

SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Staloral sublingual solution

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Active substance:

Purified allergen extracts in concentration
10, 100 IR/mL (standardised allergens)
or 10, 100 IC/mL (non-standardised allergens)

The active substance corresponds to a mannitole freeze-dried allergen extract, or to a glycerinated mannitole allergen extract solution.

→ IR (Index of Reactivity): An allergen extract titrates 100 IR/mL when, used by prick-test with a Stallerpoint on 30 individuals sensitized to this allergen, it elicits a skin reaction in average of 7mm diameter weal (geometric mean). Skin reactivity in these subjects is verified independently by the rate of their positive response to prick test made by codeine phosphate (9%).

→ IC (Index of Concentration): An allergen extract has an Index of Concentration of 100 IC/mL when its concentration equals to that of standardized extract at 100 IR/mL from the same family, taken as a reference. When the family does not contain any standardized reference extract, the value 100 IC/mL corresponds to an extract where the dilution ratio is established according to clinical experience.

These units are not interchangeable with the units used to express the potency of other allergen extracts preparations.

MOULDS

Individual allergen extracts

Extracts in IC/mL

Moulds

Alternaria alternata

ANIMAL ALLERGENS

Individual allergen extracts

Extracts in IR/mL

Cat

3. PHARMACEUTICAL FORM

Sublingual solution

Product description: colourless to off yellow solution according to allergen concentration

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Type 1 allergy according to Gell and Coombs classification, presenting mainly as seasonal or perennial rhinitis, conjunctivitis, rhino-conjunctivitis or asthma (mild to moderate) in persons aged over 5 years.

Allergen immunotherapy acts as a prevention of clinical manifestations of allergic reaction that is induced by the contact of sensitized organism with the allergen.

4.2 Posology and method of administration

- General conditions of use

Allergen immunotherapy should be initiated as soon as diagnose is made. This is due to much higher effectiveness of the treatment if it is commenced early.

Allergen immunotherapy is not recommended before the age of 5.

- Posology and method of administration

Dosing of Staloral is independent from age, but it should always be individually adjusted according to patient's reactivity.

For seasonal allergies, it is recommended to start the treatment before the pollen season and pursue until the end of the season.

For perennial allergies, it is recommended to maintain the treatment all year round.

The treatment is divided into two phases:

- Initial treatment when the dose of the allergen extract is gradually increased
- and maintenance treatment when constant (maximum tolerated) dose is used.

In the case of administering a product prepared for a specific patient, the patient's name, composition, concentration and expiry date should always be checked before using the product.

Before every use, check:

- the expiry date
- whether the vial corresponds to doctor's prescription (composition, patient name, concentration, dosage)

Clean the mouthpiece after use.

Staloral is used daily in a mouth without food or beverage. The solution is to be placed directly just under the tongue and it should be left under the tongue for 2 minutes before swallowing (sublingual use).

Use in children should be supervised by an adult.

1. Initial treatment: increasing doses

Number of actuations is increased gradually each day until the highest tolerated dose is achieved with the use of the following scheme:

Day	Vial concentration	Number of depressions	Dose (IR or IC)
D1	10 IR or IC/ml (blue cap)	1	2
D2		2	4
D3		3	6
D4		4	8
D5		5	10

D6	100 IR or IC/ml (red cap)	1	20
D7		2	40
D8		3	60
D9		4	80
D10		5	100

The treatment schedule above is only for indicative purposes and the allergologist can adjust it on the basis of patient's clinical status his/her reactivity and the allergen type used.

2. Maintenance treatment: the use of the highest tolerated dose.

Once the initiation phase is completed, the maintenance dose is administered:

- Either daily: 100 IR or IC corresponding to 5 actuations with the 100 IR/ml or IC/ml vial concentration
 - o or
- Three times a week: 100 IR or IC corresponding to 5 actuations with the 100 IR/ml or IC/ml vial concentration.

In general, daily administration is associated with better compliance than three times a week administration. Therefore, if well tolerated, daily administration is recommended.

- Duration of the treatment

It is generally recommended that the allergen immunotherapy lasts for 3-5 years.

Treatment should be reassessed in absence of significant improvement of symptoms after 1 year (perennial allergy) or after the first pollen season (seasonal allergy).

- Temporary interruption of treatment

For interruption of less than 1 week, it is recommended to resume the treatment at the last dose. For interruption of more than 1 week, it is recommended to resume the treatment with one actuation of the last vial used and to increase the dose according to the initiation scheme until the maintenance dose is reached.

