



Aservo[®]
EquiHaler[®]
Veterinary
Manual

Every Cough
Means
Something



Introduction	3
Equine asthma syndrome	4
Aetiology	5
Genetics	5
Role of infectious agents	5
Pathophysiology	6
Diagnosis of equine asthma syndrome	7
Signalment, history and clinical signs	7
Clinical examination	7
Airway endoscopy	8
Treatment of equine asthma syndrome	10
Aims of treatment	10
Corticosteroids	11
Bronchodilators	12
Mucolytics	12
Environmental modification	12
The Aservo® EquiHaler®	14
Ciclesonide	14
Soft Mist™ Inhaler Technology	17
Clinical efficacy trials	21
Pulmonary function in a mouldy hay challenge model	21
European clinical efficacy study	22
How to use	25
Environmental modification guide	26
References	30
Notes	31

Equine asthma has long been recognised by veterinary surgeons as the most common disease affecting the lower respiratory tract of horses. Our understanding of the syndrome has grown in recent years but there is still much to learn. The clinical signs experienced may range from poor performance to acute dyspnoea but the outcome is the same – removing from horses, ponies and their owners the freedom to do what they love – whatever that may be.

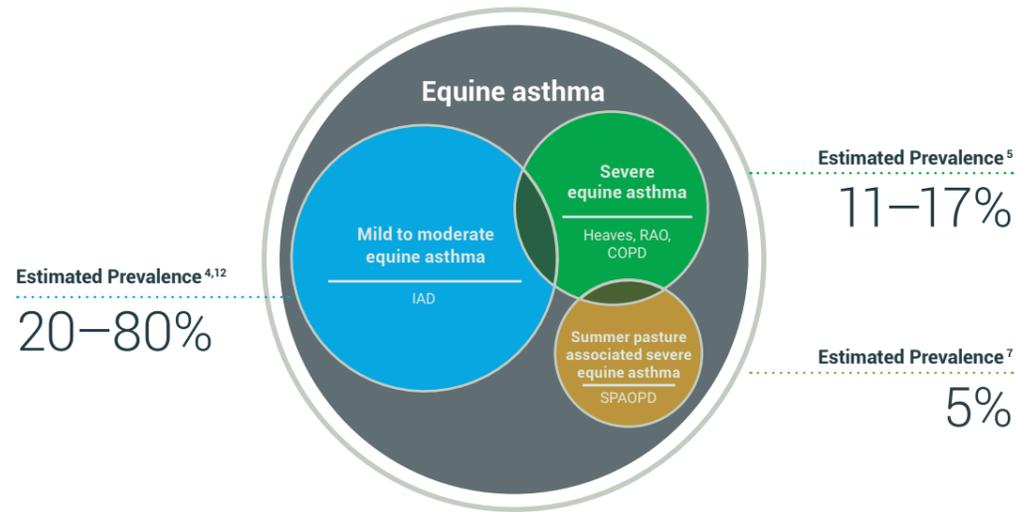
Vets work tirelessly to provide the best treatment options for their patients. But until now, there has always had to be a compromise – whether that was in consistency of drug delivery, targeting treatment to the lung, systemic cortisol suppression, owner and horse compliance or lack of robust clinical data.

Boehringer Ingelheim are passionate about respiratory health, both in the human and equine sphere. We don't believe that vets should have to compromise on any of these areas and so, after a 10 year development programme, we are proud to introduce a new way to treat severe equine asthma.

Aservo® EquiHaler® uses the prodrug ciclesonide to directly target inflammation deep in the lungs, its precise delivery aided by our Soft Mist™ Inhalation technology and a design that is made for horses and the people that care for them.

Find out more about equine asthma syndrome and the Aservo® EquiHaler® in this manual and at www.equihaler.uk





Equine asthma syndrome is an all-encompassing umbrella term to describe all chronic non-infectious inflammatory diseases affecting the lower airway in horses.

The term 'equine asthma syndrome' now replaces what was formerly referred to as inflammatory airway disease (IAD), recurrent airway obstruction (RAO), summer pasture-associated obstructive pulmonary disease (SPAOPD), heaves, chronic obstructive pulmonary disease (COPD), chronic obstructive pulmonary bronchiolitis (COB), equine emphysema and heaves.

Equine asthma syndrome can be further sub-classified based on the disease severity^{2,3}:

- Mild to moderate equine asthma (formerly IAD)
- Severe equine asthma (formerly RAO and SPAOPD)

	Mild to Moderate Equine Asthma (formerly IAD)	Severe Equine Asthma (formerly RAO, SPAOPD and heaves)
Age of onset	Likely younger horses (sport and racehorses), but all ages can be affected	Typically >7 years old
Clinical signs	<ul style="list-style-type: none"> • Poor performance • Occasional coughing during exercise or at rest • Nasal discharge may be present • Excess tracheal mucus 	<ul style="list-style-type: none"> • Increased respiratory effort at rest, with abdominal lift and nasal flaring • Frequent coughing • Nasal discharge • Exercise intolerance
Recurrence	May completely resolve with or without treatment - low risk of recurrence	Recurrent and progressive; incurable, requires lifelong management
BAL* cytology	<ul style="list-style-type: none"> • Mast cells >5% and/or mild increase in neutrophils >10% and/or eosinophils >5% 	Moderate to severe increase in neutrophils >25%
Airway obstruction	<ul style="list-style-type: none"> • Subclinical • No evidence of airflow limitation based on oesophageal balloon catheter technique ($\Delta P_{max} < 10 \text{ cm H}_2\text{O}$) 	<ul style="list-style-type: none"> • Dyspnea at rest • Moderate to severe airflow limitation during disease exacerbation based on oesophageal balloon catheter technique ($\Delta P_{max} > 15 \text{ cm H}_2\text{O}$)
Airway hyperresponsiveness	Yes	Yes
Airway remodeling	No data/conflicting evidence	Airway smooth muscle hypertrophy and extracellular matrix deposition
Arterial blood gas	During maximal exercise, gas exchange may be impaired, with decreased partial pressure of oxygen (hypoxemia)	Impaired gas exchange has been found at rest (both during disease exacerbation and remission) and during exercise. At rest: hypoxemia. During submaximal exercise: hypercapnia, hypoxia and hyperlactatemia

* Bronchoalveolar lavage

Aetiology

Airborne environmental exposures, especially to suspended organic dust particulates, play a pivotal role in the induction and progression of equine asthma^{2,12}; however, the severity of disease is also determined by the inherent responsiveness of the individual horse to the various inhaled environmental challenges (e.g. mould spores, endotoxins, etc.). For example, in horses with a genetically linked susceptibility to **severe equine asthma**, such environmental challenges, particularly moulds, induce an inappropriately exaggerated pulmonary inflammatory response.

Although the term 'equine asthma' incorporates a spectrum of environmentally-induced, non-infectious airway inflammatory diseases of varying clinical severities (i.e. mild/moderate equine asthma and severe equine asthma), there are likely to exist, in addition to "clinical severity", a plethora of other factors which, in the future may help to distinguish between the likely numerous equine asthma subtypes^{2,28}.

