

## **Postmarketing surveillance**

# **Diffuse effluvium, damage to hair structure, and disturbances of nail growth treated successfully**

## **Results of a multicenter study**

Thomas Bergner

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Hair loss, damage to hair structure, and disturbances of nail growth often lead patients to visit the physician [1, 2]. There are many possible causes of these diseases. Increased diffuse hair loss often occurs as a result of somatic or psychosomatic diseases or in connection with stress situations. Malnutrition or hormonal changes (e.g. after pregnancy or during the menopause) can also play a role [3]. The question for the therapist is how to help such patients. The efficacy and tolerability of Pantovigar® in the treatment of diffuse effluvium, degenerative changes to the hair structure, and disturbances in nail growth has been re-examined in an open multicenter study involving 1629 patients.

**L**aboratory diagnostic procedures can be helpful in the exact diagnostic clarification of hair loss, but it is usually easy to distinguish diffuse effluvium from hormonally determined hair loss on the basis of the clinical picture; whereas the whole of the scalp is affected in cases of diffuse effluvium, hair loss resulting from hormonal factors usually shows a typical sex-specific pattern [3]. A trichogram in the parietal and occipital areas of the scalp can always provide an unambiguous diagnosis [3, 4].

Degenerative changes in the hair structure usually have exogenous causes, i.e. they are due to excessive cosmetic measures. Nutritional physiology and metabolic changes can also play a role. A genetic disturbance of the differentiation of the hair follicle is a less common possibility [3, 4]. Non-infection-related disturbances of nail growth are often concomitant symptoms of one of a variety of skin diseases such as onychomycosis, psoriasis, eczema, etc., but they are also frequently the result of exogenous influences or poor nutrition [14].

### **Stimulation of hair-follicle metabolism is often the treatment of choice**

Along with elimination of the cause, the provision of substances involved in hair formation is of particular importance in diffuse effluvium and degenerative changes to the hair structure [4]. Because the hair roots are among the most metabolically active tissues in the human body [3], the stimulation of follicular metabolism in the form of substitution therapy is the treatment of choice in many patients with the above indications. A properly functioning cellular

metabolism increases the resistance of the hair to external noxae and encourages healthy hair growth. A similar situation applies in non-infection-related disturbances of nail growth.

The progressive reduction in size and associated exhaustion of the hair follicle plays the decisive role in the course of androgenetic alopecia [1, 2, 3, 4]. Causal treatment is in the forefront in relation to this condition. Tinctures containing minoxidil were regarded as promising as much as ten years ago, but are still not registered in Germany [5]. The inhibition of  $5\alpha$ -reductase by the local application of  $17\alpha$ -estradiol (Pantostin<sup>®</sup>, for men or women) [8, 9] or systemic administration of finasteride (Propecia<sup>®</sup>, only in men) [6, 7] is a fairly new method of treatment. Along with causal treatment, administration of substances involved in hair formation can also be helpful in hormonally related hair loss.

Pantovigar<sup>®</sup>, a medicament which includes sulfur-containing amino acids and B-group vitamins, has proved to be very valuable in the above disturbances of hair and nail growth. The high efficacy and tolerability of Pantovigar<sup>®</sup>, which has already been documented in detail in a number of studies [10-14], has been confirmed again within the framework of a multicenter study.

### Study design

Study procedure, inclusion and exclusion criteria: This was an open, multicenter, postmarketing surveillance study in outpatients carried out by dermatologists and general practitioners. The following subjects were included in the study:

- patients with diffuse hair loss with no evidence of underlying disease in the medical history and/or
- patients with acquired or age-related damage to the hair structure, including thin, brittle, fragile, or split hair and/or
- patients with disturbances of nail growth such as soft, fragile, easily chipped, or brittle finger nails with no evidence of underlying disease in the medical history.

Patients whose hair loss was due to a known hormonal disturbance were excluded from the study.

