APPROVED PACKAGE INSERT - BEROTEC 100 HFA

SCHEDULING STATUS: **S2**

PROPRIETARY NAME: **BEROTEC® 100 HFA**

(and dosage form) metered dose inhaler

COMPOSITION:
Each metered dose (puff) provides fenoterol hydrobromide 100 µg
Propellant: 1,1,1,2 – Tetrafluoroethane (HFA 134a)
Other excipients: citric acid anhydrous, purified water, ethanol absolute (30 % *m/m*)

PHARMACOLOGICAL CLASSIFICATION:
A 10.2.1 Bronchodilators - Inhalants

PHARMACOLOGICAL ACTION:
Fenoterol hydrobromide is a $beta_2$ selective bronchodilator with a direct local effect which relaxes the constricted bronchial muscles.
The bronchodilator effect lasts 3 – 5 hours.

INDICATIONS:
a) Symptomatic treatment of acute asthma attacks.
b) Prophylaxis of exercise induced asthma.
c) Symptomatic treatment of bronchial asthma and other conditions with reversible airway narrowing e.g. chronic obstructive bronchitis.

Concomitant anti-inflammatory therapy should be considered for patients with bronchial asthma and steroid responsive chronic obstructive pulmonary disease (COPD).

CONTRA-INDICATIONS:
Hypertrophic obstructive cardiomyopathy, tachyarrythmias.
Hypersensitivity to fenoterol hydrobromide or inactive ingredients in the product.

INTERACTIONS:
Beta-adrenergics, anticholinergics, and xanthine derivatives (such as theophylline) may enhance the effect of fenoterol. The concurrent administration of other beta-mimetics, systemically available anticholinergics and xanthine derivatives (e.g. theophylline) may increase the side-effects.
A potentially serious reduction in bronchodilatation may occur during concurrent administration of beta-blockers.
Beta-adrenergic agonists should be administered with caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of beta-adrenergic agonists may be enhanced.

Inhalation of halogenated hydrocarbon anaesthetics such as halothane, trichloroethylene and enflurane may increase the susceptibility to the cardiovascular effects of beta-agonists.

PREGNANCY AND LACTATION:
Safety of use in pregnancy and lactation has not been established.
Fenoterol may inhibit uterine contractions in pregnancy.
Pre-clinical studies have shown that fenoterol is excreted into breast milk.

DOSAGE AND DIRECTIONS FOR USE:
Acute asthma episodes:
One puff is sufficient for prompt symptom relief in many cases. In more severe cases, if breathing has not noticeably improved after 5 minutes, a second dose may be taken.
If an attack has not been relieved by 2 puffs, further puffs may be required. In these cases, patients should consult the doctor or the nearest hospital immediately.

Prophylaxis of exercise induced asthma:
One to two puffs for each administration, up to a maximum of eight puffs per day.

Bronchial asthma and other conditions with reversible airways narrowing:
If repeated dosing is required, one to two puffs for each administration, up to a maximum of eight puffs per day.

In children BEROTEC 100 HFA should be used only on medical advice and under the supervision of an adult.
DO NOT EXCEED THE RECOMMENDED DOSE.

Instructions for use/handling:
The correct administration of the metered aerosol is essential for successful therapy.
Depress the valve twice before the apparatus is used for the first time.
Before **each** use the following directions should be followed:

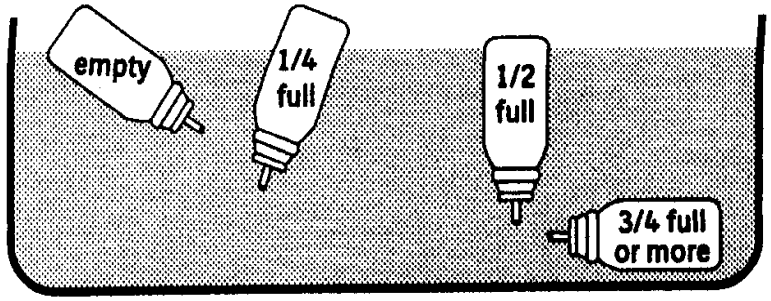
1. Remove the protective plastic cap.

(Fig 1.)

2. Breathe out deeply.
3. Hold the metered aerosol as shown in Fig. 1, and close the lips over the mouthpiece. The arrow and the base of the container should be pointing upwards.
4. Breathe in as deeply as possible, pressing the base of the container firmly at the same time, this releases one metered dose. Hold your breath for a few seconds, then remove the mouthpiece and breathe out. The same action should be repeated for a second inhalation.
5. Replace the protective cap after use.
6. After not using the metered aerosol for three days the valve has to be actuated once.

