NICE National Institute for Health and Care Excellence

NICE guidance

Neuropad for detecting preclinical diabetic peripheral neuropathy

HealthTech guidance
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www.nice.org.uk/guidance/htg486

Your responsibility

This guidance represents the view of NICE, arrived at after careful consideration of the evidence available. When exercising their judgement, healthcare professionals are expected to take this guidance fully into account, and specifically any special arrangements relating to the introduction of new interventional procedures. The guidance does not override the individual responsibility of healthcare professionals to make decisions appropriate to the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

All problems (adverse events) related to a medicine or medical device used for treatment or in a procedure should be reported to the Medicines and Healthcare products Regulatory Agency using the Yellow Card Scheme.

Commissioners and/or providers have a responsibility to implement the guidance, in their local context, in light of their duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations. Nothing in this guidance should be interpreted in a way that would be inconsistent with compliance with those duties. Providers should ensure that governance structures are in place to review, authorise and monitor the introduction of new devices and procedures.

Commissioners and providers have a responsibility to promote an environmentally sustainable health and care system and should assess and reduce the environmental impact of implementing NICE recommendations wherever possible.

Contents

This guidance replaces MTG38.

1 Recommendations

1.1 The case for adopting Neuropad to detect preclinical diabetic peripheral neuropathy is not supported by the evidence.

Why the committee made these recommendations

Neuropad detects abnormal sweating in people with diabetes. But the clinical importance of this is poorly defined. There is insufficient evidence to support the use of Neuropad in people in whom 10 g monofilament testing for diabetic peripheral neuropathy is not possible.

Using Neuropad instead of 10 g monofilament testing would likely increase costs because Neuropad has a lower specificity for detecting diabetic peripheral neuropathy. Cost modelling is uncertain because of the limited clinical-effectiveness evidence. Further research is needed on the benefits and consequences of detecting preclinical diabetic peripheral neuropathy.

2 The technology

Description of the technology

2.1 Neuropad (TRIGOcare International) is a point-of-care test for use in people with diabetes. The test detects sudomotor dysfunction (inadequate sweat production), which may indicate that a person is in the early stages of developing diabetic peripheral neuropathy (DPN). The 10-minute test is non-invasive and involves applying a single-size plaster to the sole of the foot. The plaster contains cobalt chloride, which changes colour as it absorbs sweat. The colour changing from blue to pink indicates normal sweat production and implies preserved autonomic nerve function. If the plaster stays blue or does not turn fully pink, it is assumed that there is reduced sweating which carries with it an increased risk of diabetic foot complications. The Neuropad test can be done in a clinic by a healthcare professional during a routine foot check, or at home by the person themselves or their carer. Neuropad can be used either as a standalone test or in conjunction with other standard sensory neuropathy testing.

2.2 Neuropad is a class 1 diagnostic device. The cost of Neuropad stated in the company's submission is £7.28 (excluding VAT).

2.3 The summary of claimed benefits of Neuropad in the case for adoption presented by the company are that it:

- is simple and can be done at home by the person with diabetes or their carer, or in a clinic by a healthcare professional
- is non-invasive, painless and safe
- provides results in 10 minutes that are easy to interpret
- can detect DPN earlier than monofilament and vibration tests, so is useful for the early identification of people at the greatest risk of complications.

Current management

2.4 NICE's guideline on diabetic foot problems recommends that adults with diabetes should have a risk assessment for diabetic foot problems at diagnosis, at least every year thereafter, whenever foot problems arise and at the time of any admission to hospital. During the risk assessment, both feet should be examined for any risk factors, including manifestations of DPN, which should be tested using a 10 g monofilament as part of a foot sensory examination. If DPN is detected, a person's risk is classified as being moderate or high (depending on the presence or absence of other comorbidities). This should trigger referral to a foot protection service and more frequent subsequent foot assessments.

2.5 NICE's healthtech guidance on VibraTip for testing vibration perception to detect DPN states that the technology shows potential but more research is needed.

2.6 NICE's guideline on diabetic foot problems does not refer specifically to testing for preclinical DPN using, for example, sudomotor function (on which Neuropad is based) or any other modality. Preclinical DPN refers to the early-stage development of the condition before it becomes clinically apparent (see section 4.2).

3 Evidence

Summary of clinical evidence

3.1 The evidence for Neuropad assessed by the external assessment centre (EAC) comprised 18 studies, of which 13 were full text articles and 5 were abstracts. Of the 18 studies, 17 investigated the diagnostic accuracy of Neuropad against a reference standard and 1 reported its ability to predict the risk of diabetic foot ulceration. In addition to examining diagnostic accuracy, 1 study looked at the reproducibility of results when using Neuropad and 3 assessed the association between Neuropad testing and developing foot ulcers. The most common reference standard used was the neuropathy disability score. All the studies were prospective observational, cross-sectional or longitudinal cohort studies. For full details of the clinical evidence, see section 3 of the assessment report.

