SUMMARY OF PRODUCT CHARACTERISTICS

1. NAME OF THE MEDICINAL PRODUCT

Alutard SQ Phleum pratense, 100,000 SQ-U/ml, suspension for injection
Alutard SQ Phleum pratense 10,000 SQ-U/ml, suspension for injection
Alutard SQ Phleum pratense up-dosing pack (100 SQ-U/ml, 1,000 SQ-U/ml, 10,000 SQ-U/ml and 100,000 SQ- U/ml), suspension for injection

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Alutard SQ Phleum pratense is a depot preparation containing standardised allergen from timothy pollen (*Phleum pratense*) adsorbed to aluminium hydroxide.

The biological activity of Alutard SQ Phleum pratense is related to the concentration of the allergens expressed in the unit SQ-U/ml. Additionally, the content of the individual allergen Phl p 5 is determined according to Ph. Eur. to be 7 micrograms on average per 100,000 SQ-U. Clinical efficacy and clinical safety of allergy immunotherapy (AIT) products also depend on other factors e.g. manufacturing process, formulation, product composition and administration.

The vial numbers are colour coded so that they can be easily distinguished.

Table 1: Vial and strength

Vial No. (Colour code)	Strength (SQ-U/ml)	Adjuvant (aluminium hydroxide) (mg/ml)
1 (grey)	100	0.0033
2 (green)	1,000	0.033
3 (orange)	10,000	0.33
4 (red)	100,000	3.3

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Suspension for injection

Clear liquid with or without a precipitate. The precipitate might be white to faintly brown or green.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

Allergy immunotherapy is indicated for the treatment of clinically relevant symptoms of IgE-mediated moderate to severe allergic rhinoconjunctivitis induced by pollen from the Pooideae (temperate) grass homologous group[1], diagnosed with a positive skin prick test and/or specific IgE test to pollen from the Pooideae grass homologous group.

4.2 Posology and method of administration

Treatment with Alutard SQ Phleum pratense should be carried out under well-controlled conditions with immediate access to an anaphylactic emergency kit and well-trained staff. After each injection the patient must be observed for at least 30 minutes.
Alutard SQ Phleum pratense is intended for long term treatment. The need for continued therapy should be considered at least on an annual basis as determined by physician's assessment of the patient's disease severity and level of control of allergic symptoms.

Posology
The treatment is divided into two phases: up-dosing phase and maintenance phase. The aim is to gradually increase the dose until the highest tolerated maintenance dose is reached. The highest recommended maintenance dose is 1 ml of 100,000 SQ-U/ml (vial 4). The dosing of Alutard SQ Phleum pratense must always be based on the allergenic anamnesis and the patient's sensitivity to the specific allergen (see section 4.4).

Up-dosing phase:
Recommendations for up-dosing are given in Table 2 and 3. Recommendation for up-dosing in the tables below (Table 2 and 3) should only be considered as a guide. During the up-dosing phase, one injection is administered weekly. Treatment should be initiated in due time before the pollen season.

If the patient responds with severe allergic reactions during the up-dosing phase, dose adjustment shall be done (see section 4.2 Dose reduction and section 4.4).

[1] Pooideae (temperate) grass homologous group: *Phleum pratense* (Timothy grass), *Anthoxanthum odoratum* (Sweet vernal grass), *Avena sativa* (Oat), *Dactylis glomerata* (Orchard grass/Cocksfoot), *Festuca* spp. (Meadow fescue), *Holcus lanatus* (Velvet grass/Yorkshire fog), *Hordeum vulgare* (Barley), *Lolium perenne* (Perennial ryegrass), *Poa pratensis* (Kentucky bluegrass), *Secale cereale* (Cultivated rye), *Triticum aestivum* (Cultivated wheat).

Table 2: 15 week up-dosing scheme (conventional)

Vial No	Strength SQ-U/ml	Week no	Injection no	Volume ml	Dosage SQ-U
1	100	1	1	0.2	20
	100	2	2	0.4	40
	100	3	3	0.8	80
2	1,000	4	4	0.2	200
	1,000	5	5	0.4	400
	1,000	6	6	0.8	800
3	10,000	7	7	0.2	2,000
	10,000	8	8	0.4	4,000
	10,000	9	9	0.8	8,000
4	100,000	10	10	0.1	10,000
	100,000	11	11	0.2	20,000
	100,000	12	12	0.4	40,000
	100,000	13	13	0.6	60,000
	100,000	14	14	0.8	80,000
	100,000	15	15	1.0	100,000

If the patient is eligible for allergy immunotherapy with any of the risk factors listed in section 4.4, the conventional up-dosing scheme is recommended.

