Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test
(histamine dihydrochloride)
Soluprick® Negative control, Solution for skin-prick test

PL 10085/0019

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Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test (histamine dihydrochloride)

Soluprick® Negative control, Solution for skin-prick test

PL 10085/0019

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted ALK-Abelló A/S a Marketing Authorisation (licence) for the medicinal product, Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test (PL 10085/0019) on 23rd June 2011. This is a prescription-only product (POM).

Soluprick® is a solution for skin-prick testing. Soluprick® Positive and Negative control are for diagnostic use only. They are used as a reference with other skin-prick tests to determine which substances cause an allergic reaction. The histamine dihydrochloride in the Soluprick® Positive control will produce a hard raised wheal, which may be surrounded by a red area and this is called a positive response. This response is compared with the responses from substances that the person might be allergic to. Soluprick® Negative Control will usually not cause any reaction, and is used to ensure that positive responses are not caused by the prick of the lancet.

No new or unexpected safety concerns arose from this application and it was therefore judged that the benefits of Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test outweigh the risks; hence a Marketing Authorisation has been granted.
Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test
(histamine dihydrochloride)
Soluprick® Negative control, Solution for skin-prick test

PL 10085/0019

SCIENTIFIC DISCUSSION

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INTRODUCTION

Based on the review of the data on quality, safety and efficacy, the MHRA granted ALK-Abelló A/S a Marketing Authorisation for the medicinal product Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test (PL 10085/0019) on 23rd June 2011. The product is a prescription-only medicine (POM).

This is an abridged, bibliographic application for Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test, submitted under Article 10a (well-established use) of Directive 2001/83/EC, as amended.

This medicinal product is for diagnostic use only. It is used for positive and negative control of skin-prick tests for diagnosis of specific IgE-mediated allergy. Soluprick® Positive control contains the active ingredient, histamine dihydrochloride in a concentration of 10 mg/ml. Histamine will cause an imitation of the local allergic reaction within 10-20 minutes, characterized by development of a wheal and erythema. The wheals and erythema are caused by the vaso-active effect of histamine. The negative control contains no active ingredient. Soluprick Positive control is applied epicutaneously to obtain a local reaction. Soluprick Negative control is used to evaluate the general skin-prick test reactivity of allergic patients. The solutions are sterile.

No new non-clinical or clinical efficacy studies were necessary for this application, which is acceptable given that this was a bibliographic application for a product containing an active of well-established use. Bioequivalence studies are not necessary to support this bibliographic application.

The MHRA considers that the pharmacovigilance system as described by the Marketing Authorisation Holder (MAH) fulfils the requirements and provides adequate evidence that the MAH has the services of a Qualified Person (QP) responsible for pharmacovigilance and has the necessary means for the notification of any adverse reaction suspected of occurring either in the Community or in a third country.

It is not considered that this medicinal product represents any risk to the environment. An Environmental Risk Assessment (ERA) is not considered necessary.
PHARMACEUTICAL ASSESSMENT

ACTIVE SUBSTANCE

Histamine dihydrochloride

Nomenclature:

INN: Histamine dihydrochloride

Structure:

\[
\text{H}_2\text{N} - \text{CH} - \text{CH} = \text{CH} - \text{CH} = \text{N} - \text{H}
\text{Cl}_2
\]

Molecular formula: \( \text{C}_5\text{H}_9\text{N}_3 \cdot 2\text{HCl} \)

Molecular weight: 184.10 g/mol

CAS No: 56-92-8

Physical form: A white or almost white, crystalline powder or colourless crystals

Solubility: Freely soluble in water, soluble in alcohol

The active substance, histamine dihydrochloride, is the subject of a European Pharmacopoeia (Ph. Eur.) monograph.

Synthesis of the active substance from the designated starting materials has been adequately described and appropriate in-process controls and intermediate specifications are applied. Satisfactory specifications are in place for all starting materials and reagents and these are supported by relevant Certificates of Analysis. Confirmation has been provided that the raw materials, intermediates and auxiliary agents used in synthesis of the active are not of animal, biological or genetically modified origin.

