SOLUPRICK SQ HOUSE DUST MITE *DERMATOPHAGOIDES PTERONYSSINUS*, 10 HEP, SOLUTION FOR SKIN PRICK TEST, 2ML PER VIAL

(Dermatophagoides pteronyssinus)

PL 10085/0047

UKPAR

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LAY SUMMARY

The MHRA today granted ALK-Abelló A/S a Marketing Authorisation (licence) for the medicinal product Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* (PL 10085/0047), which is a pollen. Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* is a glycerinated preparation containing standardised allergen extracts dissolved in equal parts of buffered saline and sterile glycerol. The active ingredient is a partly purified pollen allergen extract which contains the relevant allergens. The Soluprick SQ House Dust Mite species is *Dermatophagoides pteronyssinus.* This medicine is prescription only and may be administered to children

Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* are used in the diagnosis of specific IgE mediated allergic diseases via a skin prick test which is usually performed on the forearm but also sometimes on the back of the patient. A droplet of Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* is applied to the skin along with a droplet of a reference preparation and a droplet of a control preparation. The skin is pierced with a lancet through each of the droplets and any skin reactions are observed after 15 minutes. If the patient is allergic to any of the substances in the droplets, then a visible inflammatory reaction will usually occur.

Persons with IgE-mediated diseases, or atopy, have a hereditary predisposition to produce IgE antibodies against common environmental allergens such as plant pollens, mould spores, drugs (i.e. penicillins), foods, insect stings and animal products. Hayfever is an example of a common allergy whose symptoms are caused by airborne pollen.

The clinical data presented to the MHRA demonstrated that Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* accurately diagnoses adults and children with specific IgE mediated allergic diseases via the skin prick test and there were no unexpected safety concerns. It was therefore judged that the benefits of using this product outweigh the risks; hence a Marketing Authorisation has been granted.

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SCIENTIFIC DISCUSSION

INTRODUCTION

Based on the review of data on quality, safety and efficacy the UK granted a marketing authorisation for the medicinal product Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* (PL 10085/0047) to ALK-Abelló A/S on the 4th September 2007. The product is prescription only and intended for adults and children.

This was a simple abridged, national application for Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus*, submitted under Article 10c of Directive 2001/83/EC. The components of the product are identical to the previously approved Soluprick SQ House Dust Mites (PL 10085/0017) which contained the two species of house dust mite, *Dermatophagoides pteryonyssinus* and *Dermatophagoides farinae*.

Soluprick SQ House Dust Mites are aqueous solutions containing a partially purified extract of pollen. There are two different solutions each containing a specific pollen extract (*Dermatophagoides pteryonyssinus* or *Dermatophagoides farinae*).

Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* is used in the diagnosis of specific IgE mediated allergic diseases and may be used in adults and children.

Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* is for administration by the skin prick test only on the forearm or back of the patient.

PHARMACEUTICAL ASSESSMENT

REQUESTS FOR INSPECTION ACTION PRIOR TO AUTHORISATION
N/A

INTRODUCTION
A marketing authorisation for Soluprick House dust mites kit (PL 10085/0017) was granted by MHRA on 27th September 2006. Soluprick House dust mite kit consists of two vials of House dust mites. As ALK Abelló are launching vials of the individual House dust mites they are now applying for two abridged applications. These two abridged applications are submitted in accordance with article 10c (informed consent application) in accordance with directive 2001/83/EC. The drug product possesses the same qualitative and quantitative composition in term of active substance, excipients and the same pharmaceutical form as the Soluprick House dust mites.

The vials of the individual House dust mites are manufactured in the same way as Soluprick House dust mite kit and meet the same specifications for drug substance and drug products.

The individually packed vials are supported by the already submitted non-clinical and the clinical documentation, and the products are in relation to quality, non-clinic and clinic documentation identical to the corresponding product authorised under PL 10085/0017, the MA holder is the same.

Assessor's Overall Conclusions
All components were assessed previously and found to be approvable. Labels, leaflets, mock ups were acceptable.

Date: 4th September 2007

4 LIST OF QUESTIONS
None

CLINICAL ASSESSMENT

This application is based on a previous national abridged application for Soluprick SQ House Dust Mites which was granted on 27th September 2006.