Table 3: 7 week up-dosing scheme

Vial No	Strength SQ-U/ml	Week no	Injection no	Volume ml	Dosage SQ-U
2	1,000	1	1	0.3	300
3	10,000	2	2	0.2	2,000
	10,000	3	3	0.5	5,000
4	100,000	4	4	0.1	10,000
	100,000	5	5	0.3	30,000
	100,000	6	6	0.6	60,000
	100,000	7	7	1.0	100,000

The up-dosing scheme consists of 7 injections with increasing amounts of allergen up to 1 ml of vial 4 in accordance with Table 3. In order to reach the same cumulative dose as with the longer up-dosing scheme, at least one additional maintenance dose has to be administered prior to the start of the pollen season. The injections should be administered with injection intervals of 7 ± 2 days.

Maintenance phase:
The maintenance dose is individual, depending on the patient's tolerance towards the allergen. The recommended maintenance dose is 100,000 SQ-U. The maintenance dose 100,000 SQ-U corresponds to 1 ml of vial 4.

When the maintenance dose is reached, the interval between injections is gradually increased. The interval is increased from 1 to 2, 4 and 6 weeks. Subsequently, the maintenance dose is given every 6 ± 2 weeks. The maintenance treatment is continued for 3-5 years.

If the patient responds with severe allergic reactions during the maintenance phase, dose adjustment shall be done (see section 4.2 Dose reduction and section 4.4).

Situations where dose shall be adjusted or not be given, also see section 4.4.

Elderly population
Additional dose adjustment is not required in the elderly population. When prescribing Alutard SQ Phleum pratense for elderly patients ≥ 65 years, the increased prevalence of diseases for which additional caution is advised should be considered (see section 4.4).

Clinical experience in patients ≥ 65 years of age is limited.
The 7 week up-dosing scheme has not been evaluated in elderly above 65 years.

Paediatric population
Children under 5 years of age are normally not considered suitable for hyposensitisation because acceptance and cooperation problems are more likely in this age group than for adults.
For children > 5 years of age clinical data of efficacy are sparse and cannot prove efficacy. Data on safety do not reveal a higher risk than for adults.
No additional dose adjustment is required in the paediatric population. See section 4.4 and 4.8.
The 7 week up-dosing scheme has not been evaluated in children below 12 years.

Exceeding the time interval between two visits
If the recommended time interval between two visits has been exceeded, the dosing of the following injection is handled according to the following recommendation:

Table 4: Exceeded time interval between two visits during the up-dosing phase

Weeks between visits	Dosage
Up to 2 weeks	Continue up-dosing according to Table 2 or Table 3
2 - 3 weeks	Repeat previous given dose
3 - 4 weeks	Reduce the dose to 50 % of previous given dose
4 weeks or more	Restart up-dosing according to Table 2 or Table 3

Table 5: Exceeded time interval between two visits during the maintenance phase

Weeks between visits	Dosage
Up to 8 weeks	Continue with the maintenance dose
8 - 10 weeks	Reduce the dose to 75 % of previous given dose
10 - 12 weeks	Reduce the dose to 50 % of previous given dose
12 – 14 weeks	Reduce the dose to 25 % of previous given dose
14 - 16 weeks	Reduce the dose to 10 % of previous given dose
16 weeks or more	Restart up-dosing according to Table 2 or Table 3

In case of a dose reduction in the maintenance phase, the patient must be carefully observed after the injection. Subsequently, up-dose according to the recommendation in Table 2 until the maintenance dose is reached.

Concomitant treatment with more than one allergen
In case of concomitant treatment with more than one allergen, one allergen should be injected in each arm. In order to evaluate possible allergic reactions caused by the specific allergen it is recommended to give the injections with 30 minutes interval. The possible increased risk of allergic reactions at concomitant up-dosing with more than one allergen should be considered on an individual basis.

