

neuropad[®]

Screening for “at-risk” feet is the job of all of those caring for people with Diabetes.²⁶

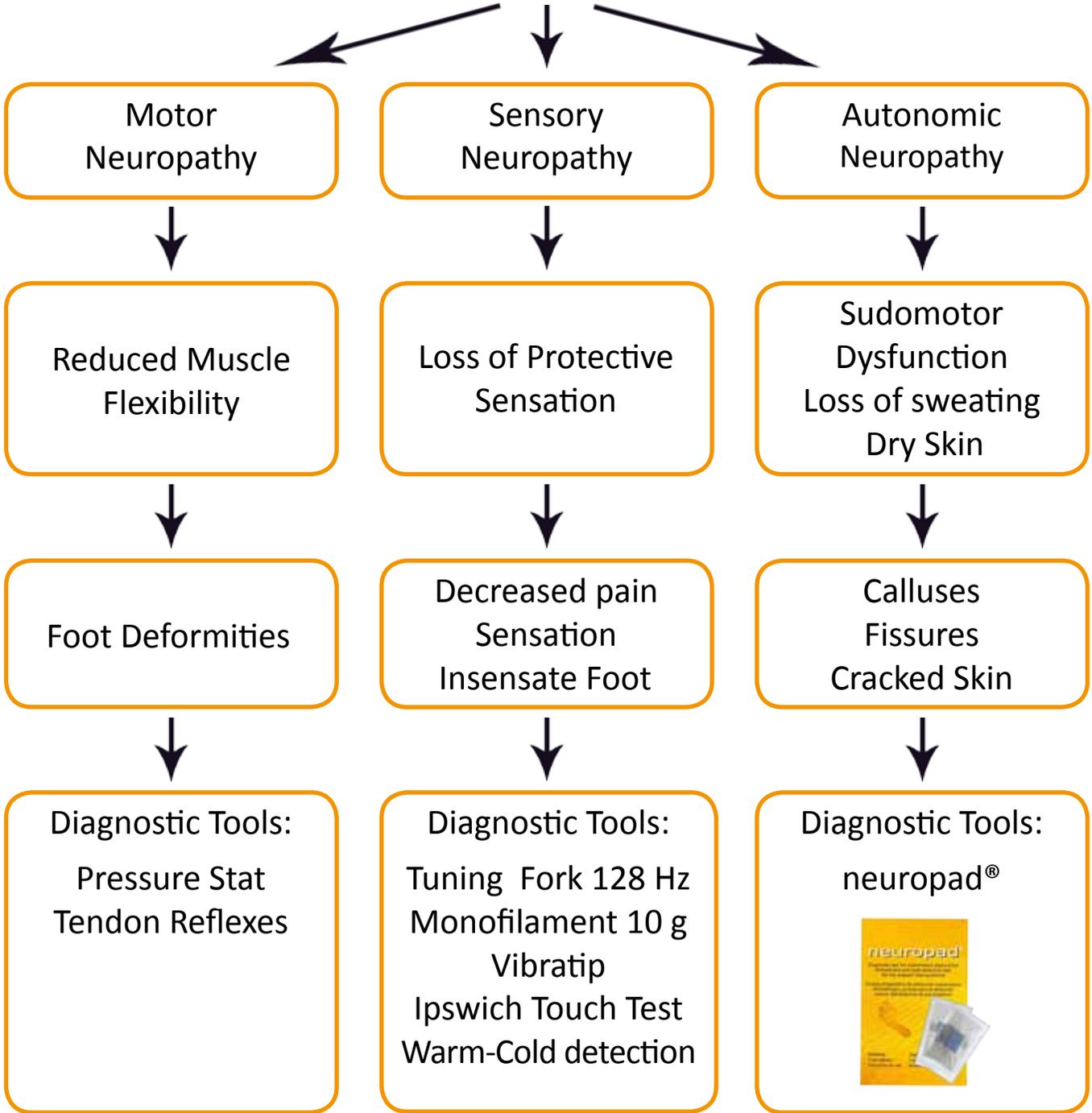


Diagnostic Test for Sudomotor Dysfunction and early detection of Diabetic Foot Syndrome, Diabetic Neuropathy^{13, 22, 23}

Included in Toronto Consensus Panel on Diabetic Neuropathy latest recommendation
Published: Diabetes - Metabolism and Reviews, Diabetes Metab Res Rev 2011; 27:

neuropad® is a simple, non-invasive indicator test that has been developed for the assessment of sweating and, hence, autonomic innervation of the diabetic foot.

