1. NAME OF THE MEDICINAL PRODUCT

Diater Prick, solution for skin-prick test

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

Diater Prick is a diagnostic medicinal product with allergenic extracts to which the patient may be sensitized as drug substance. The concentration of drug substance in Diater Prick depends on the allergen it is intended for:

Mites

ALLERGEN	*CONCENTRATION*
Acarus siro	*0.5 mg/ml*
Blomia tropicalis	*5 HEP*
Dermatophagoides farinae	*5 HEP*
Dermatophagoides pteronyssinus	*5 HEP*
Lepidoglyphus destructor	*5 HEP*
Tyrophagus putrescentiae	*2.5 HEP*
Der p 1	*15 µg/ml*
Der p 2	*16 µg/ml*
Der p 23	*3 µg/ml*

Grass pollens

ALLERGEN	*CONCENTRATION*
Cynodon dactylon	*5 HEP*
Dactylis glomerata	*5 HEP*
Wild grass mix (Dactylis, Lolium, Phleum, Poa)	*5 HEP*
Cultivated grass mix (Secale, Triticum, Hordeum)	*2.85 mg/ml*
Hordeum vulgare	*2.85 mg/ml*
Lolium perenne	*5 HEP*
Phleum pratense	*5 HEP*
Phragmites australis	*5 HEP*
Poa pratensis	*5 HEP*
Secale cereale	*2.85 mg/ml*
Triticum aestivum	*2.85 mg/ml*
Zea mays	*2.85 mg/ml*

Weed pollens

ALLERGEN	*CONCENTRATION*
Amaranthus hybridus	*2.6 mg/ml*
Ambrosia artemisiifolia	*5 HEP*
Artemisia vulgaris	*5 HEP*
Chenopodium album	*5 HEP*
Helianthus annus	*3.5 mg/ml*
Parietaria judaica	*20 HEP*
Plantago lanceolata	*5 HEP*
Rumex acetosella	*3.5 mg/ml*
Salsola kali	*5 HEP*
Taraxacum officinale	*3.5 mg/ml*

Tree pollens

ALLERGEN	*CONCENTRATION*
Cup a 1	*32 µg/ml*
Alnus glutinosa	*2.6 mg/ml*
Betula verrucosa	*2.6 mg/ml*
Corylus avellana	*2.6 mg/ml*
Cupressaceae	*5 HEP*
Fraxinus excelsior	*2.6 mg/ml*
Olea europaea	*5 HEP*
Pinus silvestris	*2.6 mg/ml*
Platanus acerifolia	*5 HEP*
Populus deltoides	*2.6 mg/ml*
Quercus ilex	*2.6 mg/ml*
Quercus robur	*2.6 mg/ml*
Spring trees mix (Alnus, Betula, Corylus, Fraxinus)	*2.6 mg/ml*

Moulds

ALLERGEN	*CONCENTRATION*
Alt a 1	*10 µg/ml*
Alternaria alternata	*2 HEP*
Aspergillus fumigatus	*1.5 mg/ml*
Candida albicans	*1.5 mg/ml*
Cladosporium herbarum	*1.5 mg/ml*
Penicillium notatum	*1.5 mg/ml*

Animal derivatives

ALLERGEN	*CONCENTRATION*
Horse	*0.1 mg/ml*
Rabbit	*2 mg/ml*
Cat	*2 HEP*
Dog	*1.5 HEP*
Cow	*2 mg/ml*

Nuts

ALLERGEN	*CONCENTRATION*
Almond	*3 mg/ml*
Cashew	*3 mg/ml*
Hazelnut	*3 mg/ml*
Peanut	*3 mg/ml*
Cacao	*3 mg/ml*
Chestnut	*3 mg/ml*
Walnut	*3 mg/ml*
Pine nut	*3 mg/ml*
Sunflower seeds	*3 mg/ml*
Pistachio	*3 mg/ml*

Cereals and legumes

ALLERGEN	*CONCENTRATION*
Rice	*3 mg/ml*
Soya husk	*3 mg/ml*
Chickpea	*2 mg/ml*
Gluten	*3 mg/ml*
Corn flour	*3 mg/ml*
Soya flour	*3 mg/ml*
Wheat flour	*3 mg/ml*