Dose reduction
Dose reduction in case of local reactions
If an injection site reaction persists for more than 6 hours after the injection, the following dose reduction is recommended depending on size of the swelling:

Table 6: Recommended dose in case of injection site swelling

Swelling, maximal diameter		Recommendation
Children over 5 years	Adults	
< 5 cm	< 8 cm	Continue up-dosing according to Table 2 or Table 3
5-7 cm	8-12 cm	Repeat previous dose
7-12 cm	12-20 cm	Reduce dose to dose given one week prior
12-17 cm	>20 cm	Reduce dose to dose given two weeks prior
>17 cm	-	Reduce dose to dose given three weeks prior

Dose reduction in case of severe systemic allergic reactions
If a severe systemic allergic reaction (see section 4.8) occurs after injection, the treatment should only be continued after careful consideration. If the treatment is continued, the following dose should be reduced to 10% of the dose provoking the reaction.

The chosen reduced dose can be split into two injections given with 30 minutes interval. The patient should be observed after the injections. Subsequently, up-dose according to recommendation in Table 2 or 3 until the maximal tolerated maintenance dose is reached.

Method of administration
After each injection, the patient must be observed for at least 30 minutes. On the day of injection, the patient must avoid physical exercise, hot baths and alcohol as these co-factors may potentially amplify an anaphylactic reaction.

Alutard SQ Phleum pratense is administered subcutaneously. The vials must be turned slowly upside down 10 - 20 times before use. For instructions on the handling of Alutard SQ Phleum pratense before administration, see section 6.6.

The injection is given either laterally in the distal part of the upper arm or dorsally in the proximal part of the forearm. Avoid intravascular injection by careful aspiration before injection. Aspiration must be repeated for every 0.2 ml during the injection and the injection must be given slowly.

Precautions in relation to administrations

Before injection:
- Double check the allergen, concentration, volume and previous injection date (dosing interval), prior to each injection.
- Alutard SQ Phleum pratense is intended for subcutaneous injection. Intravenous administration must be avoided due to the risk of allergic reactions.
- Allergic reactions (both local and systemic) which occurred during the previous injections should be recorded and the dose should be assessed on the basis of this.
- Pre-treatment with H1 antihistamines should be considered in the up-dosing phase for patients who experience large local reactions or systemic allergic reactions.
- The patient's state of health and allergy status must be evaluated as well as any changes of other medication since the last administered injection (see section 4.4 and 4.5).
- The asthma status, in patients with a medical history of asthma, must be evaluated prior to injection (see section 4.3 and 4.4).

After injection:
- The patient must be advised to consult a doctor or emergency room immediately in case of severe systemic delayed reactions.
- The patient must be advised to observe any local or systemic reactions that may occur subsequently and to inform the attending doctor at the next visit.
- Any allergic reactions (both local and systemic) should be recorded before the patient leaves the clinic.

4.3 Contraindications

- Hypersensitivity to any of the excipients listed in section 6.1.
- Asthma patients with inadequate symptom control defined as: loss of symptom control within the last four weeks (e.g. increase in daytime symptoms, nightly wakenings, increased need of medication, activity limitations).
- Asthma patients at risk of asthma exacerbation including evidence of reduced lung function defined as: FEV_1 <70% of predicted value in adults (after adequate pharmacological treatment) and FEV_1 <80% of predicted value in children and adolescents (after adequate pharmacological treatment).

- Patients with active or poorly controlled systemic autoimmune diseases and immunodeficiency disorders.
- Active malignant neoplasia (see also section 4.4)
- Severe chronic renal insufficiency
- Patients with disorders or conditions where an induced anaphylactic reaction implies an unacceptable risk such as severe cardiovascular disease.

4.4 Special warnings and precautions for use

Severe systemic allergic reactions
Due to the risk of severe allergic reactions, immediate access to full resuscitation equipment and medicines must be available, including adrenaline for injection and staff trained in the use thereof. If symptoms of a systemic reaction, such as urticaria, angioedema or severe asthma occur, symptomatic treatment should be initiated immediately.

