AIRSUPRA

Salbutamol sulfate and Budesonide

90/80 microgram

Inhalation Aerosol

1. NAME OF THE MEDICINAL PRODUCT

AIRSUPRA (salbutamol and budesonide, 90/80 mcg/actuation), inhalation aerosol.

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Each delivered dose (the dose that leaves the mouthpiece) contains 90 mcg of salbutamol (equivalent to 108 mcg of salbutamol sulfate) and 80 mcg of budesonide.

This corresponds to a metered dose of 99 mcg of salbutamol and 88 mcg of budesonide.

3. PHARMACEUTICAL FORM

Inhalation aerosol.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

AIRSUPRA is indicated for the as-needed treatment or prevention of bronchoconstriction and for the prevention of exacerbations in patients with asthma 18 years of age and older (see Clinical efficacy and safety).

4.2 Posology and method of administration

Posology

Recommended dosage for treatment or prevention of bronchoconstriction and for the prevention of exacerbations

Adult : salbutamol 180 mcg and budesonide 160 mcg (administered as 2 actuations of AIRSUPRA [salbutamol/budesonide 90 mcg/80 mcg]) as needed by oral inhalation.

Do not take more than 6 doses (12 inhalations) in a 24-hour period.

Special populations

Renal impairment
There are no data available for use of AIRSUPRA in patients with renal impairment.

Hepatic impairment
No dosage adjustment is necessary for patients with hepatic impairment (see section 5.2). As budesonide is primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver diseases.

Elderly population
No dosage adjustment is necessary for elderly patients (see section 5.2).

Paediatric population
The safety and effectiveness of AIRSUPRA have not been established in pediatric patients, and AIRSUPRA is not indicated for use in this population

Method of administration
For oral inhalation use.

For detailed instructions, refer to the patient leaflet/instructions for use.

Patients should be instructed how to administer the product correctly and advised to read the instructions for use carefully.

Patient inhaler technique should be checked to make sure that aerosol actuation is synchronised with inspiration of breath for optimum delivery of drug to the lungs.

4.3 Contraindications

Hypersensitivity to salbutamol, budesonide, or any of the excipients.

4.4 Special warnings and special precautions for use

1. **Deterioration of Asthma**
   Asthma may deteriorate acutely over a period of hours or chronically over several days or longer. If the patient continues to experience symptoms after using AIRSUPRA or requires more doses of AIRSUPRA than usual, this may be a marker of destabilization of asthma and requires evaluation of the patient and their treatment regimen.

2. **Paradoxical Bronchospasm**
   AIRSUPRA can produce paradoxical bronchospasm, which may be life threatening. If paradoxical bronchospasm occurs following dosing with AIRSUPRA, it should be discontinued immediately, and alternative therapy should be instituted. It should be recognized that paradoxical bronchospasm, when associated with inhaled formulations, frequently occurs with the first use of a new canister.

3. **Cardiovascular Effects**
   AIRSUPRA, like other drugs containing beta2-adrenergic agonists, can produce clinically significant cardiovascular effects in some patients as measured by increases in pulse rate, blood pressure, and/or other symptoms. If such effects occur, AIRSUPRA may need to be discontinued. In addition, betaagonists have been reported to produce electrocardiogram (ECG) changes, such as flattening of the T wave, prolongation of the QTc interval, and ST-segment depression. The clinical significance of these findings is unknown. Therefore, AIRSUPRA, like all sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

4. **Do Not Exceed Recommended Dosage**
   As with other inhaled drugs containing beta-adrenergic agents, AIRSUPRA should not be used more than the maximum daily dose [see 4.2 Posology and method of administration], as an overdose may result. Clinically significant cardiovascular effects and fatalities have been reported in association with excessive use of inhaled sympathomimetic drugs.

5. **Hypersensitivity Reactions, Including Anaphylaxis**
   Hypersensitivity reactions can occur after administration of salbutamol sulfate and budesonide, components of AIRSUPRA, as demonstrated by cases of anaphylaxis, angioedema, bronchospasm, oropharyngeal edema, rash, and urticaria. Discontinue AIRSUPRA if such reactions occur [see 4.3 Contraindications]

6. **Risk of Sympathomimetic Amines with Certain Coexisting Conditions**
   AIRSUPRA, like all therapies containing sympathomimetic amines, should be used with caution in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus and in patients who are unusually responsive to sympathomimetic amines. Large doses of intravenous salbutamol sulfate have been reported to aggravate preexisting diabetes mellitus and ketoacidosis.

7. **Hypokalemia**
   Beta-adrenergic agonist medicines may produce significant hypokalemia in some patients, possibly through intracellular shunting, which has the potential to produce adverse cardiovascular effects [see 4.4 Special warnings and special precaution for use, 5. Pharmacological properties]. The decrease in serum potassium is usually transient, not requiring supplementation.

8. **Immunosuppression and Risk of Infections**
   Patients who are using drugs that suppress the immune system are more susceptible to infection. Chicken pox and measles, for example, can have a more serious or even fatal course in susceptible patients using corticosteroids. In patients who have not had these diseases or been properly immunized, particular care should be taken to avoid exposure. How the dose, route, and duration of corticosteroid administration affects the risk of developing a disseminated infection is not known. The contribution of the underlying disease and/or prior

corticosteroid treatment to the risk is also not known. If a patient is exposed to chicken pox, prophylaxis with varicella zoster immune globulin (VZIG) may be indicated. If exposed to measles, prophylaxis with pooled intramuscular immunoglobulin (IG) may be indicated (see the respective Prescribing Information for VZIG and IG). If chicken pox develops, treatment with antiviral agents may be considered.

Inhaled corticosteroids should be used with caution, if at all, in patients with active or quiescent tuberculosis infection of the respiratory tract; untreated systemic fungal, bacterial, viral, or parasitic infections; or ocular herpes simplex.

9. **Oropharyngeal Candidiasis**
   AIRSUPRA contains budesonide, an inhaled corticosteroid (ICS). Localized infections of the mouth and pharynx with Candida albicans have occurred in patients treated with ICS agents. Monitor patients periodically. When such an infection develops, it should be treated with appropriate local or systemic (i.e., oral) antifungal therapy while treatment with AIRSUPRA continues. In some cases, therapy with AIRSUPRA may need to be interrupted. Advise the patient to rinse his/her mouth with water, if available, without swallowing following administration of AIRSUPRA to help reduce the risk of oropharyngeal candidiasis.

10. **Hypercorticism and Adrenal Suppression**
    Budesonide, a component of AIRSUPRA, will often help control asthma symptoms with less suppression of hypothalamic-pituitary-adrenal (HPA) function than therapeutically equivalent oral doses of prednisone. Since budesonide is absorbed into the circulation and can be systemically active at higher doses, the beneficial effects of AIRSUPRA in minimizing HPA dysfunction may be expected only when recommended dosages are not exceeded. Since individual sensitivity to effects on cortisol production exists, physicians should consider this information when prescribing AIRSUPRA.

    Because of the possibility of systemic absorption of ICS, patients treated with AIRSUPRA should be observed carefully for any evidence of systemic corticosteroid effects. Particular care should be taken in observing patients postoperatively or during periods of stress for evidence of inadequate adrenal response.

    It is possible that systemic corticosteroid effects such as hypercorticism and adrenal suppression (including adrenal crisis) may appear in a small number of patients who are sensitive to these effects. If such effects occur, appropriate therapy should be initiated as needed

11. **Reduction in Bone Mineral Density**
    Decreases in bone mineral density (BMD) have been observed with long-term administration of products containing ICS. The clinical significance of small changes in BMD with regard to long-term consequences such as fracture is unknown. Patients with major risk factors for decreased bone mineral content, such as prolonged immobilization, family history of osteoporosis, post-menopausal status, tobacco use, advanced age, poor nutrition, or chronic

use of drugs that can reduce bone mass (e.g., anticonvulsants, oral corticosteroids) should be monitored and treated with established standards of care.

12. **Glaucoma and Cataracts**
    Glaucoma, increased intraocular pressure, and cataracts have been reported following the long-term administration of ICS, including budesonide, a component of AIRSUPRA. Consider referral to an ophthalmologist in patients who develop ocular symptoms.

13. **Drug Interactions with Strong Cytochrome P450 3A4 Inhibitors**
    Caution should be exercised when considering the co-administration of AIRSUPRA with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin) because adverse effects related to increased systemic exposure to budesonide may occur [see 4.5 Interaction with other medicinal products and other forms of interaction, and 5.2 Pharmacokinetic properties].

