

## Specialist information and product information

# Epicutaneous Test Allergens

### 1. DESIGNATION OF MEDICINAL PRODUCT

See current catalog

Irritant control:

Sodium lauryl sulphate 0.25% in water

### 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

#### Active ingredients:

The medicinally effective component is part of the medicinal product designation depending on the type and amount.

#### Other components:

For a list of the other components, see Section 6.1.

### 3. FORM OF ADMINISTRATION

Solution or ointment for cutaneous application

### 4. CLINICAL DATA

#### 4.1 Areas of application

This medicinal product is a diagnostic agent.

Aqueous allergen solution or ointment for epicutaneous testing on clinical suspicion of contact allergies and photocontact allergies. Sodium lauryl sulphate 0.25% in water as irritant control.

Normally, the need for epicutaneous testing is indicated on clinical suspicion of an allergic contact skin reaction, the acute phase of which has abated by the time the test is carried out. Further possible indications are: Exclusion of a contact allergy with etiologically unexplained eczema, suspicion of provocation or aggravation of an existing dermatosis (e.g. dermatitis/eczema; in particular atopic dermatitis or psoriasis), clarification of exanthema possibly caused by medication.

#### 4.2 Dosage, type and duration of application

For epicutaneous testing, a drop or a 5 mm ribbon of ointment are applied onto the appropriate area of a suitable test chamber. This amount equals approx. 50 µl of the aqueous test preparation and approx. 17 µl of the test ointment. The application is carried out once.

The test chamber is then affixed to healthy, dry skin; generally onto the patient's back. The test area must be free of indications and a preliminary treatment with anti-eczematous active ingredients must have taken place a sufficient time ago.

The assessment of epicutaneous test reactions should take place according to the International Contact Dermatitis Research Group (ICDRG) recommendations and based on a decision passed by the German Contact Allergy Group (DKG) (For diagram see Table 1).

*Table 1*

Symbol	Appearance	Meaning
-	No reaction	Negative
?	Only erythema, no infiltrate	Questionable (allergic or irritant)
+	Erythema, infiltrate, possibly discrete papules	Single positive, allergic reaction
++	Erythema, infiltrate, papules, vesicles	Double positive, allergic reaction
+++	Erythema, infiltrate, confluent vesicles	Triple positive, allergic reaction
irr	Different changes (soap effect, vesicles, blisters, necroses)	Irritant
nt	An allergen contained in a test block but not tested	-

Unspecific irritant reactions may occur which do not indicate a contact allergy due to the current individual irritability status of the skin and the irritant characteristics of a test preparation. Such reactions are in part recognisable as typical phenomena; they can however appear as questionable reactions or, more seldom, as infiltrated erythemas.

The test with the non-allergenic obligatory irritant sodium lauryl sulphate 0.25 in water (irritant control) carried out parallel to the epicutaneous test with allergen preparations can give information on the irritability of the skin at the time of testing.

An irritant reaction (sls1 to sls4: see Table 2) on the irritant control does not necessarily mean that every minor reaction to a test allergen is also an irritant one. However, the probability is higher that irritant or minor, false positive reactions occur which therefore more likely - but not inevitably - are an expression of an irritation and are not to be considered the expression of a contact allergy.

The assessment of the irritant control (sodium lauryl sulphate 0.25% in water) takes place according to the German Contact Allergy Group e.V. (DKG) recommendations acc. the following diagram (for diagram see Table 2):

Table 2

Symbol	Appearance	Meaning
sls0	No reaction	Negative
sls1	Extremely minor/mild erythema or desquamation (selective or diffuse)	Questionable
sls2	Minor/mild erythema, desquamation, edemata or roughening of the skin	Minor
sls3	Moderate erythema, desquamation, edemata or roughness of the skin or minor/slight erosions, vesicles or fissures	Moderate
sls4	Pronounced erythema, desquamation, edemata or roughness of the skin, or erosions, vesicles or fissures	Severe

The test with SLS 0.25% in water as a marker for a hyperreactive skin therefore eases the assessment of erythematous and minor positive reactions to test allergens. Because the skin sensitivity is subject to major fluctuations over time, testing with the irritant control merely provides a statement on the current status and does not allow statements to be made on past or future tests. The fluctuations in skin irritability are also the reason for the moderate reproducibility of the test results with sodium lauryl sulphate 0.25% in water.

The following substances frequently lead to erythematous and/or irritant reactions which in part may also be associated with an infiltrate. In particular questionable and minor positive reactions must therefore be inspected particularly critically as to whether they are in fact the expression of a contact allergy or whether they are unspecific (irritant) phenomena. These test substances are therefore less suitable for general screening and should be tested in a targeted manner should clinical suspicion arise.