White bean	*2 mg/ml*
Lentil	*2 mg/ml*
Alpha-amylase	*1 mg/ml*

Milk and dairy products

ALLERGEN	*CONCENTRATION*
Alpha-lactoalbumin	*1 mg/ml*
Beta-lactoglobulin	*1 mg/ml*
Casein	*5 mg/ml*
Cow milk	*10 mg/ml*
Goat milk	*10 mg/ml*

Egg and fractions

ALLERGEN	*CONCENTRATION*
Egg white	*2 mg/ml*
Entire egg	*2 mg/ml*
Ovalbumin	*1 mg/ml*
Lysozyme	*1 mg/ml*
Yolk	*2 mg/ml*

Fish, seafood and molluscs

ALLERGEN	*CONCENTRATION*
Clam	*3 mg/ml*
Tuna	*3 mg/ml*
Cod	*3 mg/ml*
Squid	*3 mg/ml*
Prawn	*3 mg/ml*
Sole	*3 mg/ml*
Mussel	*3 mg/ml*
Hake	*3 mg/ml*
Salmon	*3 mg/ml*
Sardine	*3 mg/ml*
Cuttlefish	*3 mg/ml*

Fruits and vegetables

ALLERGEN	*CONCENTRATION*
Avocado	*15 mg/ml*
Garlic	*20 mg/ml*
Strawberry	*15 mg/ml*
Bean	*10 mg/ml*
Green bean	*10 mg/ml*
Kiwi	*10 mg/ml*
Lettuce	*10 mg/ml*
Apple	*15 mg/ml*
Peach	*10 mg/ml*
Peach peel	*10 mg/ml*
Peach pulp	*15 mg/ml*
Melon	*15 mg/ml*
Orange	*15 mg/ml*
Green pepper	*10 mg/ml*
Pineapple	*20 mg/ml*
Banana	*15 mg/ml*
Tomato	*15 mg/ml*
Grape	*20 mg/ml*

Meats

ALLERGEN	*CONCENTRATION*
Chicken	*2 mg/ml*
Cow	*2 mg/ml*
Pork	*2 mg/ml*

Spices

ALLERGEN	*CONCENTRATION*
Cinnamon	*10 mg/ml*
Cumin	*10 mg/ml*
Mustard	*5 mg/ml*
Oregano	*20 mg/ml*
Sesame	*10 mg/ml*

Insects

ALLERGEN	*CONCENTRATION*
Blatella germanica	*0.5 mg/ml*
Periplaneta americana	*0.5 mg/ml*

Miscellaneous

ALLERGEN	*CONCENTRATION*
Anisakis simplex	*1 mg/ml*
BSA	*1 mg/ml*
Latex	*10 mg/ml*

Controls

CONTROLS	*CONCENTRATION*
Positive (Histamine dihydrochloride)	*10 mg/ml*
Negative	

For the full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM

Solution for skin-prick test.

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

This medicinal product is for diagnostic use only.

Diater Prick produces a positive reaction that consists in a wheal with or without erythema in the application area in those patients that are allergic to the tested active substance (Bousquet et al. 2012).

Diater Prick test is intended for the diagnosis of specific IgE-mediated allergy, type I as described in the Gell and Coombs classification (Gell & Coombs 1963).

Literature references

- Bousquet, J., L. Heinzerling, et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" Allergy 67(1): 18-24.
- Gell, P.G.H. and Coombs, R.R.A. (1963) "The classification of allergic reactions underlying disease" Clinical Aspects of Immunology. Blackwell Science.

4.2 Posology and method of administration

Posology

A drop of Diater Prick on the surface of the skin is enough to perform a skin-prick test. Skin-prick testing should be performed by properly trained health care personnel only.

Paediatric population

The safety and efficacy of Diater Prick in the pediatric population has not been established. Nonetheless, the current guidelines on allergy diagnosis from GA^{2}LEN-ARIA ("Practical guide to skin prick tests in allergy to Aeroallergens", Bousquet et al. 2012) and EAACI ("Testing children for allergies: why, how, who and when", Eigenmann et al. 2013), recommend the use of skin prick tests for diagnosis of IgE-mediated allergies in children.

