For the use of a Registered Medical Practitioner or a Hospital or a Laboratory only OR for Specialist Use only

Beclometasone and Salbutamol Inhaler

Aerocort-A HFA Inhaler

Composition
Each actuation delivers:
Beclometasone Dipropionate BP……50 mcg
Salbutamol Sulphate BP equivalent to Salbutamol….100 mcg
Suspended in Propellant HFA-134a……..q.s

Dosage Form
Metered Dose Inhaler

Pharmacology

Pharmacodynamics

Beclomethasone dipropionate is a synthetic glucocorticoid and exerts a topical, anti-inflammatory effect on the lungs, with fewer systemic effects than oral corticosteroids.

Pharmacodynamic studies in patients with mild asthma given beclometasone for 14 days, have shown that there is a linear correlation among urinary free cortisol suppression, dose administered, and serum total-beclometasone levels obtained.

Salbutamol is a selective β_2-adrenergic receptor agonist. The pharmacological effects of salbutamol are at least in part attributable to stimulation through beta-adrenergic receptors of intracellular adenyl cyclase, the enzyme that catalyses the conversion of adenosine triphosphate (ATP) to cyclic-3',5'-adenosine monophosphate (cyclic AMP). Increased cyclic AMP levels are associated with relaxation of bronchial smooth muscle and inhibition of release of mediators of immediate hypersensitivity from cells, especially from mast cells. Salbutamol also stimulates mucous secretion and mucociliary transport in the respiratory tract. Bronchial effects of inhaled salbutamol can be detected after a few minutes and duration of action is normally 4-6 hours.

Like other β_2-adrenoceptor agonists salbutamol also has cardiovascular effects in some patients as measured by changes in pulse rate, blood pressure, symptoms and ECG changes. These effects can especially be detected after oral and intravenous administration of salbutamol. Furthermore oral and intravenous salbutamol causes reduction in uterine tonicity which has been associated with pain relief in pregnancy. In addition, salbutamol has some metabolic effects, Especially intravenous and nebulised salbutamol decreases serum potassium concentrations although the effect is generally mild and transient. Salbutamol has also lipolytic effects and it has been shown to cause increases in blood glucose and insulin probably by stimulating glycogenolysis and having a stimulatory effect on β_2-receptors in pancreas cells.

Pharmacokinetics

The pharmacokinetic profile of beclometasone shows that the peak serum concentration for total- beclometasone (BOH) (total of any beclometasone OH and beclometasone dipropionate or monopropionate hydrolysed to beclometasone OH) after single and multiple doses is achieved after 30 minutes.

The value at the peak is approximately 2 nanograms/ml after a total daily dose of 800 micrograms and the serum levels after 100, 200 and 400 micrograms are proportional. The principal route of elimination of beclometasone dipropionate and its several metabolites is in the faeces. Between 10% and 15% of an orally administered dose is excreted in the urine, as both conjugated and free metabolites of the drug.

Pharmacokinetic studies with beclometasone have not been carried out in any special populations.

Orally administered salbutamol is well absorbed with peak plasma concentrations occurring 1 to 4 hours after administration. The major proportion of inhaled Salbutamol is swallowed. The fraction that is distributed to the lung (approx. 10-25%) is rapidly seen in the circulation as free unmetabolised drug. The remainder is retained in the delivery system or is deposited in the oropharynx from where it is swallowed. The swallowed portion of an inhaled dose is absorbed from the gastrointestinal tract and undergoes considerable first-pass metabolism.

The plasma concentrations of inhaled Salbutamol are, however, lower than those produced by usual oral doses. Salbutamol and its metabolites are rapidly excreted in the urine and faeces with about 80% of the dose being recovered in urine within 24 hours. The elimination half-life of Salbutamol is 2.7 - 5.5 hours after oral and inhaled administration.

Indications
For the treatment of asthma, once the need for inhaled corticosteroid and bronchodilator therapy has been established.

Dosage and Method of Administration

Adults
Two inhalations, three or four times daily, titrated to the lowest effective dose.