Genetics

It has been suggested that there is a strong genetic, as well as environmental, cause for **severe equine asthma** susceptibility in affected horses, although the overall mode of inheritance of susceptibility to severe equine asthma is likely to be complex⁶.

A strong genetic predisposition to developing severe equine asthma has been demonstrated in several families of Warmblood and Lipizzaner horses. In these breeds the percentage of offspring affected by severe equine asthma has been shown to increase with an increasing number of affected parents; similar to findings in human medicine associated with asthma in children¹¹.



Role of infectious agents

The contribution of infectious agents to the development of equine asthma is currently uncertain². A variety of viral and bacterial aetiological agents have been linked to mild to moderate equine asthma however the causative relationship between the lower airway inflammation and infectious agent is still inconclusive and further research is required^{2,10}.

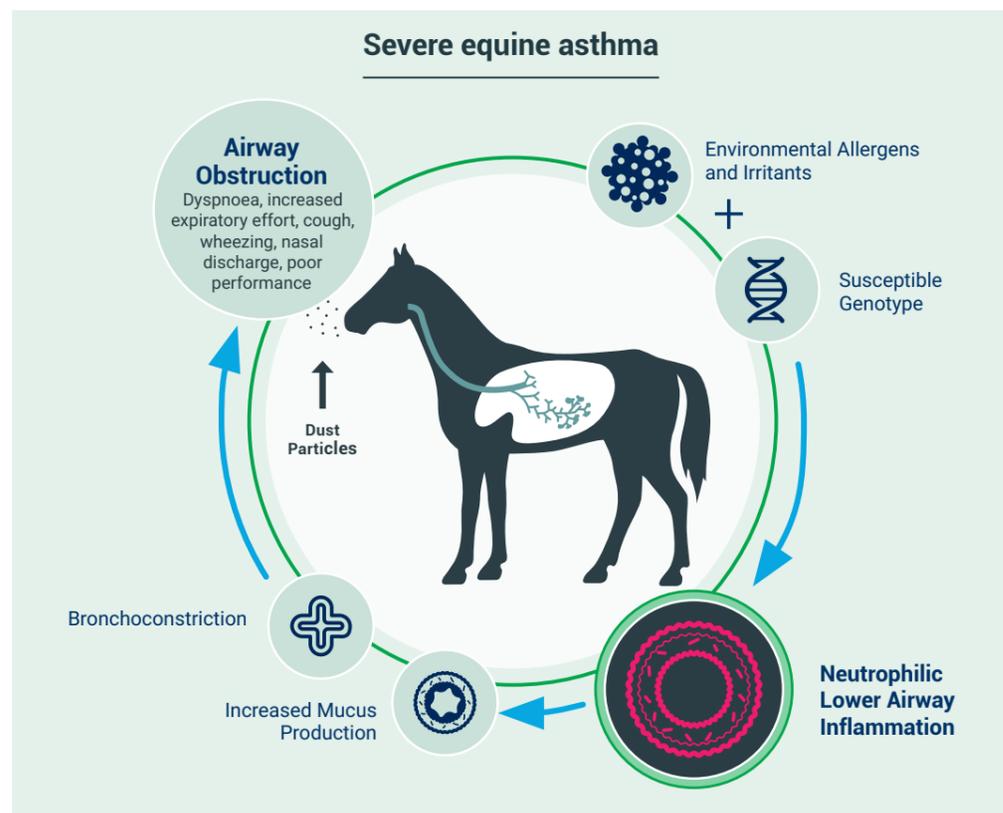
Pathophysiology

Horses affected by equine asthma develop airway inflammation and airway hyperreactivity following exposure to, and inhalation of, environmental airborne allergens^{6,12}. This inflammation results in^{6,12}:

- bronchospasm/bronchoconstriction - an exaggerated and persistent contraction of the airway smooth muscle
- inflammatory cell recruitment in the lower airways
- mucus hypersecretion
- decreased mucociliary clearance which further contributes to the accumulation of airway secretions and airway obstruction.

Although horses affected by equine asthma have increased numbers of inflammatory cells in the lower airways, the type of inflammatory cells present differ depending on the severity of disease².

Continued antigenic exposure and chronic airway inflammation in susceptible individuals, i.e. **severe equine asthma**, has been shown to result in airway remodelling and persistent structural thickening of the small airways with a three times greater increase in smooth muscle thickness than normal airways²⁷.



In **mild to moderate asthma**, it is poorly understood whether an affected animal will go on to develop the severe form of the disease^{2,28}. While severe equine asthma is recurrent, progressive and incurable, horses with mild to moderate asthma may recover and not go on to experience disease in the future².

Signalment, history and clinical signs

Horses with severe equine asthma commonly have a recent history of exposure to environmental allergens, such as hay and/or being stabled with organic bedding, and present with associated clinical signs at rest including increased expiratory rate and effort, and coughing⁶. They may have experienced these clinical signs periodically or repeatedly. Any type of horse can be affected but they are usually mature horses of >7 years old². The summer pasture-associated form of the disease is exacerbated during turnout and outdoor exercise during the relevant months.

Mild to moderate equine asthma often presents in young horses in training but can occur at any age. Poor performance or slow recovery after exercise with occasional cough is a common presentation².

Clinical examination

Pyrexia is not a feature of equine asthma syndrome². Mild to moderate cases may not demonstrate any abnormalities during pulmonary auscultation. Cases of severe equine asthma demonstrating airway obstruction can be identified by musical expiratory wheezes towards the end of the expiratory phase and early inspiratory fine crackles⁶. The use of a re-breathing bag can increase the sensitivity of thoracic auscultation and increased coughing on inducing hyperventilation indicates lower airway inflammation. This procedure is not advised in dyspnoeic cases³³.

Mild to moderate equine asthma	Severe equine asthma
Subclinical airway inflammation with lack of any clinical signs	Signs and severity may vary over time, often limiting activity and occasional acute respiratory distress
Serous to mucoid nasal discharge	Mucopurulent bilateral nasal discharge (may be observed in bedding or stable wall rather than at nares)
Occasional or chronic cough (>3 weeks duration)	Regular to frequent coughing
Poor or decreased performance	Exercise intolerance
Slower recovery post exercise	Increased expiratory effort at rest with abdominal lift and nasal flaring

Figure 2: Clinical signs of equine asthma syndrome²⁶



The diagnosis of severe equine asthma based on the history and clinical examination has been shown to be an accurate method of diagnosis¹³ however ancillary diagnostic tests are also advised to improve the diagnostic accuracy and confirm the diagnosis, especially in mild to moderate equine asthma where the more subtle clinical findings make diagnosis more challenging and other differential diagnoses need to be ruled out.

Airway endoscopy

In clinical practice airway endoscopy is commonplace and consists of either a tracheal wash (TW) and/or a bronchoalveolar lavage (BAL).