4.3 Contraindications

- Hypersensitivity to any of the excipients listed in section 6.1;
- Immune deficiency diseases or active forms of autoimmune disorder;
- Malignant disease;
- Patients with uncontrolled or severe asthma (FEV1 < 70% of predicted value);
- Oral inflammations such as oral lichen planus, oral ulcerations or oral mycosis.

4.4 Special warnings and precautions for use

Treatment with Staloral is reserved for allergologist only.

Patient should inform physician of any recent intercurrent diseases or any worsening of allergic diseases. Allergen immunotherapy should only be initiated after acute signs of the disease have been managed with adequate therapy. Treatment should be postponed in case of severe clinical symptoms of the allergic disease at the time of the treatment initiation. In case of occurrence of allergen-mediated symptoms, use of medications such as corticoids, H1-antihistamines and beta2-agonists can be necessary.

Allergen immunotherapy in patients treated with tricyclic antidepressants and mono amine oxidase inhibitors (MAOIs) should be considered carefully.

In case of mycosis, aphta, mucosa lesions, dental loss or oral surgery, including dental extraction; treatment with Staloral should be stopped until complete healing.

Eosinophilic esophagitis has been reported in association with sublingual immunotherapy. During treatment with Staloral, if severe or persistent gastroesophageal symptoms including dysphagia or chest pain occur, Staloral should be interrupted and the patient evaluated by their physician. Treatment should only be resumed upon instruction of the physician.

Patients taking beta-adrenergic blockers may be unresponsive to the usual doses of epinephrine used to treat serious systemic reactions, including anaphylaxis. Specifically, beta-adrenergic blockers antagonize the cardiostimulating and bronchodilating effects of epinephrine.

This medicine contains 23 mg of sodium in maximal dose (5 actuations – 1 ml of solution). It should be taken into account for patients following a strict low sodium diet.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

No interactions were reported in clinical trials with Staloral.

In case of severe allergic reactions, use of epinephrine may be necessary. In patients treated with tricyclic antidepressants and mono amine oxidase inhibitors (MAOIs), risk of undesirable effects of epinephrine can be increased with possible fatal consequences. This risk would have to be considered prior to treatment initiation.

Clinical experience concerning simultaneous vaccination during Staloral treatment is missing. Vaccination may be given without Staloral discontinuation after medical evaluation of the general condition of the patient.

4.6 Fertility, pregnancy and lactation

Pregnancy

No clinical data are available for the use of Staloral in pregnant women.

Animal studies do not indicate reproductive toxicity (see section 5.3).

As a precautionary measure, it is preferable to avoid initiating Staloral during pregnancy. If pregnancy occurs during treatment, the treatment may be continued with close supervision.

Breast-feeding

It is not known whether Staloral is excreted in human breast milk.

No animal studies were conducted to investigate excretion of Staloral into milk.

A risk to the newborns/infants cannot be excluded.

A decision must be made whether to discontinue breast-feeding or to discontinue Staloral therapy taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Fertility

No animal fertility study was conducted with Staloral. However histopathological examination of the male and female reproductive organs in some repeat-dose toxicity studies with pollen and mite extract contained in Staloral revealed no adverse findings.

4.7 Effects on ability to drive and use machines

Staloral has no known or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

During treatment, patients are exposed to allergens that may induce reactions which can occur immediately after administration or be delayed.

As with any sublingual allergen immunotherapy, severe allergic reactions including severe laryngopharyngeal disorder (such as dysphonia, oropharyngeal discomfort and pharyngeal oedema) or systemic allergic reactions (i.e., acute onset of an illness with involvement of the skin, mucosal tissue, or both, respiratory compromise, persistent digestive complaints, or reduced blood pressure and/or associated symptoms) can occur. Inform patients of the associated signs and symptoms and have them seek immediate medical care and discontinue therapy should these occur. Treatment should only be resumed at the instruction of a physician.

Tolerance of a given dose in a patient may vary over time depending on the patient's condition and the environment.

Pre-treatment with anti-allergic agents (for example antihistamines) may reduce frequency and severity of adverse reaction.

In case of occurrence of an adverse reaction, the treatment regimen should be reconsidered.