Children
Not recommended in children

Contraindications
Hypersensitivity to beclometasone dipropionate, salbutamol sulphate or to any of the excipients
Intravenous or oral salbutamol is used for the management of premature labour uncomplicated by conditions such as placenta praevia, ante-partum haemorrhage or toxaemia of pregnancy; however inhaled salbutamol is not appropriate for management of premature labour.
Salbutamol preparations should not be used for threatened abortion.

Warning and Precaution
Patients should be properly instructed on the use of the inhaler to ensure that the drug reaches the target areas within the lungs. To be effective, inhaler must be used by patients on a regular basis, even when patients do not have asthma symptoms, When symptoms are controlled, maintenance therapy should be reduced in a stepwise manner to the minimum effective dose. Inhaled steroid treatment should not be stopped abruptly.

Patients with asthma are at risk of acute attacks and should have regular assessments of their asthma control including pulmonary function tests.

Beclomethasone is not indicated for the immediate relief of asthma attacks. Patients therefore need to have relief medication (inhaled short-acting bronchodilator) available for such circumstances.

Beclomethasone is not indicated in the management of status asthmaticus.

Severe asthma requires regular medical assessment, including lung-function testing, as there is a risk of severe attacks and even death. Patients should be instructed to seek medical attention if short-acting relief bronchodilator treatment becomes less effective, or more inhalations than usual are required as this may indicate deterioration of asthma control. If this occurs, patients should be assessed and the need for increased anti-inflammatory therapy considered (eg. higher doses of inhaled corticosteroid or a course of oral corticosteroid)

Severe asthma exacerbations should be managed in the usual way. Subsequently, it may be necessary to increase the dose of beclomethasone up to the maximum daily dose. Systemic steroid treatment may be needed and/or an antibiotic, if there is an infection.

However, systemic effects of inhaled corticosteroids may occur, particularly at high doses prescribed for prolonged periods. These effects are much less likely to occur than with oral corticosteroids. Possible systemic effects include Cushing's syndrome, Cushingoid features, adrenal suppression, growth retardation in children and adolescents, decrease in bone mineral density, cataract, glaucoma, and more rarely, a range of psychological or behavioural effects including psychomotor hyperactivity, sleep disorders, anxiety, depression (particularly in children). It is important, therefore, that the dose of inhaled corticosteroid is titrated to the lowest dose at which effective control of asthma is maintained.

It is recommended that the height of children receiving prolonged treatment with inhaled corticosteroids is regularly monitored. If growth is slowed, therapy should be reviewed with the aim of reducing the dose of inhaled corticosteroid, if possible, to the lowest dose at which effective control of asthma is maintained. In addition, consideration should be given to referring the patient to a paediatric respiratory specialist.

Prolonged treatment with high doses of inhaled corticosteroids, particularly higher than the recommended doses, may result in clinically significant adrenal suppression.
Additional systemic corticosteroid cover should be considered during periods of stress or elective surgery.

Patients who have received systemic steroids for long periods of time or at high doses, or both, need special care and subsequent management when being transferred to inhaled steroid therapy. Patients should have stable asthma before being given inhaled steroids in addition to the usual maintenance dose of systemic steroid. Withdrawal of systemic steroids should be gradual, starting about seven days after the introduction of beclomethasone therapy. For daily oral doses of prednisolone of 10mg or less, dose reduction in 1mg steps, at intervals of not less than one week is recommended. For patients on daily maintenance doses of oral prednisolone greater than 10mg, larger weekly reductions in the dose might be acceptable. The dose reduction scheme should be chosen to correlate with the magnitude of the maintenance systemic steroid dose.

As recovery from impaired adrenocortical function, caused by prolonged systemic steroid therapy is slow, adrenocortical function should be monitored regularly.

Patients should be advised that they may feel unwell in a non-specific way during systemic steroid withdrawal despite maintenance of, or even improved respiratory function. Patients should be advised to persevere with their inhaled product and to continue withdrawal of systemic steroids, even if feeling unwell, unless there is evidence of HPA axis suppression.

Patients weaned off oral steroids whose adrenocortical function is impaired should carry a steroid warning card indicating that they may need supplementary systemic steroids during periods of stress, eg, worsening asthma attacks, chest infections, major intercurrent illness, surgery, trauma, etc.