14. **Effects on Growth in Pediatric**
    Patients Orally inhaled corticosteroids, including budesonide, may cause a reduction in growth velocity when administered to pediatric patients. The safety and effectiveness of AIRSUPRA have not been established in pediatric patients, and AIRSUPRA is not indicated for use in this population [see 4.2 Posology and method of administration]

4.5 Interaction with other medicinal products and other forms of interaction

No formal drug interaction studies have been performed with AIRSUPRA.

1. **Inhibitors of Cytochrome P450 3A4**
   The main route of metabolism of corticosteroids, including budesonide, a component of AIRSUPRA, is via cytochrome P450 (CYP) isoenzyme 3A4 (CYP3A4). After oral administration of ketoconazole, a strong inhibitor of CYP3A4, the mean plasma concentration of orally administered budesonide increased. Concomitant administration of a CYP3A4 inhibitor may inhibit the metabolism of, and increase the systemic exposure to, budesonide. Caution should be exercised when considering the co-administration of AIRSUPRA with long-term ketoconazole and other known strong CYP3A4 inhibitors (e.g., ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin) [see 4.4 Special warnings and special precaution for use].

2. **Use with Other Short-Acting Bronchodilators**
   AIRSUPRA contains the short-acting beta-agonist, salbutamol sulfate. Therefore, concomitant use of additional beta-agonists with AIRSUPRA should be used judiciously to prevent beta-agonist overdose.

3. **Beta-Blockers**

Beta-adrenergic receptor blocking agents not only block the pulmonary effect of beta-agonists, such as salbutamol sulfate, a component of AIRSUPRA, but may also produce severe bronchospasm in patients with asthma. Therefore, patients with asthma should not normally be treated with beta-blockers. However, under certain circumstances, e.g., as prophylaxis after myocardial infarction, there may be no acceptable alternatives to the use of beta-adrenergic-blocking agents in these patients. In this setting, consider cardioselective beta-blockers, although they should be administered with caution.

4. **Diuretics**
   The ECG changes and/or hypokalemia which may result from the administration of non-potassiumsparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by beta-agonists, especially when the recommended dose of the beta-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the coadministration of AIRSUPRA with non-potassiumsparing diuretics. Consider monitoring potassium levels.

5. **Digoxin**
   Mean decreases of 16% and 22% in serum digoxin levels were demonstrated after single-dose intravenous and oral administration of salbutamol sulfate, respectively, to normal volunteers who had received digoxin for 10 days. The clinical significance of these findings for patients with obstructive airway disease who are receiving salbutamol sulfate and digoxin on a chronic basis is unclear. Nevertheless, it would be prudent to carefully evaluate the serum digoxin levels in patients who are currently receiving digoxin and AIRSUPRA.

6. **Monoamine Oxidase Inhibitors or Tricyclic Antidepressants**
   AIRSUPRA should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents, because the action of salbutamol sulfate on the cardiovascular system may be potentiated.

4.6 Pregnancy and lactation

Pregnancy

Because of the potential for beta-agonist interference with uterine contractility, use of AIRSUPRA during labour should be restricted to those patients in whom the benefits clearly outweigh the risk. AIRSUPRA has not been approved for the management of pre-term labour. Serious adverse reactions, including pulmonary oedema, have been reported during or following treatment of premature labour with $beta_2$-agonists, including salbutamol.

Studies in animals have shown reproductive toxicity (see section 5.3) of salbutamol. Safety in pregnant women has not been established. No controlled clinical trials with salbutamol have been conducted in pregnant women. Rare reports of various congenital anomalies following intrauterine exposure to salbutamol (including cleft palate, limb defects and cardiac disorders) have been received. Some of the mothers were taking multiple medications during their pregnancies. AIRSUPRA should not be used during pregnancy unless clearly necessary.

Despite a large amount of data (more than 1000 pregnancy outcomes) on pregnant women, there is insufficient robust evidence to indicate malformative toxicity of inhaled budesonide.

Breast-feeding
As salbutamol is probably secreted in breast milk, its use in nursing mothers requires careful consideration. It is not known whether salbutamol has a harmful effect on the neonate, and so its use should be restricted to situations where the expected benefit to the mother is likely to outweigh any potential risk to the neonate.

Budesonide is excreted in breast milk. However, at therapeutic doses of AIRSUPRA no effects on the suckling child are anticipated.

Fertility
There is no information on the effects of salbutamol on human fertility. There were no adverse effects on fertility in animals (see section 5.3).

Budesonide did not cause any adverse effects on fertility in rats. It is unlikely that AIRSUPRA administered at the recommended dose will affect fertility in humans.

4.7 Effects on ability to drive and use machines

AIRSUPRA is not expected to adversely affect the ability to drive or use machines.

Driving or using machinery should be undertaken with caution until the effect of Airsupra on the individual is established

4.8 Undesirable effects

Overall summary of the safety profile

Since AIRSUPRA contains both salbutamol and budesonide, the safety profile is related to the individual components of the combination. No increased incidence of adverse reactions has been seen following concurrent administration of the two compounds. The most common drug related adverse reactions are pharmacologically predictable side effects of beta$_2$-agonist therapy, such as tremor.

Adverse Drug Reactions
Adverse drug reactions (ADRs) are organised by MedDRA System Organ Class (SOC). Within each SOC, preferred terms are arranged by decreasing frequency and then by decreasing seriousness. Frequencies of occurrence of adverse reactions are defined as: very common (≥1/10); common (≥1/100 to <1/10); uncommon (≥1/1,000 to <1/100); rare (≥1/10,000 to <1/1000); very rare (<1/10,000) and not known (cannot be estimated from available data).

Adverse drug reactions which have been associated with the individual components of AIRSUPRA, either alone or in combination, as evaluated in clinical trials, literature reports, or in a post-marketing setting, are given in Table 1.

Table 1. Adverse drug reactions

MedDRA SOC	MedDRA Term	Frequency
Infections and infestations	Candida infection in the oropharynx	Common
Immune system disorders	Immediate and delayed hypersensitivity reactions including rash, contact dermatitis, urticaria, angioedema, bronchospasm and anaphylactic reaction	Rare
Endocrine disorders	Signs or symptoms of systemic glucocorticosteroid effect, including hypofunction of the adrenal gland and reduction of growth rate	Rare
Metabolism and nutrition disorders	Hypokalaemia	Rare
Psychiatric disorders	Nervousness, restlessness, depression, behavioural disturbances	Rare
Nervous system disorders	Tremor, headache	Common
	Hyperactivity	Very rare
Cardiac disorders	Tachycardia	Common
	Palpitations	Uncommon
	Cardiac arrhythmias (including atrial fibrillation, supraventricular tachycardia and extrasystoles)	Very rare
	Myocardial ischaemia	Unknown
Vascular disorders	Peripheral vasodilatation	Rare
Respiratory, thoracic and mediastinal disorders	Mild irritation in the throat, dysphonia, cough	Common
	Paradoxical bronchospasm	Very rare
Gastrointestinal disorders	Mouth irritation	Uncommon
Skin and subcutaneous tissue disorders	Skin bruising	Rare
Musculoskeletal and connective tissue disorders	Muscle cramps	Uncommon

Description of selected adverse reaction

Symptoms of systemic glucocorticosteroid effect, including hypofunction of the adrenal gland and reduction of growth rate, may occur with inhaled glucocorticosteroids, probably depending on dose, exposure time, concomitant and previous glucocorticosteroid exposure, and individual sensitivity.

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorization of AIRSUPRA is important. It allows continued monitoring of the benefit/risk balance of the medicinal product.

Suspected side effects of PT AstraZeneca Indonesia's products can be reported online via the link http://contactazmedical.astrazeneca.com or by scanning the following QR code:

Reporting suspected product side effects to PT AstraZeneca Indonesia **does not replace medical consultation or treatment by a doctor**. For medical advice, diagnosis or treatment, please consult your doctor or healthcare professional.