The following adverse reactions were either reported in clinical trials or spontaneously reported in pharmacovigilance settings. The adverse reactions are presented by MedDRA preferred terms, and classified by MedDRA System Organ Class and by frequency according to the convention below:

Common ($\geq 1/100$ to $<1/10$)

Uncommon ($\geq 1/1,000$ to $<1/100$)

Rare ($\geq 1/10,000$ to $<1/1,000$)

Not known (frequency cannot be established)

System Organ Class	Frequency	Adverse reactions
Blood and lymphatic system disorders	Rare	Lymphadenopathy
Immune system disorders	Uncommon	Hypersensitivity
	Rare	Serum-sickness like reaction
	Not known*	Angioedema, anaphylactic shock
Nervous system disorders	Uncommon	Paraesthesia
	Rare	Headache
Eye disorders	Common	Eye pruritus
	Uncommon	Conjunctivitis
Ear and labyrinth disorders	Common	Ear pruritus
Respiratory, thoracic and mediastinal disorders	Common	Throat irritation, pharyngeal edema, oropharyngeal blistering, rhinitis, cough
	Uncommon	Asthma, dyspnea, dysphonia, nasopharyngitis
	Not known*	Laryngeal oedema
Gastrointestinal disorders	Common	Lip edema, Oral pruritus, mouth edema, tongue edema, paraesthesia oral, oropharyngeal discomfort, stomatitis, salivary gland disorders, nausea, abdominal pain, vomiting, diarrhoea
	Uncommon	Oral pain, gastritis, oesophageal spasm
	Not known*	Oropharyngeal oedema, dysgeusia, dry mouth, eosinophilic esophagitis
Skin and subcutaneous tissue disorders	Common	Pruritus, erythema
	Uncommon	Urticaria
	Rare	Eczema
Musculoskeletal and connective tissue disorders	Rare	Arthralgia, myalgia

System Organ Class	Frequency	Adverse reactions
General disorders and administration site conditions	Rare	Asthenia, pyrexia
	Not known*	Dizziness

*Preferred terms reported from post-marketing experience

Reporting of suspected adverse reactions

Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system at the following address:

Státní ústav pro kontrolu léčiv
Šrobárova 48
100 41 Praha 10

Webové stránky: www.sukl.cz/nahlasit-nezadouci-ucinek

4.9 Overdose

If doses higher than recommended are used, the risk of occurrence of adverse reaction and its severity may be increased.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Allergen extracts, various allergens
ATC code: V01AA20.

The precise mechanism of action of allergens administered during the course of allergen immunotherapy (AIT) is not clearly understood.

Treatment with ATI has shown to induce changes in T-lymphocyte responses, followed by elevations in allergen-specific IgG4, and/or IgG1 and sometimes IgA and decrease of specific IgE. A second and probably later immunologic response is immune deviation with a shift in the allergen specific T cell response.

5.2 Pharmacokinetic properties

The greater part of allergens in STALORAL is a mixture of proteins and glycoproteins. Due to the nature of the extracts, there is no expected blood bioavailability of intact allergens after sublingual administration.

Therefore, no pharmacokinetic studies in animals or in human have been carried out to investigate the pharmacokinetic profile and metabolism of allergen extracts.

5.3 Preclinical safety data

Preclinical data reveal no special hazard for humans based on conventional studies conducted with allergen extracts contained in Staloral to evaluate safety pharmacology, repeat-dose toxicity, genotoxicity, toxicity to reproduction and development.

6. PHARMACEUTICAL PARTICULARS

6.1 List of all excipients

Sodium chloride, glycerol, mannitol, water for injection

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months before opening and 30 days after first opening

6.4 Special precautions for storage

Store in a refrigerator (2°C – 8°C).

In any case when vials are transferred, keep them in an upright position.

6.5 Nature and contents of container

Brown type I glass vial, rubber stopper, aluminium tear-off cap with plastic lid differentiated by colour (according to concentration).

The packaging contains dosing pumps (one for each vial) and a package leaflet.

Pack size:

2×1 bottle (10 ml) in 1 pack for initial treatment

a)

blue cap:	10 IR/mL
red cap:	100 IR/mL

b)

blue cap:	10 IC/mL
red cap:	100 IC/mL

2×1 bottle (10 ml) for maintenance treatment

a) 2 bottles 10 mL each (100 IR/mL) with red cap

b) 2 bottles 10 mL each (100 IC/mL) with red cap

Not all pack sizes may be marketed.

6.6 Special precautions for disposal and other handling

Any unused product or waste material should be disposed of in accordance with local requirements.

7. MARKETING AUTHORISATION HOLDER

Stallergenes
6, rue Alexis de Tocqueville
F-92160 Antony
France

8. MARKETING AUTHORISATION NUMBER(S)

59/736/96-C

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 18. 12. 1996

Date of latest renewal: 8. 10. 2014

10. DATE OF REVISION OF THE TEXT

17. 3. 2026