This leaflet format has been determined by the Ministry of Health and the content has been checked and approved in February 2018

## 1. NAME OF THE MEDICINAL PRODUCT

TRUE Test 24, plaster for provocation test

## 2. QUALITATIVE AND QUANTITATIVE COMPOSITION

| | Active substance | microgram/cm$^2$ | microgram/patch |
|---|---|---|---|
| Panel 1 | 1. Nickel sulphate | 200 | 162 |
| | 2. Wool alcohols | 1000 | 810 |
| | 3. Neomycin sulphate | 600 | 486 |
| | 4. Potassium dichromate | 54 | 44 |
| | 5. Caine mix[a)] | 630 | 510 |
| | 6. Fragrance mix[b)] | 430 | 348 |
| | 7. Colophony | 1200 | 972 |
| | 8. Paraben mix[c)] | 1000 | 810 |
| | 9. Quinoline mix[d)] | 190 | 154 |
| | 10. Balsam of Peru | 800 | 648 |
| | 11. Ethylenediamine dihydrochloride | 50 | 41 |
| | 12. Cobalt chloride | 20 | 16 |
| Panel 2 | 13. p-tert Butylphenol formaldehyde resin | 45 | 36 |
| | 14. Epoxy resin | 50 | 41 |
| | 15. Carba mix[e)] | 250 | 203 |
| | 16. Black rubber mix[f)] | 75 | 61 |
| | 17. Cl+Me-Isothiazolinone | 4 | 3 |
| | 18. Quaternium-15 | 100 | 81 |
| | 19. Mercaptobenzothiazole | 75 | 61 |
| | 20. p-Phenylenediamine | 80 | 65 |
| | 21. Formaldehyde[g)] | 180 | 146 |
| | 22. Mercapto mix[h)] | 75 | 61 |
| | 23. Thiomersal | 7 | 6 |
| | 24. Thiuram mix[i)] | 27 | 22 |

a) Five parts of benzocaine, one part of dibucaine hydrochloride and tetracaine hydrochloride.
b) Five parts of geraniol and oak moss, four parts of hydroxycitronellal and cinnamylalcohol, two parts of cinnamaldehyde and eugenol and one part of isoeugenol and α-amylcinnamaldehyde.
c) Equal weights of methyl parahydroxybenzoate, ethyl parahydroxybenzoate, propyl parahydroxybenzoate, butyl parahydroxybenzoate and benzyl parahydroxybenzoate.
d) Equal weights of clioquinol and chlorquinaldol.
e) Equal weights of diphenylguanidine, zincdiethyldithiocarbamate and zincdibutyldithiocarbamate.
f) Two parts of N-isopropyl-N'-phenyl paraphenylenediamine, five parts of N-cyclohexyl-N'-phenyl paraphenylenediamine and five parts of N,N'-diphenyl paraphenylenediamine.
g) Actually contains N-hydroxymethyl succinimide.
h) Equal weights of morpholinylmercaptobenzothiazole, N-cyclohexylbenzothiazylsulphenamide and dibenzothiazyl disulphide.
i) Equal weights of disulfiram, dipentamethylenethiuram disulphide, tetramethylthiuram disulphide and tetramethylthiuram monosulphide.

For the full list of excipients, see section 6.1.

## 3. PHARMACEUTICAL FORM

Plaster for provocation test

TRUE Test 24 consists of 2 panels of surgical plaster each with 12 patches. Each patch is coated with a film containing the test substance.

## 4. CLINICAL PARTICULARS

### 4.1 Therapeutic indications

This medicinal product is for diagnostic use in adults only.

Diagnosis of allergic contact dermatitis.

### 4.2 Posology and method of administration

1) Open the package and remove the test panel.

2) Remove the protective plastic from the test surface of the panel. Be careful not to touch the test substances.

3) Position the test on the patient's back - the outer part of the upper arm can eventually be used. Smooth gently outward toward the edges, making sure each allergen makes firm contact with the skin. The 2 panels are placed on each side a few cm from the midline.

4) Indicate on the skin the location of the two notches on each panel with a medical marking pen.