Reporting of suspected adverse drug events can also be sent to Pusat Farmakovigilans/MESO Nasional Badan Pengawas Obat dan Makanan (BPOM) by filling out the online form: https://e-meso.pom.go.id/ADR or via email pv-center@pom.go.id or by direct reporting addressed to:
Pusat Farmakovigilans/MESO Nasional
Badan Pengawas Obat dan Makanan (BPOM)
Direktorat Pengawasan Keamanan, Mutu, dan Ekspor Impor Obat, Narkotika, Psikotropika, Prekursor dan Zat Adiktif
Badan Pengawas Obat dan Makanan RI
Jl. Percetakan Negara No. 23
Jakarta 10560

4.9 Overdose

AIRSUPRA contains both salbutamol and budesonide; therefore, the risks associated with overdosage for the individual components described below apply to AIRSUPRA.

Salbutamol
The most common signs and symptoms of overdose with salbutamol are transient beta agonist pharmacologically mediated events, including tachycardia, tremor, hyperactivity and metabolic effects including hypokalaemia (see sections 4.4 and 4.8).

Hypokalaemia may occur following overdose with salbutamol. Serum potassium levels should be monitored. Lactic acidosis has been reported in association with high therapeutic doses as well as overdoses of short-acting beta-agonist therapy, therefore monitoring for elevated serum lactate and consequent metabolic acidosis (particularly if there is persistence or worsening of tachypnoea despite resolution of other signs of bronchospasm such as wheezing) may be indicated in the setting of overdose.

Budesonide
Acute overdosage with budesonide, even in excessive doses, is not expected to be a clinical problem. However, the plasma cortisol level will decrease and number and percentage of circulating neutrophils

will increase. The number and percentage of lymphocytes and eosinophils will decrease concurrently. When used chronically in excessive doses, systemic glucocorticosteroid effects, such as hyper corticism and adrenal suppresion, may appear.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Mechanism of action

AIRSUPRA contains both salbutamol and budesonide; therefore, the mechanisms of action described below for the individual components apply to AIRSUPRA. These drugs represent two classes of medications (a short-acting selective beta$_2$-adrenergic agonist and a synthetic corticosteroid) that have different effects on clinical, physiological, and inflammatory indices of asthma.

Salbutamol is a selective beta$_2$-adrenoceptor agonist. At therapeutic doses it acts on the beta$_2$-adrenoceptors of bronchial muscle providing short acting (4-6 hour) bronchodilation with a fast onset (within 5 minutes) in reversible airways obstruction.

Budesonide is a glucocorticosteroid which when inhaled has a rapid (within hours) and dose-dependent anti-inflammatory action in the airways, resulting in reduced symptoms and fewer asthma exacerbations. Inhaled budesonide has a lower incidence and severity of adverse effects than those seen with oral corticosteroids. The exact mechanism responsible for the anti-inflammatory effect of glucocorticosteroids is unknown.

Clinical efficacy and safety

The efficacy of AIRSUPRA was evaluated in the 2 clinical randomized, double-blind, multicenter studies MANDALA and DENALI in subjects with mild to severe asthma as described below. While patients 12 to 17 years of age were included in these trials, AIRSUPRA is not approved in this age group; therefore, efficacy results are presented for adults only

MANDALA
The efficacy of AIRSUPRA 180 mcg/160 mcg was evaluated in patients 12 years of age and older with moderate to severe asthma in MANDALA, a randomised, double-blind, multicentre study. MANDALA was a variable length exacerbation study with at least 24 weeks duration.

Patients 12 years of age and older were randomised (1:1:1) and received at least one dose of AIRSUPRA, salbutamol/budesonide 180 mcg/80 mcg or salbutamol 180 mcg as needed. Patients were required to be receiving medium to high dose inhaled corticosteroids (ICS) or low to high dose ICS/long-acting beta$_2$-adrenergic agonists (LABA), with or without another controller medicine as maintenance therapy. All patients continued their own maintenance therapy throughout the trial. MANDALA was conducted in symptomatic patients with moderate to severe asthma, a history of at least 1 severe asthma exacerbation in the year prior to screening, pre-bronchodilator $FEV_1 \geq 40$ to $< 90\%$ of predicted normal (for patients aged 12 to < 18 years old, $\geq 60\%$) and a confirmed reversibility to salbutamol.

The efficacy population (n=3040) in MANDALA had a mean age of 51 years (range: 12 to 84 years), with 66% female, 82% Caucasian, and 25% of Hispanic or Latino ethnicity. The median duration of

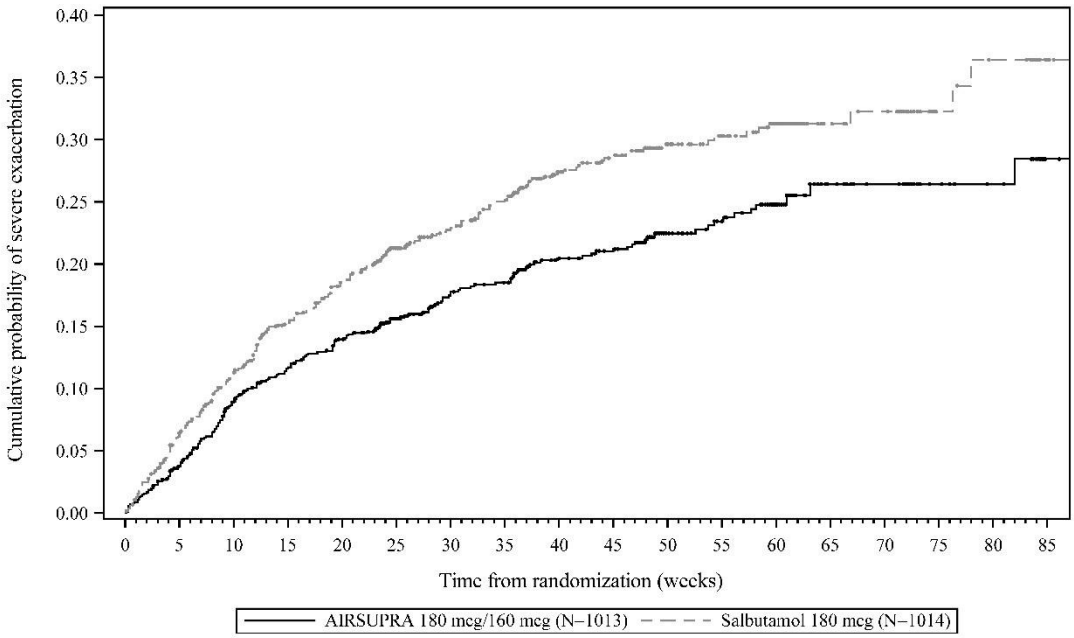
asthma was 20 years (range: 1 to 80 years) since the first diagnosis of asthma. The mean pre-bronchodilator percent predicted FEV_1 was 68% (range 22% to 126%).

The overall patterns of use of AIRSUPRA and salbutamol 180 mcg were similar during the randomised treatment period.

The primary efficacy endpoint was the time to first severe asthma exacerbation (defined as worsening or onset of asthma symptoms that required systemic corticosteroids for at least 3 days or an emergency room visit that led to the use of systemic corticosteroids for at least 3 days or a hospitalisation for at least 24 hours due to asthma).

Treatment with AIRSUPRA, compared with salbutamol 180 mcg, demonstrated statistically significant reductions in the risk of severe asthma exacerbations, as assessed by the time to first severe asthma exacerbation as described in Figure 1. Compared with salbutamol 180 mcg, patients receiving AIRSUPRA experienced a statistically significant 27% reduction (Hazard Ratio [HR] 0.73; 95% CI: 0.61, 0.88) in the risk of a severe asthma exacerbation (p<0.001).

Figure 1. Kaplan-Meier cumulative incidence curve for time to first exacerbation*



Number of patients at risk

AIRSUPRA 180 mcg/160 mcg	1013	963	903	870	839	601	557	546	442	431	248	233	194	75	68	41	37	11
Salbutamol 180 mcg	1014	937	875	817	775	555	514	492	392	373	224	210	172	75	70	33	29	9

*Curve truncated when < 1% of patient population remained at risk.

There were reductions in severe asthma exacerbation risk regardless of exacerbation history (1 or > 1 in the past year), baseline lung function, and asthma severity (defined by background maintenance therapy) compared with salbutamol 180 mcg.

Treatment with AIRSUPRA demonstrated a statistically significant reduction in the annual rate of severe asthma exacerbations by 24% compared with salbutamol 180 mcg as shown in Table 2.