No new clinical data have been supplied with these applications and none are required for an application of this type.

PRE-CLINICAL ASSESSMENT

This application is based on a previous national abridged application for Soluprick SQ House Dust Mites which was granted on 27th September 2006.

No new preclinical data have been supplied with these applications and none are required for an application of this type.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The important quality characteristics of Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* are well defined and controlled. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

EFFICACY

Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus* is used in the diagnosis of specific IgE mediated allergic diseases via a skin prick test. No new or unexpected safety concerns arose from this application.

The SPC, PIL and labelling are satisfactory.

RISK BENEFIT ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified. The components of the product are identical to those previously assessed under PL 10085/0017. The risk benefit is therefore considered to be positive.

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STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the marketing authorisation application on 3rd May 2007

2 The MHRA completed its assessment of the application on 30th August 2007

3 The application was determined on 4th September 2007

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STEPS TAKEN AFTER AUTHORISATION - SUMMARY

Date submitted	Application type	Scope	Outcome

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Soluprick SQ House Dust Mite *Dermatophagoides pteronyssinus,* 10 HEP, Solution for skin prick test, 2 ml per vial

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Soluprick SQ House Dust Mite is a glycerinated preparation containing standardised allergen extracts dissolved in equal parts of buffered saline and sterile glycerol.

Active ingredients:
The active ingredient is a partly purified pollen allergen extract which contains the relevant allergen. The active ingredient is standardised with respect to the content of major allergen and the biological activity is controlled by a total potency assay. The potency is expressed in HEP (Histamine Equivalent in Prick testing). The biological activity of Soluprick SQ House Dust Mite is related to the reaction in the skin of an allergic patient measured relative to a histamine dihydrochloride solution.

For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Solution for a skin prick test (SPT)

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Soluprick SQ House Dust Mite is used in the diagnosis of specific IgE mediated allergic diseases.

4.2 Posology and method of administration

Dosage:
Soluprick SQ House Dust Mite 10 HEP is recommended as the optimal biological potency of the allergen when taking into account the meaning of high sensitivity related to high specificity. The potency is expressed in HEP (Histamine Equivalent in Prick testing) which is related to the allergenic activity of the allergen product in the skin of the allergic patient.

ALK Positive control (histamine dihydrochloride 10 mg/ml) is used as reference and ALK Negative control (Saline solution) is used to evaluate unspecific reactions.

When performing a SPT the amount of solution introduced into the superficial layer of the skin is extremely low, approximately 3×10^{-3} µl. (S. Dreborg, Allergy no. 10, Vol 44, 1989)

Skin prick test technique

- The SPT is preferably performed on the volar side of the forearm. Alternatively the test can be performed on the back of the patient.

- The skin must be dry and clean and may be disinfected with 70% alcohol.

- Each test preparation and the controls are applied in droplets on the skin in an appropriate distance from each other (a numbered tape can be used).

- The superficial layer of the skin is pierced with an ALK Lancet perpendicular to the skin through the droplet. Hold it for 1 second and draw back the lancet. For each test preparation and control a new sterile, disposable ALK Lancet is used. The positive control is applied last.

- The droplets are wiped off with a tissue. Do not mix the preparations by sweeping!

- Start to read the reaction of the preparations after 15 minutes beginning with the positive control. A positive reaction is a pale weal (oedema) with a red flare (erythema). To record the weal in the patient's report: mark the contour of the weal with a pen, stick transparent tape over the weal. Press and transfer the tape to the report. The flare can be recorded likewise.

Size of the weal

The mean weal diameter of the allergen product ($D_{a)}$ and of the histamine control (D_h) is calculated as $D = (D_l + d_p)/2$, where D_l is the longest diameter and d_p is the diameter mid-ortogonal to D_l.

Interpretation of results

- Reactions of the allergen product can be graded in relation to the histamine control reaction. This relation is called the skin index (SI).

$SI = D_a/D_h$

0	: negative reaction
+	: $SI \leq 0.5$
++	: $0.5 < SI \leq 1.0$
+++	: $1.0 < SI \leq 2.0$
++++	: $2.0 < SI$

- By use of a biological standardised allergen product a mean weal diameter _≥3 mm indicates that the patient is sensitized to the respective allergen source.