Discontinuation of systemic steroids may also cause exacerbation of allergic diseases such as atopic eczema and rhinitis. These should be treated as required with topical therapy, including corticosteroids and/or antihistamines.

Like other corticosteroids, caution is necessary in patients with active or latent pulmonary tuberculosis.

Patients should be advised to seek medical attention for review of maintenance beclomethasone therapy if peak flow falls, symptoms worsen or if the short-acting bronchodilator becomes less effective and increased inhalations are required. This may indicate worsening asthma.

Most patients can be successfully transferred to inhaled steroids with maintenance of good respiratory function, but special care is necessary for the first few months after the transfer, until the hypothalamic-pituitary-adrenal (HPA) system has sufficiently recovered to enable the patient to cope with stressful emergencies such as trauma, surgery or serious infections, Patients should, therefore, carry a steroid warning card to indicate the possible need to re-instate systemic steroid therapy rapidly during periods of stress or where airways obstruction or mucus significantly compromises the inhaled route of administration. In addition, it may be advisable to provide such patients with a supply of corticosteroid tablets to use in these circumstances. The dose of inhaled steroids should be increased at this time and then gradually reduced to the maintenance level after the systemic steroid has been discontinued.

Beclometasone dipropionate, like other inhaled steroids, is absorbed into the systemic circulation from the lungs. Beclometasone dipropionate and its metabolites may exert detectable suppression of adrenal function. Within the dose range 100-800 micrograms daily, clinical studies with beclomethasone have demonstrated mean values for adrenal function and responsiveness within the normal range.

In the event of a previous effective dose of inhaled salbutamol failing to give relief for at least three hours or if they need more inhalations than usual, the patient should be advised to seek medical advice as soon as possible. In this situation patients should be reassessed and consideration given to an increase in their anti-inflammatory therapy, (e.g. higher doses of inhaled corticosteroids or a course of oral corticosteroids). A regular anti-inflammatory controller medication taken on a daily basis is required as soon as the patient needs inhaled β_2-agonists more than twice a week. Severe episodes of asthma must be treated in the normal way.

As there may be adverse effects associated with excessive dosing, the dosage and frequency of administration should only be increased on medical advice.

Salbutamol should be administered with caution in patients with thyrotoxicosis, cardiac insufficiency, hypokalaemia, myocardial ischaemia, tachyarrhythmia and hypertrophic obstructive cardiomyopathy.

Potentially serious hypokalaemia may result from β_2 agonist therapy, mainly from parenteral and nebulised therapy. Particular caution is advised in acute severe asthma, as this effect may be potentiated by concomitant treatment with xanthine derivatives, steroids, diuretics and by hypoxia. It is recommended that serum potassium levels are monitored in such situations.

Rarely inhalation therapy may cause bronchospasm after dosing. In this event, treatment with Salbutamol must be immediately discontinued and, if need be, replaced with another therapy.

Cardiovascular effects may be seen with sympathomimetic drugs, including salbutamol. There is some evidence from post-marketing data and published literature of rare occurrences of myocardial ischaemia associated with salbutamol. Patients with underlying severe heart disease (e.g. ischaemic heart disease, arrhythmia or severe heart failure) who are receiving salbutamol should be warned to seek medical advice if they experience chest pain or other symptoms of worsening heart disease. Attention should be paid to assessment of symptoms such as dyspnoea and chest pain, as they may be of either respiratory or cardiac origin.

Drug Interaction

If additional adrenergic drugs are administered to patients using Aerocort-A HFA they should be used with caution to avoid deleterious cardiovascular effects.

Concomitant administration of salbutamol and non-selective ß-blocking drugs such as Propranolol is not recommended.

Patients treated with monoamine oxidase inhibitors or tricyclic antidepressants should be followed clinically in the beginning of salbutamol treatment, because the action of salbutamol on the vascular system may be potentiated.

The simultaneous administration of xanthines, corticosteroids or potassium excreting diuretics may increase hypokalaemia.