Appropriate specifications have been provided for the active substance. Analytical methods have been appropriately validated and are satisfactory for ensuring compliance with the relevant specifications. Batch analysis data are provided and comply with the proposed specifications. Satisfactory Certificates of Analysis have been provided for any reference standards used by the active substance manufacturer.

The active substance is stored in appropriate packaging. Specifications and Certificates of Analysis have been provided for the packaging materials used. The primary packaging in direct contact with the active substance complies with relevant Ph. Eur. requirements and satisfies Directive 2002/72/EC (as amended); it is suitable for contact with foodstuffs.

Appropriate stability data have been generated for the active substance stored in the proposed commercial packaging. These data demonstrate the stability of the active substance and an appropriate retest period has been applied.
MEDICINAL PRODUCT

Description & Composition

Soluprick® Positive and Negative controls, Solutions for skin-prick tests are presented as 2 ml of clear, aqueous, sterile solutions. The positive control contains the active ingredient, histamine dihydrochloride in a concentration of 10 mg/ml.

Other ingredients consist of pharmaceutical excipients, namely phenol, sodium dihydrogen phosphate dihydrate, disodium phosphate dehydrate, sodium chloride, glycerol, water for injections, and sodium hydroxide and hydrochloric acid (for pH adjustment). The negative control contains only the excipients. Appropriate justification for the inclusion of each excipient has been provided.

All excipients used comply with their respective European Pharmacopoeia monographs. Satisfactory Certificates of Analysis have been provided for all excipients.

The applicant has provided a declaration confirming that there are no materials of human or animal origin contained in or used in the manufacturing process for the proposed product. None of the excipients are sourced from genetically modified organisms.

There were no novel excipients used and no overages.

Pharmaceutical development

Details of the pharmaceutical development of the medicinal product have been supplied and are satisfactory. The objective was to develop sterile, stable aqueous solutions that act as positive and negative controls for skin-prick testing.

Manufacture

A description and flow-chart of the manufacturing method has been provided.

In-process controls are appropriate considering the nature of the product and the method of manufacture. Process validation studies were conducted and the results were satisfactory.

Finished product specification

Finished product specifications are provided for both release and shelf-life and are satisfactory. Acceptance limits have been justified with respect to conventional pharmaceutical requirements and, where appropriate, safety. Test methods have been described and have been adequately validated, as appropriate. Satisfactory batch analysis data are provided and accepted. The data demonstrate that the batches are compliant with the proposed specifications. Certificates of Analysis have been provided for any reference standards used.

Container Closure System

The control solutions are licensed for marketing as 2 ml sterile, aqueous solution in clear type I glass vials, closed with bromobutyl rubber stoppers and propylene screw caps. The sealed vials are packaged individually with the Patient Information Leaflet (PIL) into cardboard outer cartons.
Satisfactory specifications and Certificates of Analysis for all packaging components have been provided. All primary product packaging complies with EU legislation, Directive 2002/72/EC (as amended), and is suitable for contact with parenteral preparations.

**Stability**

Finished product stability studies have been conducted in accordance with current guidelines, using product stored in the packaging proposed for marketing. The stability data support a shelf-life of 3 years for the unopened vial. Once opened, the shelf-life of the product is 6 months; this is satisfactory. Storage instructions are ‘Store in a refrigerator (2°C - 8°C)’.

**Quality Overall Summary**

A satisfactory quality overall summary is provided, and has been prepared by an appropriately qualified expert. The CV of the expert has been supplied.

**PRODUCT INFORMATION:**

The approved Summary of Product Characteristics (SmPC), Patient Information Leaflet (PIL) and labelling are satisfactory. Mock-ups of the PIL and labelling have been provided. The user-testing of the PIL has been evaluated and is accepted.