Table 2. Annualized rate of severe exacerbations in patients 12 years of age and older with moderate to severe asthma

	n	Number of severe exacerbations	Annualized Rate	Rate Ratio vs Salbutamol (95% CI)	P-value
AIRSUPRA	1013	334	0.45	0.76 (0.62, 0.93)	p=0.008
Salbutamol 180 mcg	1014	413	0.59		

The annualised total systemic corticosteroid (SCS) dose due to asthma was calculated for each patient during the study period. For patients treated with AIRSUPRA, the annualised total SCS dose when compared with salbutamol 180 mcg demonstrated a statistically significant reduction in mean annualized dose of 43 mg per patient [AIRSUPRA (86 mg) vs salbutamol 180 mcg (129 mg)].

Asthma control was assessed using the Asthma Control Questionnaire (ACQ-5) responder analysis. Responders were defined as patients with an improvement of 0.5 or more in overall ACQ-5 score at Week 24 compared to baseline. The percentage of ACQ-5 responders at Week 24 for AIRSUPRA was 67% compared with 62% for salbutamol 180 mcg (odds ratio 1.22; 95% CI: 1.02, 1.47).

Asthma quality of life was assessed using the Asthma Quality of Life Questionnaire (AQLQ+12). Responders were defined as those with an improvement of 0.5 or more in AQLQ score at Week 24 compared to baseline. The percentage of responders at Week 24 for AIRSUPRA was 51% compared with 46% for salbutamol 180 mcg (odds ratio 1.23; 95% CI: 1.02, 1.48).

DENALI
The efficacy of AIRSUPRA on lung function was evaluated in patients 12 years of age and older with mild to moderate asthma who were previously treated with as-needed short-acting beta$_2$-agonists (SABA) alone or with low-dose ICS maintenance therapy plus as-needed SABA. DENALI was a double-blind, active-comparator and placebo-controlled lung function study conducted over 12 weeks. Patients were randomized 1:1:1:1:1 to receive AIRSUPRA, salbutamol/budesonide 180 mcg/80 mcg, budesonide 160 mcg, salbutamol 180 mcg, or placebo, all administered 4 times daily. Only the results for the approved dose of AIRSUPRA are described below.

The study population (n=989) had a mean age of 49 years (range: 12 to 90 years) with 62% female, 89% Caucasian, and 28% of Hispanic or Latino ethnicity, and a median duration of asthma of 21 years. At screening, subjects had a pre-bronchodilator FEV_1 of 50 to < 85% predicted normal value for subjects 18 years of age and older and ≥ 50% predicted normal value for subjects 12 to 17 years of age. All subjects were required to demonstrate reversibility to salbutamol. The mean pre-bronchodilator percent predicted FEV_1 was 66% (range: 45 to 107%).

The dual primary endpoints were change from baseline in FEV_1 $AUC_{0\text{-}6\ hours}$ over the 12-week treatment period comparing AIRSUPRA with budesonide 160 mcg and change from baseline in trough FEV_1 at Week 12 comparing AIRSUPRA with salbutamol 180 mcg.

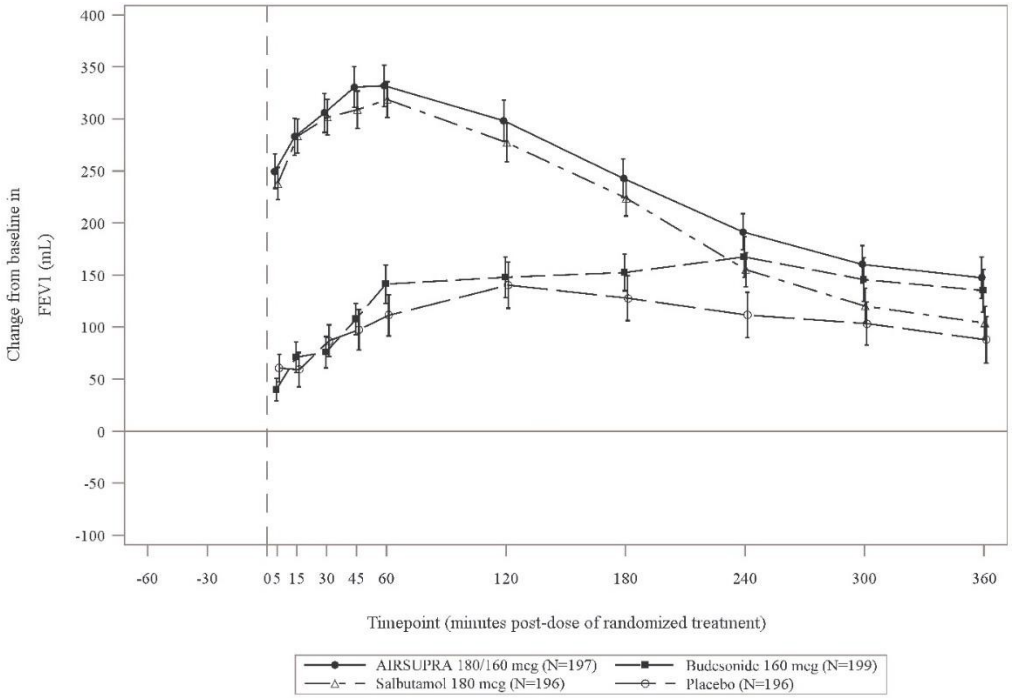
For FEV_1 $AUC_{0\text{-}6\ hours}$, AIRSUPRA showed statistically significantly greater improvements compared with budesonide 160 mcg (80.7 mL; 95% CI: 28.4, 132.9; p-value=0.003).

For trough FEV_1, AIRSUPRA showed statistically significantly greater improvements compared with salbutamol 180 mcg (132.8 mL; 95% CI: 63.6, 201.9; p-value <0.001).

Onset of bronchodilation (as defined by a ≥ 15% increase in FEV_1 post-dose within 30 minutes on Day 1) was observed in 50% of subjects treated with AIRSUPRA and 43% of subjects treated with salbutamol 180 mcg. Following a single dose on Day 1, the median time to onset and mean duration of bronchodilation were 7.5 and 186.9 minutes with AIRSUPRA and 9.5 and 168.2 minutes with salbutamol 180 mcg, respectively.

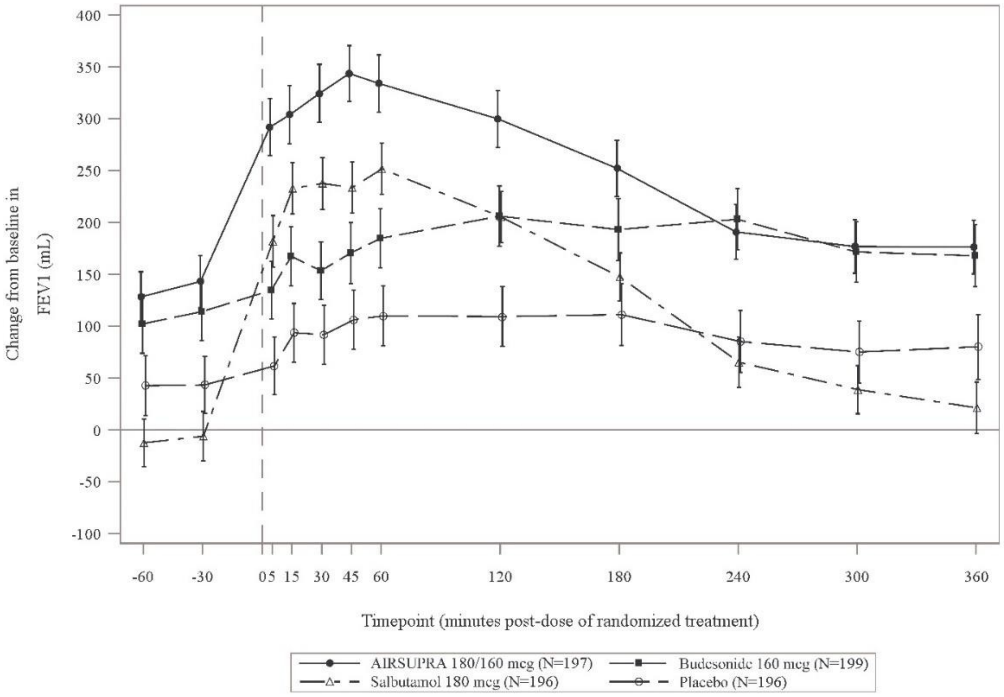
No diminution in the 6-hour bronchodilator effect was observed with AIRSUPRA as assessed by FEV_1 following 12 weeks of treatment (Figures 2 and 3). Post-dose FEV_1 AUC_{0-6} for AIRSUPRA was at Day One 240.8 mL and after 12 weeks 247.9 mL, compared to 212.6 mL and 137.5 mL respectively for salbutamol 180 mcg.