Pregnancy and Lactation

Pregnancy
There is inadequate evidence of safety in human pregnancy. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate and intra-uterine growth retardation. There may therefore, be a risk of such effects in the human foetus. It should be noted, however, that the foetal changes in animals occur after relatively high systemic exposure. Beclometasone dipropionate is delivered directly to the lungs by the inhaled route and so avoids the high level of exposure that occurs when corticosteroids are given by systemic routes.

Lactation
It is probable that beclometasone dipropionate is excreted in milk. However, given the relatively low doses used by the inhalation route, the levels are likely to be low. As salbutamol is excreted in breast milk. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where it is felt that the expected benefit to the mother outweighs any potential risk to the neonate.

The use of beclometasone Dipropionate/ salbutamol in pregnancy requires that the possible benefits of the drug be weighed against the possible hazards. The drug has been in widespread use for many years without apparent ill consequence.

There is no experience with or evidence of safety of propellant HFA 134a in human pregnancy or lactation. However, studies on the effect of HFA 134a on reproductive function and embryofoetal development in animals have revealed no clinically relevant adverse effects.

Undesirable Effect

Beclometasone Dipropionate

A serious hypersensitivity reaction including oedema of the eye, face, lips and throat (angioedema) has been reported rarely.

As with other inhaled therapy, paradoxical bronchospasm may occur after dosing. Immediate treatment with a short-acting bronchodilator should be initiated, beclometasone should be discontinued immediately and an alternate prophylactic treatment introduced.

Systemic effects of inhaled corticosteroids may occur, particularly with high doses prescribed for prolonged periods. These include adrenal suppression, growth retardation in children, decrease in bone mineral density and the occurrence of cataract and glaucoma.

Commonly, when taking beclometasone, hoarseness and candidiasis of the throat and mouth may occur. To reduce the risk of hoarseness and candida infection, patients are advised to rinse their mouth after using their inhaler.

Based on the MedDra system organ class and frequencies, adverse events are listed in the table below according to the following frequency estimate: very common (≥ 1/10); common (≥1/100 to <1/10); Uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1,000); very rare (<1/10,000), not known (cannot be estimated from the available data).

MedDra – system organ class	Frequency and Symptom
Infections and infestations	*Common*: Candidiasis in mouth and throat
Immune system disorders	*Rare*: Allergic reactions, angioedema in eyes, throat, lips and face
Endocrine disorders	*Very rare*: Adrenal suppression, growth retardation in children
Nervous system disorders	*Uncommon*: Headache, vertigo, tremor
Eye disorders	*Very rare*: Cataract, glaucoma
Respiratory, thoracic and mediastinal disorders	*Common*: Hoarseness, pharyngitis *Uncommon*: Cough, increased asthma symptoms *Rare*: Paradoxical bronchospasm
Gastrointestinal disorders	*Common*: Taste disturbances *Uncommon*: Nausea
Skin and subcutaneous tissue disorders	*Uncommon*: Urticaria, rash, pruritus, erythema, purpura
Musculoskeletal and connective tissue disorders	*Very rare*: Decrease bone mineral density
Psychiatric Disorders	*Unknown*: Psychomotor hyperactivity, sleep disorders, anxiety, depression, aggression, behavioural changes (predominantly in children)

Salbutamol sulphate

The undesirable effects caused by normally used inhaled doses of salbutamol are mild, typical for sympathomimetic agents, and they usually disappear with continued treatment.

Frequencies are defined as: very common (≥1/10), common, (≥1/100 and <1/10), uncommon (≥1/1000 and <1/100), rare (≥1/10,000 and <1/1000), very rare (<1/10,000) and not known (cannot be estimated from available data).

