
Clinical – Bronchial asthma
PULMICORT is a corticosteroid for inhalation use in the treatment and prophylaxis of asthma.

Studies in animals and humans have shown an advantageous ratio between topical anti-inflammatory activity and systemic glucocorticoid effect over a wide dose range. This is explained by the extensive first pass hepatic degradation of budesonide after systemic absorption, approximately 85-90%, in combination with the low potency of formed metabolites.

Budesonide is approximately twice as potent as beclomethasone dipropionate as shown in the skin blanching test for anti-inflammatory activity of topical steroids in humans. Budesonide has, however, less systemic effect than beclomethasone dipropionate, as measured by depression of morning plasma cortisol and effect on differential WBC count. The improved ratio of topical anti-inflammatory activity to systemic effect of budesonide is due to high glucocorticoid receptor affinity combined with a high first pass metabolism and a short half-life.

Doses of 0.8mg have been found to suppress plasma cortisol levels and urinary cortisol secretion. A single inhalation of 3.2mg budesonide was found to suppress plasma cortisol levels to a degree similar to 10mg oral prednisolone.

Budesonide has been shown to counteract the mainly "IgE" but not the mainly "IgG" mediated lung anaphylaxis in guinea pigs. Pre-treatment for one to four weeks with inhaled budesonide 1mg daily in asthmatic patients inhibited the immediate bronchial reaction to allergen challenge in a time-related manner; the late reaction is inhibited after one week of inhaled treatment.

Inhaled budesonide pre-treatment for 2 to 4 weeks has also been shown to reduce non-specific bronchial hyper-responsiveness in asthmatic patients to both direct (histamine, methacholine) and indirect (exercise) provocative stimuli in a time-related manner.

Budesonide did not potentiate ß-receptor-mediated bronchodilation and did not affect theophylline-induced relaxation of respiratory airway smooth muscle in guinea pigs. In man, single oral inhalations of up to 1.6mg budesonide produced mild bronchodilation. This effect is maximal at 6 hours after inhalation with a duration of 12 hours.

Clinical – Croup
A number of studies in children with croup have compared Pulmicort Respules with placebo. Examples of representative studies evaluating the use of Pulmicort Respules for the treatment of children with croup are given below.

Efficacy in children with mild to moderate croup
A randomised, double-blind placebo-controlled trial in 87 children (aged 7 months to 9 years), admitted to hospital with a clinical diagnosis of croup, was conducted to determine whether Pulmicort Respules improves croup symptom scores or shortens the duration of stay in hospital. An initial dose of Pulmicort Respules (2mg) or placebo was given followed by either Pulmicort Respules 1mg or placebo every 12 hours. Pulmicort Respules statistically significantly improved croup score at 12 and 24 hours and at 2 hours in patients with an initial croup symptom score above 3. There was also a 33% reduction in the length of stay.

Efficacy in children with moderate to severe croup
A randomised, double-blind, placebo-controlled study compared the efficacy of Pulmicort Respules and placebo in the treatment of croup in 83 infants and children (aged 6 months to 8 years) admitted to hospital for croup. Patients received either Pulmicort Respules 2mg or placebo every 12 h for a maximum of 36 h or until discharge from hospital. The total croup symptom score was assessed at 0, 2, 6, 12, 24, 36 and 48 hours after initial dose. At 2 hours, both the Pulmicort Respules and placebo groups showed a similar improvement in croup symptom score, with no statistically significant difference between the groups. By 6 hours, the croup symptom score in the Pulmicort Respules group was statistically significantly improved compared with the placebo group, and this improvement versus placebo was similarly evident at 12 and 24 hours.

Clinical – Exacerbation of chronic obstructive pulmonary disease (COPD)
Several studies on nebulised budesonide, 4-8mg/day have shown to effectively treat exacerbations of COPD.

The efficacy of budesonide was evaluated in an open-label, randomised, comparative study in 78 hospitalised patients with acute exacerbations of COPD in two parallel groups receiving nebulised budesonide (n=37) 4 mg/day (2 mg twice daily) or intravenous infusion of prednisolone 120-180 mg/day (n=41) for 7-14 days. Patients treated with nebulised budesonide or prednisolone showed similar improvements in FEV1, SpO2 (saturation as measured by pulse oximetry) and symptoms (COPD Assessment Test™ (CAT)).