(Nitrobutyl)morpholine/(ethylnitrotrimethylene)dimorpholine 1%	Disperse red 11 1%
1,2-benzisothiazoline-3-on, sodium salt 0.1%	Disperse red 17 1%
1,3-diphenylguanidine 1%	Disperse blue 106 0.3%
4,4'-dihydroxybiphenyl 0.1%	Dodecyl gallate 0.3%
Alpha-amyl cinnamic aldehyde 1%	Edate disodium 1%
Alpha-hexyl cinnamic aldehyde 10%	Farnesol 5%
Amalgam alloy metals 20%	Gamma methylionone 1%
Ammonium tetrachloroplatinate 0.25%	Hexylresorcinol 0.25%
Amylcinnamic alcohol 1%	Iodopropinyl butylcarbamate 0.2%
Anisyl alcohol 1%	Isopropyl myristate 10%
Benzophenone-4 (sulisobenzon) 10%	Linalool (stabilised) 10%
Benzotriazole 1%	Methylheptin carbonate 1%
Benzoyl peroxide 1%	Monobenzene 1%
Benzyl benzoate 1%	Narcissus absolute 2%
Benzyl salicylate 1%	Octyl gallate 0.3%
Benzylcinnamate 5%	Octylisothiazolinone 0.025%
bis(dibenzylthiocarbamate)zinc 1%	Orange oil 2%
Bismark Brown R 0.5%	Parabene mix 16%
Butylhydroxytoluene 2%	Phenylephrine hydrochloride 10%
Cetalkoniumchloride 0.1%	Propylene glycol 20% in water
Cetylpyridinium chloride 0.1%	Propylene glycol 5%
Chlorhexidine digluconate 0.5%	Pyrogallol 1%
Cocamidopropylbetaine 1%	Sodium benzoate 5%
Coconutdiethanolamide 0.5%	Sorbic acid 2%
Copper sulphate x 5 H <sub>2</sub> O 1% Di-2-ethylhexylphthalate 5%	Triclosan 2%
Dibutyl phthalate 5%	Tricresyl phosphate 5%
Diethanolamine 2%	Trolamine 2.5%
Diphenyl thiourea 1%	

In general, those test reactions which are assessed via readings taken after 72 (or 96) hours as "+" to "+++" indicate a contact allergy. During the assessment as to whether a test reaction is allergic or irritant, the reaction dynamics can also play a role: A crescendo progression (increase in reaction strength from the 24/48-hour reading to the 72-hour reading) or a plateau reaction (reaction severity remains the same) tend to indicate a true allergic reaction; and a decrescendo progression (reduction in the reaction severity from the 24/48-hour reading to the 72-hour reading) is more likely to indicate an irritation.

The relevance assessment forms the closure of each epicutaneous test. It must be determined, for those allergens to which a reaction has been observed, which meaning this contact allergy has had for patients in the past (anamnestic relevance) and will have in the future (prospective relevance – important for future avoidance of contact with the allergen). The patient must be issued with appropriate information, preferably in the form of an allergy record.

In order to test for a photocontact allergy, the substances are applied in duplicate after determination of the individual MED on UV-A and UV-B. One set is exposed after 24 hours; the second set remains 48 hours and serves as an unexposed epicutaneous control test. The exposed test fields are then covered up with material impervious to light, in order to avoid further light influence. The reading and assessment takes place immediately as well as after 24, 48 and 72 hours. Fluorescent spotlights are suitable for exposing the samples to a light source similar to sunlight (e.g. Philips TL-K40W/09N) with a wavelength of 320-400 nm. For exclusive irradiation with UV-A, the samples are exposed with 5 to 10 J/cm<sup>2</sup>.

#### Children and the elderly

Children from the age of 2 and elderly people can be tested with the specified concentrations and dosages. Small children under 2 years of age should only be subjected to epicutaneous tests if indications are severe, and the number of tests should be limited to the anamnesticly suspicious substances.

#### 4.3 Contraindications

- Known hypersensitivity to one of the other components in the test preparations
- Acute or generalised dermatitis; the test area must have been free of eczematous indications for at least 14 days.
- Therapy with systemic and/or local corticoids  
The application of corticoids must be ceased 7 – 10 days before the epicutaneous test. The intake of a 10 – 20 mg prednisolone equivalent will not influence the test.
- After strong solar irradiation or UV irradiation, you must wait for four weeks before carrying out an epicutaneous test.
- An epicutaneous test cannot be assessed if the patient is being treated with cyostatic medicinal products or is undergoing an immunosuppressive therapy.

Because sodium lauryl sulphate 0.25% in water is an obligatory irritant, the test should never take place alone, but rather should be carried out exclusively as an irritant control parallel to testing the epicutaneous test allergens.  
(For application of the irritant control sodium lauryl sulphate 0.25% in water, see 4.2. Dosage, type and duration of the application.)

#### 4.4 Special warning guidelines and precautionary measures for the application

In order to avoid falsification of the test results, please observe the following points:

The test area must have been free of eczematous indications for at least 14 days. The administration of systemic corticoids and/or topical corticoids must have ceased 7 – 10 days before. You must wait 4 weeks after the patient has been subjected to strong sunlight irradiation or UV irradiation. Whilst the allergens are applied, severe physical movements, exertion or soaking of the test patch (e.g. when having showers or baths) must be avoided.

If the test result is doubtful or unclear, the test can be repeated at the earliest after all test reactions have abated; a waiting period of at least approx. 2 months must be maintained.