Diabetic Neuropathy (Distal Symmetric Polyneuropathy)



Today neuropad® test is the only simple and low cost medical device which documents sudomotor dysfunction, validated with more than 30 clinical study publications.

The pathway to foot ulceration:

A combination of risk factors that ultimately results in the pathway to skin breakdown.

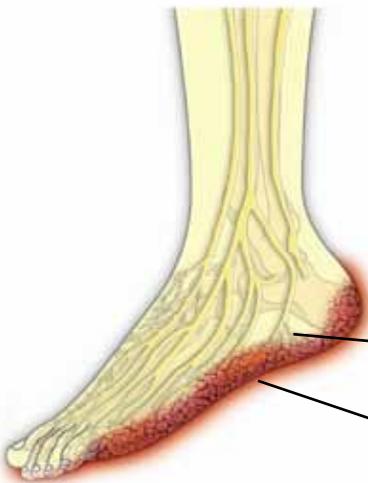
Autonomic neuropathy leading to dry skin and callus build up at such sites, and can also be regarded as a component cause.²⁶



Peripheral Vascular Disease

Peripheral vascular disease leads to ischaemia

Arteries of the foot



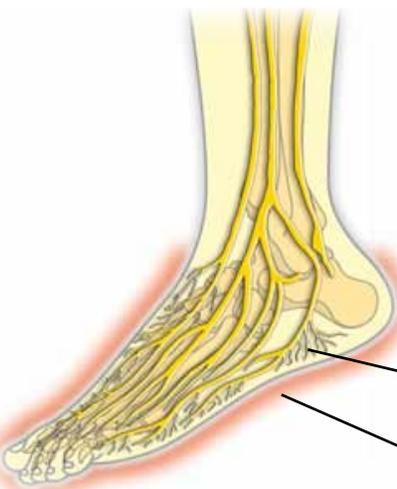
Small Fibre Neuropathy

Small nerve fibres regulate several key functions such as sweating. Peripheral sympathetic autonomic neuropathy leads to sudomotor dysfunction and dry cracked skin.

Nerve fibres

Dry Cracked Skin

Painful Diabetic Neuropathy



Large Fibre Neuropathy

Large nerve fibres neuropathy affects sensory and motor components leading to walking abnormalities and insensate feet. An increasing body of data shows that small fibre damage may precede large fibre damage in diabetic neuropathy.²²

Nerve fibres

Insensate feet

Diabetic Foot Syndrome Small Fibre Neuropathy

Small fibres constitute 70–90% of peripheral nerve fibres and regulate several key functions such as tissue blood flow, temperature and pain perception as well as sweating, all of which are highly relevant to the clinical presentation and adverse outcomes **associated with foot ulcerations in patients with diabetes**²².

neuropad[®] response indicates both functional and structural denervation in the feet of diabetic patients. This has considerable clinical relevance in screening for diabetic neuropathy.¹²

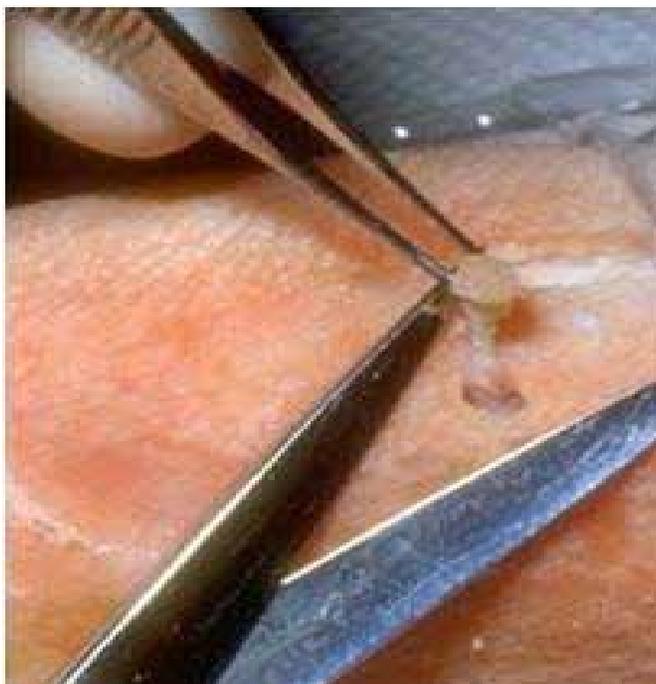


Figure 1: Skin biopsy

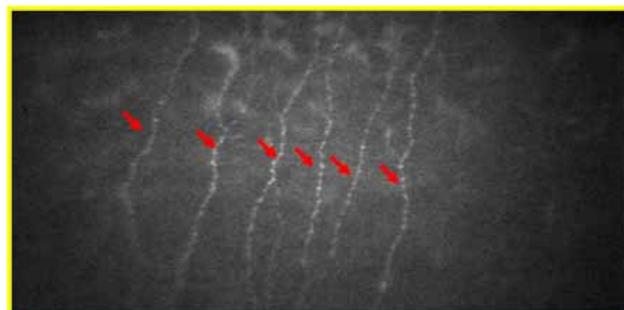


Figure 2: Corneal confocal microscopy image of a control subject with normal corneal nerve density

