

# Alocado™

## Test Report

**Kedo Eurocosmetics** Ltd. and **Spider Pharm Industries** Ltd. entered an agreement in September 2006, to test the Alocado™ product line on volunteers suffering from psoriasis as requested by **Teva Pharmaceuticals** Ltd. Hungary. This document contains the test results, which are available for anyone wishing to be informed about the products. Our aim is to address physicians, specialists (dermatologists), pharmacists and patients all at the same time.

### Section 1

Psoriasis is a classic and common dermatological condition. It is defined as follows: an **“inflammatory skin condition with increased epithelial proliferation, characterized by infiltrated plaques and silvery scaling”**. According to international statistics 2-3% of the overall population are affected by this condition in varying degrees. (Varies geographically).

In Hungary, the estimated number of patients lies between 200,000 and 300,000, although much fewer visit their physicians, because part of them have already lost faith in receiving effective treatment; the other reason for not seeing a physician is that they are in remission and do not see its importance. The causes of psoriasis are still unclear, but research has significantly advanced our understanding concerning the inflammatory process and the immunological background of the illness.

The cause of this condition is believed to be genetic in nature. The condition is characterized by an increased sensitivity of the skin, reacting to external and internal stimuli. These stimuli are the so-called “provoking factors”. The most important provoking factors are mechanical (injury or irritation of the skin), immunological, metabolic stimuli, and provocation by medicine and stress.

A characteristic feature of the illness is the deterioration of quality of life. This is not a life-threatening illness and its gravity is determined not by the physician, but the patient. This condition influences the patient’s everyday life as well as their social and working activities. Deterioration of the quality of life due to psoriasis can be as serious as that caused by heart disease or depression.

Clinically speaking, it is the most versatile skin disease. The most often affected parts of the body are: the scalp, the knees, the elbow, the buttocks, the genitalia, the navel, the flexures and the nails. Its most frequent forms: thick, silvery plaque, extensive, inflammatory plaque, tiny, punctiform lesions and incidental small blisters.

From a medical point of view, the degrees of illness can range from an asymptomatic state through mild symptoms, with isolated plaques to persistent, thick plaques; from a gradual spread to a degree when joints are also affected and the complete surface of the skin is covered by erythroderma.

According to **Prof. Christopher Griffith**, the gravity of the illness depends on the degree of deterioration of quality of life, the resistance to therapy and the degree lesion spreading.

Seeing as psoriasis is an illness that influences the quality of life and its gravity is determined by the patient, the physician compares his or her own findings with the evaluation of the patient and offers the patient all available therapeutic alternatives. Finally they will be able to mutually choose the best one.

The therapy can be either local or systemic.

Local treatment consists of two phases: the first is stopping acute symptoms, and the second is maintaining therapy with the aim of avoiding a relapse. As for the medication used in maintenance therapy it is of utmost importance that they be well tolerated by the patient, without any side effects.

**There are very few preparations used so far, that comply with the above requirements.** Traditional treatment possibilities for the acute phase are: coal tar, local corticosteroids, vitamin D analogues, local retinoids, and keratolytic agents (compounds containing salicylic acid, for external application). Besides these, Photo-therapy (PUVA, UVB) and bath therapy may also be applied.

The above therapies are effective, but they have several side effects.

- Corticosteroids can cause atrophy of the skin, vasodilation may occur; fungal or bacterial infections may emerge.
- Vitamin D may be irritating and expensive.
- The application of coal tar and some of the photo-therapies in large doses are carcinogenic.
- Salicylic acid in high concentrations is irritating.

From the list of above-mentioned therapies only vitamin D is suitable for maintenance therapy.

So the need for a phase-specific, non-aggressive (non-irritating) maintenance therapy is justified.

## **Section 2**

The Alocado™ product line was developed in 1988 based on formulas developed by physicians and pharmacists working in clinics near the Dead Sea. At that time it was recognized that the surroundings, the water and the mud of the Dead Sea had a healing effect on the patients suffering from skin diseases.

This was also the time when some publications on side effects and disadvantageous features of steroids appeared. Realizing these facts, the inventors were inspired to develop a range of products solving all varying problems using a phase specific range of products that were a revolutionary departure from the “all in one” existing medicines. During their work, they could make use of some publications analysing therapeutic effects of some vegetable oils like Avocado oil and the Aloe Vera extract. Besides this, patients wished to enjoy remission not only for a week for as long as their treatment at the Dead Sea lasted, but for a longer period of time. This was made possible by being able to take these natural remedies back home.