The injection should be postponed:
- if the patient has a fever or shows other clinical signs of a chronic or acute infection
- if the patient has an atopic dermatitis that has exacerbated

Treatment with TCA, MAO-inhibitors or COMT-inhibitors
One option for treating severe systemic allergic reactions is adrenaline. The effects of adrenaline may be potentiated in patients treated with tricyclic antidepressants (TCA), mono amino oxidase inhibitors (MAOIs) and/or COMT inhibitors with possible fatal consequences.

Immunogenic vaccination for infectious pathogens
To avoid any interference in immune response, there should be at least one week between vaccination with Alutard SQ Phleum pratense and immunogenic vaccination with infectious pathogens (see section 4.5).

Cardiovascular diseases
Patients with cardiac diseases may be at increased risk in case of systemic allergic reactions. Patients with cardiovascular diseases must be sufficiently treated for the underlying condition prior to the initiation of Alutard SQ Phleum pratense treatment. In connection with the treatment with Alutard SQ Phleum pratense special attention should be given. See section 4.3. Clinical experience in treatment with Alutard SQ Phleum pratense of patients with cardiac diseases is limited.

The effects of adrenaline may be reduced in patients treated with beta-blockers. In addition, the effects of adrenaline may exacerbate cardiovascular disease, e.g. cause cardiac arrythmia. Patients in treatment with beta-blockers should be carefully monitored during the up-dosing phase.

Asthma
Asthma is a known risk factor for severe systemic allergic reactions. In patients with asthma, the asthma symptoms should be adequately controlled prior to the initiation of Alutard SQ Phleum pratense In connection with the treatment with Alutard SQ Phleum pratense special attention should be given. The patient's asthma condition must be assessed prior to each injection (see section 4.3). Patients must be informed of the need to seek medical attention immediately if their asthma deteriorates suddenly. Clinical experience in treatment with Alutard SQ Phleum pratense of patients with asthma is limited.

Autoimmune diseases
There are no controlled studies on the influence of autoimmune disorders on the efficacy of allergy immunotherapy (AIT), or on autoimmune disorders as a predisposing factor for severe side effects during AIT. AIT may only be initiated in patients with autoimmune diseases in case of disease remission or well-adjusted therapy. Alutard SQ Phleum pratense should therefore be prescribed with caution in these patients.

Malignant neoplastic diseases
There are no controlled studies on the influence of malignant neoplastic diseases on the efficacy of AIT, or on malignant neoplastic diseases as a predisposing factor for severe side effects during Alutard SQ Phleum pratense immunotherapy. AIT may only be initiated when the malignant disease is stable. In case of aggravation treatment with Alutard SQ Phleum pratense should be discontinued. Alutard SQ Phleum pratense should therefore be prescribed with caution in these patients.

Other populations (including patients with renal dysfunction)
As Alutard SQ Phleum pratense contains aluminium, there is a theoretical risk of aluminium accumulation in patients at high risk (i.e. patients with renal dysfunction and patients concomitantly treated with other aluminium containing drugs (e.g. antacids)). This should be considered when initiating therapy with Alutard SQ Phleum pratense.
The effect of the systemic use of immunosuppressive treatment and the concomitant use of immunotherapy with AIT is not known. The concomitant use of immunosuppressive products should therefore be weighted case by case.

Elderly population
Available data obtained from clinical studies are limited. Therefore, special care should be given to the benefit/risk assessment with regards to the treatment of elderly patients (see section 4.2).

Paediatric population
Children under 5 years of age are normally not considered suitable for hyposensitisation because acceptance and cooperation problems are more likely in this age group than for adults. For children ≥5 years of age, clinical data of efficacy are sparse, however safety data do not suggest a higher risk than for adults.
The 7 week up-dosing scheme has not been evaluated in children below 12 years.

This medical product contains less than 1 mmol sodium (23 mg) per dose, i.e. it is essentially 'sodium-free'.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction trials have been performed in humans and no potential drug interactions have been identified from any source. Concomitant treatment with symptomatic anti-allergy medications, e.g. antihistamines, corticosteroids and mast cell stabilisers may increase the patient's tolerance level towards the allergen injections. This should be considered at discontinuation of such medications.

Postpone the injection if immunogenic vaccination for infectious pathogens (e.g., tetanus vaccine) has been given, wait at least a week before treatment with Alutard SQ Phleum pratense is continued. Immunogenic vaccination for infectious pathogens should not be given earlier than a week after an Alutard SQ Phleum pratense injection.