Both a TW and a BAL enable:

- visualisation of the airways
- assessment of mucous accumulations
- collection of respiratory secretions for cytological evaluations.

TW is frequently carried out in clinical practice and is often considered an easier method of obtaining fluid samples from the lower respiratory tract than a BAL. However, although cytological evaluation from TW aspirates provides some information about the inflammatory status of the airways, BAL is considered a more sensitive technique for identifying lower airway inflammation and is recommended as the primary method of confirming equine asthma-associated lower airway inflammation^{2,6,29}.

Ideally, cytology from both techniques (TW and BAL) and microbiology of TW samples should be carried out to give the best picture of what is going on in the airways. Correlation of bacteriological, cytological and clinical findings should always be performed but care should be taken when interpreting bacteriology results as bacteria cultured are not always significant and can even be the result of contamination³⁰.



Inflammatory Cells in BALF	Healthy horses	Mild to moderate equine asthma	Severe equine asthma
Neutrophils	≤5%	>10%	>25%
Mast Cells	≤2%	>5%	≤2%
Eosinophils	≤1%	>5%	≤1%

Figure 3: Suggested Bronchoalveolar Lavage Fluid (BALF) Reference Ranges for Equine Asthma Syndrome²

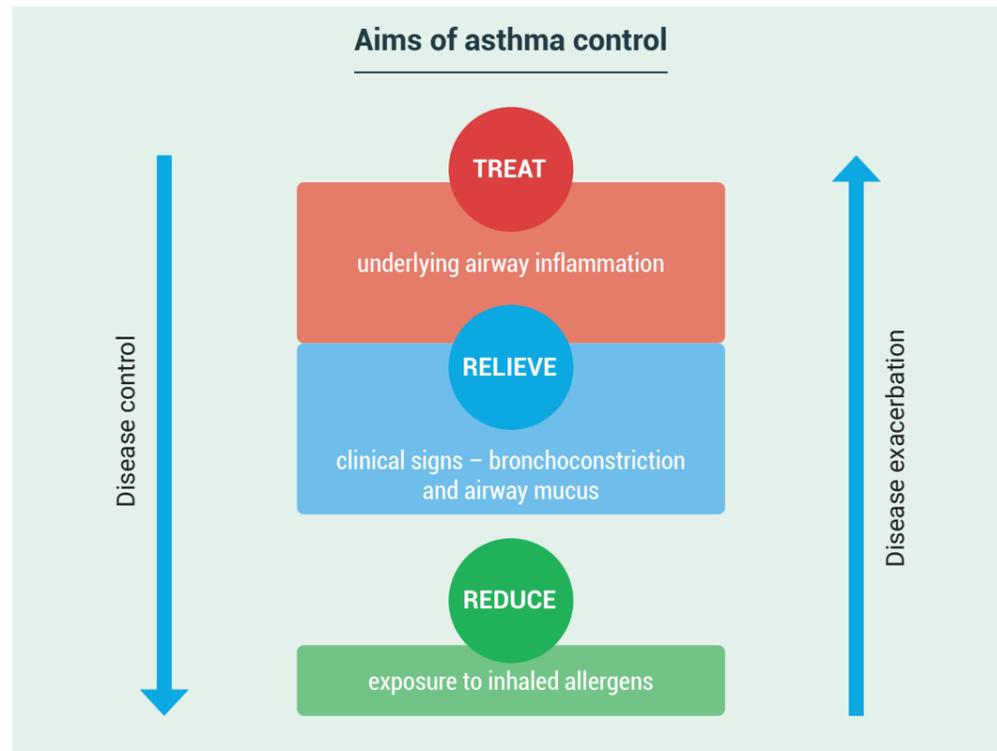
A detailed discussion of airway sampling, interpretation of laboratory results and a how-to TW and BAL guide can be found in the Airway Sampling CPD video on the Boehringer Academy: www.boehringer-academy.co.uk > **Equine** > **Respiratory**

Aims of treatment

Acute cases of severe equine asthma may require immediate rescue therapy with intravenous corticosteroids and bronchodilators. Once initial dyspnoea is controlled, follow up treatment can be initiated.

There is little published data concerning the treatment of mild to moderate equine asthma and therefore the principles of severe equine asthma are often applied, namely controlling airway inflammation and modifying the environment to improve airway hygiene².

The aims of treating severe equine asthma can be summarised using the following algorithm:



TREAT underlying airway inflammation. All of the clinicopathological features associated with severe equine asthma, including airway hyperreactivity, bronchoconstriction, mucus hypersecretion and cough, are as a result of the inflammatory response that occurs within the lower airways. Therefore, pharmacological therapy with corticosteroids, specifically glucocorticoids, remain the cornerstone of therapy for severe equine asthma⁶.

Resolution of clinical signs can take time and therefore in cases which require rapid resolution of bronchoconstriction on welfare grounds a secondary aim is recommended:

RELIEVE clinical signs of bronchoconstriction and airway mucus, using bronchodilators and mucolytics if required. Bronchodilators improve the clinical picture rapidly, allowing corticosteroids time to take effect.

All of this should be underpinned by the final aim:

REDUCE exposure to inhaled allergens and irritants which will enable the patient to achieve disease remission and keep inflammation and clinical signs under control as long as they are in place.

If disease is periodically exacerbated, this process can be reinstated. These aims allow vets to reduce the amount of pharmaceuticals that are prescribed in the management of severe equine asthma. In the treatment of human asthma, continuous treatment with inhaled corticosteroids and bronchodilators is recommended¹⁸. This is due to the ubiquitous nature of inhaled allergens in the environment; only where there is opportunity to identify a particular trigger and avoid it can prescriptions be reduced.

Corticosteroids

Treatment with corticosteroids, in combination with continuous environmental modification and antigen avoidance, have been shown to improve airway inflammation and promote disease remission¹⁴. In some horses these interventions may be all that is required to alleviate the lower respiratory tract inflammation and associated bronchospasm and ultimately control the associated clinical signs.



In clinical practice multiple options are available in terms of the drugs available, the doses used and the routes of administration. When administering corticosteroids the aims of treatment are:

- to achieve higher concentrations of corticosteroid directly at the site of airway inflammation, relative to the rest of the body
- to have minimal systemic effect as measured by adrenal cortisol suppression
- to have minimal associated side effects
- to partially reverse airway remodelling in severely asthmatic horses

In order to meet these treatment aims and achieve a more targeted therapy it is considered preferable to administer corticosteroids via inhalation rather than systemic administration. However, there have historically been no licensed treatments administered via this route. Use of inhaled beclomethasone via a spacer device has been demonstrated to be effective if compliance can be achieved but it has also been shown that 5 actuations BID (250µg per actuation) can cause a similar level of cortisol suppression as parenteral dexamethasone³⁴. Nebulised dexamethasone has not been extensively studied, however not all preparations available are suitable for nebulisation. A recent study demonstrated both suppression of the hypothalamic pituitary axis and a lack of clinical improvement following nebulisation with dexamethasone³⁵.