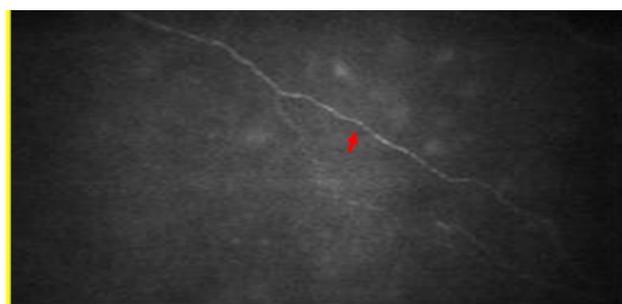


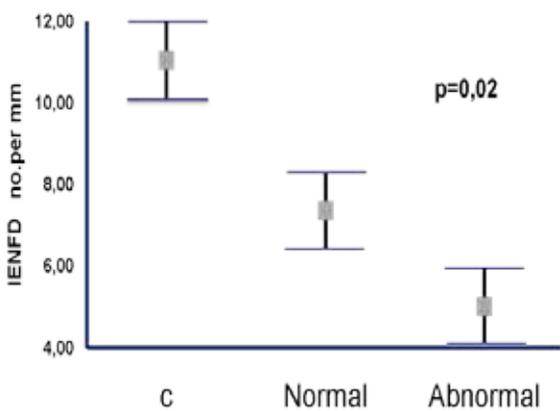
Figure 3: image from a diabetic patient with severe neuropathy and marked loss of corneal nerve fibres

Sudomotor innervation: a novel stereologic technique in skin biopsies showed a correlation between sweat gland nerve fibre density, neuropathic symptoms, neurological deficits and sweat production.²²

neuropad® test response strongly correlated to other test for Small Fibre Neuropathy

neuropad® test vs Intraepidermal Nerve Fibre Density (IENFD)

All diabetic patients with an abnormal neuropad® test had structural denervation of the feet¹².



A comparative study of the neuropad® test versus skin biopsies from the dorsum of the foot showed that all diabetic patients with abnormal neuropad® test had significantly lower IENFDs compared to diabetic patients with a normal neuropad® response and healthy subjects¹².

neuropad® test vs Non-Contact Corneal Aesthesiometry

Using multi-dimensional scaling, Non-Contact Corneal Aesthesiometry was closer to the Neuropathy Disability Score, Diabetic Neuropathy Symptom Score and neuropad®²⁵.

Association between corneal sensation threshold in millibars and specific neuropathy parameters in the study cohort expressed as correlation coefficient (Pearson for continuous variables, Spearman for non-continuous variables)

Corneal Sensation threshold (mbars)	Pearson Correlation(.r)	p
Neuropathy Disability Score (0-10)	0.2*	0.001
neuropad® (blue/patchy/pink)	-0.13*	0.032
Diabetic Neuropathy Symptom Score (0-4)	0.19*	0.002

*spearman rho (ρ)

Sensitivity and Specificity of neuropad® for the diagnosis of Diabetic Neuropathy: comparison with clinical examination and Nerve Conduction Study¹⁰

neuropad® test revealed a sensitivity $\geq 86\%$ and specificity $\geq 67\%$ for the diagnosis of diabetic neuropathy with a cut-off time of 10 minutes comparing a clinical examination (NDS).^{4, 8, 9, 18}

	N° of patients	Sensitivity (%)	Specificity (%)
Papanas et al	104	94.4	69.7
Liatis et al	117	86	67
Shen et al	98	92.8	78.5

The sensitivity of the indicator test for abnormal NCS was 97.8%, and its specificity was 96.4%.¹⁰

The indicator test has a validity comparable to that of NCS for the diagnosis of diabetic neuropathy.¹⁰

Clinical Neuropathy Status			
Patients	with clinical neuropathy (n=83) [n (%)]	without clinical neuropathy (n=37) [n (%)]	p ^a
Abnormal neuropad®	79 (95.2)	12 (32.4)	0.0001
Normal neuropad®	4 (4.8)	25 (67.6)	
Abnormal NCS	78 (94)	14 (37.8)	0.0001
Normal NCS	5 (6)	23 (62.2)	