### **Advantages of the Alocado™ product line are as follows:**

- ✓ It does not contain steroids.
- ✓ It does not contain tar.
- ✓ It does not contain synthetic vitamin D.
- ✓ The acid content never exceeds 2%.
- ✓ The active ingredients are combined with very strong emollients.
- ✓ A unique composition of natural oils (mainly Avocado), Aloe Vera extract and salt from the Dead Sea (not reaching salt concentration levels that could irritate skin).
- ✓ There are special products to treat different symptoms, including open wounds.
- ✓ We offer products for maintenance therapy to be used in state of remission to contribute to palliate symptoms of the next relapse.
- ✓ These products do not have any side effects neither after short- nor after long-term treatment.

### **Section 3**

We began testing Alocado™ products in September 2006. Approximately 25-30 volunteers were recruited to take part in the test, which was not launched at the most favourable period, because psoriasis generally relapses when cold weather is to be expected. Baseline data were collected along with the dermatological examination, i.e. personal data, medical history, and all medication taken before and at the time of this examination were recorded. The state of the skin was photographed, some of these photos will be shown later and are saved on the enclosed DVD. The photos don't always document the changes of conditions exactly, since there was no possibility to take professional photos, and in many cases the pictures are distorted by inappropriate lighting or positioning. This is why we used the PASI index widely accepted in specialist literature to establish condition changes. We established values on the basis of PASI index from the starting state of illness, and during the repeated follow-ups. A short summary on PASI:

The objective skin condition of the patient is expressed by the so called PASI index. This is an internationally accepted index to demonstrate the state of the skin and to establish efficacy of the therapy.

The index evaluates the main symptoms of psoriasis: erythema, induration, and scaling, and the size of the affected area are taken into consideration as well. All these factors are taken into account in the regions of the head, the upper limbs, the torso and the lower limbs. Using different multipliers a relative number is achieved from the sum of these values. This relative number is not quite perfect; e.g. changing from PASI 20 to PASI 10 is much easier than to change from 10 to 5. There is a version of this index where the patients analyse the values themselves. (This happened in our case, when we had weekly or bi-weekly phone consultations with the patients.)

Due to the fact that psoriasis is an illness influencing the quality of life, it is the patient who evaluates the illness most precisely; his or her opinion is crucial.

Administering ALOCADO™ products, our aim was to give emollient, nourishing and calming preparations to the patient. These products are phase-specific, meaning that they always exert their effect against the most irritating symptom and they support maintenance therapy in conjunction with drug therapy or without. The products prolong the period between relapses and make the patients feel more comfortable with their skin.

## Section 4, Results

Table summarizing PASI index scores

1	26.4	20.4	15.8	12	10.7	4.9	
2	6.2	6	6	7.2	7.2	0	Discontinued due to lack of improvement
3	12.5	12.5	12.5	9.26	8.2	0	
4	4.1	2	2	1.6	1.6	1.6	
5	0.8	0.8	0.3	0	0	0	
6	9.6	6.6	3.9	3.6	3.6	1.2	
7	13.2	6	4.8	4.8	0	0	
8	15.6	15.35	9.5	10.7	0	0	
9	26.2	0	0	0	0	0	Discontinued the test due to operation
10	3.9	2.4	6	0	0	0	Appeared on a new body part
11	36	20.5	6.6	11.4	1	0	
12	39.2	55	25	20	20	13.2	
13	6.2	5.8	3.7	3.2	2.8	0	
14	19.2	20.4	19.8	13.2	0	0	
15	20.3	11.6	11.6	29	14.1	1.2	
16	2.4	3	0	0	0	0	Discontinued the test because could not wait for the effect
17	2	2.4	0	0	0	0	Discontinued the test because could not wait for the effect
18	34.2	18.6	18.6	18.6	0	0	
19	22.3	22.3	21.4	21.4	0	0	
20	0	0	0	0	0	0	Atopic dermatitis
21	7.3	5.15	4.45	6	6	0	Scaling resolved, erythroderma increased
22	14.4	10.9	7.6	0	0	0	
23	6.6	4.8	3.6	0	0	0	

24	36.7	23.1	16.5	20.7	21.6	0	Did not receive the products by mail
25	3.6	3.2	2	1.6	3.2	0	
26	12.4	9.8	7.85	5.9	4.6	0	
27	28.8	28.52	12	0	0	0	
28	2.2	1.2	0.9	0	0	0	
29	26.4	18	9.45	0	0	0	
30	44	42.8	0	0	0	0	
	0	0	0	0	0	0	
Follow-up	1	2	3	4	5		
Summary	381.3	288.6	209.5	200.16	104.6	22.1	
	29	28	25	18	13	5	
<b>Mean value</b>	<b>13.15</b>	<b>10.31</b>	<b>8.38</b>	<b>11.12</b>	<b>8.05</b>	<b>4.42</b>	