**Conclusion**

All pharmaceutical issues have been resolved and the quality grounds for this application are considered adequate. There are no objections to approval of Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test from a pharmaceutical point of view.
NON-CLINICAL ASSESSMENT

This is an abridged, bibliographic application for Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test, submitted under Article 10a (well-established use) of Directive 2001/83/EC, as amended.

Specific non-clinical studies have not been performed, which is acceptable considering that this was a bibliographic application for a product containing an active of well-established use.

A non-clinical overview has been written by a suitably qualified person and is satisfactory. The overview justifies the dosage adequately in terms of known data on the in-vivo turnover rate of histamine in man. References to lack of mutagenic and genotoxic effects are given and pregnancy is reasonable considered not to be an absolute contra-indication for the diagnostic use of this product. The CV of the non-clinical expert has been supplied.

There are no objections to approval of Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test from a non-clinical point of view.
CLINICAL ASSESSMENT

1. INTRODUCTION AND BACKGROUND

This is an abridged, bibliographic application for Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test, submitted under Article 10a (well-established use) of Directive 2001/83/EC, as amended.

Soluprick Positive control contains the active ingredient histamine dihydrochloride in a concentration of 10 mg/ml. The Negative control contains no active ingredient. The product is intended to evaluate the general skin-prick test reactivity of allergic patients.

Histamine is a potent inflammatory mediator and elicits the wheal and flare reaction typical of the immediate part of type I hypersensitivity reactions. The basis of this reaction is a local vasodilation and plasma extravasation causing local oedema that typically develops instantaneously and gradually subsides within half an hour. Histamine has therefore long been accepted as the most suitable positive control for skin tests. A concentration of 10 mg/ml of histamine dihydrochloride has been shown to give the most reproducible and reliable results for skin-prick test.

Soluprick® controls have been marketed in Denmark since 1988. The product also has Marketing Authorisations obtained by national procedures in the Czech Republic, Denmark, Finland, Germany, Slovakia, Sweden and Switzerland.

1.1 Indications

This medicinal product is for diagnostic use only. It is used for positive and negative control of skin-prick tests for diagnosis of specific IgE-mediated allergy.

The indications are satisfactory and are the same as have been approved by Mutual Recognition (MR) procedure for Soluprick® Positive and Negative controls [DK/H/0860/01-2/MR]. The Reference Member State in this MR procedure was Denmark; Concerned Member States were Austria, Belgium, Estonia, France, Greece, Iceland, Ireland, Latvia, Lithuania, Luxembourg, Norway, Portugal and Slovenia.

1.2 Dose and Dose Schedule

Full details concerning the posology are provided in the SmPC. The posology is satisfactory. The dose and dose schedule instructions in adults and children, as proposed in the SmPC, are supported by the literature presented in the clinical overview.

2. TOXICOLOGY

The toxicology of histamine dihydrochloride is well-known. No new data have been submitted and none are required for this application, considering the small dose of this naturally occurring autacoid, the route of administration and established clinical safety over several decades of use.
3. CLINICAL PHARMACOLOGY

The clinical pharmacology of the cutaneous wheal and flare reaction secondary to intracutaneous histamine administration is widely known and accepted. Appropriate references are given. No clinical studies were performed, which is appropriate for this application. An adequate description of the pharmacodynamic effects of intracutaneous histamine using similar dosages is given.

4. CLINICAL EFFICACY

This section is based on a literature review provided by the applicant and does not contain any new clinical data. The applicant has provided sufficient data to support the conclusions. The histamine skin-prick test is a well-accepted technique. The European Academy of Allergology and Clinical Immunology (EAACI) has published a position paper for ‘Skin test used in type I allergy testing’ (1989) and a position paper for ‘Allergen standardisation and skin tests’ (1993). These publications are used in practice as the basic knowledge for skin-prick testing.

5. CLINICAL SAFETY

No new data have been submitted and none are required for applications of this type. No new or unexpected safety concerns arose from this application. Safety is reviewed in the clinical overview. The safety profile of histamine dihydrochloride is well-known. The evidence presented to support the clinical safety of histamine dihydrochloride is adequate. The applicant has provided supportive evidence for the adverse events listed in Section 4.8 of the SmPC.