For information considering concomitant use of TCA, MAOIs, COMT-inhibitors, beta-blockers and antacids, see section 4.4.

4.6 Fertility, pregnancy and lactation

Pregnancy
There is no clinical experience of the use of Alutard SQ Phleum pratense during pregnancy. Up-dosing treatment should not be initiated during pregnancy. If pregnancy occurs during maintenance treatment, the maintenance treatment may continue after a careful evaluation of the patient's general condition and reactions to previous injections with Alutard SQ Phleum pratense.

Breastfeeding
No clinical data is available on the use of Alutard SQ Phleum pratense during breastfeeding. No effects on the breastfed infant are anticipated.

Fertility
There is no clinical data with respect to fertility for the use of Alutard SQ Phleum pratense.

4.7 Effects on ability to drive and use machines

Alutard SQ Phleum pratense has no or negligible influence on the ability to drive and use machines. However, some of the adverse reactions mentioned under section 4.8 may temporarily affect the ability to drive or use machines.

4.8 Undesirable effects

Summary of the safety profile
Generally, reactions appearing in connection with Alutard SQ Phleum pratense treatment occur due to an immunological reaction (local and/or systemic) to the respective allergen.
Symptoms of an immediate reaction appear within the first 30 minutes after the injection. Delayed symptoms normally appear within the first 24 hours after the injection. Commonly reported adverse reactions in patients treated with Alutard SQ Phleum pratense are local reactions at the injection site. The most serious adverse drug reaction occurring in patients treated with Alutard SQ Phleum pratense is anaphylactic shock. It is a life-threatening condition which demands immediate treatment.

Tabulated list of adverse reactions
The adverse reactions are divided into groups according to the MedDRA convention frequencies: Very common (≥1/10), common (≥1/100 to <1/10), uncommon (≥1/1,000 to <1/100), rare (≥1/10,000 to <1/1,000), very rare (<1/10,000), not known (cannot be estimated from the available data). Adverse drug reactions and frequencies in the table below are based on one clinical trial with Alutard SQ 6-grass mix and rye. Additional adverse reactions reported spontaneously from the market for Alutard SQ grass products are included in the table below.

System Organ Class	**Frequency**	**Adverse Drug Reaction**
Immune system disorders	Common	Anaphylactic reaction
	Uncommon	Anaphylactic shock
Nervous system disorders	Not known	Dizziness, paraesthesia
Eye disorders	Common	Conjunctivitis, eye pruritus, eye swelling
	Uncommon	Eyelid oedema
Ear and labyrinth disorders	Common	Vertigo
	Uncommon	Ear pruritus
Cardiac disorders	Not known	Palpitations, tachycardia, cyanosis
Vascular disorders	Not known	Hypotension, pallor, flushing
Respiratory, thoracic and mediastinal disorders	Common	Cough, dyspnoea, nasal congestion, allergic rhinitis, sneezing, throat irritation, rhinorrhoea, nasal pruritus
	Not known	Bronchospasm, throat tightness, wheezing, asthma
Gastrointestinal disorders	Common	Diarrhoea, vomiting, nausea, abdominal pain
	Uncommon	Dyspepsia
Skin and subcutaneous tissue disorders	Common	Urticaria, pruritus, rash, erythema
	Uncommon	Swelling face, eczema
	Not known	Angioedema
Musculoskeletal and connective tissue disorders	Not known	Joint swelling, arthralgia
General disorders and administration site conditions	Very common	Injection site reaction*
	Common	Fatigue, chills, feeling hot, discomfort
	Not known	Chest discomfort, injection site hypertrichosis, sensation of a foreign body

* Injection site reactions may present events such as injection site pruritus/swelling/urticaria/ erythema/nodules/pain/bruising/haematoma/induration/inflammation/oedema/rash/warmth/ discolouration/papule, localised oedema, administration site pain, pain in extremity.

Data from a 7-weeks-updosing trial indicates a slightly increased risk of eye symptoms such as eye swelling and eye pruritus and of skin reactions such as erythema, rash and urticaria with fast up-dosing, 7 weeks compared to 11 weeks.

Local reactions
Local reactions can be treated with symptomatic medication such as e.g. antihistamines.