	Common	Uncommon	Rare	Very Rare
Immune System disorders		hypersensitivity reactions (angioedema, urticaria, hypotension and collapse)		
Metabolism and nutrition disorders			hypokalaemia	
Nervous system disorders:		Headache	hyperactivity, restlessness, dizziness	
Cardiac disorders	palpitations			myocardial ischaemia Cardiac arrhythmias including atrial fibrillation, supraventricular tachycardia and extra systoles
Vascular disorders	peripheral vasodilatation, and as a result small increase in heart rate			
Respiratory, thoracic and mediastinal disorders			bronchospasm (*see Warnings and precautions*), cough, irritation of mouth and throat which may be prevented by rinsing the mouth after inhalation,	
Musculoskeletal and connective tissue and bone disorders:	tremor		muscle cramps,	

Overdose
Acute overdosage is unlikely to cause problems with beclomethasone, The only harmful effect that follows inhalation of large amounts of the drug over a short time period is suppression of HPA function. Specific emergency action need not be taken. Treatment with beclomethasone should be continued at the recommended dose to control the asthma; HPA function recovers in a day or two,

Excess repeat use of salbutamol inhalations may produce adverse effects such as tachycardia, CNS stimulation, tremor, hypokalaemia and hyperglycaemia,

If excessive doses of beclomethasone dipropionate were taken over a prolonged period a degree of atrophy of the adrenal cortex could occur in addition to HPA suppression, In this event the patient should be treated as steroid dependent and transferred to a suitable maintenance dose of a systemic steroid such as prednisolone. Once the condition is stabilised, the patient should be returned to beclometasone by the method described above in *Warnings and precautions*,

Treatment consists of discontinuation of salbutamol together with appropriate symptomatic therapy. The preferred antidote for overdosage with salbutamol is a cardio-selective beta-blocking agent, but beta-blocking drugs should be used with caution in patients with a history of bronchospasm. Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored. If hypokalaemia occurs potassium replacement via the oral route should be given. In patients with severe hypokalaemia intravenous replacement may be necessary.

Incompatibility
NA

Shelf Life
36 months

Storage
Store below 30°C. Avoid storage in direct sunlight or heat. Protect from frost.

Packaging information
Aerocort-A HFA Inhaler is available in canister containing 200 metered dose.

Last Updated: *November 2014*

21070341

Cipla

Cipla

Bedometasone and Salbutamol Inhaler

Aerocort-A HFA inhaler

with dose indicator

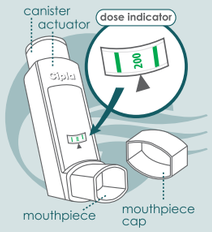
patient information leaflet

please read this leaflet completely before use

CFC-FREE

ABOUT YOUR AEROCORT-A HFA INHALER

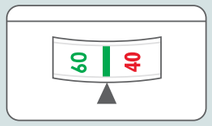
PARTS OF THE INHALER



Your **AEROCORT-A HFA** inhaler now comes with a dose indicator. It shows the number of puffs in the inhaler. As you use the inhaler, the dose indicator will countdown and indicate the number of puffs remaining.

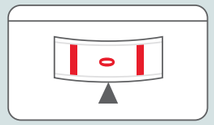
HOW TO KNOW THAT YOUR AEROCORT-A HFA INHALER IS GETTING OVER

When there are 40 puffs remaining, the colour of the numbers will change from green to red.



This indicates that fewer doses are remaining in the inhaler. You should now consider getting a new inhaler or ask your doctor if you need another one.

When the dose indicator displays '0', this means that there is no more medicine left in the inhaler & you need to discard the inhaler. Your inhaler may not feel empty & it may continue to operate, but you will not get the right amount of medicine, if you keep using it beyond '0'.



BEFORE USING YOUR AEROCORT-A HFA INHALER

A. Remove the cap from the mouthpiece & make sure that the mouthpiece is clean.

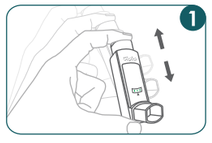
B. Hold the inhaler away from your face. Shake it well & release two puffs into the air.

C. Your **AEROCORT-A HFA** inhaler is now ready for use.

IF you have not used your inhaler for a week or more, shake well and release one puff into the air.

USING YOUR AEROCORT-A HFA INHALER

1. Sit or stand upright. Remove the mouthpiece cap & shake the inhaler well. Hold it upright as shown, with your thumb at the base below the mouthpiece. Place either one or two fingers on top of the canister.