Figure 2. Mean change from baseline FEV_1 on Day 1 (≥ 12 years of age)*



*Baseline FEV1 is defined as the average of the 60- and 30-minute pre-dose results on the date of randomization. Error bars represent the standard error of mean estimates.

Figure 3. Mean change from baseline FEV_1 at Week 12 (≥ 12 years of age)*



*Baseline FEV1 is defined as the average of the 60- and 30-minute pre-dose results on the date of randomization. Error bars represent the standard error of mean estimates.

Subjects receiving AIRSUPRA demonstrated an improvement from baseline in trough FEV_1 at Week 1 when compared with salbutamol 180 mcg (107.9 mL; 95% CI: 48.1, 167.8).

Asthma control was assessed in subjects who were uncontrolled at baseline using the ACQ-7 responder analysis. Responders were defined as those with an improvement of 0.5 or more from baseline to Week 12. The percentage of responders for AIRSUPRA were 66% compared with 47% for salbutamol 180 mcg (odds ratio 2.3; 95% CI: 1.47, 3.69).

The incidence of severe exacerbations was an exploratory endpoint in DENALI. The number (percentage) of subjects with at least 1 severe asthma exacerbation was lower in AIRSUPRA and budesonide 160 mcg treatment groups at 4 (2.0%), and 4 (2.0%), respectively when compared with salbutamol 180 mcg at 20 (10.2%) and placebo at 14 (7.1%).

5.2 Pharmacokinetic properties

Absorption

Salbutamol

Following inhaled administration of AIRSUPRA in healthy subjects, the median t_{max} of salbutamol was 1.00 hour (individual values ranged from 0.08 to 6.05 hours). Geometric mean C_{max} was 472.2 pg/mL (individual values ranged from 38.4 to 971 pg/mL).

Budesonide
Following inhaled administration in healthy subjects of AIRSUPRA, the median t_{max} of budesonide was 0.33 hours (individual values ranged from 0.08 to 4.00 hours). Geometric mean C_{max} was 272.8 pg/mL (individual values ranged from 51.7 to 819 pg/mL). Systemic exposure to budesonide with AIRSUPRA did not exceed that from inhaled budesonide via a dry powder inhaler comparator in healthy subjects.

Distribution

Salbutamol
Following inhaled administration of AIRSUPRA in healthy subjects, the mean apparent volume of distribution (Vz/F) of salbutamol was 565.7 L. Salbutamol is bound to plasma proteins to the extent of 10%.

Budesonide
Following inhaled administration of AIRSUPRA in healthy subjects, the mean apparent volume of distribution (Vz/F) of budesonide administered in AIRSUPRA was 1002.0 L. Budesonide plasma protein binding averages 85-90%.

Biotransformation

Salbutamol
Salbutamol administered intravenously is cleared partly renally and partly by metabolism to the inactive 4'-O-sulfate (phenolic sulfate).

Budesonide
Budesonide undergoes an extensive degree (≈90%) of biotransformation on first passage through the liver to metabolites of low glucocorticosteroid activity. The glucocorticosteroid activity of the major metabolites, 6β-hydroxybudesonide and 16α-hydroxyprednisolone, is less than 1% of that of budesonide. The metabolism of budesonide is primarily mediated by CYP3A, a subfamily of cytochrome p450.

Elimination

Following inhaled single-dose administration with AIRSUPRA in healthy subjects, the mean terminal half-life of salbutamol was estimated to be 7.1 hours (individual values ranged from 4.62 to 10.0 hours) and the mean terminal half-life of budesonide was estimated to be 4.1 hours (individual values ranges from 2.46 to 6.15 hours).

Linearity/non-linearity

The kinetics of budesonide is dose-proportional at clinically relevant doses.

Special populations

Specific studies to examine the effects of age, sex, gender/ethnicity, or body weight on the pharmacokinetics of AIRSUPRA have not been conducted.

Elderly patients
Based on available data, no adjustment of the dosage of AIRSUPRA in elderly patients is necessary.

The confirmatory trial of AIRSUPRA for asthma included 566 subjects aged 65 and older. No overall differences in safety or effectiveness were observed between these subjects and younger subjects.

Renal impairment
There are no data regarding the specific use of AIRSUPRA in patients with renal impairment.

Hepatic impairment
There are no data regarding the specific use of AIRSUPRA in patients with hepatic impairment.

However, because budesonide is primarily eliminated via hepatic metabolism, an increased exposure can be expected in patients with severe liver impairment.

Paediatric patients
The safety and effectiveness of AIRSUPRA have not been established in pediatric patients, and AIRSUPRA is not indicated for use in this population.

Drug-Drug Interaction
Inhibitors of cytochrome P450 enzymes
Ketoconazole: As a strong inhibitor of cytochrome P450 (CYP) isoenzyme 3A4 (CYP3A4), the main metabolic enzyme for corticosteroids, ketoconazole increased plasma levels of orally ingested budesonide.

Cimetidine: At recommended doses, cimetidine, a nonspecific inhibitor of CYP enzymes, had a slight but clinically insignificant effect on the pharmacokinetics of oral budesonide.

5.3 Preclinical safety data

Non-clinical data reveal no specific hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity and carcinogenic potential.

The toxicity observed in animal studies with budesonide and salbutamol were associated with pharmacological actions or minor adaptive responses commonly observed in inhalation toxicology studies and dose-dependent.

No non-clinical repeat dose toxicology, genotoxicity, carcinogenicity or reproductive toxicology studies have been conducted with AIRSUPRA.

Salbutamol

In common with other potent selective beta$_2$-agonists, salbutamol has been shown to be teratogenic in mice when given subcutaneously. In a reproductive study, 9.3% of foetuses were found to have cleft palate at 2.5 mg/kg dose. In rats, treatment at the levels of 0.5, 2.32, 10.75 and 50 mg/kg/day orally throughout pregnancy resulted in no significant foetal abnormalities. The only toxic effect was an increase in neonatal mortality at the highest dose level as the result of lack of maternal care. Reproductive studies in the rabbit at doses of 50 mg/kg/day orally (900 times higher than the maximum dose in humans on a mcg/m2 basis) have shown foetuses with treatment related changes; these included open eyelids (ablepharia), secondary palate clefts (palatoschisis), changes in ossification of the frontal bones of the cranium (cranioschisis) and limb flexure.

In an oral fertility and general reproductive performance study in rats at doses of 2 and 50 mg/kg/day (450 times higher than the maximum dose in humans on a mcg/m2 basis), with the exception of a reduction in number of weanlings surviving to day 21 post-partum at 50 mg/kg/day, there were no adverse effects on fertility, embryofoetal development, litter size, birth weight or growth rate.

Budesonide

In animal reproduction studies, glucocorticosteroids such as budesonide have been shown to induce malformations (cleft palate, skeletal malformations). However, these animal experimental results are not relevant in humans at the recommended doses (see section 4.6). Budesonide demonstrated no tumourigenic potential in mice. In rats, an increased incidence of hepatocellular tumours was observed, considered to be a class-effect in rats from long-term exposure to corticosteroids.

AIRSUPRA contains the excipients 1,2-distearoyl-sn-glycero-3-phosphocholine (DSPC) and calcium chloride as part of the spray-dried porous particle technology in the pressurised liquid propellant HFA-134a. The safety of HFA-134a has been fully evaluated in preclinical studies. DSPC and calcium chloride have a long history of safe use in man and are approved excipients worldwide.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Norflurane
1,2-distearoyl-*sn*-glycero-3-phosphocholine (DSPC)
Calcium chloride

6.2 Incompatibilities

Not applicable.

6.3 Shelf-life

Please refer to expiry date on the outer carton.
To be used within 9 months of opening the pouch

6.4 Special precautions for storage

Do not store above 30°C.

Store in a dry place.

6.5 Nature and contents of container

A pressurised metered dose inhaler, comprising an internally-coated aluminium canister, sealed with a metering valve, fitted with an attached dose indicator and fitted into a white plastic actuator body with a frosted clear plastic dust cap. Each inhaler is individually packaged in a foil laminate pouch containing a desiccant sachet and placed into a carton.

6.6 Instructions for use, handling and disposal

The canister should not be broken, punctured or burnt, even when apparently empty. Do not use or store near heat or open flames. Do not expose to temperatures above 49ºC.