- Injection site reactions consist of one or several of the following symptoms: diffuse swelling, redness, pain, itching, discolouration, haematoma and injection site urticaria. These symptoms most often appear within 30 minutes and may also persist after 6 hours. Generalized pruritus may also occur.

- Subcutaneous nodules at the injection site have been observed after repeated injections.

The aluminium content may contribute to the occurrence of local adverse effects including positive skin patch test for aluminium.

Systemic allergic reactions
Mild to moderate systemic allergic reactions might occur and are effectively treated with symptomatic medications such as e.g. antihistamines.

Symptoms that may be associated with a systemic allergic reaction may include but are not limited to urticaria, angioedema, dyspnoea, cough, bronchospasm, rhinitis, wheezing, chest tightness, asthma, tachycardia and hypotension. Other symptoms of a systemic allergic reaction can be fatigue, general discomfort, headache, abdominal pain, vomiting, diarrhoea, flushing, rash, pruritus or sneezing.

A severe systemic allergic reaction is a potentially life-threatening reaction that usually occurs within a few minutes after the patient has been exposed to the allergen. A severe systemic allergic reaction requires immediate treatment with e.g. adrenaline and/or other anaphylactic treatment.

In case of large local reactions and systemic reactions an evaluation of the treatment must be performed (see section 4.2 and section 4.4).

Atopic dermatitis may be exacerbated during treatment.

<u>Paediatric population</u>
Limited data from clinical trials on the adverse events in children is available. Available safety data does not indicate additional risks related to the use of Alutard SQ Phleum pratense in the paediatric population (see section 4.2 and 4.4).

<u>Other special populations</u>
No data from clinical trials on the adverse events in other populations available.

<u>Reporting of suspected adverse reactions</u>
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 [To be completed nationally]

4.9 Overdose

If a higher dose of Alutard SQ Phleum pratense than intended is injected, the risk of systemic reactions increases. The patient must be observed, and any reaction must be treated with relevant symptomatic medication.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Allergen extracts
ATC code: V01AA02

Alutard SQ Phleum pratense is used for treatment of patients with specific IgE-mediated allergy. The target organ for the pharmacodynamic effect is the immune system. The aim is to suppress the reaction toward the allergen that the patient is treated with. Alutard SQ Phleum pratense has several effects. The recruitment of T-lymphocytes and eosinophilic granulocytes to the target organ is inhibited and is followed by a pronounced shift from the production of Th2 cytokines to the production of Th1 cytokines. In addition, the synthesis of IL-10 is increased which may lead to T-lymphocyte anergy. Release of histamine from peripheral blood basophiles is decreased. This is the result of the decreased number of recirculating basophils.

Clinical efficacy and safety
Alutard SQ Phleum pratense has been investigated in numerous clinical trials and has a well-established use, as it has been used for several decades in adults and children above 5 years. Pivotal trials are described in the following.

Clinical efficacy
Adult population
Trial UK22, a double-blind, placebo-controlled trial included 410 patients (18-60 years of age) with seasonal allergic rhinoconjunctivitis, receiving treatment with Alutard SQ Phleum pratense (100,000 SQ-U) for one year. In subjects treated with 100,000 SQ-U, the mean symptom and medication scores were 28% (absolute treatment difference: 1.26) and 32% (1.36) lower than those in the placebo group across the entire pollen season, and during the peak pollen season, the mean symptom and medication scores were 32% (2.09) and 41% (2.51) lower than those in the placebo group.

Paediatric population
There are limited efficacy data in children > 5 years of age (see also section 4.4).

Clinical safety
Adult population
In trial UK22, safety of Alutard SQ Phleum pratense was investigated in double-blind, randomised, placebo-controlled trial conducted in 410 subjects with moderate/severe seasonal allergic rhinoconjunctivitis. 181 (44%) subjects reported local side effects and 252 (61.5%) subjects reported systemic reactions. Local side effects and systemic reactions reported were in general delayed and mild, and more pronounced in subjects treated with 100,000 SQ-U. No life-threatening reactions were reported.