*Dosage and duration of the study:*

Pantovigar<sup>®1</sup> was administered at a dose of 3 × 1 capsules per day for at least three, and up to six, months, depending on the clinical course. Cosmetic procedures such as permanent waves and hair coloring were not permitted, though patients were to continue other hair-care measures.

*Study parameters:*

The physician assessed the severity of the three possible diagnoses – hair loss, damage to the hair structure, and disturbances of nail growth – at the start of the study, after six weeks, after three months, and after the completion of treatment, using the following four-point scale: absent, slight, moderate, severe. The patients also had to collect and count the hairs which fell out at each of these four occasions for three consecutive days, and document the results in a patient card.

*Efficacy and tolerability:*

Both the physician and the patient assessed the therapeutic effect of the treatment with Pantovigar<sup>®</sup> at the end of treatment, using the following four-point scale:

- very good (cure)
- good (considerable improvement)
- moderate (some improvement) and
- unsatisfactory (no improvement or deterioration of the clinical picture).

The tolerability was also documented on the basis of a four-point scale:

- very good (no adverse events)
- good (mild, transient malaise)
- moderate (tolerable adverse events)
- poor (persistent and severe adverse events).

The individual adverse events were documented using a standardized Case Report Form.

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<sup>1</sup> 1 Pantogar capsule contains: thiamine mononitrate 60 mg, calcium D-pantothenate 60 mg, medicinal yeast 100 mg, L-cystine 20 mg, keratin 20 mg, p-aminobenzoic acid 20 mg

## Study evaluation

Unless otherwise stated, all percentages relate to the whole study population of n = 1629 patients.

### *Statistical methods:*

The statistical evaluation was carried out by Jung & Jung of Planegg bei München, using descriptive methods. The usual statistical characteristics (including the group size [n], arithmetic mean, and standard deviation) were calculated for continuous data. Four new variables were calculated to assess the efficacy in hair loss. They were obtained from the mean value of the number of hairs counted by the patients over three days at each of the four measurement times. Only complete sets of patient data were included. The change in the number of hairs lost was checked for statistical significance using the t-test.

### *Patient-related data, treatments, and duration of the disease:*

A total of 1629 patients took part in the multicenter study. The data on all the patients, who were an average of 43.6 years old (Fig. 1), were suitable for inclusion in the evaluation. 84.6% of the patients were women and 15.2% were men. Table 1 shows the frequencies of the diagnoses. Investigators could also cite two (544 times, 33.4%) or three (174 times, 10.7%) diagnoses.

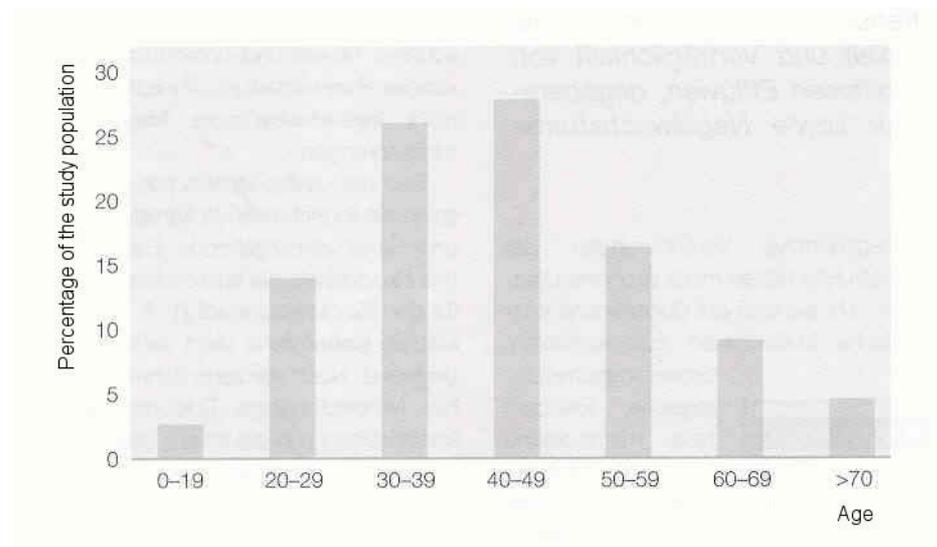


Fig. 1: Age distribution of the patients

**Table 1:** Distribution of the diagnoses

Diagnosis	Number	%
Diffuse effluvium	1194	73.3
Damage to hair structure	684	42.0
Disturbances of nail growth	642	39.4
n = 2523 (multiple responses permitted)		