In the above table, the first column shows the number of volunteers, and the other columns contain PASI index scores as per follow-up. The dates of follow-ups vary from volunteer to volunteer. Due to the fact that they did not start at the same time, but one after the other, in some cases it was possible to have even six follow-ups whereas in other cases only 1-2. The intervals between the follow-ups also vary; they changed individually. In some cases, this interval was 10-14 days, while in others, it was several weeks. So the columns show PASI index scores registered during follow-ups, irrespective of the time elapsed. At the bottom of the table, the index scores measured during the first, second, third, etc. follow-ups are summarized, where a decreasing trend can already be identified. Besides this, we have calculated the mean index scores as well, this can be seen in the bottom row.

The index scores do not show a smooth decrease, which means that there have been relapses. Further on, individual data will also be introduced.

In the first column, PASI index score changes are highlighted in a different colour. In the case of volunteer 20, the dark green colour means that this patient suffered from **Atopic Dermatitis** (and in his row the PASI index score is zero throughout the test). This case has demonstrated that certain preparations of the Alocado™ product line, suitable for the treatment of very dry skin, may be useful for other conditions as well.

We can see very fast and very effective results in this case as shown by those before and after pictures:

## ATOPIC DERMATITIS (case 20) Clinical test for ALOCADO™

- A woman of 29 years of age
- Suffering from Atopic Dermatitis for 12 years.
- Treated with all kinds of medicine, including injections and steroids.
- Past two years, no changes.
- Start of treatment 8.11.06 – before photo.
- Last check 31.12.06 – after photo.
- Treated with Alocado™ Cream and Alocado™ Skin Softener, to be applied three times a day, first Alocado™ Skin Softener and when absorbed, Alocado™ Cream. When itchy, Alocado™ Cream can be applied as much as needed.
- In 31.12.06 Alocado™ Gold was added to treat open wounds left on the body,
- 10.01.07 wounds are closed; most of the skin is clear, continue maintenance treatment with the Alocado™ Cream.

Before



After



In the **case no' 9**, highlighted in red, the data could not be evaluated, because the patient could not continue this test owing to another type of health problem unrelated to Psoriasis. There were three cases, indicated by the pink fields (**cases 2, 16, 17**), where no improvement was observed, which is why these volunteers did not continue our test. The other fields, indicated by light green, show the results of those volunteers, where improvement could be observed in comparison with their initial condition, irrespectively of whether their PASI curve showed a decline or whether it was fluctuating.

Based on the table summarizing PASI index scores we may summarise the 30 tested volunteers as follows:

One patient's data could not be evaluated due to his Atopic Dermatitis, but it should be mentioned that this volunteer gave positive feedback about the emollient effect of the preparations (case no' 20).

3 patients aborted treatment right at the beginning, stating that it was ineffective (case no' 2 – reduced from 6.2 to 6 and then had a renewed outbreak to 7.2 then stopped, case no' 9 tried for a few days only, then stopped, case no' 17 didn't wait for an effect and stopped).

1 patient was hospitalised with an-other health problem unrelated (case no' 9).

Evaluating patients over a given time span, the number of follow-ups varied. PASI index scores fluctuated heavily, with 7 patients, improvement was followed by deterioration (case no' 2, case no' 8 – got scared from the remission and stopped although showing good improvement before, case no' 10 had an out break on a new part of the body, blamed the products and stopped, case no' 15 – showed great improvement, in midst of treatment suffered a more severe outbreak then the one he begin with, continued treatment, achieved almost clear skin, case no' 21 – showed improvement and then erythroderma increased, needed a change in products to suit the new condition, decided to stop, case no' 24 – showed more than 50% improvement but when products did not arrive by mail, the situation deteriorated and the connection broke, case no' 25 – showed 50% improvement when had a new outbreak, connection broke), and then improvement could be observed once more.

We advised patients many times not to become disappointed in case of deterioration, but continue with their treatment.

This fluctuation is part of the natural process of psoriasis, because improvement and deterioration will keep alternating owing to different provoking factors.

With 11 patients (cases no' 1, 6, 11, 12, 13, 22, 23, 25, 26, 28, 29) a relatively steady improvement could be noted.

When starting the Alocado™ treatment, we tried to choose patients who had not been treated with any steroids or other medicines within a given period before the test. However, taking these preparations was not a criterion for exclusion, since it is necessary to have some emollient treatment for those who took the aforementioned medication as in case no' 12 here the test started whilst the patient was taking steroids (39.2 in the PASI index), we asked him to stop, once doing that the PASI level was increased by more than 40%, but with the continuation of treatment with the Alocado™ products it was reduced to 13.2 in the PASI index, an improvement of 76%. A discontinuation of treatment with steroids might trigger a relapse but the situation can be improved with a continuous usage of the Alocado™ products.