In a multi-center randomised controlled, single-blind study involving 471 patients with acute exacerbations of COPD, patients were treated with nebulised budesonide 6 mg/day (2 mg three times/day); or intravenously injected methylprednisolone (40 mg/day) for 10 days. Clinical efficacy of nebulised budesonide in comparison to systemic methylprednisolone as measured by FEV1, PaCO2 and symptoms (CAT) was comparable, while PaO2 improved more in the methylprednisolone group.

In a double-blind, randomised, placebo-controlled study involving 199 patients with acute exacerbations of COPD, patients were treated with nebulised budesonide 8 mg/day (2 mg four times a day) (n=71) or 30 mg oral prednisolone every 12 hours (n=62) or placebo (n=66) for 3 days. Improvement in post-bronchodilator FEV1 compared to placebo was 0.10 L for budesonide and 0.16 L for prednisolone; the difference between the active treatments was not statistically significant. The proportion of patients showing clinical improvement in post-bronchodilator FEV1 of at least 0.15 L was greater in the nebulised budesonide group (34%) and the prednisolone group (48%) than in the placebo group (18%). The differences were statistically significant for both active treatments versus placebo ($p<0.05$) but not between the active treatments.

PHARMACOKINETICS
Approximately 10% of the discharged dose of PULMICORT aerosol is deposited in the lungs.

The volume of distribution of budesonide in adult man is approximately 300L and in children is 3.1 to 4.8 L/kg indicating a high tissue affinity. Plasma protein binding is 88.3 ±1.5% in humans.

In adults the plasma half-life following inhalation via aerosol was 2.0 ± 0.2 hours and in children 1.5 hour with peak plasma levels occurring immediately after administration.

Negligible biotransformation was observed in human lung and serum preparations.

PULMICORT is 90% inactivated on first pass through the liver, via metabolism to more polar metabolites with a more than 100-fold lower glucocorticosteroid systemic activity than the parent compound.

In human volunteers who inhaled tritiated budesonide, 31.8 ± 7.5% of the discharged dose was recovered in urine and 15.1 ± 4.3% in faeces (0-96h). Plasma clearance of unchanged budesonide was calculated to be 84 L/h in adults and 1.5 to 2 L/h/kg in children.

INDICATIONS

PULMICORT RESPULES contain the potent non-halogenated corticosteroid budesonide for use in bronchial asthma in patients where use of a pressurized inhaler or dry powder formulation is unsatisfactory or inappropriate.

PULMICORT RESPULES can be used for the treatment of acute laryngotracheobronchitis (croup) in infants and children.

PULMICORT RESPULES can be used in patients with exacerbations of chronic obstructive pulmonary disease (COPD) in persons without signs of acute respiratory insufficiency.

CONTRAINDICATIONS

Hypersensitivity to budesonide or any other ingredients.

PRECAUTIONS

Bronchospasm

PULMICORT is not indicated for rapid relief of bronchospasm. PULMICORT is therefore not suitable as sole therapy for the treatment of status asthmaticus or other acute exacerbations of asthma where intensive measures are required.

If patients find short-acting bronchodilator treatment ineffective, or they need more inhalations than usual, medical attention must be sought. This indicates a worsening of the underlying conditions, and warrants a reassessment of the therapy.

Oral corticosteroid usage

Particular care is needed in patients who are being transferred from oral corticosteroids to PULMICORT, since they may remain at risk of impaired adrenal function for some considerable time (see PRECAUTIONS - Potential systemic effect of inhaled corticosteroids: HPA axis suppression and adrenal insufficiency). These patients should be instructed to carry an appropriate warning card (see Clinical Management: Patients - Oral corticosteroid dependent).

Patients previously receiving high doses of systemic steroids may regain earlier allergic symptoms such as rhinitis and eczema when transferred from oral therapy to PULMICORT due to the reduced systemic steroid effect of budesonide (see Clinical Management: Patients - oral corticosteroid dependent).

Potential systemic effects of inhaled corticosteroids

Inhaled steroids are designed to direct glucocorticoid delivery to the lungs in order to reduce overall systemic glucocorticoid exposure and side effects. However inhaled steroids may have adverse effects; possible systemic effects of inhaled steroids include depression of the HPA axis, reduction of bone density, cataracts and glaucoma and retardation of growth rate in children. In steroid-dependant patients, prior systemic steroid usage may be a contributing factor (see Precautions - Oral corticosteroid usage), but such effects may occur amongst patients who use only inhaled steroids regularly.