See also section 4.2 Posology and method of administration, and the patient information leaflet.

HARUS DENGAN RESEP DOKTER

Box, 1 inhaler @ 120 actuations (Reg.No. : DKIXXXXXXXXXXXX)

Manufactured by
AstraZeneca Dunkerque Production, France

Imported by
PT AstraZeneca Indonesia Cikarang, Bekasi – Indonesia

Date of revision text : 11 May 2026
Document number : VV-RIM-07225876

INFORMASI PRODUK UNTUK PASIEN
AIRSUPRA®
Salbutamol sulfate dan Budesonide
90 microgram /80 mikrogram
Aerosol Inhalasi

Bacalah seluruh selebaran ini dengan cermat sebelum mulai menggunakan obat ini.

- Simpan leaflet ini. Anda mungkin perlu membacanya di kemudian hari.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter Anda atau apoteker.
- Obat ini diresepkan khusus untuk Anda. Jangan berikan obat ini kepada orang lain karena dapat membahayakan mereka meskipun tanda dan gejala penyakitnya sama dengan Anda.

Informasi yang terkandung pada leaflet ini

1 AIRSUPRA DAN KEGUNAANNYA

AIRSUPRA adalah inhaler yang digunakan untuk mengobati asma pada pasien berusia 18 tahun ke atas. AIRSUPRA menggabungkan 2 obat, yaitu obat agonis beta$_2$-adrenergik kerja pendek/cepat (SABA) (salbutamol) dan obat kortikosteroid inhalasi (ICS) (budesonid), dalam 1 inhaler, yang diberikan dalam bentuk semprotan dengan propeler.

- Obat SABA seperti salbutamol membantu merelaksasi otot polos saluran napas, sehingga saluran melebar dan pernapasan menjadi lebih lancar.
- Obat ICS seperti budesonid membantu mengurangi peradangan di paru-paru. Peradangan di paru-paru dapat mengakibatkan sesak napas.

AIRSUPRA adalah obat resep yang digunakan:

- sesuai kebutuhan sebagai inhaler pelega untuk mengobati atau mencegah gejala asma (penyempitan saluran napas, mengi, batuk, dan sesak napas).
- untuk membantu mencegah gangguan napas parah yang muncul tiba-tiba (serangan asma).

AIRSUPRA tidak boleh digunakan sebagai pengobatan rutin untuk asma. Jika saat ini Anda mengonsumsi obat jangka panjang untuk mengendalikan gejala asma, tetap konsumsi obat tersebut sesuai petunjuk penyedia layanan kesehatan Anda.

2 HAL YANG PERLU DIKETAHUI SEBELUM MENGGUNAKAN AIRSUPRA

Jangan menggunakan AIRSUPRA:

- jika Anda alergi terhadap budesonid, salbutamol, atau bahan AIRSUPRA lainnya (tercantum dalam bagian 6).

Kesulitan bernapas yang tiba-tiba

Jika Anda merasakan sesak di dada, batuk, mengi, atau sesak napas segera setelah menggunakan AIRSUPRA, **hentikan penggunaan obat ini** dan segera cari pertolongan medis karena mungkin Anda menderita kondisi serius yang disebut bronkospasme paradoks.

Hubungi dokter Anda sebelum menggunakan AIRSUPRA, jika:

- Anda memiliki perburukan asma
- Anda mengalami bronkospasme paradoks, yaitu gangguan saluran pernapasan sesaat setelah menggunakan bronkodilator.
- Anda memiliki riwayat gangguan jantung
- Anda ingin menggunakan obat lebih banyak dari dosis yang disarankan
- Anda memiliki riwayat alergi berat termasuk anafiksis seperti reaksi berat/bengkak pada wajah/kerongkongan, sesak hebat, atau ruam.
- Anda memiliki kelenjar tiroid yang terlalu aktif.
- Kadar kalium dalam darah rendah.
- Anda baru saja terkena infeksi
- Anda pernah mengalami riwayat infeksi jamur di mulut atau tenggorakan setelah menggunakan inhaler steroid.
- Anda memiliki hormon kortisol yang tinggi
- Anda beresiko memiliki tulang rapuh (osteoporosis) atau pernah mengalami patah tulang, atau penurunan fungsi tulang
- Anda memiliki resiko glukoma dan katarak
- Anda mengonsumsi obat yang dapat meningkatkan interaksi dengan enzim CYP3A4 (dapat merujuk pada bagian ”mengonsumsi obat lain”)
- Anda memiliki perlambatan pada pertumbuhan anak

AIRSUPRA dengan makanan dan minuman

Anda dapat menggunakan AIRSUPRA kapan saja sepanjang hari, dengan atau tanpa makanan.

Kehamilan

Sebelum menggunakan AIRSUPRA, beri tahu dokter jika Anda sedang hamil atau sedang merencanakan kehamilan.

Menyusui

Sebelum menggunakan AIRSUPRA, beri tahu dokter jika Anda sedang menyusui.

Menyetir dan mengoperasikan mesin

AIRSUPRA kemungkinan tidak akan memengaruhi kemampuan mengemudi atau menggunakan alat atau mesin apa pun.

Anak-anak dan Remaja

Keamanan dan kemanjuran Airsupra belum terbukti pada anak-anak atau remaja. Jangan berikan obat ini kepada anak-anak atau remaja berusia kurang dari 18 tahun

Mengonsumsi obat-obatan lain

Harap dicatat bahwa pernyataan ini mungkin juga berlaku untuk produk yang digunakan beberapa waktu lalu.

Beri tahu dokter atau apoteker Anda jika Anda sedang menggunakan/baru-baru ini menggunakan/akan menggunakan obat-obatan lain

Beri tahu dokter/apoteker secara khusus jika Anda sedang mengonsumsi:

- obat-obatan untuk peningkatan sitokrom P4503A4, seperti : ketoconazole, ritonavir, atazanavir, clarithromycin, indinavir, itraconazole, nefazodone, nelfinavir, saquinavir, telithromycin)
- obat-obat lain dengan agonis $beta_2$-adrenergik kerja pendek/cepat (SABA)
- obat-obatan untuk detak jantung tidak teratur atau cepat, misalnya amiodarone.
- obat-obat diuretik
- obat digoxin
- obat-obat antidepressan untuk golongan monoamine oxidase inhibitors atau *Tricyclic antidepressant*

3 CARA MENGGUNAKAN AIRSUPRA

Selalu gunakan AIRSUPRA sesuai dengan yang diinstruksikan oleh dokter Anda. Tanyakan kembali kepada dokter atau apoteker Anda jika Anda tidak yakin.

AIRSUPRA digunakan melalui 2 inhalasi (semprotan/*puff*) sesuai kebutuhan. Tiap semprotan mengandung 90 mikrogram salbutamol dan 80 mikrogram budesonid. Jangan menghirup lebih dari 12 kali (semprotan) dalam jangka waktu 24 jam.

Jika Anda merasa efek AIRSUPRA terlalu kuat atau terlalu lemah, konsultasikan dengan dokter Anda atau apoteker.

Jika Anda menggunakan AIRSUPRA lebih banyak dari yang seharusnya

Jika Anda mungkin telah berlebihan menggunakan AIRSUPRA, segera konsultasikan dengan dokter atau apoteker.

Tanda-tanda overdosis adalah gemetar dan detak jantung cepat.

4 EFEK SAMPING YANG MUNGKIN DIALAMI

Seperti semua obat-obatan lain, AIRSUPRA dapat memiliki efek samping.

Umum (dapat dialami hingga 1 dari 10 orang)

- sariawan (infeksi jamur) di mulut
- gemetar/tremor
- sakit kepala
- detak jantung cepat
- iritasi ringan pada tenggorokan
- batuk dan/atau suara serak

Tidak umum (dapat dialami hingga 1 dari 100 orang)

- jantung berdebar (palpitasi)
- iritasi mulut
- kram otot

Jarang (dapat mempengaruhi hingga 1 dari 1.000 pasien)

- reaksi hipersensitivitas termasuk, ruam kulit, gatal, biduran (urtikaria), pembengkakan pada area mulut dan tenggorokan (angioedema), bronkospasme (pengencangan otot di saluran napas yang menyebabkan mengi dan sesak napas), penurunan tekanan darah, dan pingsan.
- penurunan fungsi kelenjar adrenal
- penurunan laju pertumbuhan
- merasa gelisah atau gugup
- depresi
- perubahan perilaku

- memar pada kulit
- penurunan jumlah kalium dalam darah (jika ini terjadi, Anda mungkin merasakan detak jantung tidak teratur, kelemahan otot, atau kram)
- peningkatan aliran darah ke ekstremitas (vasodilatasi perifer)

Sangat jarang (dapat mempengaruhi hingga 1 dari 10.000 orang)

- hiperaktivitas
- gangguan irama jantung, termasuk fibrilasi atrium, peningkatan denyut jantung (takikardia supraventrikular), dan denyut nadi tidak teratur (ekstrasistol ventrikel)
- kejang bronkial (bronkospasme paradoks)

Tidak diketahui (frekuensi tidak dapat diperkirakan dari data yang tersedia)

- sirkulasi darah yang buruk ke otot jantung (iskemia miokard)

Jika Anda mengalami efek samping yang tidak tercantum dalam selebaran ini, harap beri tahu dokter Anda atau apoteker.