In trial UK23A, safety of Alutard SQ Phleum pratense was investigated in an open-label trial including 338 subjects (13-61 years of age, 4% of the subjects were <18 years of age) with allergic rhinoconjunctivitis receiving 3 years of treatment. The trial demonstrated that Alutard SQ Phleum pratense had an acceptable safety profile. Of the 338 adult subjects participating in the trial 128 subjects completed. The most frequently reported adverse events were primarily mild or moderate local and systemic reactions. Local reactions were reported in 24% of the adults during the up-dosing phase and 10% during the maintenance phase. Systemic reactions were reported in 44% of the subjects during the up-dosing phase and 14% during the maintenance phase. Early non-life-threatening severe

systemic reactions were reported in 4% in the adults. Early life-threatening systemic reactions were reported in < 1% of the adults.

Paediatric population
In parallel to trial UK23A (described above) and with similar trial design, in UK23P safety of Alutard SQ Phleum pratense was investigated in 81 children (5-16 years of age), with allergic rhinoconjunctivitis receiving 3 years of treatment demonstrating an acceptable safety profile. Of the 81 children participating in the trial 47 subjects completed.
Like for the trial UK23A, the most frequently reported adverse events in UK23P were primarily mild or moderate local and systemic reactions. Local reactions were reported in 75% of the children during the up-dosing phase and 52% during the maintenance phase.
Systemic reactions in UK23P were reported in 72% of the children during the up-dosing phase and 35% during the maintenance phase. Early non-life-threatening severe systemic reactions were reported in 1% in the paediatric population, and no early life-threatening systemic reactions were reported in the children.

5.2 Pharmacokinetic properties

Adsorption of the allergen to aluminium hydroxide results in a slow release from the injection site. By subcutaneous injection the allergen is slowly released which reduces the allergenicity and possibly prolongs the stimulation of the immune system.

5.3 Preclinical safety data
Safety pharmacology studies have not been performed. Studies of general toxicology and genotoxicity have revealed no special hazards to humans.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Aluminium hydroxide
Sodium chloride
Sodium hydrogen carbonate
Phenol
Sodium hydroxide (for pH adjustment)
Water for injections

6.2 Incompatibilities

In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Shelf life for Alutard SQ Phleum pratense is 3 years

Shelf life after opening of vial is 6 months when used for one individual patient.

6.4 Special precautions for storage

Store in refrigerator (2°C – 8°C).
Do not freeze.
Store in the original package in order to protect from light.

For storage conditions after first opening of the medicinal product, see section 6.3.

6.5 Nature and contents of container

Alutard SQ Phleum pratense is supplied in glass vials (type I) fitted with a halobutyl rubber stopper and sealed with a coloured aluminium cap with a tear-off centre. The vial numbers are colour coded so that they easily can be distinguished.

Alutard SQ Phleum pratense is available in different packs, one up-dosing pack (4 x 5 ml) and three maintenance packs (1 x 5 ml; 10,000 SQ-U/ml, 1 x 5 ml; 100,000 SQ-U/ml and 2 x 5 ml; 100,000 SQ-U/ml).
Not all pack sizes may be marketed.

Table 7: Up-dosing pack 4 x 5 ml

Vial no.	Strength (SQ-U/ml)	Colour code
1	100	grey
2	1,000	green
3	10,000	orange
4	100,000	red

Table 8: Maintenance pack 1 x 5 ml

Vial no.	Strength (SQ-U/ml)	Colour code
3	10,000	orange

Table 9: Maintenance pack 1 x 5 ml and 2 x 5 ml

Vial no.	Strength (SQ-U/ml)	Colour code
4	100,000	red

6.6 Special precautions for disposal and other handling

During storage, a precipitate and a clear liquid can be observed. This is completely normal for a suspension and does not constitute a sign of deterioration of the quality of the product. The precipitate might be white to faintly brown or green.

The vials must be turned slowly upside down 10 - 20 times to make a homogeneous suspension prior to use.

Inspect the suspension visually for particulate matter prior to administration. Discard the product if visible particles are present.

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

7. MARKETING AUTHORISATION HOLDER

ALK-Abelló A/S
Bøge Allé 6 - 8
2970 Hørsholm
Denmark

8. MARKETING AUTHORISATION NUMBER(S)

[To be completed nationally]

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

[To be completed nationally]

10. DATE OF REVISION OF THE TEXT

2025-01-15