4.3 Contraindications

In extremely rare cases allergic reactions may occur and therefore, a SPT should be avoided when patients are treated with beta-blockers. Recovery from an anaphylactic reaction through the action of adrenaline may be hindered by beta-blockers since these drugs might influence an effective anti-anaphylactic treatment. Therapy with beta-blockers has to be considered an absolute contra-indication.

4.4 Special warnings and precautions for use

Any diseases seriously affecting the patient's general condition; skin lesions in the area used for the testing; dermatographism; dermatitis. Atopic eczema may hamper the reliability of the test.

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with antiallergic symptomatics may affect the result of the test.
It is recommended that patients who are going to have a skin prick test performed discontinue treatment with:

Therapeutic agent	Interval between last given dose and the SPT
Short-acting antihistamines	2-3 days
Long-acting antihistamines	8 weeks
Hydroxyzine	2 weeks
Ketotifen	2 weeks
Tricyclic antidepressants	2 weeks
Local application of potent steroid ointment	2-3 weeks

Corticosteroids in doses lower than 30 mg of prednisone/prednisolone per day for up to one week do not reduce the response to skin tests.

Oral low dose glucocorticoids (doses less than 10 mg of prednisolone per day) need not to be discontinued prior to skin testing.

4.6 Pregnancy and lactation

Pregnancy is not an absolute contraindication for skin testing. Skin prick testing with Soluprick may be performed during lactation.

4.7 Effects on ability to drive and use machines

None

4.8 Undesirable effects

Undesirable effects occurring are related to the fact allergenic material is applied. The local reaction is an integrated part of the diagnosis, and the following type of reactions related directly to the patient's allergy might occur.

Local reactions
The weal is continuously spreading and pseudopodia may be formed during the first 15-20 minutes after application. Note that in some cases a late reaction (6-24 hours after) may occur after application of the allergen in the form of a diffuse swelling.

Systemic reaction
In rare cases a general reaction may develop which can be treated with relevant symptomatics.

Anaphylactic reaction
Although never reported a theoretical possibility exists of development of an anaphylactic reaction after a few seconds or minutes. For this reason an emergency kit with a ready for use adrenaline syringe must always be available.

4.9 Overdose

Not relevant

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Soluprick SQ House Dust Mite is used for specific diagnosis by skin prick testing. The preparation is mixtures of molecules with high molecular weight compounds.

The allergenic substance of the preparation can react with the immune system of an allergic patient provided IgE antibodies to the corresponding allergen are released. An immediate allergic reaction will occur within 10-20 minutes, characterised by a weal and flare.

This reaction is mainly caused by binding the allergen to specific IgE attached to mast cells, resulting in release of vaso-active agents like histamine. Some patients also develop a late phase reaction, i.e. a diffuse swelling and redness, starting 2 to 3 hours after the allergen piercing, peaking at 6-12 hours and disappearing within 12-24 hours.
Lymphocytes are involved in the late phase response; the exact mechanism has not yet been elucidated.

5.2 Pharmacokinetic properties

Neither the doses applied in a SPT - in terms of weight less than 0.1 µg - nor the route of administration indicate that Soluprick SQ House Dust Mite is used to acquire a clinical effect after systemic absorption.
No attempt has been made to account for the fate of the individual components.

5.3 Preclinical safety data

No toxicological studies have been performed. However, long term clinical experience confirms that non- allergic reactions are hardly of any significance.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Disodium phosphate, dihydrate
Sodium dihydrogen phosphate, dihydrate
Phenol
Sodium chloride
Glycerol
Water for Injections

The sodium content of Soluprick SQ House Dust Mite is less than 1 mmol sodium (23 mg) per dose; therefore it is essentially “sodium free”

6.2 Incompatibilities

None known. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Shelf life of medicinal product as packaged for sale: 3 years
Shelf life after opening the container: 6 months

6.4 Special precautions for storage

Store in a refrigerator at 2-8 °C
Do not freeze. Store in original packaging in order to protect from light.

6.5 Nature and contents of container

Vial (type I glass) with a halobutyl rubber stopper and a screw cap (polypropylene).

6.6 Special precautions for disposal

No special requirements.