6. CLINICAL OVERVIEW

A satisfactory clinical overview is provided and has been prepared by an appropriately qualified expert. The overview includes discussions of the safety and efficacy of the product, the selection of the histamine concentration, and the sensitivity and specificity of the skin-prick test. The CV of the clinical expert has been supplied.

7. PRODUCT INFORMATION

Summary of Product Characteristics (SmPC)

The approved SmPC is satisfactory.

Patient Information Leaflet (PIL)

The final PIL is in line with the approved SmPC and is satisfactory.

Labelling

The labelling is satisfactory.

8. CONCLUSION

This application has been submitted as a so called “bibliographic application”; the applicant has submitted no new data. The pharmacodynamics and pharmacokinetics of histamine dihydrochloride are well-documented in the literature and the clinical use is established. The product literature is approved. The grant of a Marketing Authorisation was, therefore, recommended.
OVERALL CONCLUSION AND BENEFIT-RISK ASSESSMENT

QUALITY
The important quality characteristics of Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test and Soluprick® Negative control, Solution for skin-prick test are well defined and controlled. The specifications and batch analytical results indicate consistency from batch to batch. There are no outstanding quality issues that would have a negative impact on the benefit/risk balance.

NON-CLINICAL
No new non-clinical data were submitted and none are required for an application of this type.

CLINICAL
No new data are submitted and none are required for this type of application.

The published literature supports the efficacy of this product in the proposed indication, positive and negative control of skin-prick tests for diagnosis of specific IgE-mediated allergy. The safety and efficacy of histamine dihydrochloride is well-known. The presented evidence for well-established use of the active substance is sufficient.

The literature review identifies no new safety issues or concerns. The safety profile of histamine dihydrochloride is well-known.

PRODUCT LITERATURE
The approved SmPC is satisfactory.

The PIL is in line with the SmPC and is satisfactory. The package leaflet has been evaluated via a user consultation study in accordance with the requirements of Articles 59(3) and 61(1) of Directive 2001/83/EC, as amended. The results show that the package leaflet meets the criteria for readability as set out in the Guideline on the readability of the label and package leaflet of medicinal products for human use.

The approved labelling artwork complies with statutory requirements.

BENEFIT-RISK ASSESSMENT
The quality of the product is acceptable and no new non-clinical or clinical safety concerns have been identified. Histamine dihydrochloride is an active substance of well-known safety and efficacy. It has been used for a number of decades in the EC. Extensive clinical experience with histamine dihydrochloride is considered to have demonstrated the therapeutic value of the active substance. The benefit: risk ratio is considered to be positive.
Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test  
(histamine dihydrochloride)  
Soluprick® Negative control, Solution for skin-prick test

PL 10085/0019

STEPS TAKEN FOR ASSESSMENT

1 The MHRA received the Marketing Authorisation application on 15th August 1996.

2 Following standard checks and communication with the applicant the MHRA considered the application valid on 21st August 1996.

3 Following assessment of the application the MHRA requested further information relating to the quality dossier on 27th November 1996, 21st April 1999, 7th April 2006 and 16th October 2008; and further information relating to the clinical dossier on 27th November 1996 and 19th November 2009.

4 The applicant responded to the MHRA’s requests, providing further information for the quality sections on 1st March 1999, 5th February 2004, 29th August 2006, and 29th December 2008; and further information for the clinical sections on 1st March 1999 and 28th May 2010.

5 The application was determined 23rd June 2011.
Soluprick® Positive control, 10 mg/ml, Solution for skin-prick test
(histamine dihydrochloride)
Soluprick® Negative control, Solution for skin-prick test

PL 10085/0019

STEPS TAKEN FOR ASSESSMENT

Not applicable
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Soluprick Positive control, 10 mg/ml, Solution for skin-prick test
Soluprick Negative control, Solution for skin-prick test

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Soluprick Positive control: Histamine dihydrochloride 10 mg/ml.
Soluprick Negative control: No active ingredient.
For a full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Solution for skin-prick test.
A clear aqueous solution.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
This medicinal product is for diagnostic use only.
Positive and negative control of skin-prick tests for diagnosis of specific IgE-mediated allergy.