Dugaan efek samping produk obat PT. AstraZeneca Indonesia dapat dilaporkan secara online melalui link http://contactazmedical.astrazeneca.com atau dengan *scan QR code* berikut:

Pelaporan dugaan efek samping produk kepada PT. AstraZeneca Indonesia tidak menggantikan konsultasi atau penanganan medis oleh dokter. Untuk mendapatkan saran medis, diagnosis, atau pengobatan, tetap konsultasikan keluhan pasien kepada dokter atau tenaga kesehatan profesional.

5 CARA PENYIMPANAN AIRSUPRA

- Jauhkan obat ini dari jangkauan dan pandangan anak-anak.
- Jangan simpan di atas suhu 30°C. Simpan di tempat yang kering.
- **Gunakan sebelum tanggal:** Jangan gunakan AIRSUPRA setelah tanggal kedaluwarsa pada label/karton. Tanggal kedaluwarsa mengacu pada hari terakhir bulan tersebut.
- Inhaler dapat digunakan dalam jangka waktu **9 bulan** sejak kemasan dibuka.
- Ingatlah untuk mengembalikan AIRSUPRA yang sudah tidak dipakai ke apoteker.

- **Peringatan:** Tabung tidak boleh pecah, tertusuk, atau terbakar, meskipun terlihat kosong. Jangan digunakan atau disimpan di dekat panas atau api terbuka. Jangan terkena suhu lebih tinggi dari 49°C.

6 INFORMASI LEBIH LANJUT

Kandungan AIRSUPRA

Bahan aktif AIRSUPRA terdiri atas salbutamol sulfat dan budesonide.

Tiap satu kali inhalasi (*puff*) memberikan dosis setara dengan 90 mikrogram salbutamol (setara dengan 108 mikrogram salbutamol sulfat) dan 80 mikrogram budesonide.

Bahan lainnya adalah norflurane, 1,2-distearoyl-*sn*-glycero-3-phosphocholine dan kalsium klorida.

Bentuk dan Isi Kemasan AIRSUPRA

AIRSUPRA tersedia dalam bentuk tabung *canister* yang dilengkapi indikator dosis, dilengkapi badan aktuator plastik berwarna putih, dan tutup debu (*dust cap*) plastik transparan agak buram. Tiap inhaler dikemas satu-satu dalam kantong laminasi foil yang berisi zat pengering dan dimasukkan ke dalam karton. AIRSUPRA memiliki bentuk sediaan aerosol inhalasi bertekanan dengan warna suspensi putih.

AIRSUPRA tersedia dalam kemasan yang berisi 1 inhaler dengan 120 dosis

HARUS DENGAN RESEP DOKTER
Dus, 1 pouch @ 1 inhaler @ 120 actuations (Reg. No : DKIXXXXXXXXXXXXX)

Diproduksi oleh
AstraZeneca Dunkerque Production (AZDP)
Dunkerque, France

Diimpor oleh
PT. AstraZeneca Indonesia
Cikarang, Indonesia

Document Number : VV-RIM-07251073
Leaflet terakhir direvisi : 07 April 2026

7 PETUNJUK PENGGUNAAN

AIRSUPRA®
Salbutamol sulfate dan Budesonide
90 microgram /80 mikrogram
Aerosol Inhalasi

Baca petunjuk penggunaan berikut dengan seksama
AIRSUPRA Anda (yang disebut "inhaler" dalam leaflet ini) mungkin berbeda dari inhaler yang Anda pernah gunakan sebelumnya.

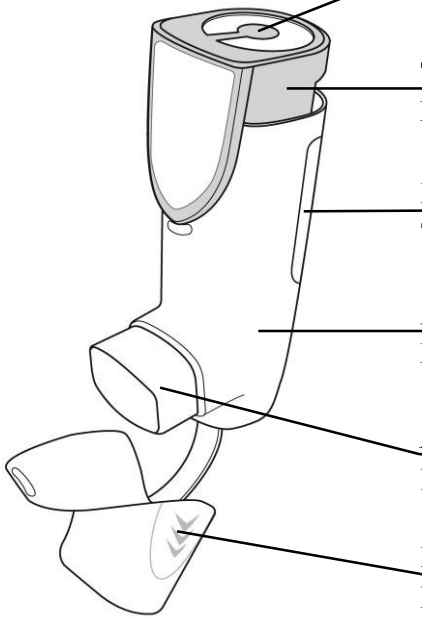
Informasi penting

- Hanya untuk penggunaan inhalasi oral
- Persiapkan inhaler Anda untuk penggunaan pertama kali dengan cara *priming* (persiapan awal)
- Lakukan *priming* inhaler sehingga Anda mendapatkan jumlah obat yang tepat saat menggunakannya
- Bilas badan aktuator plastik yang berwarna putih setiap minggu.

Menyimpan inhaler Anda

- Simpan inhaler Anda pada suhu kamar (20-25°C).
- **Jangan disimpan di lingkungan yang lembab, seperti kamar mandi.**
- Jauhkan inhaler Anda dan semua obat-obatan jauh dari pandangan dan jangkauan anak-anak.

Bagian-bagian inhaler



Indikator *Puff*
Terletak di atas tabung *canister* bertekanan

Tabung Canister bertekanan (di dalam)
Berisi bahan aktif yang terkandung

Label Aktuator
Tulis waktu penggunaan pada label

Aktuator
Berisi tabung *canister* bertekanan.

Mouthpiece
Menyemprotkan bahan aktif yang terkandung

Penutup *Mouthpiece*
Melindungi *mouthpiece* saat inhaler tidak digunakan.

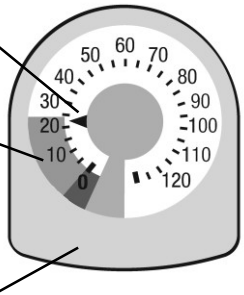
Cara membaca indicator puff/dosis

Indikator *puff* akan berkurang 1 (satu) setiap kali Anda menggunakan 1 (satu) puff/dosis.

Garis Petunjuk
Menunjukkan jumlah *puff* yang tersisa .

Zona kuning
Segera ganti dengan inhaler yang baru apabila garis petunjuk berada pada zona kuning

Zona merah
Buang inhaler Anda ketika garis petunjuknya berada di angka 0 pada zona merah



Jangan mengisap saat garis petunjuk menunjukkan angka 0 karena Anda tidak akan meendapatkan dosis penuh.

Kapan harus mengganti inhaler baru?

Ganti inhaler dengan yang baru apabila:

- garis petunjuk pada indikator puff berada dalam zona kuning.
- inhaler-nya mengalami kerusakan

Membuang inhaler Anda

Buang inhaler Anda mengikuti pedoman lokal apabila:

- Sembilan bulan setelah inhaler-Anda dikeluarkan dari kantong foil/*pouch*
  atau
- setelah tanggal kadaluwarsa pada karton dan tabung
  atau
- indikator *puff* menunjukkan 0,
- manapun dari situasi di atas yang terjadi terlebih dahulu.

Jangan menggunakan kembali atau menggunakan aktuator dengan *canister* yang berisi obat dari inhaler lain.
Jangan menusuk atau membuang canister ke dalam api atau insenerator

SEBELUM PENGGUNAAN PERTAMA KALI – Inhaler disiapkan dengan cara *priming*

- Tulis ’tanggal kadaluarsa’ (*Use by date*) pada label aktuator.
- Sebelum Anda menggunakan inhaler untuk **pertama kalinya, kocok inhaler dan semprotkan sebanyak 4 kali** dengan cara priming.