<u>HPA axis suppression and adrenal insufficiency</u>

Dose-dependent HPA axis suppression (as indicated by 24 hour urinary and/or plasma cortisol AUC) has been observed with inhaled budesonide, although the physiological circadian rhythms of plasma cortisol were preserved. This indicates that the HPA axis suppression may represent a physiological adaption in response to inhaled budesonide, not necessarily adrenal insufficiency. The lowest dose that results in clinically relevant adrenal insufficiency has not been established. Very rare cases of clinically relevant adrenal dysfunction have been reported in patients using inhaled budesonide at recommended doses.

Particular care is needed in patients who are being transferred from oral corticosteroids to PULMICORT, since they may remain at risk of impaired adrenal function for some considerable time (see PRECAUTIONS - Oral corticosteroid usage). Patients who have required high dose emergency corticosteroid therapy, prolonged treatment at the highest recommended dose of inhaled corticosteroids

or patients administering concomitant medication metabolised by CYP3A4 (see Interactions with other drugs) may also be at risk. These patients may exhibit signs and symptoms of adrenal insufficiency when exposed to severe stress such as trauma, surgery, infection (particularly gastroenteritis) or other conditions associated with severe electrolyte loss. Monitoring for signs of adrenal dysfunction is advisable in these patient groups. For these patients additional systemic glucocorticosteroid cover should be considered during periods of stress, severe asthma attack or elective surgery.

Bone density

Whilst corticosteroids may have an effect on bone mass at high doses, long term follow up (3 - 6 years) studies of budesonide treatment in adults at recommended doses, have not demonstrated a negative effect on bone mass compared to placebo, including one study conducted in patients with a high risk of osteoporosis. The lowest dose that does effect bone mass has not been established.

Bone mineral density measurements in children should be interpreted with caution as an increase in bone area in growing children may reflect an increase in bone volume. In three large medium to long term (12 months - 6 years) studies in children (5-16 years), no effects on bone mineral density were observed after treatment with Pulmicort (189 - 1322μg/day) compared to nedocromil, placebo or age matched controls. However, in a randomised 18 month study (n=176; 5-10 years), bone mineral density was significantly decreased by 0.11g/cm^2 (p=0.023) in the group treated with inhaled budesonide via Turbuhaler compared with the group treated with inhaled disodium cromoglycate. The dose of budesonide was 400μg twice daily for 1 month, 200μg twice daily for 5 months and 100μg twice daily for 12 months and the dose of disodium cromoglycate 10mg three times daily. The clinical significance of this result remains uncertain.

Growth

Long term studies show that children treated with inhaled budesonide ultimately achieve adult target height. However, an initial reduction of growth velocity (approximately 1cm) has been observed and is generally within the first year of treatment.

Rare individuals may be exceptionally sensitive to inhaled corticosteroids. Height measurements should be performed to identify patients with increased sensitivity. The potential growth effects of prolonged treatment should be weighed against the clinical benefit. To minimise the systemic effects of inhaled corticosteroids, each patient should be titrated to his/her lowest effective dose (see DOSAGE & ADMINISTRATION).

Infections and tuberculosis

High doses of glucocorticosteroids may mask some signs of existing infection and new infections may appear during their use. Special care is needed in patients with active or quiescent pulmonary tuberculosis or fungal, bacterial or viral infections of the respiratory system.

Hepatic function

Reduced liver function may affect the elimination of corticosteroids. This may be clinically relevant in patients with severely compromised liver function.

Positive pressure delivery systems

Respiratory drugs should not be used with positive pressure delivery systems (eg. IPPB) in pulmonary conditions involving pneumothorax, air cysts or mediastinal emphysema unless special drainage is performed.

Carcinogenicity and mutagenicity

The carcinogenic potential of budesonide has been evaluated in mouse and rat at oral doses up to 200 and 50μg/kg/day, respectively. No oncogenic effect was noted in the mouse. One study indicated an increased incidence of brain gliomas in male Sprague-Dawley rats given budesonide, however the results were considered equivocal. Further studies performed in male Sprague-Dawley and Fischer rats showed that the incidence of gliomas in the budesonide-treated rats was low and did not differ from that in the reference glucocorticoid groups or the controls. It has been concluded that treatment with budesonide does not increase the incidence of brain tumours in the rat.