Skin prick tests must be previously suggested by a clinical history and a physical exam. Although there is no lower age limit to perform the skin prick tests, results should be interpreted with caution in children younger than 2 years of age (Eigenmann et al. 2013).

Literature references

- Bousquet, J., L. Heinzerling, et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" *Allergy* 67(1): 18-24.
- Eigenmann PA, Atanaskovic-Markovic M. et al. (2013) "Testing children for allergies: why, how, who and when" *Pediatr Allergy Immunol* 24: 195–209.

Method of administration

- The skin prick test is usually performed on the volar surface of the forearm. Alternatively, the prick test may be carried out on the patient's back.
- The skin area is cleaned with alcoholic solution and dried.
- A drop of each of the tested substance is applied on the skin spaced at least 2 cm apart to prevent cross-contamination. The forearm should be at rest. Positive and negative controls are applied after the active tests.
- The skin is punctured by passing a lancet through the drops. A new lancet is used for every drop, discarding it after each use.
- Drop excess is carefully removed with a tissue to prevent cross-contamination.
- The patient should not scratch or rub the tested skin area.
- The result of test is read after 15 minutes.
- A wheal with a diameter of at least 3 mm, with or without erythema, is considered to be a positive reaction (Bousquet et al. 2012).
- No reaction is expected for the negative control. If a positive result is obtained, the skin-prick test is not reliable.

4.3 Contraindications

The use of Diater Prick is contraindicated in the following cases:

- Hypersensitivity to any of the excipients listed in section 6.1.
- Eczema (i.e. atopic dermatitis), dermographism and urticaria in the skin area selected to perform the skin test.
- Use of antihistamines within two days prior to the skin prick test (see section 4.5)
- The patient is taking beta-blockers for heart diseases or for controlling high blood pressure

Literature references

- Eigenmann PA, Atanaskovic-Markovic M. et al. (2013) "Testing children for allergies: why, how, who and when" Pediatr Allergy Immunol 24: 195–209.
- Bernstein, IL, Li, JT. Et al. (2008) "Allergy diagnostic testing: An updated practice parameter" Annals of Allergy, Asthma and Immunology vol 100, no. 3 SUPPL. 3.
- Bousquet, J., L. Heinzerling, et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" Allergy 67(1): 18-24.

4.4 Special warnings and precautions for use

Skin-prick testing should be performed by properly trained health care personnel only.

Prick testing solutions must not be used to perform intradermal testing.

The patient should be free of infectious diseases, fever or inflammatory reactions at the time of testing, unless the skin test is urgently needed. Also, dermographism, dermatitis and eczema in the testing area could influence the interpretation of the test (Bousquet et al. 2012).

Some medicinal products may suppress the result of the skin tests, so it is imperative to ask the patient about their use in the previous days (see section 4.5).

If the patient is receiving immunotherapy treatment for allergy, the skin test should be performed at least 1 week after the administration of the last dose of immunotherapy. Similarly, administration of the next dose of immunotherapy should be performed at least 2 or 3 days after the completion of the skin test.

The patient should not scratch or rub the area used to perform the test. After performing the skin test, the patient should be monitored for at least 30 minutes.

In exceptionally rare cases an anaphylactic reaction may appear after skin prick testing. If that reaction occurs, administer adrenaline.

Paediatric population

Skin prick tests must be previously suggested by a clinical history and a physical exam. Results should be interpreted with caution in children younger than 2 years of age (Eigenmann et al. 2013).

Literature references

- Bousquet, J., L. Heinzerling, et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" Allergy 67(1): 18-24.
- Eigenmann PA, Atanaskovic-Markovic M. et al. (2013) "Testing children for allergies: why, how, who and when" Pediatr Allergy Immunol 24: 195–209.

4.5 Interaction with other medicinal products and other forms of interaction

No interaction studies have been performed.

In general, antihistamines, corticosteroids, chromones and all medication that present a concomitant antiallergic activity, can alter the results of skin tests. In the case of oral antihistamines, it is recommended to suspend its administration two days before the cutaneous test. Other medicinal products not related to the

treatment of allergic diseases may have influence, as anxiolytics but not antidepressants (Bousquet et al. 2012).