## PSORIASIS (case 12)

Clinical test for ALOCADO™

- 75 years old
- PASI index at start 39.2 for the past 15 years no improvement whatever medicine taken.
- Very swollen, red and inflamed skin, sometimes very itchy, others not
- Some areas are covered with thin plaque.
- At current situation, using medicine with steroids, help minor.
- Started Alocado™ treatment at the 28/9/06 received Alocado™ Gold for treating inflammation and Alocado™ Pasta for treating red swollen skin.
- The moment stop taking medicines within one week situation worsen to 55 in PASI index (steroid effect).
- After 1 month when inflammation reduced, Alocado™ Body oil and Alocado™ Cream for itching and dry skin were added. So treatment included Alocado™ Gold, Alocado™ Body oil, Alocado™ Pasta and Alocado™ Cream, when inflammation was reduced to zero Alocado™ Gold was stopped.
- After 1 more month at the 3<sup>rd</sup> of December 2006 the PASI index dropped to 13.2.
- No Itching, No scaling, No inflammation, No swelling, No redness (small red dots are the only thing left, typical to old peoples skin), fingernails grew back better then before (were treated with Alocado™ Skin Softener).
- Over all, pretty satisfying results.
- On going treatment – Alocado™ Cream, Alocado™ Body oil and Alocado™ Skin Softener for maintainance.

Before



After



After



Before



After



In many cases improvement could be observed based on the regular application of the Alocado™ products. When stopping it, the skin's condition deteriorated.

We observed that the efficacy of the products and the response to them could be increased by applying the appropriate Alocado™ product several times a day.

**It has been observed that application 4 times daily (this dosage proved to be necessary to achieve maximum efficacy) resulted in the fastest improvement.**

In the course of the treatment, we had to change products with many patients, because ALOCADO™ products are phase-specific, and a different product is recommended depending on the predominant symptom (scaling, inflammation, infiltration). In patients showing improvement, the use of the compound called **Gold** should be emphasized, having a soothing effect on the itching, excoriated parts of the skin, which, quickly epithelized, and the patient soon became asymptomatic.

An example of heavy usage of the Alocado™ Gold can be observed in **case no' 1**

## PSORIASIS (case 1)

Clinical test for ALOCADO™

- 68 years old lady
- PASI index at start 26, for the past 10 years no improvement whatever medicine taken.
- Very swollen, very red and extremely inflamed skin, amazingly no itching.
- At current situation, gave up on treatment for several years.
- Started Alocado™ treatment at the 28/9/06 received Alocado™ Gold for treating inflammation and Alocado™ Pasta for treating red swollen skin and Alocado™ Cream for dry skin.
- After 1 month of treatment, PASI index dropped to 13, inflammation reduced and at one area only pinkish coloration left. (patient refuse to stop taking the Alocado™ Gold although inflammation was reduced, we let it stay).
- After two months PASI index 5 and less, No Itching, No scaling, No inflammation, No swelling, No redness but very light almost unnoticeable pink.
- Over all, pretty satisfying results.
- On going treatment – Alocado™ Cream, Alocado™ Body oil and Alocado™ Bath oil for maintenance.

Before



After



After



Because of the moderate improvement of PASI index scores and the fluctuating course of the illness, 10 patients (cases 2, 3, 8, 9, 10, 14, 16, 17, 19, 30) claimed that the treatment did not have the desired effect. Besides acknowledging the improvement in the condition of the skin, the tenderness, the decrease of infiltration, the restoration of elasticity, resolution of scaling, the majority of patients claim inflammation persisted to very small degree.

**Summary based on the objective results (PASI index scores):** based on objective symptoms, PASI index scores improved in 23 cases (79.3%); PASI improvement of 50% was observed in 13 cases (56.5%), while a 75% improvement of PASI occurred in 4 cases (17.4%).

**Subjective results based on patients' self-evaluation:** According to the volunteers, in 7 cases there was no significant improvement or the condition did not change (cases no' 2, 5, 10, 19, 30), in the other 22 cases significant improvement was reported.

**In 5 cases the condition became asymptomatic to a degree not heard of (PASI 1 –1.6) using other preparations cosmetic or medicine (cases no' 4, 6, 11, 15, 25). No side effects were observed. Some transitional irritation was reported.**

**Based on these results, it may be concluded that the phase-specific, emollient, palliative natural compounds of the ALOCADO™ product line *offer a highly effective alternative for the treatment of psoriasis.***

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