Just under 33% of the patients reported prior treatment, 12.3% of them the use of hair tinctures containing estradiol. Just under 28% of patients had concomitant illnesses, the most common being hypertension (6.3%) and diabetes mellitus (2.8%). Almost as many of them (27.6%) were taking concomitant medication for the underlying illness.

The mean duration of the condition before treatment was twelve months.

*Duration of treatment, dose, and tolerability:*

The mean duration of treatment was 18.2 weeks (*Table 2*). The standard dose was three Pantovigar® capsules daily. 98.8% of the patients took the medication at the prescribed dose during the first six weeks. After three months, 96.2% of the patients reported that they had taken the product as prescribed, and at the end of treatment the figure was 84%. The main reason for failure to take the medication regularly at the start of treatment was “lack of patient compliance” (81.8% of n = 11) and later on it was “good therapeutic outcome” (44.4% of n = 171).

**Table 2:** Duration of treatment

<b>Weeks</b>	<b>Number</b>	<b>%</b>
Up to 4	36	2.2
5-9	43	2.7
10-14	359	22.0
15-19	500	30.7
20-24	485	29.8
25-29	172	10.6
30-34	17	1.0
35 or more	17	1.0
n = 1629		

## Study results

### *Monitoring the course of the disease:*

The continuous monitoring showed significant reductions in the category “severe disease” compared with the previous observation time for all three diagnoses (*Fig. 2*). There were evaluable results relating to the number of hairs lost over three days at all four measurement times for a total of 951 patients (*Fig. 3*). The mean value fell from 142 per day before treatment to 108 per day after six weeks of treatment then continued to fall to 73 per day after three months and 53 per day at the end of treatment. These reductions were statistically significant ( $p < 0.01$ ) and were due to the treatment with Pantovigar®.