7 MARKETING AUTHORISATION HOLDER

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

8 MARKETING AUTHORISATION NUMBER

PL 10085/0047

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

04/092007

10 DATE OF REVISION OF THE TEXT

04/09/2007

Patient Information Leaflet

SOLUPRICK SQ HOUSE DUST MITE *DERMATOPHAGOIDES PTERONYSSINUS*, 10 HEP, SOLUTION FOR SKIN PRICK TEST, 2ML PER VIAL

(Dermatophagoides pteronyssinus)

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PATIENT INFORMATION LEAFLET

SOLUPRICK SQ 10 HEP
Solution for skin prick testing

Grass Pollen, Tree Pollen, Weed Pollen, Animal Hair and Dander and House Dust Mites

1. WHAT YOU SHOULD KNOW ABOUT SOLUPRICK SQ

Please read this leaflet carefully before you start treatment with Soluprick SQ. Soluprick SQ is a solution for skin prick testing (SPT). It is used in the diagnosis of specific allergenic diseases. If you have any questions or are in any doubt about anything, please ask your doctor or nurse.

2. WHAT IS THE SKIN PRICK TESTING FOR?

Soluprick SQ is used to check if you have an allergy to one of the following groups of allergens:

Grass pollen
Tree pollen
Weed pollen
Animal hair and dander
House dust mites

See section number 7

3. BEFORE YOU ARE GIVEN YOUR SKIN PRICK TEST

- Are you regularly taking Beta-blockers to control your blood pressure?
- Have you any skin problems in the area to be used for testing?
- Are you allergic to any of the ingredients in Soluprick SQ?
- Are you taking, antihistamines, hydroxyzine, ketotifen, tricyclic antidepressants or using steroid ointment?
- If the answer to any or all of the above questions is YES, TELL YOUR DOCTOR/NURSE BEFORE HE/SHE GIVES YOU SOLUPRICK SQ

4. HOW WILL YOU BE GIVEN THE SKIN PRICK TEST?

- The Skin Prick Test is usually carried out on the inner side of the forearm. Alternatively the test can be done on your back.
- Your skin must be dry and clean and may be disinfected with alcohol by the nurse or doctor
- Test preparations and the controls are applied in droplets on the skin at an appropriate distance from each other (a numbered tape may be used).
- The top layer of the skin is pierced by the doctor/nurse with an ALK lancet through the droplets.
- The reaction is read after 15 minutes. A positive reaction is a pale small raised swelling or weal with a red edge.

5. AFTER YOU HAVE BEEN GIVEN THE SKIN PRICK TEST

Normally a Skin Prick Test does not cause any problems but occasionally some people may get side effects such as:

- A continuously spreading weal may be formed at the site during the first 10-20 minutes after application of the allergen.
- Widespread swelling and redness may happen 6-24 hours after the application of the allergen.

If you experience any of these side effects, and they stay or become troublesome, tell your doctor or pharmacist.
If you get any other unusual or unexpected side effect, you should tell your doctor or pharmacist at once.

Anaphylactic reaction
In extremely rare cases an anaphylactic reaction (a severe reaction throughout the body that is recognised by difficulty in breathing, fainting, itching, and weals) may develop after a few seconds or minutes. For this reason an emergency kit with a 'ready for use' adrenalin syringe will always be available.

TELL YOUR DOCTOR/NURSE IMMEDIATELY IF YOU FEEL ANY OF THESE CHANGES. He or she will be able to give you the right treatment at once to make you feel well.

6. HOW SHOULD THE SKIN PRICK TEST BE STORED?

- The clinic/hospital will store the Skin Prick Test, solution.
- This medicine should be kept in a refrigerator (between 2ºC and 8ºC) out of the reach and sight of children, as the medicine could harm them.
- Do not freeze the solution.
- Keep the vials in the outer carton to protect it from light.
- Do not use the skin prick test solution after the expiry date, which is printed on the carton and label.

7. WHAT IS IN THE MEDICINE?

Soluprick SQ is a solution for skin prick testing that contains an extract of specific allergen. The allergen is the substance that causes the allergic disease. Soluprick SQ also contains the inactive ingredients, disodium phosphate, sodium dihydrogen phosphate, phenol, sodium chloride, glycerol and water for injections.