The container is not transparent. It is not therefore possible to see when it is empty. The aerosol will deliver 200 doses. When these have all been used the aerosol may still appear to contain a small amount of fluid. The aerosol should, however, be replaced because you may not get the right amount of treatment.

The amount of treatment in your aerosol can be checked as follows:
Remove the aerosol from the plastic mouthpiece and put the aerosol into a container of water. The contents of the aerosol can be estimated by observing its position in the water (see Fig. 2).



(Fig. 2)

The mouthpiece can be washed with warm water and should always be kept clean. If soap or detergent is used, the mouthpiece should be thoroughly rinsed in clean water.

WARNING: The plastic mouthpiece has been specially designed for use with BEROTEC 100 HFA to ensure that you always get the right amount of the medicine. The mouthpiece must never be used with any other metered aerosol nor must the BEROTEC 100 HFA aerosol be used with any mouthpiece other than the one supplied with the product.

The container is under pressure and should on no account be opened by force or exposed to temperatures exceeding 50 °C.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:
Side-Effects:
Frequent undesirable side-effects of BEROTEC 100 HFA are fine tremor of skeletal muscles and restlessness, headache, dizziness, tachycardia and palpitations.
Nausea, vomiting, sweating, weakness and myalgia/muscle cramps may occur.
Hypokalaemia may occur.
Overdosage may cause cardiac effects.
High dosages may increase the risk of serious side-effects, including cardiac dysrhythmias.
The risk is further aggravated if administered concomitantly with other medicines that cause hypokalaemia and cardiac dysrhythmias or in the presence of hypoxia and acidosis.
It is recommended that serum potassium levels are monitored in such situations.
The maximum dose should not be exceeded.
Particularly after higher doses, a decrease in diastolic blood pressure, an increase in systolic blood pressure or arrhythmias may occur.
Cough, local irritation and less common, paradoxical bronchoconstriction have been reported.

In less frequent cases skin reactions or allergic reactions have been reported, especially in hypersensitive patients.
In individual cases psychological changes have been reported with inhalation therapy with beta-mimetics.

Special Precautions:
When using the new formulation of BEROTEC metered dose inhaler for the first time, some patients may notice that the taste is slightly different from that of the CFC-containing formulation. Patients should be made aware of this when changing from one formulation to the other. They should also be told that the formulations have been shown to be interchangeable for all practical purposes and that the difference in taste has no consequences in terms of the safety or the efficacy of the new formulation.

Other sympathomimetic bronchodilators should only be used with BEROTEC 100 HFA under medical supervision. Anticholinergic bronchodilators may however be inhaled at the same time.
In the following conditions BEROTEC 100 HFA should only be used after careful risk/benefit assessment, especially when doses higher than recommended are used:
Insufficiently controlled diabetes mellitus, recent myocardial infarction, severe organic heart or vascular disorders, hyperthyroidism, pheochromocytoma.
In the case of acute, rapidly worsening dyspnoea (difficulty in breathing) a doctor should be consulted immediately.

Prolonged use:
- On demand treatment (symptom oriented) may be preferable to regular use.
- Patients should be evaluated for the addition or the increase of anti-inflammatory therapy (e.g. inhaled corticosteroids) to control airway inflammation and to prevent long term lung damage.

If bronchial obstruction deteriorates it is inappropriate and possibly hazardous to simply increase the use of beta$_2$-agonists containing products such as BEROTEC 100 HFA beyond the recommended dose over extended periods. The use of increasing amounts of beta$_2$-agonists containing products on a regular basis to control symptoms of bronchial obstruction may suggest declining disease control. In this situation, the patient's therapy plan, and in particular the adequacy of anti-inflammatory therapy, should be reviewed to prevent potentially life threatening deterioration of disease control.

Not to be used in children under six years of age.

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:
Symptoms:
The expected symptoms with overdosage are those of excessive beta-adrenergic-stimulation, including exaggeration of the known pharmacologic effects, i.e. any of the symptoms listed under side-effects, the most prominent being tachycardia, palpitation, tremor, hypertension, hypotension, widening of the pulse pressure, anginal pain, arrhythmias and flushing.

Treatment:
Administration of sedatives, tranquillizers, in severe cases intensive therapy.
Beta-receptor blockers, preferably $beta_1$-receptor blockers, are suitable as specific antidotes; however, a possible increase in bronchial obstruction must be taken into account and the dose should be adjusted carefully in patients suffering from bronchial asthma.
Further treatment should be symptomatic and supportive.