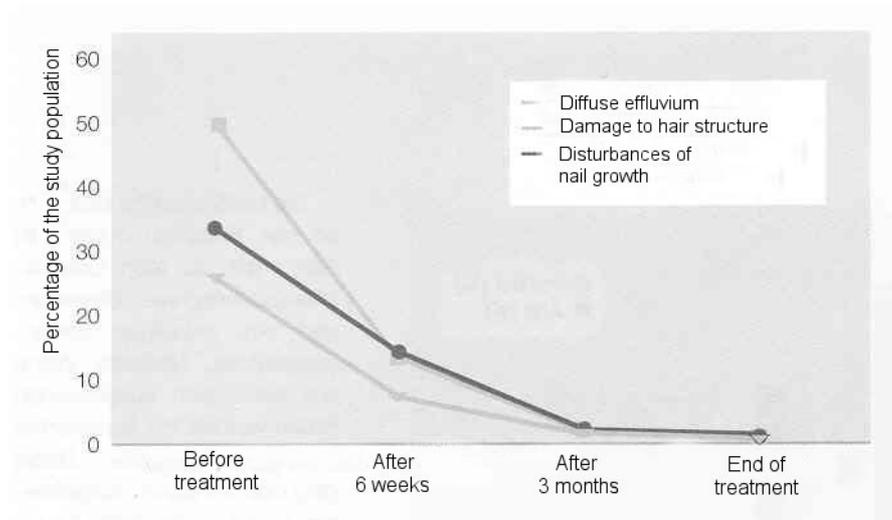


Fig. 2: Number of clinical pictures described as “severe” by the physician

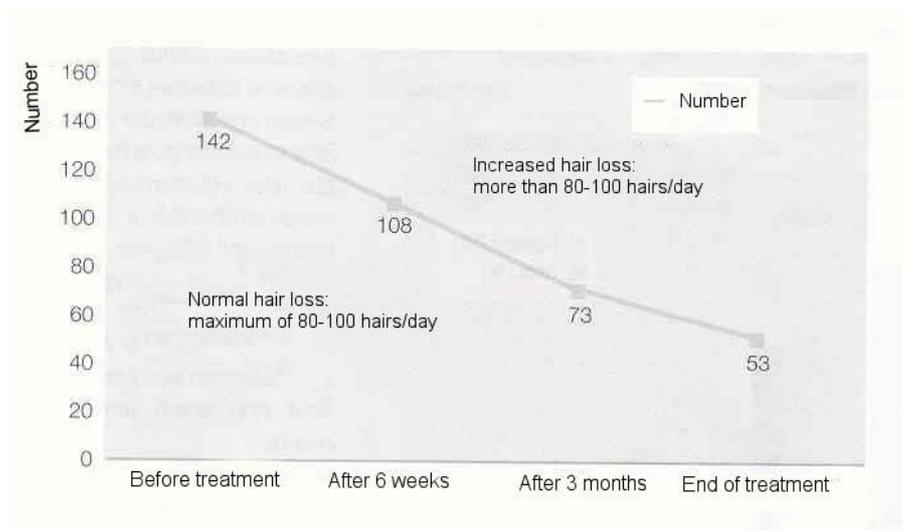


Fig. 3: Number of hairs lost per day (mean value over 3 days)

*Therapeutic effect and tolerability:*

Both the physician and patient assessed the efficacy in relation to the individual diagnoses after the end of treatment. The physician classified the efficacy as very good or good in relation to diffuse effluvium in 90.2% of cases, in relation to damage to hair structure in 88.3% of cases, and in relation to disturbances of nail growth in 87.5% of cases.

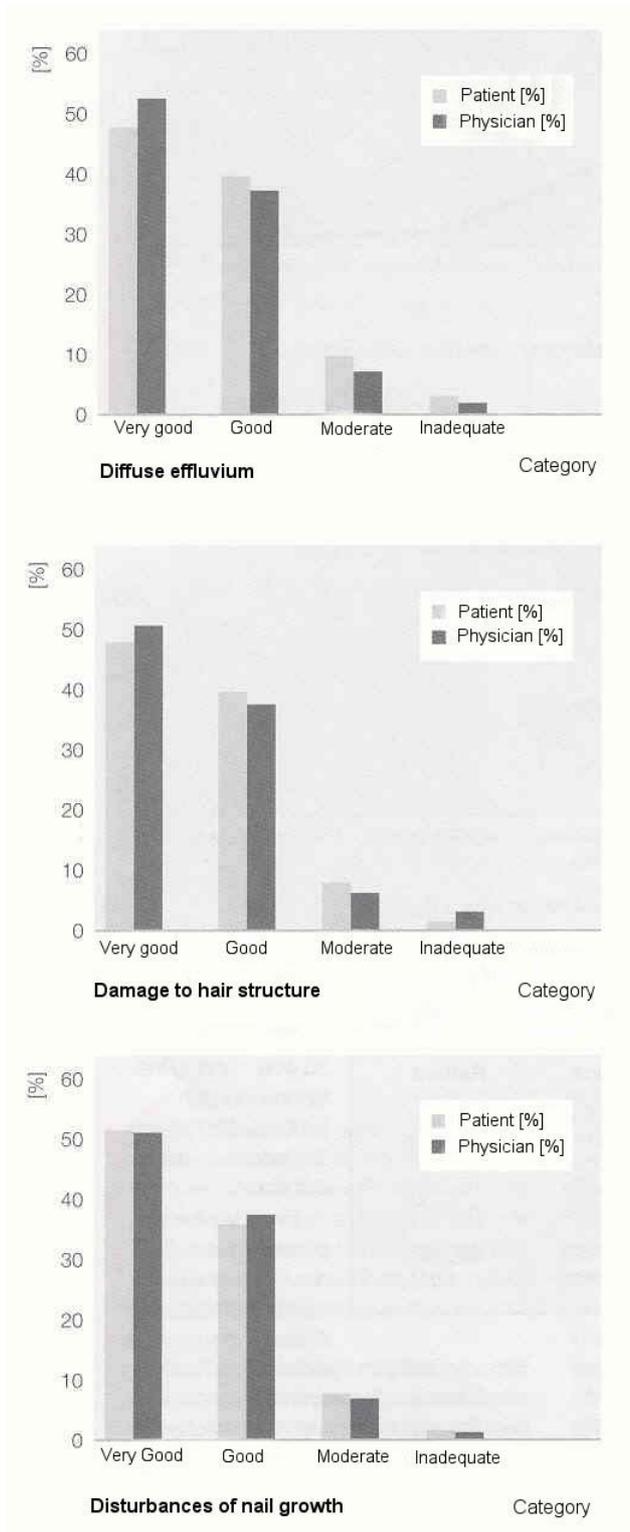
The patients also classified the efficacy of the product in respect of each of the three diagnoses as very good or good in 87% of cases. *Table 3* shows the exact figures for each of the categories. *Figs. 4a-c* illustrates the assessments graphically.