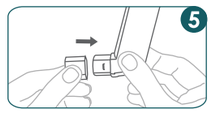


2. Breathe out fully, through your mouth.

3. Place the mouthpiece of the inhaler in your mouth between your teeth & close your lips around it (do not bite it). **Start breathing in slowly through your mouth. Press down the canister firmly & fully to release one spray while continuing to breathe in slowly & deeply.**

4. Remove the inhaler from your mouth & hold your breath for 10 seconds, or for as long as is comfortable. Breathe out normally.

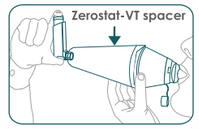
5. If another puff is required, wait for at least 1 minute. Shake inhaler well & repeat steps 2 to 4. After use, replace the mouthpiece cap firmly & snap it into position.



6. After taking each dose, rinse your mouth with water & spit it out.

IMPORTANT:
Do not rush steps 2, 3 & 4. It is important that you start to breathe in slowly before releasing a puff.
To ensure correct use of the inhaler, use it in front of a mirror for the first few times. If you see 'mist' coming out from the top of the inhaler or the sides of your mouth, start again from step 1. This escaping mist indicates incorrect technique.

In case of difficulty in using the inhaler correctly, you may use it along with a Zerostat-VT spacer.

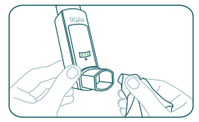


CLEANING YOUR AEROCORT-A HFA INHALER

It is important to keep your inhaler clean. Clean your inhaler atleast once a week.

1. Take the mouthpiece cap off. **DO NOT take the metal canister out of the actuator.**

2. Wipe the inside & the outside of the mouthpiece with a clean, dry cloth.



3. Replace the mouthpiece cap.

4. DO NOT wash or soak any part of the inhaler in water.

STORING YOUR AEROCORT-A HFA INHALER

Store below 30°C.
Avoid storage in direct sunlight or heat.
Protect from frost.
Keep the inhaler in an upright position, with the mouthpiece down.

DO NOT

- × *Spray the inhaler in your eyes.*
- × *Exceed the recommended dose.*
- × *Change/tamper with the numbers on the dose indicator.*
- × *Puncture or burn the inhaler even when empty as it is pressurized.*

Keep the inhaler out of the reach of children.

21070341

PACKAGING DEVELOPMENT

Product Name: Aerocort-A HFA Inhaler	**Material No.:** 21070341	**Version:** 01	**Item:** Leaflet	**Co-ordinator:** Shilpa	**Artist:** Manish	**Date:** 23/05/2018
Colours: BLUE WOOL TEST VALUE 5-8 (LIGHT FASTENING DATA) Front Side: Pantone 5473 C, Pantone 425 C, Pantone 185 C, Pantone 354 C; Back Side: Pantone 425 C				**INK:** Oil based Ink from DIC OR MICRO		
Design: Unfolded	**Reference:** 21048078			**Software:** Illustrator CC		
Fonts: ——	**Links:** Aerocort Inhaler.tif					
Actual Size: 280 x 170 mm	**Size after folding:** NA	**2D Code:** 21070341(F) & 21070341(B)	**Grain Direction :** Parallel to length			**Screen : #** __
Material: 70 GSM Maplitho Paper (From Andhra OR Ballarpur Paper Mill ONLY)			**Varnish:**	**Artwork Print Size:** ☐ actual ☐ scaled		
Path: D:\Manish\April 2018 to March 2019\Shilpa\Lebanon\Aerocort A Inhaler\21070341 Aerocort-A HFA Inhaler Dose Indicator Leaflet Lebanon.ai						

- **Instructions / Remark:** NA
- Any deviation must be brought to the notice of packaging development co-ordinator immediately.
- For any clarification, please contact packaging development co-ordinator immediately.
  NO CHANGES IN ARTWORK SHOULD BE DONE BY THE PRINTER
- The printer should verify the e-proof against the approved artwork before submitting for approval and the e-proof should have printer details .

Checked by	Artist	Cordinator	file loaded in Server	Section Head
Pharma Code	☐	☐		
2D Code	☐	☐		
QR Code	☐	☐		
Bar Code	☐	☐		
Artwork	☐	☐		
Spell check	☐	☐		