#### 4.5 Interactions with other medicinal products and other interactions

No interaction trials have been carried out.

#### 4.6 Pregnancy and breastfeeding

During pregnancy and breastfeeding, epicutaneous tests should not be carried out if possible.

#### 4.7 Effects on roadworthiness and capability when operating machines

Not applicable.

#### 4.8 Side effects

Any skin reactions occurring, for example itching or reddening of the skin with formation of blisters at the point of application must be interpreted in terms of the contact allergy to be tested or a photocontact allergy.

The assessment of side effects is based on the following frequency data:

<b>Very frequent:</b>	> 1 of 10 people tested
<b>Frequent:</b>	< 1 of 10, > 1 of 100 people tested
<b>Occasional:</b>	< 1 of 100, > 1 of 1000 people tested
<b>Seldom:</b>	< 1 of 1,000, > 1 of 10,000 people tested
<b>Very seldom:</b>	< 1 of 10,000 people tested, including individual cases

The side effects in order of severity are stated in each frequency group.

Sensitisations due to the epicutaneous test (active sensitisation) are seldom.

An active sensitisation can be suspected after late reactions which occur for the *first* time approx. 10-21 days after application of the epicutaneous test. However, because such late reactions alone are not proof of an active sensitisation, this must be determined via a repeat test. If a positive reaction then results within 72-96 hours, this allows to conclude that an active sensitisation due to the first test is probable. Late reactions after 10-21 days can however be due to other reasons. On some patients, they occur habitually and do not indicate an active sensitisation.

#### General illness and complaints at the place of application

Frequent: Active sensitisation due to the test allergen p-phenylendiamine 1%

Occasional: Active sensitisation due to the test allergen epoxy resin 1%

Seldom: Sensitisation due to epicutaneous tests

Very seldom: Immediate allergic reaction (Type I)

Frequency unknown (frequency cannot be estimated based on the data available):

Tests using p-tert.-butylphenol-formaldehyde resin 1% may cause depigmentation of the skin.

Should sweating, dizziness or similar symptoms occur after application of the test allergens, the doctor must be informed immediately.

#### Emergency measures for side effects:

Unexpectedly severe local or general reactions occur very seldom during epicutaneous tests, but anaphylactic reactions have been described in individual cases. For this reason, emergency equipment must be available. Typical alarm symptoms for an impending anaphylactic shock are burning, itching and a feeling of heat on and under the tongue, in the throat, in the palms of the hands and on the soles of the feet. The therapy must be carried out acc. the current results of the Consensus Conference "Acute therapy of anaphylactoid reactions".

#### 4.9 Overdosage

There have been no reports of overdosage.

### 5. PHARMACOLOGICAL CHARACTERISTICS

#### 5.1 Pharmacodynamic characteristics

Pharmacotherapeutic Group: Allergy tests; ATC code: V04C L

The pharmacodynamics of the epicutaneous test preparations correspond to the pathogenesis of the allergic contact eczemas.

#### 5.2 Pharmacokinetic characteristics

There is no special pharmacokinetic data relating to only one substance for the epicutaneous test preparations.

### 5.3 Preclinical safety data

The concentrations in which the substances to be tested are contained in the test preparations lie between 0.002% and 100%. This means that in the prescribed application of 17 µl ointment or one drop of solution (approx. 50 µl), between 0.29 µg and 50 mg of active ingredient are applied to the skin once. Even if complete resorption is assumed, no toxic effects are to be expected.

## 6. PHARMACEUTICAL DATA

### 6.1 List of other components

**White petrolatum, purified water, glycerine or ethanol.**

**Sorbitan sesquioleate** contained in  
Cinnamic aldehyde 1 %  
Amylcinnamic aldehyde 1%  
Fragrance mix 8%  
Oakmoss absolute 1%  
Geraniol 1%  
Hydroxycitronellal 1%  
Isoeugenol 1%  
Cinnamic aldehyde 1 %

**Magnesium nitrate** contained in  
MCI/MI 0.01%

**Paraffin, liquid** contained in  
Wool wax alcohols 30%

**Paraffin, hard** contained in  
Amerchol® L 101 50%  
Fragrance mix II 14%  
Cananga odorata (Ylang ylang III) 10%

### 6.2 Incompatibilities

Not applicable.

### 6.3 Storage life

The expiry date is printed onto every test syringe and applies to unopened containers.  
You must not use the medicinal product after the expiry date stated on the label.

### 6.4 Special precautionary measures for storage

The substances should be stored at temperatures between 2° – 8° C.

The following substance must be stored protected from light:  
Primine 0.01%

**Keep out of the reach and sight of children.**

### 6.5 Type and content of container

Container: pre-filled syringe (PP) with plunger (PE) and cap (PE)  
Package size: 1 syringe with 5ml ointment/solution

### 6.6 Special precautionary measures for disposal and other guidelines on handling

No special requirements.

## 7. HOLDER OF AUTHORISATION

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## 8. INFORMATION STATUS

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## 9. DISTRIBUTION INFORMATION



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