Bronchodilators

In some cases which are demonstrating acute, severe airway obstruction additional adjunctive treatment with systemic bronchodilators may also be required to rapidly improve respiratory function and relieve bronchospasm.

Clenbuterol (Ventipulmin®; Boehringer Ingelheim) is the most frequently prescribed bronchodilator in equine medicine, and is licensed for the treatment of respiratory disease in horses where airway obstruction due to bronchospasm and/or accumulation of mucus is a contributing factor. It is understandable that bronchodilators have historically been prescribed in preference to corticosteroids where there are concerns regarding the impact of systemic corticosteroids on a particular patient, however bronchodilator monotherapy is no longer recommended as underlying inflammation is not addressed directly.

Mucolytics

Effective suppression of the inflammatory response should result in a reduction in airway mucus production. However if an abnormal amount of mucus, with increased viscosity, remains in the airways despite treatment with corticosteroids then mucolytics, such as dembrexine (Sputulosin®; Boehringer Ingelheim), may be administered concurrently¹⁹.

Environmental modification

Environmental modification remains the most important non-therapeutic intervention for horses with asthma and should primarily focus on reducing the concentration of airborne respirable dust in the horse's breathing zone.

Exposure to airborne organic dust plays a pivotal role in the development of equine asthma and progression of the disease⁶; occurring predominantly from stabling and from hay.

Airborne organic dust contains various potentially pro-inflammatory agents such as^{2,6}:

- bacterial endotoxins
- moulds
- microbial toxins
- forage mites
- plant debris

Contributing environmental trigger factors and irritants include:

- inorganic dust – for example in arenas and racetracks⁹
- ammonia – for example in a poorly ventilated or deep littered stable⁶



Horses with summer pasture-associated severe equine asthma are likely triggered by⁸:

- airborne pasture-associated mould spores and grass pollens
- hot and humid conditions



It is thought that environmental moulds are the inciting cause of most severe equine asthma exacerbations. The severity of the response in susceptible animals can then be attributed to other agents within respirable dust, notably bacterial endotoxins³⁶. Airway irritants such as ammonia and cold air can further affect patients demonstrating airway hyper-responsiveness.

Commonly horse owners may report that they have implemented changes to the environment but despite this the affected horse continues to have frequent episodes of clinical signs associated with equine asthma. In these circumstances it is likely that the affected horse continues to be exposed to airborne environmental allergens and so a full environment assessment should be carried out to determine the potential cause.

Common mis-steps when implementing environmental modification are:

- Not addressing poor ventilation in stables
- Shared airspace with other horses not subject to environmental change
- Storage of forage/bedding or proximity of muck heaps to horse's stable
- Feeding mouldy haylage
- Use of homemade steamers / allowing soaked hay to dry out before feeding
- Old/mouldy hay in the bottom of mangers
- Deep litter bedding
- Feeding from a hay net rather than a clean floor
- Straw bedding in field shelters or dry hay fed at pasture
- Mucking out/sweeping while horse in stable

A guide to environmental management can be found on p26. of this manual and an instructional video at www.equihaler.uk. Owner support materials to assist in case management are available from your Boehringer Ingelheim territory manager.

The Aservo® EquiHaler® is a combination of a novel corticosteroid (ciclesonide) and advanced inhalation technology (Soft Mist™ Inhaler) designed specifically for horses. It is indicated for the alleviation of clinical signs of severe equine asthma. Ciclesonide is a prodrug that is activated in the airway epithelium, making it truly targeted to the lung. It has demonstrated no statistically significant cortisol suppression in clinical trials²³, making it completely different to other corticosteroids on the veterinary market. The Soft Mist™ generated in the product is a slow moving medicated mist with a consistent high fine particle fraction that allows horse to breathe it in naturally, deep into the lung, without a spacer or other device that may reduce the amount of medication delivered.

Ciclesonide

Ciclesonide is an inactive prodrug* that is enzymatically converted to the pharmacologically active metabolite **desisobutyryl-ciclesonide (des-ciclesonide)** in the airway epithelium following inhalation.

*What is a prodrug?

Prodrugs are chemicals with little or no pharmacological activity that undergo biotransformation to a therapeutically active metabolite.

Ciclesonide potency

The potency of inhaled corticosteroids is expressed as the **relative receptor affinity (RRA)** which reflects the binding affinity to the glucocorticoid receptor, relative to dexamethasone (Figure 4).

Glucocorticoid	Relative Receptor Affinity
Dexamethasone	100
Des-ciclesonide	1200

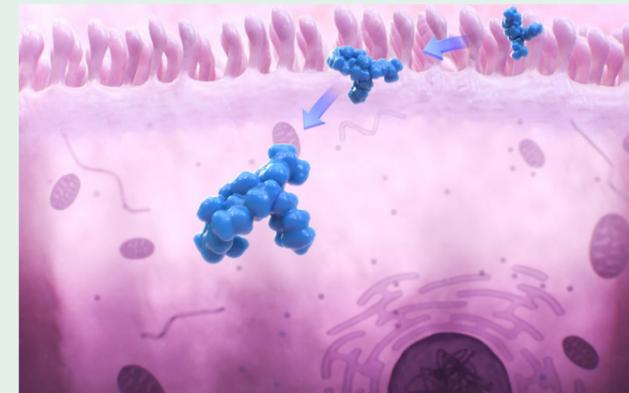
Figure 4: Relative Receptor Affinities of inhaled glucocorticoids³⁷

The prodrug ciclesonide has a very low affinity for glucocorticoid receptors with an RRA of 12 however the active metabolite, des-ciclesonide, has:

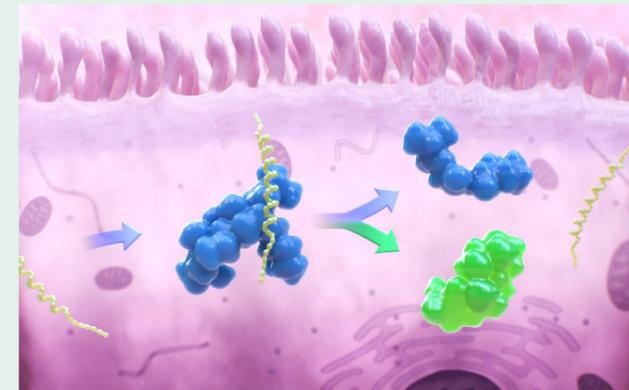
- 12 times greater RRA than dexamethasone
- 100 times greater RRA than ciclesonide.

Conversion to the active metabolite at the site of action has the potential to significantly reduce the systemic concentrations of active drug following inhalation and thus minimise the likelihood of undesirable side effects²².