^a patients with neuropathy vs patients without neuropathy

Sudomotor Dysfunction diagnosis with neuropad® test provides an earlier diagnosis of Diabetic Neuropathy.^{17, 22}

The invariably lower specificity than sensitivity is due to the fact that neuropad® is abnormal in about one third of patients with clinical examination negative for neuropathy. It has been proposed that this result may be ascribed to earlier diagnosis of neuropathy by means of neuropad® before conventional clinical signs become positive.²⁴

neuropad® test positive result in diabetic patients without clinical neuropathy is a remarkable indicator for the development of clinical neuropathy in the future.^{17, 22}

This appears to reflect early small fibre involvement which is missed using NDS as a measure of neuropathy.²²

Patient Group	with neuro- pathy 2nd examination after 5 years	without neuro- pathy 2nd examination after 5 years	NDS 1st examination	NDS 2nd examination	p value
with normal neuropad® on 1st examination (n=70)	2 (2.86%)	68	2.97 ± 0.72	4.23 ± 0.99	p < 0.001
with abnormal neuropad® on 1st examination (n=39)	10 (25.64%)	29	3.39 ± 0.91	4.63 ± 1.33	p < 0.001

Diabetic patients with abnormal neuropad® test result have higher risk of foot ulceration¹⁶

Dryness of the skin of the feet assessed by neuropad® test correlates with foot ulceration.¹⁶

A study with 379 patients with diabetes has shown that dryness of the skin of the feet correlates with foot ulceration. Subclinical sudomotor dysfunction can be detected early in diabetes, even in subjects with normal nerve conduction velocities. We showed that dryness of the skin of the feet was detected in 95% of the patients with foot ulceration using the neuropad® test.

An abnormal neuropad® response correlates with foot ulceration in subjects with diabetes. Patients with foot ulceration had more severe peripheral neuropathy and more often an abnormal neuropad® response.

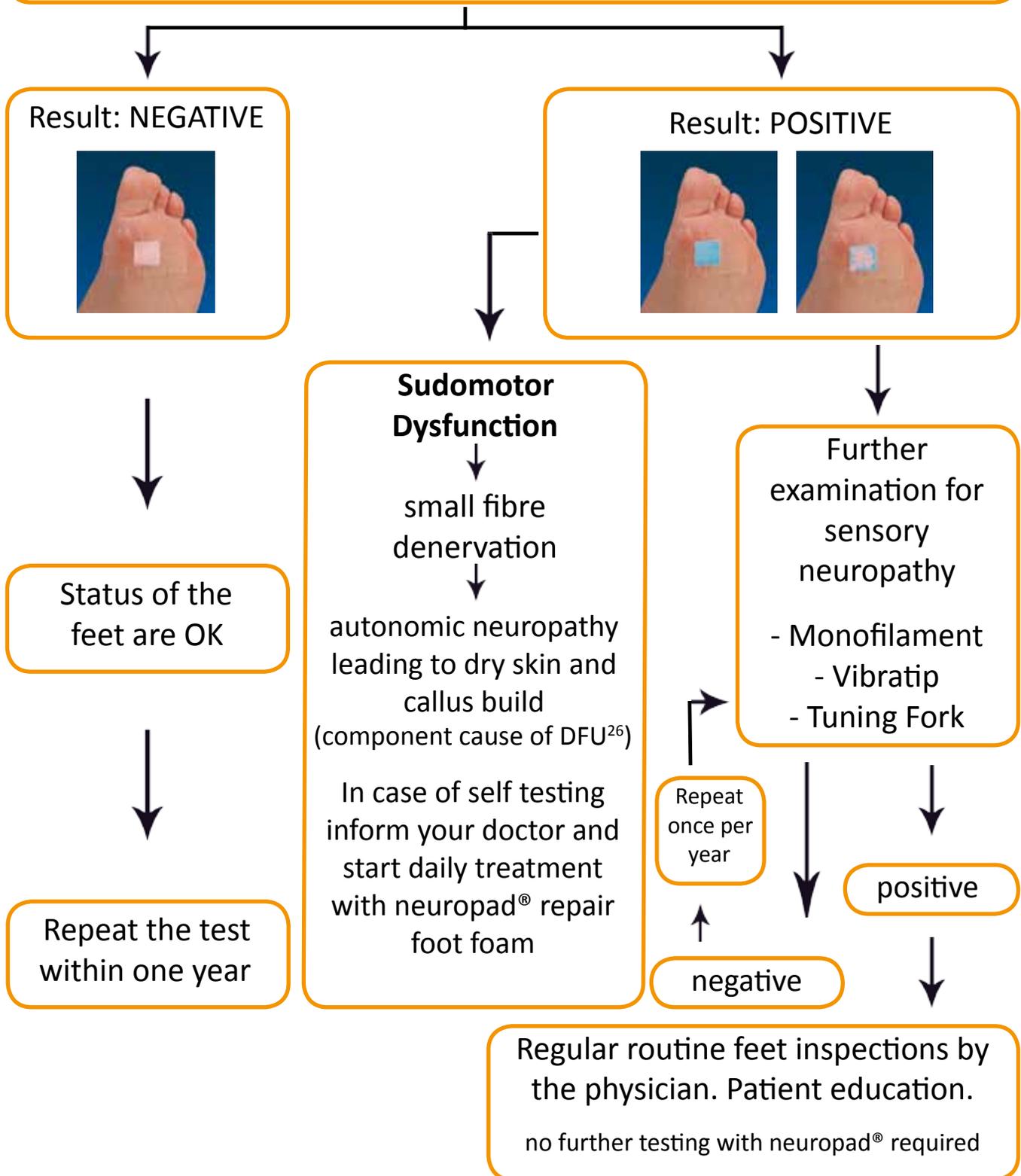
Multivariate statistical analysis demonstrated that patients with diabetes with abnormal neuropad® response are **16 times** more likely to develop foot ulceration compared to those with a normal neuropad® test result.¹⁶