IDENTIFICATION:
Clear, colourless or almost colourless liquid under pressure in a one-piece stainless steel canister fitted with a metering valve.

PRESENTATION:
Metered aerosol complete with a mouthpiece.
Canister of 10 ml, providing 200 metered doses.

STORAGE INSTRUCTIONS:
Store at or below 30 °C in a dry place out of the reach of children.
Do not force container open.

REGISTRATION NUMBER:
34/10.2.1/0367

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:
Ingelheim Pharmaceuticals (Pty) Ltd
407 Pine Avenue
Randburg
South Africa

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GOEDGEKEURDE VOUBILJET – BEROTEC 100 HFA

SKEDULERINGSTATUS: **S2**

EIENDOMSNAAM: **BEROTEC 100 HFA**
(en doseervorm) afgemete dosis inasemtoestel

SAMESTELLING:
Elke afgemete dosis (inhalasie) verskaf fenoterolhidrobromied 100 µg.
Dryfmiddel: 1,1,1,2-tetrafluoro-etaan (HFA 134a).
Ander eksipiënte: Sitroensuur anhidries, gesuiwerde water, etanol absoluut (30 % *m/m*).

FARMAKOLOGIESE KLASSIFIKASIE:
A 10.2.1 Brongodilators – Inasemmiddels

FARMAKOLOGIESE WERKING:
Fenoterolhidrobromied is ‘n $beta_2$-selektiewe brongodilator met ‘n direkte plaaslike effek wat die saamgetrekte brongiale spiere laat ontspan.
Die brongodilaterende effek duur vir 3 – 5 ure.

INDIKASIES:
a) Simptomatiese behandeling van akute asma-aanvalle.
b) Voorkoming van oefeningsgeïnduseerde asma.
c) Simptomatiese behandeling van brongiale asma en ander kondisies met omkeerbare lugwegvernouing bv. chroniese obstruktiewe brongitis.

Meegaande anti-inflammatoriese terapie behoort oorweeg te word in pasiënte met brongiale asma en steroïedreagerende chroniese obstruktiewe longsiekte (COLS).

KONTRA-INDIKASIES:
Hipertrofiese obstruktiewe kardiomiopatie, tagi-aritmië.
Hipersensitiwiteit teen fenoterolhidrobromied of die onaktiewe bestanddele van hierdie produk.

INTERAKSIES:
Beta-adrenergiese middels, anticholinergiese middels, xantienderivate (soos teofillien) mag die effek van fenoterol versterk. Die gelyktydige toediening van ander betamimetika, sistemies beskikbare anticholinergiese middels en xantienderivate (bv. teofillien) mag die newe-effekte vererger.
‘n Potensieel ernstige afname in brongodilatering mag gedurende die meegaande gebruik van betablokkeerders plaasvind.
Beta-adrenergiese agoniste behoort met sorg toegedien te word in pasiënte wat met monoamienoksidaseïnhibeerders of trisikliese antidepressante behandel word, aangesien die werking van beta-adrenergiese agoniste versterk mag word.
Die inhalering van gehalogeneerde hidrokoolstof narkosemiddels soos halotaan, trichlooretileen en enfluraan mag die vatbaarheid tot kardiovaskulêre effekte van beta-agoniste laat toeneem.

SWANGERSKAP EN LAKTASIE:
Die veiligheid van gebruik gedurende swangerskap en laktasie is nie vasgestel nie.
Fenoterol mag sametrekkings van die baarmoeder gedurende swangerskap inhibeer.
Pre-kliniese studies het aangetoon dat fenoterol in borsmelk uitgeskei word.

DOSIS EN GEBRUIKSAANWYSINGS:
Akute asma episodes:
In baie gevalle is een inhalasie voldoende vir die vinnige verligting van simptome. In meer ernstige gevalle, indien die asemhaling nie binne 5 minute merkbaar verbeter het nie, kan ‘n tweede dosis geneem word.
Indien ‘n aanval nie deur twee inhalasies verlig is nie, mag verdere inhalasies nodig wees. In sulke gevalle behoort pasiënte onmiddellik hul dokter of die naaste hospitaal te raadpleeg.

Profilakse van oefeningsgeïnduseerde asma:
Een tot twee inhalasies met elke toediening, tot ‘n maksimum van agt inhalasies per dag.

Brongiale asma en ander kondisies met omkeerbare lugwegvernouing:
Indien herhaalde dosering nodig is, een tot twee inhalasies met elke toediening, tot ‘n maksimum van agt inhalasies per dag.

In kinders behoort BEROTEC 100 HFA slegs op mediese advies en onder die toesig van ‘n volwassene gebruik te word.
MOENIE DIE AANBEVOLE DOSIS OORSKRY NIE.