The test should be applied on a healthy skin, free from scars, acne, dermatitis, or any other condition which may interfere with interpretation of test reactions (see section 4.4).

The patient should wear TRUE Test 24 for 48 hours without removing it and being careful not to get the test area wet (water, sweat).

Following this period, the test is removed. The reaction should be read 1/2 an hour after removal of the test and again 1-2 days after removal, when the allergic reactions are fully developed and mild irritant reactions have faded.

Neomycin sulphate and p-phenylenediamine, however sometimes cause reactions, which may not appear until 4-5 days after the application. Patients should be instructed to report this. If appropriate, an additional office visit with a late reading at day 5-7 will verify a late reaction.

Reading of the test should be done by the doctor.

**Interpretation**

An identification template is provided with each package of TRUE Test 24 for quick identification of any allergen, which causes a reaction. To assure correct positioning, marks on the skin should correlate with the notches on the template. Notice the difference between page 1 and 2 on the template corresponding to panel 1 and 2.

The interpretation method recommended by the International Contact Dermatitis Research Group is:

| | |
|---|---|
| - | Negative reaction |
| ? | Doubtful reaction; faint macular erythema, none or insignificant infiltration |
| + | Weak (nonvesicular) positive reaction; erythema, weak infiltration, possible papules |
| ++ | Strong (vesicular) positive reaction; erythema, infiltration, papules, vesicles |
| +++ | Extreme positive reaction: intense erythema, infiltrate, coalescing vesicles |
| IR | Irritant reaction of different types |
| NT | Not tested |

**Note**

- Patients showing a negative reaction may still be sensitised to another substance not included in this test panel. Furthermore, false-negative results may occur. Retesting or testing with complementary substances may be indicated.

- A positive reaction should meet the criteria for an allergic reaction (papular or vesicular erythema and infiltration).

- Pustules, as well as patchy follicular or homogeneous erythema without infiltration are usually signs of irritation and do not indicate allergy.

What is important in evaluation a positive test response is not the number of plusses assigned to the test response, but determining whether the response is a truly positive reaction (caused by allergy) or a non-specific irritant reaction.

*Paediatric use:*
TRUE Test 24 is recommended for use in adults only, as safety and effectiveness of TRUE Test 24 in children has not been established.

## 4.3 Contraindications

Severe or generalized active dermatitis. Testing should be postponed until the acute course has past.

Known hypersensitivity towards other excipients contained in the test besides the active substances (see 6.1 List of excipients)

## 4.4 Special warnings and precautions for use

Sensitisation to a substance on the test panel only seldom occurs. A test reaction that appears on day 10 or later may be a sign of contact sensitisation.

Excited skin syndrome (angry back) is a state of hyperreactivity induced by dermatitis on other parts of the body or by a strong positive skin test reaction. Therefore, test results should be evaluated carefully in patients with multiple, positive, concomitant patch test results. To determine which reactions are false positive, retesting at a later date may be necessary.

The use of TRUE Test 24 in patients with a known history of anaphylactoid reactions should be carefully evaluated before application.

Excessive sweating and sun exposure of the test site is to be avoided. Sun tan may decrease patch test reactivity and cause false negative tests.

Avoid applying the test on skin with acne, scars, dermatitis or any other condition that may interfere with test results.

If a severe patch test reaction develops, the patient may be treated with a topical corticosteroid. In rare case treatment with systemic corticosteroid may be necessary.

Butylated hydroxyanisole (BHA) (E320) and Butylated hydroxytoluene (BHT) (E312) are present as antioxidants in allergen patch no. 7 Colophony (panel 1). BHA and BHT may cause local skin reactions (e.g. contact dermatitis), so a false positive reaction for Colophony may occur.

## 4.5 Interaction with other medicinal products and other forms of interaction

Use of immunosuppressants (including steroids) may suppress a positive patch test reaction. Use of topical steroids on the test site or oral steroids (equivalent to 20 mg prednisolone or more on a daily basis) should be discontinued for at least two weeks prior to testing.

No interaction studies have been performed.