The following individual allergens are available:

Grass pollen: Meadow Foxtail, Cock's Foot, Meadow Fescue, Perennial Ryegrass, Timothy Grass, Kentucky Blue Grass, Cultivated Rye.
Tree pollen: European Alder, Grey Alder, Silver Birch, Hazel
Weed pollen: Mugwort, Pellitory of the Wall, Upright Pellitory.
Animal hair and dander: Horse Dander, Dog Hair, Cat Hair
House dust mites: Dermatophagoides farinae, Dermatophagoides pteronyssinus

Each single allergen is provided in a 2 ml glass vial.

The strength of the products is 10 HEP

The biological activity of Soluprick SQ is related to the reaction in the skin of an allergic patient measured relative to a histamine dihydrochloride solution.

8. MANUFACTURER AND PRODUCT LICENCE HOLDER

Product Licence Holder:
ALK-Abelló A/S
Bøge Allé 6-8
DK-2970 Hørsholm
Denmark

Manufacturer:
ALK-Abelló S.A.
Miguel Fleta 19
E-28037 Madrid
Spain

9. DISTRIBUTOR

ALK-Abelló Ltd.
1 Tealgate
Hungerford
Berkshire RG17 OYT
United Kingdom
Tel: 01488 686 016

10. DATE ON WHICH THE PACKAGE LEAFLET WAS LAST REVISED

June 2007

11. FURTHER INFORMATION

Allergy UK
Tel: 01322 619 898
www.allergyuk.org