Aanwysings vir gebruik/hantering:
Die korrekte toediening van die afgemete aërosol is noodsaaklik vir suksesvolle terapie.
Druk die klep twee keer in voordat die apparaat vir die eerste keer gebruik word.
Voor **elke** gebruik behoort die volgende aanwysings gevolg te word:
1. Verwyder die beskermende plastiese dop.

Fig. 1

2. Asem heeltemal uit.
3. Hou die afgemete aërosol soos aangedui in Fig. 1 en sluit die lippe om die mondstuk. Die pyltjie en die basis van die houer behoort na bo te wys.
4. Asem so diep as moontlik in, terwyl die basis van die houer terselfdertyd ferm ingedruk word. Dit stel een afgemete dosis vry. Hou jou asem vir ‘n paar sekondes in en verwyder dan die mondstuk en asem uit. Dieselfde aksie behoort vir die tweede inhalasie gevolg te word.
5. Plaas die beskermende dop na gebruik terug.
6. Wanneer die afgemete aërosol vir drie dae nie gebruik is nie, moet dit weer een keer geaktiveer word.

Die houer is nie deursigtig nie. Dit is derhalwe nie moontlik om te sien wanneer dit leeg is nie. Die aërosol sal 200 dosisse lewer. Wanneer hierdie dosisse almal opgebruik is, mag dit

voel asof daar nog ‘n klein hoeveelheid vloeistof in die houer is. Die houer behoort dan egter vervang te word, aangesien jy andersins dalk nie die korrekte hoeveelheid van die medikasie sal inneem nie.

Die hoeveelheid vloeistof in die houer kan as volg nagegaan word:
Verwyder die aërosol uit die plastiese mondstuk en plaas dit in ‘n houer met water. Die hoeveelheid aërosol kan geskat word deur na die posisie van die houer in die water te kyk (sien Fig. 2).

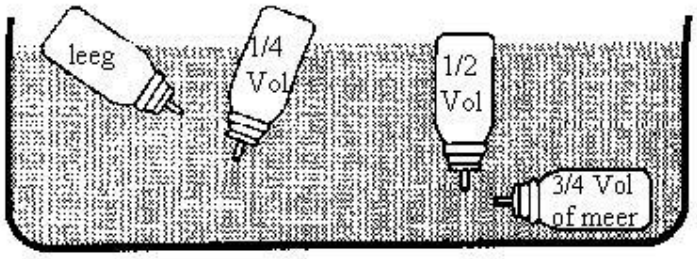

Fig. 2

Die mondstuk kan met warm water gewas word en behoort altyd skoon gehou te word. Indien seep of reinigingsmiddels gebruik word, behoort die mondstuk deeglik met skoon water gespoel te word.

WAARSKUWING: Die plastiese mondstuk is spesifiek ontwerp vir gebruik saam met BEROTEC 100 HFA, om te verseker dat jy altyd die korrekte hoeveelheid van die medisyne inneem. Die mondstuk moet nooit met enige ander afgemete aërosol gebruik word nie, en BEROTEC 100 HFA behoort ook nooit met enige ander mondstuk, behalwe die een wat saam met die produk verskaf word, gebruik te word nie.

Die houer is onder druk en behoort onder geen omstandighede oopgeforseer te word of aan temperature hoër as 50 °C blootgestel te word nie.

NEWE-EFFEKTE EN SPESIALE VOORSORGMAATREëLS:
Newe-effekte:
Ongewenste newe-effekte van BEROTEC 100 HFA wat dikwels voorkom is fyn bewerasie van die skeletspiere en rusteloosheid, hoofpyn, duiseligheid, tagikardie en hartkloppings.
Naarheid, braking, sweet, swakheid en mialgie/spierkrampe mag voorkom.
Hipokalemie mag voorkom.
Oordosering mag harteffekte veroorsaak.
Hoë dosisse mag die risiko van ernstige newe-effekte, insluitende hartdisritmië, verhoog. Hierdie risiko word verder vererger wanneer dit saam met ander medisyne wat hipokalemie en hartdisritmieë veroorsaak, gebruik word, of in die teenwoordigheid van hipoksie en asidose.
In hierdie situasies word dit aanbeveel dat die serum kaliumvlakke gemonitor word.
Die maksimum dosis behoort nie oorskry te word nie.
Veral na hoër dosisse mag ‘n afname in diastoliese bloeddruk en ‘n toename in sistoliese bloeddruk of aritmië voorkom.