## 4.6 Fertility, pregnancy and lactation

There are no data from the use of TRUE Test 24 in pregnant women. Animal studies are insufficient with respect to reproductive toxicity. TRUE Test 24 is not recommended during pregnancy, unless indispensable, and should not be used during breast-feeding.

## 4.7 Effects on ability to drive and use machines

Not relevant.

## 4.8 Undesirable effects

| System organ classes | Frequency | Undesirable effect |
|---|---|---|
| Skin and subcutaneous tissue disorders | Very common (≥1/10) | long-lasting reaction, irritation caused by the surgical tape |
| | Common (≥1/100 to <1/10) | transient hypopigmentation/hyperpigmentation |
| | Uncommon (≥1/1,000 to <1/100) | flare-up of dermatitis |
| | Rare (≥1/10,000 to <1/1,000) | sensitisation |

In extremely rare cases and only in relation to certain substances, anaphylactic reactions (systemic reaction, possibly with a life-threatening drop of blood pressure) have occurred. The allergy departments are for other reasons prepared to treat such incidences. Anaphylactic type reactions in relation to application of TRUE tests are not documented.

Irritation caused by the surgical tape adhesive disappears rapidly.

A positive test reaction usually disappears within 1-2 weeks. Long-term reactions are positive reactions, which persist for weeks or months.

Positive test reaction may leave an area of transient hypopigmentation/hyperpigmentation at application site.

A flare-up of dermatitis may be observed when testing during an active phase of dermatitis.

Sensitisation. See section 4.4 (special warnings and special precautions for use).

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. Any suspected adverse events should be reported to the Ministry of Health according to the National Regulation by using an online form

https://forms.gov.il/globaldata/getsequence/getsequence.aspx?formType=AdversEffectMedic@moh.gov.il

## 4.9 Overdose

Not relevant.

# 5. PHARMACOLOGICAL PROPERTIES

## 5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other diagnostic agent, ATC code: V 04 CL

A positive response to the patch test is a classical delayed hypersensitivity reaction (type IV), which can appear within 6-96 hours after exposure.

The cell-mediated response involves the Langerhans' cell and T-lymphocytes, which interact and produce lymphokines. These lymphokines then form lymphocyte clones with trigger macrophages to cause a cutaneous inflammation.

Clinical signs of a positive contact dermatitis reaction are: erythema, oedema papules, vesicles and a palpable dermal inflammatory infiltrate at the test area.

### 5.2 Pharmacokinetic properties

Not applicable.

### 5.3 Preclinical safety data

Preclinical data do not indicate a risk for acute toxicity. Some of the substances have shown carcinogenic potential in animal studies. Nevertheless, these findings do not represent a significant additional risk for the clinical use of TRUE Test 24 taking into consideration dose levels, time of exposure and/or other modes of exposure to the same substances.

## 6. PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Besides the active substances, stated under 2. the test contains the following excipients: Plaster of polyester fibres plus binder (ethyleneacetate copolymer) with acrylic adhesive, polyester patches, povidone 90, hydroxypropyl cellulose, methyl cellulose , ß-cyclodextrin, sodium carbonate, sodium bicarbonate, butylhydroxyanisole and butylhydroxytoluene.

### 6.2 Incompatibilities

Not applicable.

### 6.3 Shelf life

The expiry date of the product is indicated on the packaging materials.

### 6.4 Special precautions for storage

Store in a refrigerator (2-8 °C).

### 6.5 Nature and contents of container

Each panel is covered by a protective sheet of silicone-treated polyethylene and then packed in airtight pouches of packaging laminate.

For stabilization purposes, panel 2 contains a desiccant.

Pack size:
Carton box with 1 test unit
Carton box with 10 test units

1 unit = one panel 1, one panel 2 and a reading template.
Not all pack sizes may be marketed.

## 6.6 Special precautions for disposal and other handling

No special requirements for disposal.

## 7. MANUFACTURER

SMARTPRACTICE DENMARK ApS
Herredsvejen 2
3400 Hilleroed
Denmark

## 8. REGISTRATION HOLDER

Gamida Ltd.
32 Shaham, Keiryat Matalon,
Petach Tikva

## 9. MARKETING AUTHORISATION NUMBER(S)

159-71-34684-00