4.2 Posology and method of administration
A skin-prick test (SPT) is performed by administering a drop of the product on the surface of the skin. The skin is penetrated using a lancet. The skin-prick test may be performed on the volar side of the forearm or on the back.
Soluprick Positive control (Histamine dihydrochloride 10 mg/ml) is applied as reference to evaluate the general reactivity of the skin-prick test, and Soluprick Negative control is applied to evaluate unspecific reactions.
Skin-prick testing should be performed by experienced personnel only.

Paediatric population
Prick testing in children is already possible after the first year of life depending on the child’s constitution, but in general should not be performed before the age of 4.

Instructions for use
• The skin-prick test is normally performed on the volar side of the forearm. Alternatively the test may be performed on the patient’s back.
• The skin must be dry and clean. It is recommended to wash the test area with an alcoholic solution.
• Each test solution and the Positive and the Negative control are applied in droplets on the skin placed at least 1.5 cm. apart. The forearm should be at rest. Apply the Positive and the Negative control after the active tests.
• The superficial layer of the skin is pierced through the droplet perpendicular to the skin using a 1 mm tip standardized lancet. A new lancet must be used for each allergen.
• Apply a slight, constant pressure for approximately 1 second. Draw the lancet straight back.
• Surplus allergen extract is removed with a tissue. It is important to avoid contamination between the allergens.
• The reactions are read after 15 minutes.
• A positive reaction is a wheal with or without erythema.
The result may be transferred to a test form as follows: Mark the contour of the actual wheal. Transfer the result to the test form with the adhesive side of transparent tape, where after the reaction can be read on graph paper.

A wheal with a diameter of at least 3 mm is considered to be a positive reaction.

For the Negative Control no reaction is expected. In case of a positive reaction with the Negative Control the skin-prick test in general must be regarded as not reliable.

4.3 Contraindications

Acute or chronic atopic dermatitis in the area used for testing.

Hypersensitivity to phenol or any other excipient in Soluprick Positive and Negative Control

4.4 Special warnings and precautions for use

Caution should be exercised if the patient is suffering from one or more of the following conditions: Any diseases seriously affecting the patient’s general condition, skin lesions in the area used for testing, dermatographism, dermatitis and active eczema in the area used for testing (test should be postponed). These conditions may influence the interpretation of the test outcome.

In case of axillary lymph node dissection, it is preferable to perform the skin tests on the opposite arm.

Skin-prick testing should be performed by experienced personnel.

In extremely rare cases an anaphylactic reaction may occur after skin-prick testing with active allergen.

For skin-prick tests with active allergen performed concomitantly with Soluprick Positive and Negative Control, an emergency kit with a ready for use adrenaline syringe must always be available. The concomitant use of beta-blocking agents may influence efficiency of anti-anaphylactic treatment (e.g. adrenaline).

4.5 Interaction with other medicinal products and other forms of interaction

Concomitant treatment with anti allergic or other medication 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:

<table>
<thead>
<tr>
<th>Therapeutic agent</th>
<th>Interval between last given dose and SPT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Short-acting antihistamines (fexofenadine, ebastine, promethazine)</td>
<td>2-3 days</td>
</tr>
<tr>
<td>Long-acting antihistamines (cetirizine, clemastatine, hydroxyzine, promethazine, loratadine)</td>
<td>5-7 days</td>
</tr>
<tr>
<td>Local application of potent steroid ointment</td>
<td>2-3 weeks</td>
</tr>
</tbody>
</table>

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

Long-term treatment with oral low dose glucocorticoids (doses lower than 10 mg of prednisolone per day) need not be discontinued prior to the skin-prick test. Locally applied steroid drugs must be avoided in the area use for testing 2-3 weeks prior to the test.
Antidepressants may interfere with the result of the skin-prick test due to potential effect on the histamine H1 receptors. Tricyclic antidepressants may interfere with the result of the skin-prick test for up to 1 week after the last administration of antidepressants. There is no data regarding interactions with other antidepressants. Therefore, the rate of elimination and the H1 antihistamine potency of the given antidepressants should be taken into consideration. The risks of discontinuing treatment with an antidepressant should carefully be considered with the benefits of the skin-prick test.