Hoes, plaaslike irritasie en minder dikwels paradoksale brongokonstriksie, is aangemeld.
In gevalle wat minder dikwels voorkom is velreaksies of allergiese reaksies aangemeld, veral in hipersensitiewe pasiënte.
In individuele gevalle is sielkundige veranderinge met inhaleringsterapie met beta-mimetika aangemeld.

Spesiale voorsorgmaatreëls:
Wanneer die BEROTEC 100 HFA afgemete dosis inasemtoestel vir die eerste keer gebruik word, mag sommige mense opmerk dat die smaak effens verskil van dié van die CFK bevattende formulasie. Pasiënte behoort daarvan bewus gemaak te word wanneer daar van een formulasie na die ander oorgeskakel word. Hulle behoort ook ingelig te word dat dit aangetoon is dat die formulasies vir alle praktiese doeleindes uitruilbaar is en dat die verskil in smaak geen gevolge in terme van veiligheid of doeltreffendheid van die nuwe formulasie het nie.

Ander simpatomimetiese brongodilators moet slegs onder mediese toesig saam met BEROTEC 100 HFA gebruik word. Anticholinergiese brongodilators mag egter terselfdertyd gebruik word.
Tydens die volgende toestande behoort BEROTEC 100 HFA slegs na ‘n deeglike risiko/voordeel bepaling gebruik te word, veral wanneer hoër as aanbevole dosisse gebruik word:
Onvoldoende beheerde diabetes mellitus, onlangse miokardiese infarksie, erge organiese hart- of vaskulêre afwykings, hipertiroïdisme, feochromositoom.
In die geval van akute, vinnig ergerwordende dispnee (moeite met asemhaling), behoort ‘n dokter onmiddellik geraadpleeg te word.

Verlengde gebruik:
- Wanneer-nodig-behandeling (simptoom georiënteerd) mag bo gereelde gebruik verkies word.
- Pasiënte behoort vir die toevoeging of die toename van anti-inflammatoriese terapie (bv. ingeasemde kortikosteroïede) geëvalueer te word om die inflammasie van die lugweë te beheer en om langtermyn longbeskadiging te voorkom.

Indien die brongiale obstruksie vererger is dit onvanpas en moontlik gevaarlik om bloot die gebruik van beta$_2$-agonisbevattende produkte soos BEROTEC 100 HFA vir verlengde periodes bokant die aanbevole dosis te vermeerder. Die gebruik van toenemende hoeveelhede beta$_2$-agonisbevattende produkte op ‘n gereelde basis om die simptome van brongiale obstruksie te beheer mag op ‘n afname van siektebeheer dui. In só ‘n situasie behoort die pasiënt se terapieplan, en veral die toereikendheid van die anti-inflammatoriese terapie, heroorweeg te word om potensieel lewensbedreigende agteruitgang van siektebeheer te voorkom.

Moet nie in kinders jonger as 6 jaar oud gebruik word nie.

BEKENDE SIMPTOME VAN OORDOSERING EN BESONDERHEDE VAN DIE BEHANDELING DAARVAN:
Simptome:
Die verwagte simptome van oordosering is dié van oormatige beta-adrenergiese stimulasie, insluitende verergering van die bekende farmakologiese effekte, d.i. enige van die simptome

gelys onder newe-effekte, waarvan die mees prominente newe-effekte tagikardie, hartkloppings, bewerasie, hipertensie, hipotensie, verwyding van die polsdruk, anginapyn, aritmië en hittegloede is.

Behandeling:
Toediening van sedeermiddels, kalmeermiddels en in erge gevalle intensiewe terapie. Beta-reseptorblokkeerders, verkieslik $beta_1$-reseptorblokkeerders, is geskik as spesifieke teenmiddels; ‘n moontlike toename in brongiale obstruksie moet egter in gedagte gehou word en die dosis behoort versigtig in pasiënte wat aan brongiale asma ly, aangepas te word. Verdere behandeling behoort simptomaties en ondersteunend te wees.

IDENTIFIKASIE:
Helder, kleurlose tot byna kleurlose vloeistof onder druk in ‘n eenstuk vlekvrye staal houer met ‘n metingsklep daarop aangebring.

AANBIEDING:
Afgemete aërosol volledig met ‘n mondstuk.
Houer met 10 mℓ, wat 200 dosisse lewer.

BERGINGSAANWYSINGS:
Bewaar teen of benede 30 °C in ‘n droë plek buite bereik van kinders.
Moenie die houer oopforseer nie.

REGISTRASIENOMMER:
34/10.2.1/0367

NAAM EN BESIGHEIDSADRES VAN DIE HOUER VAN DIE SERTIFIKAAT VAN REGISTRASIE:
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