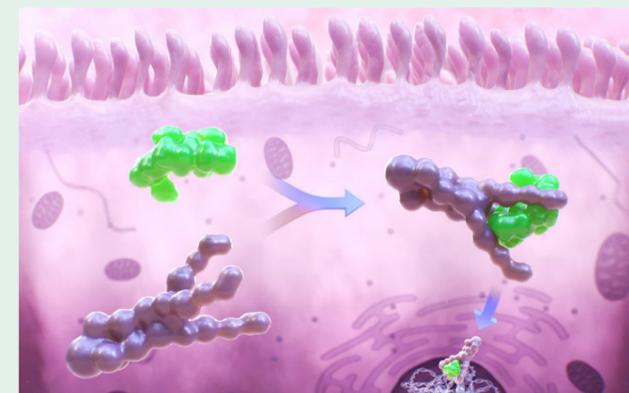
Mode of action²²



Ciclesonide is inhaled as a prodrug with low activity and enters the airway respiratory epithelium.



In the airway epithelium ciclesonide (blue) is enzymatically converted to the pharmacologically active metabolite des-ciclesonide (green) by the enzyme esterase.



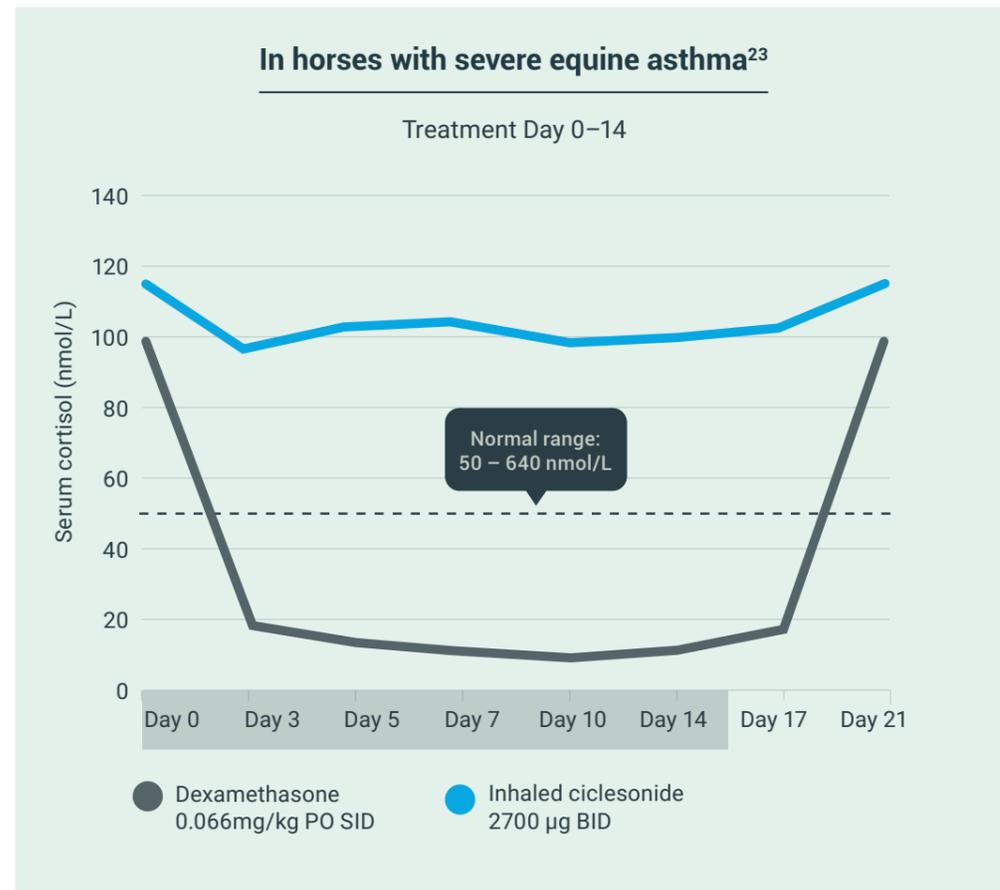
Des-ciclesonide forms reversible depots with fatty acids (oleate) and binds to the glucocorticoid receptors in the lungs to exert its anti-inflammatory action.

Cortisol suppression

A decrease in serum cortisol levels is an indirect marker of systemic exposure to administered corticosteroids, and may reflect potential for increased risk of adverse consequences.

Two studies have evaluated cortisol suppression in horses treated with inhaled ciclesonide vs a positive control and placebo respectively.

The first study, conducted at the University of Montreal, compared serum cortisol levels of severely asthmatic horses treated with dexamethasone or inhaled ciclesonide (at the licensed dose rate) for 14 days^{22,23}. They found no significant reduction in cortisol suppression in the ciclesonide treated group compared to a significant level of cortisol suppression in the dexamethasone group as would be expected. This effect continued beyond cessation of treatment.



A further study was conducted to evaluate safety². This study assessed serum cortisol levels in healthy horses treated with ciclesonide for 30 days at 3 times the recommended dose. No statistically significant effect on serum cortisol was identified in this study.

Vets are often reluctant to treat horses and ponies diagnosed with PPID with corticosteroids however studies have shown no significant systemic effect of inhaled ciclesonide on serum cortisol levels. Treatment with Aservo® EquiHaler® is not contra-indicated and it has been used in horses diagnosed with PPID with no relevant adverse events³⁸.

- Inhaled ciclesonide is well tolerated, even in horses with PPID
- There is no statistically significant effect on serum cortisol levels in asthmatic horses when treated for 14 days at the recommended dose
- A study has shown that there is no statistically significant effect on serum cortisol levels in healthy horses when treated for 30 days at 3 x the recommended dose

Soft Mist™ Inhaler Technology

Aservo® EquiHaler® uses Soft Mist™ Inhaler (SMI) technology to achieve highly efficient deep lung delivery of ciclesonide.

This unique technology is significantly different from pMDI inhalers, which utilise a gaseous propellant to create a high velocity spray which can deposit in the upper airway or on a spacer device.