4.6 Pregnancy and lactation
The risk of performing skin-prick test during pregnancy must be carefully evaluated together with the patient in order to identify the specific clinical need for identifying the trigger allergen during the period of pregnancy.

Skin-prick testing with Soluprick Positive and Negative Control may be performed during lactation.

4.7 Effects on ability to drive and use machines
Soluprick Positive and Negative Controls have no influence on the ability to drive and use machines.

4.8 UNDESIRABLE EFFECTS
Soluprick Positive control (histamine dihydrochloride) will cause a local reaction with development of wheal and erythema with local itching after the test. In some cases a slight local pain may appear (See Section 4.2).

Administration site reactions:

<table>
<thead>
<tr>
<th>MedDRA SOC</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>General disorder and administration site condition</td>
<td>Common (≥1/100 to &lt;1/10): Pain</td>
</tr>
</tbody>
</table>

4.9 Overdose
No event of overdose is reported upon correct usage. Undesirable effects, in the form of exaggerated pharmacological effects, can be caused by wrong administration.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Pharmacotherapeutic group: Test for allergic diseases

ATC Code: V04 CL
Soluprick Positive Control: Histamine will cause an imitation of the local allergic reaction within 10-20 minutes, characterized by development of a wheal and erythema. The wheals and erythema are caused by the vaso-active effect of histamine.

5.2 Pharmacokinetic properties
Soluprick Positive control is applied epicutaneously to obtain a local reaction. Soluprick Negative control is used to evaluate unspecific reactions. The amount of solution applied epicutaneously at skin-prick testing corresponds to 3 x 10⁻³ μl.

5.3 Preclinical safety data
No non-clinical studies have been carried out.
Many years of clinical experience with the compounds used in the formulation confirms an acceptable level of safety in the amounts administered to the patient.
6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients
Phenol
Sodium dihydrogen phosphate dihydrate
Disodium phosphate dehydrate
Sodium chloride
Glycerol
Water for injections
Sodium hydroxide (for pH adjustment)
Hydrochloric acid (for pH adjustment)

6.2 Incompatibilities
Not applicable

6.3 Shelf life
3 years.
6 months after first opening of the vial.

6.4 Special precautions for storage
Store in a refrigerator (2°C - 8°C).

6.5 Nature and contents of container
2 ml solution in a clear type I glass vial closed with a bromobutyl rubber stopper and a propylene screw cap.

6.6 Special precautions for disposal
The solution is ready for use.

7 MARKETING AUTHORISATION HOLDER
ALK-Abelló A/S
Bøge Allé 6-8
DK-2970 Hørsholm
Denmark

8 MARKETING AUTHORISATION NUMBER(S)
PL 10085/0019

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
23/06/2011

10 DATE OF REVISION OF THE TEXT
23/06/2011
SOLUPRICK® POSITIVE CONTROL, 10 mg/ml, Solution for Skin-prick test Histamine Dihydrochloride AND SOLUPRICK® NEGATIVE CONTROL,

Solution for Skin-prick Test

Read this leaflet before you start using this medicine.
- Keep this leaflet. You may need to read it again.
- If you have any further questions, please ask your doctor or pharmacist.
- If any of the side effects gets serious or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.

In this leaflet:
1. What Soluprick® is and what it is used for?
2. Before you use Soluprick®
3. How to use Soluprick®
4. Possible side effects
5. How to store Soluprick®
6. Further information

1. WHAT SOLUPRICK® IS AND WHAT IT IS USED FOR?
Soluprick® is a solution for skin prick testing.

Soluprick® Positive and Negative Control are for diagnostic use only. They are used as a reference with other skin prick tests to determine which substances cause your allergic reaction.