In male rats dosed with 10, 25 and 50μg/kg/day, those receiving 25 and 50μg/kg/day showed an increased incidence of primary hepatocellular tumours. This was observed in all three steroid groups (budesonide, prednisolone, triamcinolone acetonide) in a repeat study in male Sprague-Dawley rats thus indicating a class effect of corticosteroids.

The mutagenic potential of budesonide was evaluated in 6 different test systems. No mutagenic or clastogenic effects of budesonide were found.

Pneumonia in patients with COPD
An increase in the incidence of pneumonia, including pneumonia requiring hospitalisation, has been observed in patients with COPD receiving inhaled corticosteroids. There is some evidence of an increased risk of pneumonia with increasing steroid dose but this has not been demonstrated conclusively across all studies.

There is no conclusive clinical evidence for intra-class differences in the magnitude of the pneumonia risk among inhaled corticosteroid products.

Physicians should remain vigilant for the possible development of pneumonia in patients with COPD as the clinical features of such infections overlap with the symptoms of COPD exacerbations.

Risk factors for pneumonia in patients with COPD include current smoking status, older age, low body mass index (BMI) and severe COPD.

Visual disturbance
Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

USE IN PREGNANCY - Category A
The benefits of asthma control outweigh any potential for an adverse pregnancy outcome.

Results from a large prospective epidemiological study and from world-wide post marketing experience indicate that inhaled budesonide during pregnancy has no adverse effects on the health of the foetus or new born child.

Inhaled glucocorticosteroids, such as budesonide, should be considered because of the lower systemic effects of doses, compared to those of oral glucocorticosteroids, required to achieve similar pulmonary responses.

USE IN LACTATION
Budesonide is excreted in breast milk. However, due to the relatively low doses used via the inhalational route the amount of drug present in the breast milk, if any, is likely to be low. Breastfeeding can be considered if the potential benefit outweighs any potential risks.

INTERACTIONS WITH OTHER DRUGS
The metabolism of budesonide is primarily mediated by CYP3A, a subfamily of cytochrome P450. Inhibitors of this enzyme e.g. ketoconazole and itraconazole, can therefore increase systemic exposure to budesonide. This is of limited clinical importance for short-term (1-2 weeks) treatment with CYP3A inhibitors, but should be taken into consideration during long-term treatment.

ADVERSE REACTIONS
PULMICORT is generally well tolerated. Most adverse reactions have been mild and of a local character. Systemic effects and oropharyngeal complications caused by budesonide were found to be dose dependent.

Clinical signs of steroid excess were present in 50% of patients (n=10) taking 1.6mg or more daily of budesonide alone for long periods.

Clinical trials, literature reports and post-marketing experience suggest that the following adverse drug reactions may occur:

Common (more than 1%)

Nose and throat:	hoarseness; sore, irritated throat; irritation of the tongue and mouth; dry mouth; oral candidiasis
Respiratory:	cough
Infections and infestations:	pneumonia (in COPD patients)

Uncommon (less than 1%)

Nose and throat:	irritation of the larynx; bad taste
Gastrointestinal:	diarrhoea; nausea
Hypersensitivity reactions:	Immediate and delayed hypersensitivity reactions such as skin reactions (eg. urticaria, rash, dermatitis), bronchospasm, angioedema and anaphylactic reaction.
Central Nervous System:	headache; lightheadedness; thirst; tiredness
Metabolic and nutritional disorders:	weight gain
Eye disorders:	Vision blurred

If oropharyngeal candidiasis develops, it may be treated with appropriate anti-fungal therapy whilst still continuing with PULMICORT therapy. The incidence of candidiasis can generally be held to a minimum by having patients rinse their mouth with water after each inhalation.

Inhaled steroids may have adverse effects in higher than recommended doses; possible systemic effects of inhaled steroids include depression of the HPA axis, reduction of bone density and retardation of growth rate in children (see PRECAUTIONS – Potential systemic effects of inhaled corticosteroids).

- Reduction in growth velocity has been reported in association with administration of inhaled corticosteroids, however studies with budesonide indicate that this is transient and that final adult height may ultimately be achieved (see PRECAUTIONS - Growth).
- Dose dependant HPA axis suppression has been observed with budesonide, however this may represent a physiological adaption rather than adrenal insufficiency (see PRECAUTIONS - HPA axis suppression and adrenal insufficiency). The lowest dose that results in clinically relevant adrenal insufficiency has not been established.
- No negative effects on bone mass have been observed in adults treated with inhaled budesonide at recommended doses. In children, bone mineral density should be interpreted with caution as an increase in bone area may reflect an increase in bone volume (see PRECAUTIONS - Bone density).