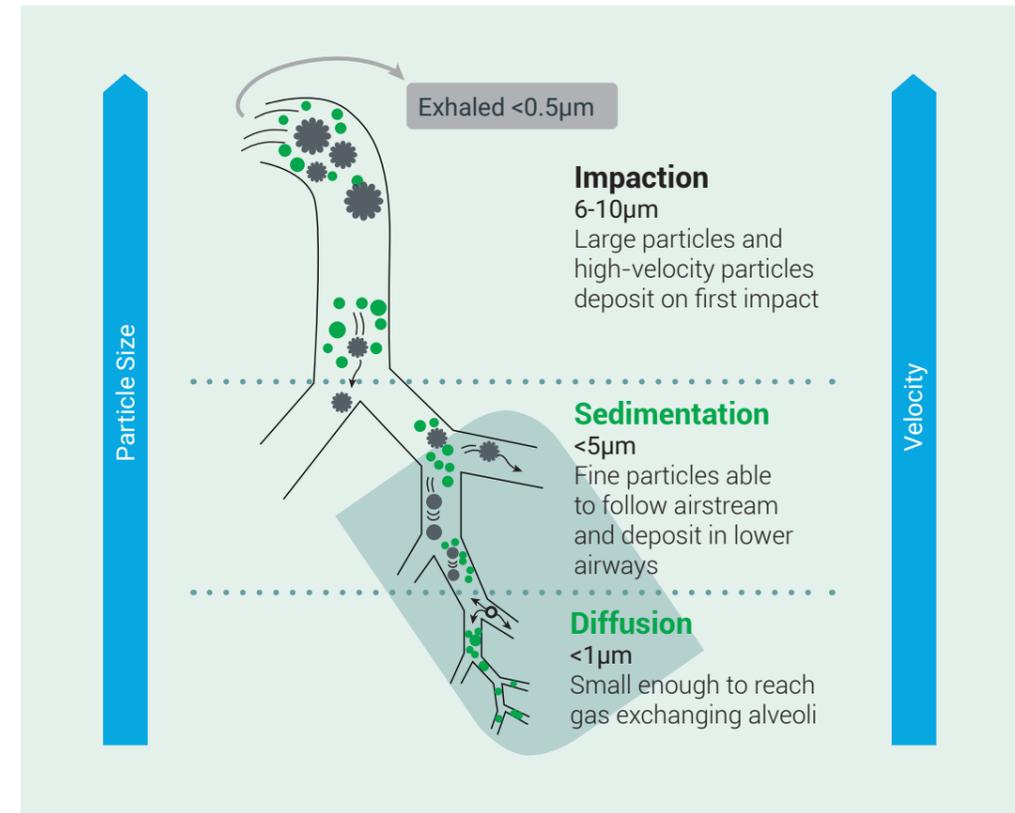


Soft Mist™ in the nostril adaptor of the Aservo® EquiHaler®

<p>High fine particle fraction</p> 	<p>Over 90% of the particles generated in the mist of the Aservo® EquiHaler® are <math><5\mu\text{m}</math>.</p> <p>Deposition of the aerosolised substance within the lungs depends primarily on the mean aerodynamic particle size fraction. Fine particles <math><5\mu\text{m}</math> have been shown to be the optimal particle size for deep peripheral lung deposition¹⁶.</p>
<p>Low velocity stream</p> 	<p>The Soft Mist™ in the Aservo® EquiHaler® is released at low velocity (0.8m/second) for a longer duration (>1 second).</p> <p>This duration has been validated as optimal considering the breathing patterns of asthmatic horses²³.</p> <p>In humans a spray of lower velocity and longer duration has been shown to decrease oropharyngeal deposition and increase deep lung deposition²⁴.</p>
<p>Propellant-free</p> 	<p>The Aservo® EquiHaler® is free from HFA greenhouse gases.</p> <p>The energy to generate the Soft Mist™ within the SMI is mechanical and comes from a compressed spring within the inhaler (Figure 5).</p> <p>A propellant-free inhaler has been shown to have a lower carbon footprint when compared to a pressurised metered dose inhaler (pMDI)²⁵.</p>
<p>Dosing accuracy</p> 	<p>Each actuation of the Aservo® EquiHaler® consistently delivers:</p> <ul style="list-style-type: none"> • A pre-determined dose • A uniform particle size • The ciclesonide in the SMI is delivered as a solution preserved with ethanol which maintains the microbial stability following initial puncture of the cartridge prior to first use.

Soft Mist™ Technology = small particle size x low velocity

Smaller particles (respirable size) administered at low velocity travel with inhaled air deep into peripheral lung²⁶.



How is the Soft Mist™ generated?

Soft Mist™ is generated mechanically by the energy released from a powerful spring. Medication drawn into the Uniblock (Figure 5) by capillary action is forced into two jets that converge at an angle, which turns a stream of medication into a slow-moving mist.

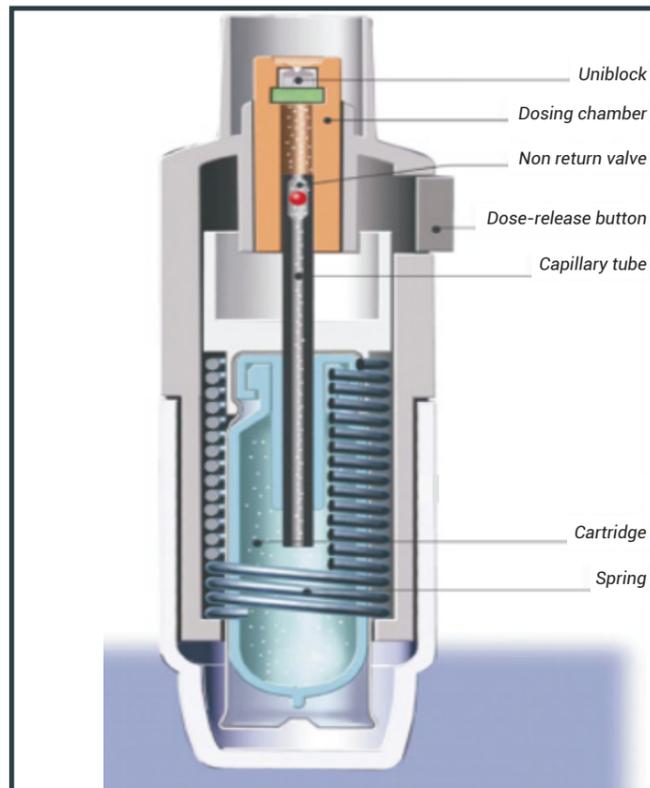
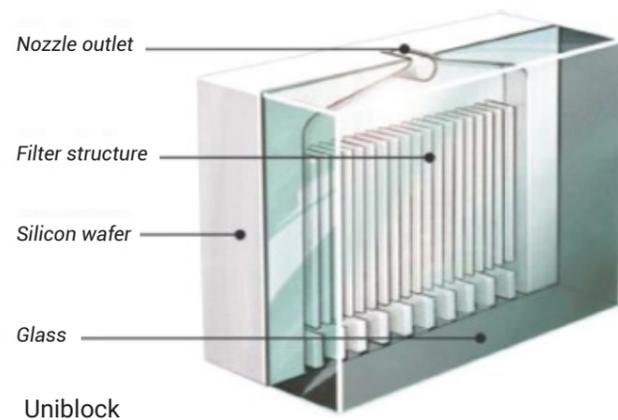


Figure 5: Soft Mist™ Inhaler Engineering



Clinical efficacy trials

Aservo® EquiHaler® has been extensively studied for both safety and efficacy in clinical trials with more than 600 horses.