The use of beta-blockers or ACE inhibitors should be discontinued 48 hours before the test, under medical supervision and adequate control of blood pressure (Bernstein et al. 2008). For patients following immunotherapy treatment, see section 4.4.

The drug clearance periods recommended by the EAACI (European Academy of Allergy and Clinical Immunology) in their "Practical Guide to Skin Prick Tests in Allergy to Aeroallergens" (Bousquet et al. 2012) for drugs with inhibitory effect on the skin prick tests are summarized in the table below:

Treatment	**Clearance period**
Oral H1-antihistamines	2-7 days
Imipramine	Up to 21 days
Phenothiazines	Up to 10 days
Topical skin corticosteroids	Up to 7 days
UV light treatment systemic depending on light source, most intensive with PUVA	Up to 4 weeks

Literature references

- Bousquet, J., L. Heinzerling, et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" Allergy 67(1): 18-24.
- Bernstein, IL, Li, JT. Et al. (2008) "Allergy diagnostic testing: An updated practice parameter" Annals of Allergy, Asthma and Immunology vol 100, no. 3 SUPPL. 3.

4.6 Fertility, pregnancy and lactation

Pregnancy

There are no or limited amount of data from the use of Diater Prick in pregnant women.

Breast-feeding

It is unknown whether these allergenic extracts/metabolites are excreted in human milk. A risk to the newborns/infants cannot be excluded.

Fertility

No information on the safety of the medicinal product for fertility is available.

4.7 Effects on ability to drive and use machines

Diater prick has no or negligible influence on the ability to drive and use machines.

4.8 Undesirable effects

Adverse reactions occur immediately or hours after the administration. They are classified into:

Local reactions
Such as erythema, edema or swelling, with or without itching at the puncture site. Typically, they appear after 10-60 minutes and persist for several hours, disappearing without treatment.

Moderate systemic reactions
Such as large papules, erythema and pruritus that may lead to a generalized urticaria or rash with the presence of ocular and nasal symptoms and Quincke's edema. The onset of symptoms usually occurs between a few minutes and 4-6 hours after the test.

Severe systemic reactions:
Anaphylactic syndrome can appear immediately or within minutes of performing the test. Usually, it is preceded by symptoms such as palmar and plantar pruritus, itching on the tongue and the throat and can lead to a rapid collapse that affects multiple organ systems: vascular collapse with strong hypotension, nasal congestion, bronchospasm and laryngeal edema, generalized pruritus, urticaria and angioedema, abdominal pain, nausea, vomiting and diarrhea; tinnitus, dizziness, relaxation of the sphincters, convulsions and loss of consciousness.

Paediatric population
Overall, the adverse reactions found in children and adolescents are similar to those found in adults.

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

4.9 Overdose

No overdosing is expected from the correct usage of Diater Prick as the product is administered locally as a skin-prick test in very low doses (approximately 16 x 10^{-3} µl, Antico et al. 2000).

Literature references

- Antico A, Lima G, Arisi M, Ostan A, Morrica B. (2000) "Assay of prick test inoculum volume. II Average values and individual variability" Ann Allergy Asthma Immunol. 85(2):145–149.

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Group V (Various). ATC code: V04CL Test for allergic diseases

Mechanism of action

Skin IgE mediated reactions occur within minutes (Early Phase Reaction = EPR) as a wheal and flare. The EPR depends on both pro inflammatory mediators and neurogenic cell and it is taken into account when interpreting this type of cutaneous test. The EPR is frequently followed by a late phase reaction (LPR = Late Phase Reaction) that manifests itself as an erythematous indurated inflammatory reaction that starts 1-2 hours after completion of the skin test, it reaches the peak within 6-12 h and then solves after 24-48 h.