Rare reports of skin bruising have occurred following treatment with inhaled glucocorticosteroids.

Psychiatric symptoms such as behavioural disturbances, nervousness, restlessness and depression have been observed with budesonide as well as other glucocorticosteroids.

Facial skin irritation has occurred in a few cases when a nebuliser with a face mask has been used. To prevent irritation the face should be washed after each use of PULMICORT RESPULES delivered via a nebuliser with a face mask.

Rarely, PULMICORT may provoke bronchoconstriction in hyperreactive patients. Bronchospasm may be treated with an inhaled β_2- agonist.

DOSAGE AND ADMINISTRATION

BRONCHIAL ASTHMA:

PULMICORT RESPULES should be administered from a suitable nebuliser. The dose delivered to the patient varies between 40-60% of the nominal dose depending on the nebulising equipment used. The nebulisation time and the dose delivered are dependent on flow rate, volume of nebuliser chamber and volume fill. A suitable fill for most nebulisers is 2-4mL.

Some sedimentation may occur during storage of PULMICORT RESPULES. If this does not readily resuspend completely upon shaking, the RESPULE should be discarded.

Dosage initially, or during periods of severe asthma, or while reducing oral corticosteroids

Adults

1-2mg twice daily.

Children

0.5-1mg twice daily.

Maintenance
The maintenance dose should be individualised and should be the lowest dose, which keeps the patient symptom-free. Recommended doses are:

Adults
0.5-1mg twice daily.

Children
0.25-0.5mg twice daily.

Clinical Management
Patients - not oral corticosteroid dependent
Treatment with the recommended doses of PULMICORT usually gives a therapeutic effect within 10 days.

In patients with excessive mucus secretion in the bronchi, an initial short course (about 2 weeks) of an oral corticosteroid, commencing with a high dose and gradually reducing, should be given in addition to PULMICORT. Treatment should be continued for at least one month before determining the maximal response to a given dose of PULMICORT.

Patients - oral corticosteroid dependent
Transfer of patients dependent on oral corticosteroids to PULMICORT requires special care because of slow normalisation of the disturbed hypothalamic-pituitary-adrenal function caused by extended treatment with oral corticosteroids (see PRECAUTIONS - Oral Corticosteroid usage and Potential systemic effects of inhaled corticosteroids - HPA axis suppression and adrenal insufficiency).

When PULMICORT treatment is initiated, the patient's asthma should be in a relatively stable phase. A high dose of PULMICORT should then be given in combination with the previously used oral corticosteroid dose for about 2 weeks. The dose of oral corticosteroid should then be reduced gradually (for example 1mg prednisolone or equivalent every four days, however, the exact rate of reduction will depend on individual clinical response) to the lowest possible level. The dose of PULMICORT should not be changed while the patient remains on oral corticosteroids.

In many cases, it may be possible to completely replace the oral corticosteroid with inhaled PULMICORT. In other patients, a low oral steroid maintenance dose may be necessary. Some patients may experience uneasiness during the withdrawal of oral corticosteroids due to the decreased systemic corticosteroid effect. The physician may need to actively support the patient and to stress the reason for the PULMICORT treatment.

The length of time needed for the body to regain sufficient natural corticosteroid production is often extended and may be as long as 12 months. Transferred patients should carry a warning card indicating that they may need supplementary systemic corticosteroids during periods of stress, such as severe infection, trauma or surgery. During such times it may be necessary to give additional oral corticosteroids.

During transfer from oral therapy to PULMICORT, a lower systemic steroid action is experienced. Earlier allergic symptoms may recur (eg. rhinitis, eczema, conjunctivitis) or patients may suffer from tiredness, headache, muscle and joint pain, lassitude and depression or occasionally nausea and vomiting. In these cases, further medical support may be required.

CROUP:
In infants and children with croup, the usual dose is 2mg of nebulised budesonide. This dose is given as a single administration, or as two 1mg doses separated by 30 minutes. Dosing can be repeated every 12 hours up to 36 hours or until clinical improvement.

EXACERBATIONS OF COPD:
Patients should be treated with daily doses of 4 to 8 mg of PULMICORT RESPULES, divided into two to four administrations, until clinical improvement is achieved, but for no longer than 10 days.

The use of nebulised budesonide has not been evaluated in clinical trials in patients with an exacerbation of COPD with respiratory failure requiring invasive mechanical ventilation or admission to intensive care

unit.