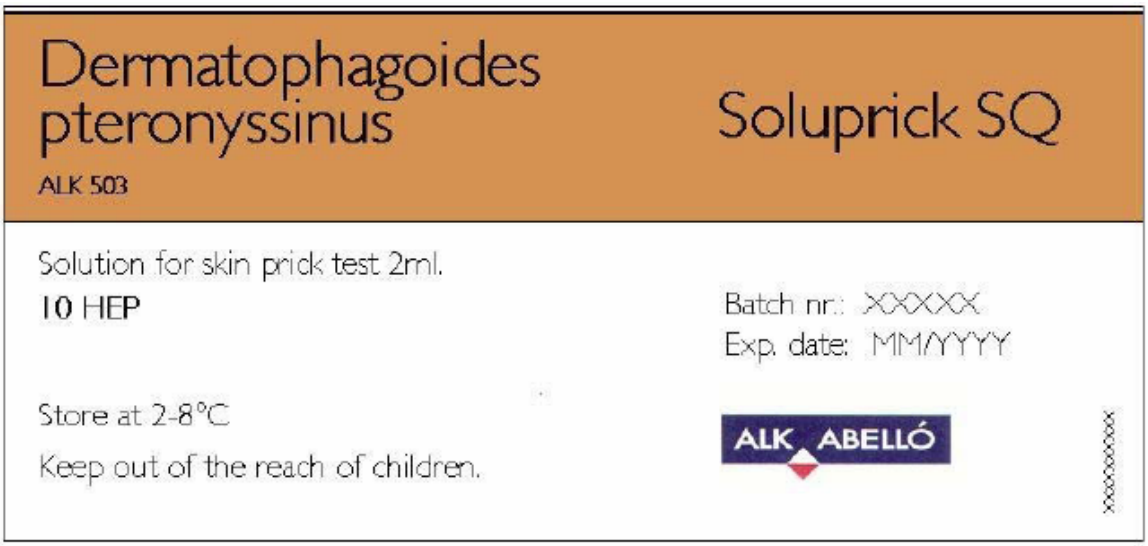
Labelling

SOLUPRICK SQ HOUSE DUST MITE *DERMATOPHAGOIDES PTERONYSSINUS*, 10 HEP, SOLUTION FOR SKIN PRICK TEST, 2ML PER VIAL

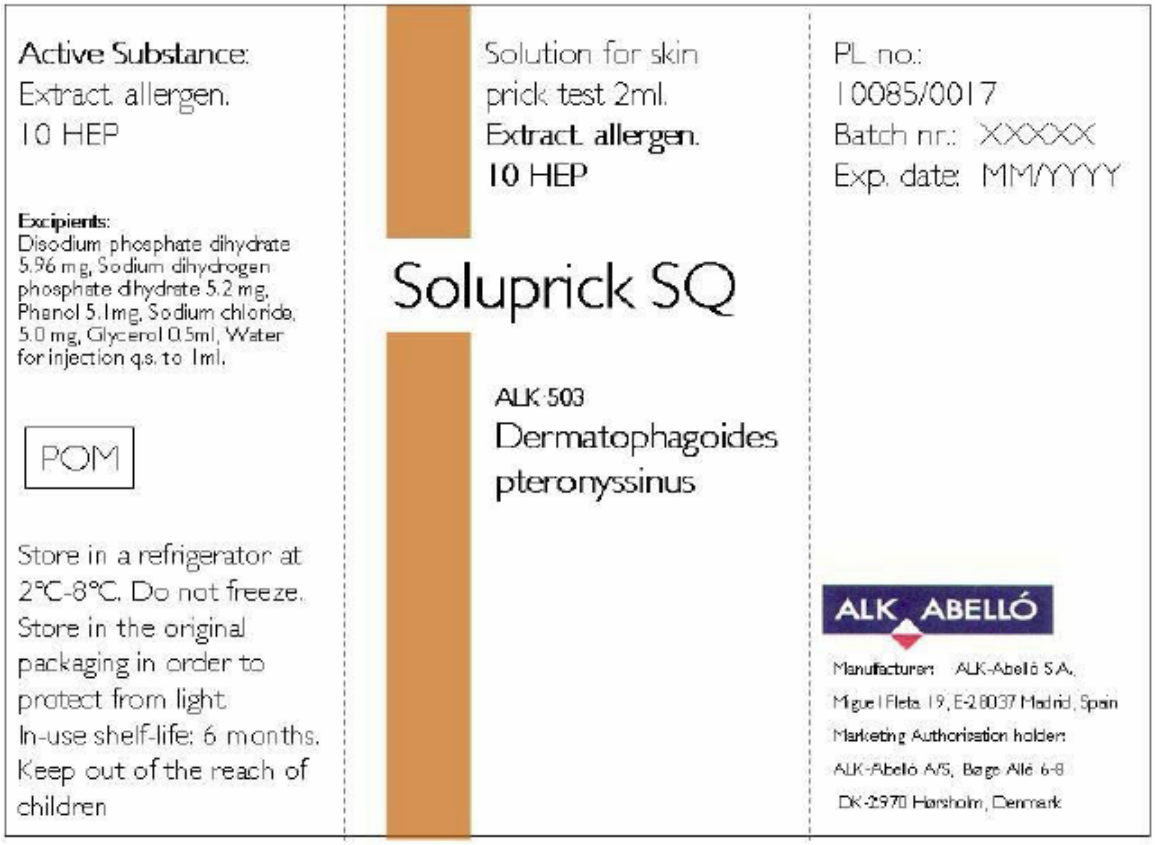
(Dermatophagoides pteronyssinus)

PL 10085/0047

VIAL


Dermatophagoides pteronyssinus
ALK 503
Soluprick SQ
Solution for skin prick test 2ml.
10 HEP
Batch nr.: XXXXX
Exp. date: MM/YYYY
Store at 2-8°C
Keep out of the reach of children.
ALK ABELLÓ

BOX


Active Substance:
Extract allergen.
10 HEP
Excipients:
Disodium phosphate dihydrate 5.96 mg, Sodium dihydrogen phosphate dihydrate 5.2 mg, Phenol 5.1mg, Sodium chloride, 5.0 mg, Glycerol 0.5ml, Water for injection q.s. to 1ml.
POM
Store in a refrigerator at 2°C-8°C. Do not freeze.
Store in the original packaging in order to protect from light
In-use shelf-life: 6 months.
Keep out of the reach of children
Solution for skin prick test 2ml.
Extract allergen.
10 HEP
Soluprick SQ
ALK 503
Dermatophagoides pteronyssinus
PL no.:
10085/0017
Batch nr.: XXXXX
Exp. date: MM/YYYY
ALK ABELLÓ
Manufacturer: ALK-Abelló S.A.
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