1. Tulis tanggal kadaluarsa (*Use by date*)

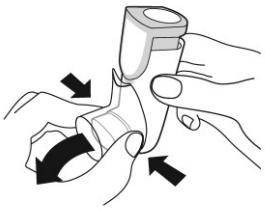
Tulis tanggal kadaluarsa (*Use by date*) (dihitung dari 9 bulan setelah Anda membuka kantong foil pertama kali) pada label aktuator menggunakan tinta permanen.

Tulis ‘tanggal kadaluarsa’ (*Use by date)* pada label aktuator.

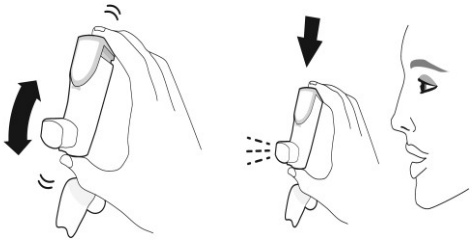
2. Tingkatkan inhaler Anda sebelum pemakaian pertama

Lepaskan penutup *mouthpiece*

Kocok inhaler dengan baik dan semprotkan **4 puff** (hanya untuk uji priming) dengan mengarah jauh dari Anda, kocok setiap sebelum menyemprotkan *puff* uji.



Kocok sebelum disemprotkan. Ulangi kedua tindakan tersebut sebanyak4 kali.



Puff ekstra disediakan untuk *priming*. **Jangan melewatkan tahapan *priming*.**

Kapan dan bagaimana cara *priming* ulang inhaler Anda?

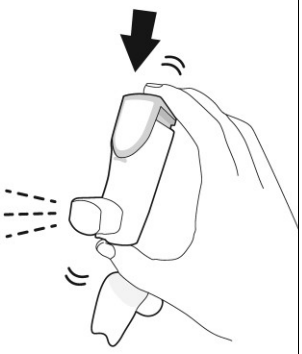
Lakukan *priming* ulang inhaler Anda:

- Setelah membilas aktuator putih
- Bila terjatuh
- Bila tidak digunakan selama lebih dari 7 hari.

Bagaimana melakukan *priming* ulang inhaler Anda?

Lepaskan penutup *mouthpiece* dan semprotkan **2 *puff* uji,** kocok sebelum menyemprotkan setiap *puff* uji

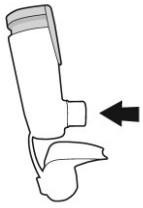
Kocok sebelum disemprotkan.
Ulangi kedua tindakan sebanyak dua kali

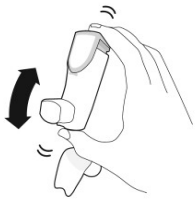
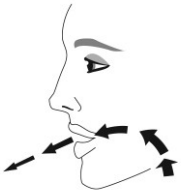
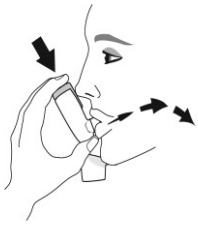


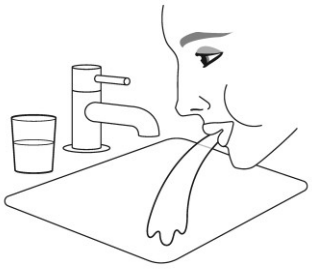
Puff ekstra disediakan untuk *priming*. **Jangan melewatkan tahapan *priming*.**

Bagaimana Cara Menggunakan Inhaler Anda – Inhalasi obat Anda

- Gunakan 2 semprotan **(= 1 dosis)** sesuai kebutuhan. **Jangan** menggunakan lebih dari 12 puffs dalam 24 jam.
- Setelah digunakan, bilas mulut Anda jika air tersedia, tanpa menelan, untuk mencegah infeksi jamur oral.

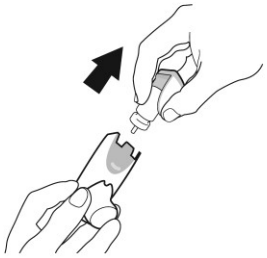
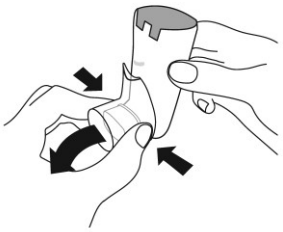
1. Cek inhaler terlebih dahulu
Lepaskan penutup *mouthpiece*. **Periksa mouthpiece untuk melihat apakah ada benda asing dan singkirikan benda tersebut sebelum digunakan**  Periksa pada bagian dalam *mouthpiece*.

2. Kocok dan Lakukan Inhalasi				
Kocok inhaler terlebih dahulu dengan baik.	Hembuskan napas secara dalam.	Posisikan *mouthpiece* ke mulut dan tutup bibir di sekitar lubang mulut.	Tarik napas dalam-dalam dan perlahan-lahan saat menyemprotkan **1 puff**. Lanjutkan menarik napas sampai secara maksimal.	Lepaskan *mouthpiece* dari mulut. Tahan napas selama Anda bisa atau sampai 10 detik.
				 

3. Ulangi	4. Pasang *mouthpiece* kembali	5. Bilas
Segera ulangi langkah kocok dan inhalasi untuk mengambil semprotan kedua.  **2 kepulan = 1 dosis.**	Pasang kembali *mouthpiece*. 	Bilas mulut jika air tersedia **(jangan ditelan)** untuk mencegah infeksi jamur oral. 

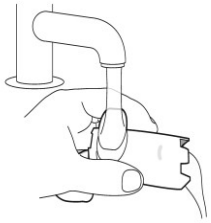
Pembersihan Mingguan - Mencuci aktuator Anda 1 kali setiap minggu

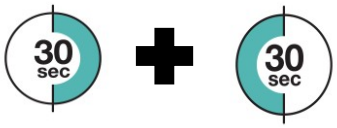
- Bilas aktuator putih setiap minggu agar obat tidak menumpuk dan menghalangi semprotan melalui *mouthpiece*.
- **Jangan biarkan tabung menjadi basah.**
- Lakukan *priming* ulang setelah pembilasan.

1. Lepaskan *canister*
Lepaskan *canister* dan sisihkan. Lepaskan *mouthpiece*.  

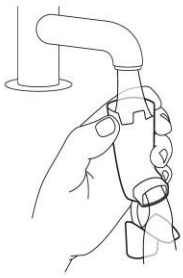
2. Bilas melalui kedua ujung

Bilas dengan air hangat selama 30 detik pada setiap ujung aktuator. Kocok perlahan untuk menghilangkan sisa air. **Jangan menggunakan sabun. Jangan dikeringkan dengan handuk atau tisu.**

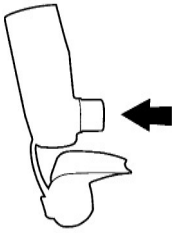


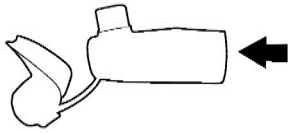


Total 60 detik



Periksa *mouthpiece* dan aktuator untuk memastikan apakah masih tersisa tumpukan obat. Lakukan pembilasan, apabila masih ada tumpukan obat.

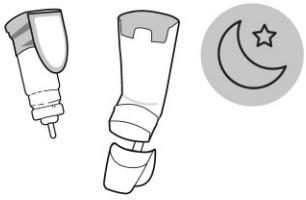




Periksa bagian dalam *mouthpiece* dan aktuator .

3. Biarkan aktuator hingga mengering

Biarkan actuator hingga mongering (air-dry), lebih baik semalaman.



4. Memasang kembali dan melakukan priming ulang

Pertama, pasang kembali penutup *mouthpiece*. Setelah *mouthpiece* terpasang, tekan *canister* ke dalam tabung aktuator secara perlahan. **Jangan memasang kembali sampai inhaler benar-benar kering. Jangan memasukkan tabung canister ketika *mouthpiece* terlepas.** Lakukan *priming* ulang inhaler dengan mengikuti langkah-langkah *priming* ulang sebagaimana di atas.

Penggunaan inhaler sebelum kering dalam keadaan darurat

Jika Anda perlu menggunakan inhaler sebelum kering:

- kocok untuk menghilangkan sisa air
- masukkan tabung dalam alat
- kocok alat dan semprotkan sebanyak dua kali ke udara, menjauhi dari wajah
- gunakan dosis yang diresepkan
- bilas kembali inhaler sesuai dengan langkah pembilasan .