Time to effect in exacerbations of COPD
Following inhaled administration of PULMICORT RESPULES for the treatment of exacerbations of COPD the time to symptom improvement is comparable to administration of systemic corticosteroids.

OVERDOSAGE
Symptoms
In most cases, occasional overdosing will not produce any obvious symptoms but will decrease the plasma cortisol level and increase the number and percentage of circulating neutrophils. The number and percentage of lymphocytes and eosinophils will decrease concurrently. Habitual overdosing may cause hypercorticism and hypothalamic-pituitary-adrenal suppression.

Treatment
Withdrawing PULMICORT or decreasing the dose will abolish these effects, although the normalization of the HPA-axis may be a slow process.

PRESENTATION
0.25mg per 1ml and 0.5mg per 1ml sterile nebuliser suspension in single dose polyethylene (plastic) units.

Pack size available: 30 single dose units of 2 ml (for 0.25mg/ml and 0.5mg/ml), 5 single dose units of 2 ml (for 0.5mg/ml only).

SHELF-LIFE
24 months

STORAGE CONDITION
Store below 30°C. Do not refrigerate. Unused Respules should be discarded three months after opening of foil packs.

NAME AND ADDRESS OF THE MANUFACTURER
AstraZeneca AB
Forskargatan 18,
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Sweden.

DATE OF REVISION OF TEXT
07 January 2025
VV-RIM-01321498

INSTRUCTION LEAFLET
Before using Pulmicort Respules, please read this leaflet and follow the instructions carefully.

IMPORTANT
Pulmicort (budesonide) is a preventative agent and should not be used as sole therapy in the case of an acute asthma attack. If your asthma worsens you should consult your treatment plan or consult your physician.

CAUTION
The contents of Pulmicort Respules are for inhalation via a nebuliser, and should not be swallowed or injected.
Use only as directed by your physician.
Avoid getting the aerosol in the eyes (we suggest that you use eye goggles).
Wash the face and rinse the mouth out with water after administration of each dose of Pulmicort.
Do not exceed the prescribed dose.
Pulmicort may be nebulised in combination with Bricanyl®, Ventolin™, Intal™, Atrovent™ or normal saline.
Pulmicort should be added to the nebuliser immediately before use.
Medications for nebulisation should not be mixed in advance.

WARNING
Unused, unopened Respules should be discarded 3 months after opening of the foil pack.
During storage Pulmicort Respules should be protected from light by keeping them in the foil envelope.

Instructions for the use of Pulmicort Respules
1. Prepare the nebuliser for filling.
2. Detach one Pulmicort Respule from the rack by twisting it firmly.
3. Shake the Respule.
4. Twist the top off the Respule.
5. Squeeze the contents into the reservoir of the nebuliser.
   Do not dilute the contents unless instructed to do so by your physician.
   In some cases, it may be necessary to use only a part of the Respule content to obtain the prescribed dose.
   Your physician or pharmacist will advise you accordingly.
6. Use the nebuliser as directed, ensuring that the contents of the reservoir are completely used up.
7. After use, clean your nebuliser in accordance with the manufacturer's recommendations.

Also remember to wash your face and rinse your mouth out with water.
After each nebulisation, the mouthpiece or facemask should be rinsed in warm water and dried.

Nebulisers and Pulmicort (budesonide) Respules
For all solutions used in a nebuliser, it is very important that the mist (aerosol) produced is the right size and strength to work correctly in your lungs.
With Pulmicort Respules, this can best be achieved by **using a compressed air jet nebuliser which gives an output of at least 6 to 8 litres per minute.**
A jet nebuliser creates the aerosol mist for you to inhale by using air pumped via an electric compressor or compressed oxygen from a tank.
Please check the instruction manual, or with the manufacturer of your nebuliser to ensure your nebuliser fulfils these requirements.
Please note that it is **not** recommended that the **ultrasonic nebuliser** is used with Pulmicort Respules.
An ultrasonic nebuliser creates a high frequency signal to produce vibrations in the liquid and to provide a fog of small droplets which can be inhaled. Use of this type of nebuliser may cause your treatment with Pulmicort Respules to be ineffective.
Opened single-dose units should be used within 12 hours.
Sterile single-dose units in a opened envelope should be used within 3 months.
Always keep unopened units in the foil envelope in order to protect from light.
Please also follow the other instructions in this pack.

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