Only ten patients reported adverse events under treatment with Pantovigar® (0.6%). The events reported were mainly transient gastrointestinal disturbances (stomach aches, pressure over the stomach, gastric spasms). An association between the adverse event and the administration of Pantovigar® was suspected in three cases. The physicians classified the tolerability as good or very good in 98.5% of cases.

**Table 3:** Evaluation of the therapeutic effect – very good or good

Diagnosis	Physician	Patient
Diffuse effluvium (n = 1194)	90.2% (n = 1077)	87.5% (n = 1044)
Damage to hair structure (n = 684)	88.3% (n = 604)	87.3% (n = 597)
Disturbances of nail growth (n = 642)	87.5% (n = 562)	87.4% (n = 561)

**Diffuse effluvium, damage to hair structure, and disturbances of nail growth treated successfully**



**Fig. 4a-c:** Therapeutic effect – diffuse effluvium/damage to hair structure/disturbances of nail growth

## Evaluation of the results

Although disturbances of hair or nail growth are indications which do not have adverse physical effects on patients, their mental suffering can be considerable. The urgent need for an effective and well tolerated treatment is thus beyond question.

The postmarketing surveillance study in 1629 patients again confirms the good experience with Pantovigar® in general and clinical practice. Pantovigar® can be regarded as very effective in all three indications investigated, i.e. diffuse hair loss, damage to hair structure, and disturbances of nail growth.

The continuous monitoring of these patients by the physician showed improvements of the individual clinical pictures at each of the examination times. Measurable values, such as the number of hairs lost per day, showed statistically significant reductions. The number of hairs lost per day fell back into the normal physiological range (max. 80-100 hairs per day). In terms of the therapeutic efficacy, 87% of patients and 90% of physicians classified the results in diffuse effluvium as very good or good. In damage to hair structure the figures were 87% of patients and 88% of physicians, and in disturbances of nail growth 87% of patients and 88% of physicians. The assessments by the physicians and the patients were thus in agreement.

Pantovigar® is thus of high therapeutic value in the diseases cited, whether used on its own or as an adjuvant treatment, while having excellent tolerability. Adverse events were only documented in ten cases, and they were transient. The physicians classified the tolerability of Pantovigar® as good or very good in 98.5% of all patients.

This multicenter study once more confirms that Pantovigar® is an effective and safe treatment for diffuse hair loss, damage to hair structure, and disturbances of nail growth.

References are available from the author:

Dr. med. Thomas Bergner, Räterstr. 20, 85551 Kirchheim bei München, Germany