Pulmonary function in a mouldy hay challenge model²³

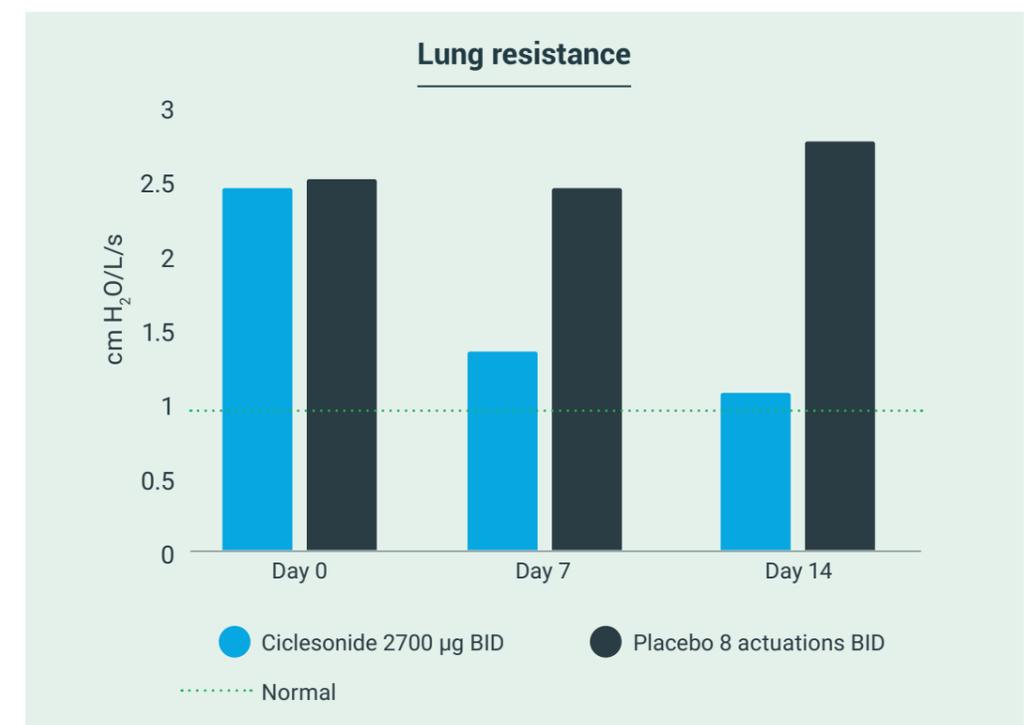
A cross-over placebo controlled, blinded, randomised study was performed in 8 horses to investigate the effects of different doses of inhaled ciclesonide on the pulmonary function of asthmatic horses undergoing experimentally induced airway obstruction in a mouldy hay challenge model.

Mouldy hay challenge model

- Proven experimental model to induce airway obstruction and clinical exacerbations in asthmatic horses²⁷.
- Each horse included in this study underwent a personalised mouldy hay challenge in order to induce a steady degree of airflow obstruction during a 2 week conditioning phase before treatment, and throughout the duration of the study.

Inhaled ciclesonide at 2,700µg twice daily significantly improved both pulmonary function and weighted clinical score on day 7, with a further improvement observed on day 14, when compared to placebo.

Pulmonary function is considered the gold standard for measuring response to treatment of severe equine asthma. The average lung resistance on day 0 was 2.5 cm H₂O/L/s, consistent with a diagnosis of severe equine asthma. A lung resistance of up to 1 cm H₂O/L/s is considered normal.



European clinical efficacy study²²

A prospective, multicentre, double blind, randomised, placebo-controlled clinical trial was conducted with 224 client owned horses by 24 vet clinics in 3 countries under field conditions.

To be included in the study horses had to have a diagnosis of severe equine asthma based on:

- History of chronicity of equine asthma previously responsive to administration of a bronchodilator, and/or glucocorticoid and/or change in environment
- Laboured breathing observed at rest and an abdominal lift score ≥ 1
- Weighted clinical score ≥ 11
- Duration of current episode over 14 days with observation of at least one clinical sign of moderate to severe equine asthma
- No environmental changes were allowed 2 weeks prior and throughout the study

A Weighted Clinical Score (WCS) was used by vets to monitor response to treatment with Aservo® EquiHaler® (at the licensed dose and duration) or placebo. This clinical score has been validated by pulmonary function testing and the average WCS of a horse on day 0 of the study was 15: which equates to a lung resistance of 2.5 cm H₂O/L/s, as per the previous study.

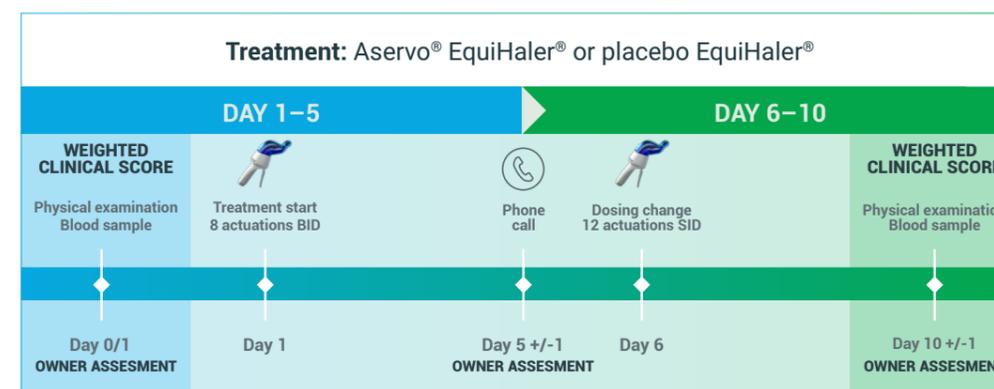
Weighted Clinical Score (WCS)

WCS is a total score (out of 23) assigned to an individual horse based on 9 clinical parameters. WCS has been positively correlated with severity of pulmonary obstruction as defined by pulmonary resistance in horses with severe equine asthma²³.

Pulmonary obstruction	R _L (cm H ₂ O/L/s)	Weighted Clinical Score
Mild	1.0–1.8	≤ 10
Moderate	1.8–2.5	11–14
Severe	>2.5	≥ 15