The Histamine Dihydrochloride in the Soluprick® Positive Control will produce a hard raised wheal, which may be surrounded by a red area and this is called a positive response. This response is compared with the responses from substances that you might be allergic to.

Soluprick® Negative Control will usually not cause any reaction, and is used to ensure that positive responses are not caused by the prick of the lancet.
2. BEFORE YOU USE SOLUPRICK®

Do not use Soluprick® Positive and Negative control

- If you have ever experienced a bad reaction when using this product or any other product containing phenol or any other ingredient contained in the solution (see Section 6).
- If you have skin problems (atopic dermatitis) in the area in which the skin prick test is to be applied.

Please inform your doctor if any of these statements apply to you.

Take special care with Soluprick® Positive and Negative control

Some conditions can affect the results of the skin prick test, therefore please tell your doctor or health professional before the skin prick test is carried out if:

- Your general health condition is seriously affected by any disease;
- You suffer from active eczema or other skin diseases in the area of the skin used for testing;
- You have had a lymph node in the armpit removed.

In extremely rare cases an anaphylactic reaction (a severe reaction throughout the body that is recognized by wheals, itching, shortness of breath and fainting) may occur after skin prick testing with substances that you are allergic to. Therefore your doctor or health professional should have an appropriate emergency kit available before conducting the skin prick test, to be able to take adequate emergency measures which may include injection of adrenaline.

Beta-blocking medication (used for example for high blood pressure and several heart diseases) may influence the efficacy of adrenaline, so please tell your doctor if you are taking beta-blocking medication.

Using other medicines

Please tell your doctor or health professional if you are taking or have recently taken any other medicines including those obtained without a prescription.

Some medicines can affect the results of the skin prick test, therefore: Please tell your doctor or health professional before the skin prick test is carried out if you are taking any of the following medicines:

- Short-acting antihistamines (usually used to treat hayfever or skin hives), such as fexofenadine, ebastine, promethazine within the last two to three days;
- Long-acting antihistamines (usually used to treat hayfever or skin hives), such as cetirizine, clemastine, hydroxyzine, promethazine, loratadine within the last week;
- Antidepressants (of the type called 'tricyclic antidepressant'), such as amitriptyline, clomipramine, imipramine, maprotiline, nortriptyline, dosulepin and doxepin, within the last week;
• Corticosteroids (sometimes called steroids), such as prednisolone and prednisone, which may be taken to treat arthritis, inflammation of blood vessels (called vasculitis), asthma and other diseases
• Corticosteroid creams and ointments (which are used to treat eczema and other types of skin inflammation) such as hydrocortisone, triamcinolone acetonide, fluocortolone 21-pivalate, betamethasone 17-valerate, betamethasone dipropionate and fluocinolone acetonide that you have applied to your skin within the last two to three weeks

Pregnancy and breast-feeding
In case of pregnancy, ask your doctor, pharmacist, or health professional for advice before having a skin prick test done. Skin prick testing can be performed if you are breast feeding.

Driving and using machines
Soluprick® Positive and Negative controls have no known negative effect on the ability to drive and use machines.

3. HOW TO USE SOLUPRICK®
Prick testing may be performed in children over the age of one if the child is able to tolerate the procedure, but in general should not be performed before of the age of 4.

Your doctor or health professional will carry out the skin prick test for you. The procedure is as follows:
• 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 doctor or healthcare professional.
• The test solutions, Soluprick® Positive control and Soluprick® Negative control are applied in droplets on the skin at an appropriate distance from each other.
• The top layer of the skin is pierced by the doctor or nurse with a lancet through the droplets.
• The reaction is read after 15 minutes. A positive reaction is a pale small raised swelling or wheal with a red edge.