The association (odds ratio, 95% CI) between the studied parameters and foot ulceration by multivariate logistic regression analysis.

	Odds ratio	95% CI	p value
Model 1 VPT (≥ 25 vs < 25 V)	11.91	6.03-21.86	<0.001
Model 2 NDS (≥ 6 vs < 6)	6.70	3.31-13.35	<0.001
Model 3 Monofilament score (<3 vs >3)	6.75	3.27-13.95	<0.001
Model 4 neuropad result (abnormal vs normal)	16.28	6.27-38.24	<0.001

Early detection of Diabetic Neuropathy and diagnosis of Sudomotor Dysfunction

Screening with neuropad® GP Practice or Self-Testing



The treatment of the symptoms (dry and cracked skin)

The unique and effective combination:

Diagnoses & Management of the feet for patients with Diabetes Mellitus

Complete solution for:

- ✓ Effective treatment and management of pathological dry diabetic foot (neuropad® test abnormal).
- ✓ Prevention and foot care for patients with Diabetes Mellitus
- ✓ Highly user friendly (comfortable in use – 86%, absorbed quickly by the skin – 88%, doesn't feel fatty – 91%)¹⁹
- ✓ A significant beneficial effect was noticeable as early as after 7 treatment days²¹
- ✓ Effect was enhanced after further 7 treatment days²¹
- ✓ Paraffin-, vaseline-, lanolin-free: non-comedogenic



Unique combination with 5 active ingredients plus Urea. Covers all aspects for the need of neuropathic skin.

	10% Urea	Oenothera Biennis Oil (g linoleic Acid)	Extract Centella Asiatica	Panthenol	Alpha Hydroxy Acid AHA-Complex	Allantoin
Hydration	✓	✓	✓	✓		
Exfoliation	✓				✓	
Regeneration		✓	✓	✓		✓
increases elasticity		✓				

Application of moisturizers

containing humectants like lactic acid, urea, glycerin and alpha-hydroxy acids is clearly effective in reducing dry skin conditions and enhancing the skin barrier function.²⁷

An innovative unique standardized diagnostic tool to complete Diabetic Foot Examination. The only simple test for documentation of Sudomotor Dysfunction.

Simple visual indicator test which uses a colour change to define the integrity of skin sympathetic cholinergic innervation²².

Benefits of neuropad[®] test:

- high sensitivity^{18,22,23} of NDS, ideal for screening
- detects small fibre denervation^{12,25,22}
- test for sudomotor dysfunction
- non-invasive, direct result
- objective visual test with high reproducibility⁵
- validated for self-examination¹¹
- easy to use¹¹, simple, economic
- increases patient`s compliance

neuropad[®] test results:

Always apply to both feet:



pink =
normal result



blue/pink =
abnormal result
Sudomotor Dysfunction
Foot at risk of ulceration



blue =
abnormal result
Sudomotor Dysfunction
Foot at risk of ulceration



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www.trigocare.com • info@trigocare.com