R_L, pulmonary resistance

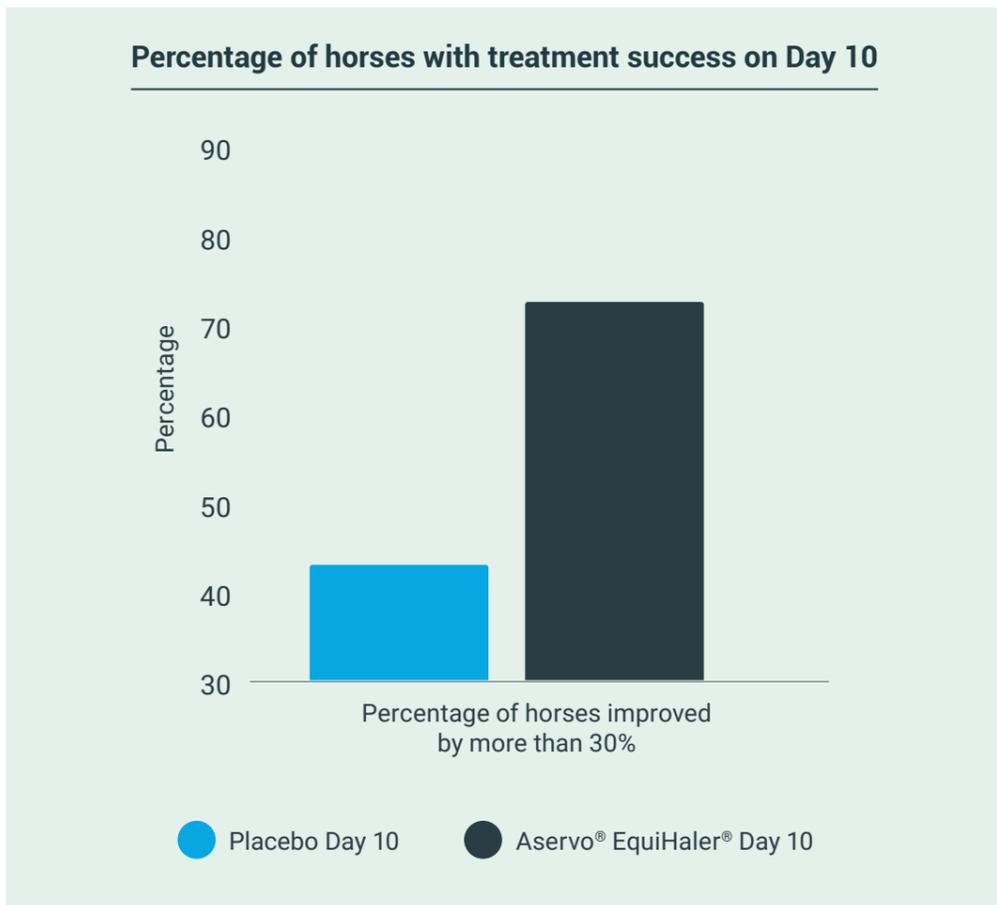
The study started on day 0 and continued to day 10 +/-1. All treatments were administered by the horse owners. The horses were randomly assigned to either treatment with Aservo® EquiHaler® or placebo and both the owners and investigators were blinded to which was administered. The owners were instructed not to change the horses' environment in any way during the trial.



Results

The mean WCS of Aservo® EquiHaler® treated patients on day 10 was 7.8, compared to a starting WCS of 15. This corresponds to a patient with severe pulmonary obstruction becoming mild, as per the definitions in the Weighted Clinical Score table.

Treatment with the Aservo® EquiHaler® was considered successful in 73.4% of horses receiving the treatment between day 0 and day 10 +/-1, as compared to placebo.



The results of this study demonstrate that:

- Aservo® EquiHaler® is effective in improving clinical signs related to severe equine asthma (including summer pasture-associated equine asthma)
- Horse acceptance of the Aservo® EquiHaler® is >95%³⁹



10 days total treatment duration

DAY 1-5 8 ACTUATIONS (2,744 µg) TWICE DAILY

DAY 6-10 12 ACTUATIONS (4,116 µg) ONCE DAILY

Detailed administration instructions are available in the package insert and on the digital leaflet: www.info.equi-haler.com

For tips on how to introduce Aservo® EquiHaler® to a patient for the first time, working with their natural behaviour, see the video at www.equihaler.uk

Forage recommendations

Feeding dry hay should be avoided and instead replaced with either haylage, soaked hay or steamed hay as appropriate to reduce respirable particulates.

Soaked hay

- Must be soaked immediately before use in clean water.
- Hay should be soaked in a hay net so that hay is loose. This will ensure that all of the hay is soaked.
- Immersion in water for maximum 30 minutes appropriately reduces the respirable particulate numbers.



Haylage

- Storage of haylage is important. It is advised that only small bales are used and that bales are used within 3 days.
- Once opened haylage should be stored in an easy to clean environment as remnants of mould from the haylage may be present. This area should be regularly cleaned and disinfected.

Steamed hay

- When steaming hay a commercial steamer should be used.
- Hay steamers must be regularly cleaned to prevent accumulation of hay, dust, debris and mould.

General forage management

- Breathing zone respirable particulate concentrations are significantly greater when horses are fed from a hay net rather than when fed hay on the ground³². Therefore all forage should be fed on a clean, dry floor.
- Forage should not be transported and moved in a wheelbarrow that is also used to move bedding and faeces.
- Forage should not be stored in the same airspace as an affected horse.

Bedding

- Straw bedding should be avoided and replaced with low dust alternatives such as rubber matting, cardboard or dust extracted large flake woodshavings.
- Rubber matting should be used where possible to minimise the amount of bedding used in the stable. However the following considerations need to be made when using rubber matting:
 - Loose mats should be moved and the surface underneath cleaned and disinfected every 2 weeks
 - Sealed mats should be regularly checked to ensure that there is no damage to the seal
- Ensure that soiled bedding is regularly changed to minimise ammonia exposure.



Feed and turnout

Feed

- Pelleted feeds have less particulate matter so should be fed where possible. Avoid feeding chaff due to an increased risk of respirable dust – if chaff must be used then ensure that the feed is dampened or oil is added prior to being fed.
- Keep all feeds in their bags if possible. If feed is removed from the bag then ensure that the feed bin is cleared out and cleaned regularly.

Turnout

- Where possible horses should be turned out 24/7 or as near to this as possible (unless affected by summer pasture-associated equine asthma). However ensure that horses are not turned out on dust tracks and dusty paddocks.
 - In contrast, horses with pasture-associated asthma are more likely to benefit from being stabled in a well-ventilated, cool and low-dust environment throughout the 'at-risk' periods of the year.
- Supplementary dry forage in paddocks should be avoided. If supplementary additional forage is required then ensure that the forage meets the same requirements as for use when stabled.
- Ensure outdoor feed containers are regularly cleaned and disinfected to minimise mould contamination.

Exercise areas

- Ensure that horse walkers are regularly cleaned and disinfected to minimise the potential accumulation of dust and growth of moulds and bacteria.
- Some arena surfaces may increase a horse's exposure to dust particles, particularly those containing latex⁹, which means that where possible owners should minimise the amount of time spent exercising an infected horse on an arena surface.



Housing and stabling

Ventilation

Stables and housing buildings require an air inlet and outlet for appropriate airflow and these inlets/outlets should be present in the front and back walls, ideally above horse head height, and also in the roof. If there are no openings in the roof or the back of the stable then the ventilation in that stable is likely to be inadequate.

Visual signs that may indicate the ventilation is inadequate are:

- Condensation
- Rusting
- Cobwebs
- Birds roosting (stable too warm)
- Visible mould on the roof

Additional openings should be created in the stable walls and roof above horse head height, if and where appropriate, to increase stable ventilation.

Housing recommendations

- Cobwebs and dust should be regularly cleared from the stable and the stable should be regularly disinfected.
- The affected horse should be removed from the stable when either their stable, or neighbouring stables, are being mucked out. A minimum of 30 minutes should be left after mucking out before the horse is returned to their stable.
- If the affected horse shares airspace with neighbouring horses, such as in a barn layout, then it is important that the necessary environmental changes are also made to all the stables sharing the airspace, not just the affected horse.
- The yard should not be swept when the affected horse is in the stable or on the yard.

Optimal management involves complete antigen avoidance where possible and, although in certain circumstances may be hard to achieve, has been shown to improve both lung function and airway inflammation when implemented¹⁴ and so is vital when managing a horse with equine asthma.



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