4. POSSIBLE SIDE EFFECTS
Like all medicines, Soluprick® can cause side effects, although not everybody gets them.

Soluprick® Positive Control will cause the expected local effects associated with histamine. The Positive control will produce a hard raised wheal, which may be surrounded by a red area and local itching.

In some cases you may experience slight pain at the skin prick test control site.

If any of the side effects gets serious, or if you notice any side effects not listed in this leaflet, please tell your doctor or pharmacist.
5. HOW TO STORE SOLUPRICK®

- Keep out of the reach and sight of children.
- The clinic/hospital will store the skin prick test solution.
- Store in a refrigerator (2°C – 8°C).
- Do not use Soluprick® after the expiry date which is stated on the label and carton.
- Soluprick® should be used within six months after first opening.

Medicines should not be disposed of via wastewater or household waste. Ask your pharmacist how to dispose of medicines no longer required. This will help to protect the environment.

6. FURTHER INFORMATION

The active substance in Soluprick® Positive Control is Histamine Dihydrochloride. There is no active substance in Soluprick® Negative Control.

The solutions also contain Glycerol, Phenol, Disodium phosphate dihydrate, Sodium dihydrogen phosphate dihydrate, Sodium Chloride, Sodium hydroxide, Hydrochloric acid and Water for Injection.

What Soluprick® looks like and the content of the pack

Soluprick® is supplied in a glass vial containing 2 ml clear solution.

The vial is closed with a rubber stopper and a screw cap.

Marketing Authorisation Holder:

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

Manufacturer:

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

This medicinal product is authorised in the member states of EEA under the following names:

Soluprick® Positive Control, Soluprick® Negative Control

Marketing Authorisation Number: PL 10085/0019

This leaflet was last approved in: 02/2011

This leaflet will be made available in formats appropriate for the blind and partially sighted people upon request. Please contact: ALK-Abelló Ltd, Tealgate, Hungerford, Berkshire. RG17 OY. United Kingdom. Tel: 01488 686 016
UKPAR Soluprick® Positive and Negative controls, Solutions for skin-prick tests  PL 10085/0019

LABELLING

Soluprick® Positive Control

Carton

Solution for skin prick testing, 2ml.
Histamine dihydrochloride 10mg/ml

Excipients:
Disodium phosphate dihydrate 5.96 mg, Sodium dihydrogen phosphate dihydrate 5.2 mg, Phenol 5.1 mg, Sodium chloride 5.0 mg, Glycerol 0.5 ml, Water for injection q.s. to 1 ml.

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 sight and reach of children.

Soluprick

Positive Control

Histamine dihydrochloride ALK 001

PL no.:10085/0019
Batch nr.: 12345_GB01
Exp. date: 12-2009

Manufacturer
Miguel Sierra, 19 Madrid
ES 28037 Spain
M.A. holder ALK-ABELLO A/S
Bøge Allé 6-8
DK-2970 Hørsholm Denmark

Vial label

Positive Control Histamine dihydrochloride ALK 001

Solution for skin prick testing, 2ml.
10mg/ml

Store at 2°C-8°C. Keep out of sight and reach of children.
Soluprick® Negative Control

Carton

Solution for skin prick testing, 2ml.

Excipients:
Disodium phosphate dihydrate 5.96 mg,
Sodium dihydrogen phosphate dihydrate 5.2 mg,
Phenol 0.1 mg, Sodium chloride 0.0 mg,
Glycerol 0.5 ml, Water for injection q.s. to 1ml.

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 sight and reach of children.

PL no.: 10085/0019
Batch nr.: 12345_GB01
Exp. date: 12-2008

ALK 002

Manufacturer
Miguel Fleta, 19 Madrid
ES-28037 Spain
M.A. holder ALK-ABELLÓ A/S
Bleg Allé 8-8
DK-2970 Horsholm Denmark

Vial label

Negative Control

Solution for skin prick testing, 2ml.

Store at 2°C-8°C.
Keep out of sight and reach of children.

Soluprick

PL no.: 10085/0019
Batch nr.: 12345_GB01
Exp. date: 12-2008