The immediate response is induced by mast cell degranulation upon contact with the allergen. Histamine is the main mediator but not the only one. Other mediators involved are tryptase D2 PG, LT C4, kallikrein, Tx B2, PAF and neurogenic mediators as Substance P, Neurokinin A and related peptide calcitonin gene (CGRP). Recently, it has been shown that the presence of mast cells IL4 + is correlated with the size of the wheal (Saarinen, Harvima et al. 2001). In the delayed reaction involves mast cells, CD4 + RO (memory phenotype), eosinophils and basophils lymphocytes. Histamine plays a more limited role with a higher participation of PG D2 and LT C4 and cytokines such as IL-1β, IL-6, GM-CSF, IL-4 and 5, IL-2 and IFN-γ, chemokines, RANTES and MCP-3.

Diagnostic skin tests for IgE-dependent reactions (immediate hypersensitivity), evaluate IgE-mediated responses. The results of the test together with a clinical history suggestive of allergy confirm the etiology of the process and allow to introduce environmental control measures to avoid the allergen and ultimately can be used to indicate an specific immunotherapy treatment for the patient (Zacharisen 2000).

Skin prick test main limitation is that a positive reaction does not necessarily mean that the symptoms are caused by an IgE-mediated reaction because symptom-free subjects may also have allergen-specific IgE and therefore give a positive cutaneous response.

Even asymptomatic relatives of allergic individuals have more positive tests than the general population. This requires a careful interpretation of the skin test results always correlated with the clinical history of the patient (Adinoff, Rosloniec et al. 1990).

Paediatric population

The current guidelines on allergy diagnosis from GA^{2}LEN-ARIA ("Practical guide to skin prick tests in allergy to Aeroallergens", Bousquet et al. 2012) and EAACI ("Testing children for allergies: why, how, who and when", Eigenmann et al. 2013), recommend the use of skin prick tests for diagnosis of IgE-mediated allergies in children.

Mechanism of action is similar to that in adults. Skin prick tests are easily performed in children, and are essential for deciding treatment, either it is allergen avoidance or specific immunotherapy (Eigenmann et al. 2013).

Literature references

- Saarinen, J. V., R. J. Harvima, et al. (2001) "Interleukin-4-positive mast cells are highly associated with the extent of immediate allergic wheal reaction in the skin" Allergy 56(1): 58-64.
- Zacharisen, M. C. (2000) "Allergy skin testing infants: a safe or risky procedure?" Ann Allergy Asthma Immunol 85(6 Pt 1): 429-430.
- Adinoff, A. D., D. M. Rosloniec, et al. (1990) "Immediate skin test reactivity to Food and Drug Administration-approved standardized extracts" J Allergy Clin Immunol 86(5): 766-774.
- Bousquet, J., Heinzerling, L., et al. (2012) "Practical guide to skin prick tests in allergy to aeroallergens" Allergy, 67: 18–24.
- Eigenmann PA, Atanaskovic-Markovic M. et al. (2013) "Testing children for allergies: why, how, who and when" Pediatr Allergy Immunol 24: 195–209.

5.2 Pharmacokinetic properties

Diagnostic skin-prick tests are intended for local use at very low quantities and are administered as a single-dose treatment in a punctual occasion. Therefore, the patient is in contact with very low concentrations of the product and a insignificant absorption of the product at the systemic level is expected, so no data on pharmacokinetics can be collected.

5.3 Preclinical safety data

No data are available.

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Glycerol
Sodium chloride
Sodium dihydrogen phosphate monohydrate
Disodium hydrogen phosphate dihydrate

Phenol
Water for injection

6.2 Incompatibilities

No compatibility studies have been performed. In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.

6.3 Shelf life

Do not use this medicine after the expiry date which is stated on the packaging.

6.4 Special precautions for storage

Store in a refrigerator (2ºC-8ºC). Do not freeze.

Store in the original packaging.

Do not use Diater Prick if the vial has lost some of its contents or if the packaging has been damaged.

6.5 Nature and contents of container

Glass vial (Type I) with rubber stopper (Type I) and dropper.

Each vial contains 2 ml (1 ml for moulds and animal derivatives) solution of allergenic extract.

6.6 Special precautions for disposal

No special requeriments.

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

Do not use this medicinal product if there are visible signs of damage.

7. MARKETING AUTHORISATION HOLDER

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

10. DATE OF REVISION OF THE TEXT

April 2023.