EAC's analysis of the clinical evidence

3.2 The EAC considered that the 2 published UK studies (Ponirakis et al. 2014 and Quattrini et al. 2008) were fully relevant to the scope. The EAC also did a meta-analysis of 5 diagnostic accuracy studies that used a neuropathy disability score of 5 or more as the reference standard: Freitas et al. 2009, Kamenov et al. 2010, Liatis et al. 2007, Manes et al. 2016 and Tentolouris et al. 2008.

3.3 The EAC used its meta-analysis results comparing Neuropad with a neuropathy disability score of 5 or more with the results obtained for 10 g monofilament. It concluded that Neuropad may be more sensitive than 10 g monofilament testing in detecting diabetic peripheral neuropathy (DPN) but has lower specificity. In addition, the EAC noted that the current care pathway includes interventions that are triggered only by clinically apparent DPN, which would be regarded as moderate or advanced, so the benefit of detecting preclinical DPN in the current care pathway is uncertain.

2021 guidance review: summary of clinical evidence

New evidence was not robust to support the use of Neuropad as an alternative to monofilament

3.4 The EAC reviewed evidence published since April 2017. There were 8 publications, including 7 comparative clinical studies, on Neuropad. None of the studies used a single comparator, with all using multiple tests to diagnose diabetic peripheral neuropathy, which indicates variation in the care pathway. The EAC found that the new evidence was heterogeneous and did not help to clarify Neuropad's position in the care pathway. The most common comparators (reference tests) were in line with the final scope (for details see the review report – August 2022). Four studies reported the diagnostic accuracy of using Neuropad to diagnose diabetic peripheral neuropathy compared with standard care (10 g monofilament alone). Neuropad's sensitivity ranged between 24.3% (Gomez-Banoy et al. 2017, n=93) and 95% (Zografou et al. 2020, n=174) with a specificity ranging between 29% (Lorenzini et al. 2020, n=42) and 94.2% (Gomez-Banoy et al. 2017, n=93). It is unclear to the EAC why the sensitivity and specificity reported by Gomez-Banoy et al. (2017) were outliers to the other 3 studies. The EAC concluded that the new evidence was not sufficiently robust to support the use of Neuropad in people who would currently undergo testing with monofilament. This is because the evidence reported a wide variation in sensitivity and specificity for Neuropad, compared with monofilament. **[2021]**

None of the new evidence showed particular benefits of Neuropad for specific population groups, including people in care homes

3.5 The EAC reported that Zografou et al. (2020) claimed Neuropad was a useful screening tool for diagnosing diabetic peripheral neuropathy in terms of time saving and objectivity during clinical examination and educational benefit for the patient. However, none of the new evidence explicitly measured and compared the time taken with Neuropad against a comparator. And none of the new evidence demonstrated particular benefits for specific patient groups, including people in care homes. **[2021]**

Summary of economic evidence

3.6 Neither the company nor the EAC identified any relevant published economic evidence. The company submitted a Markov model with 2 comparisons: Neuropad testing compared with 10 g monofilament testing, and Neuropad testing compared with Neuropad testing then 10 g monofilament testing. The time horizon of the model was 3 years. The EAC made a number of changes, including: adding the implications of false-negative and false-positive results; adding a death state; extending the time horizon to 10 years; and adding a third comparison of Neuropad testing with no testing. For full details of the economic evidence, see section 4 of the assessment report.

EAC's analysis of the economic evidence

3.7 The EAC disagreed with a number of the sources used to generate parameter values in the company's model. It also noted discrepancies between the values used in the model and those quoted in the referenced sources. Moreover, the EAC considered that the cost of 10 g monofilament testing in the model had been overestimated, because it included the cost of the reusable holder. For full details of the EAC's changes to the company's economic model, see sections 4.2 and 4.3 of the assessment report.

3.8 Results from the EAC's revised model showed that Neuropad testing incurs additional cost over a 10-year time horizon compared with all other comparators:

- £775 per patient compared with 10 g monofilament testing
- £1,075 per patient compared with Neuropad testing then 10 g monofilament testing
- £1,792 per patient compared with no testing.

The EAC did sensitivity analyses which showed that Neuropad testing alone was not cost saving in any considered scenario.

2021 guidance review: summary of economic

evidence

The new evidence did not address the issues in the original cost model

3.9 An economic study was published after the original guidance was published (Rodriguez-Sanchez et al. 2020). The EAC reviewed it and noted that it was a cost-effectiveness analysis. The EAC did not consider that the study fully addressed the issues outlined by the original EAC (King's College Technology Evaluation Centre [KiTEC]; for details see the review report – August 2022). It concluded that the results of Rodriguez-Sanchez et al. (2020) were consistent with the findings presented in the original assessment report, and the economic case remains unchanged. **[2021]**

4 Committee discussion

Clinical effectiveness

4.1 The evidence for the accuracy of Neuropad in diagnosing preclinical diabetic peripheral neuropathy (DPN) comprises longitudinal observational studies that mainly compared testing in terms of neuropathy scoring systems (most commonly the neuropathy disability score). The committee was aware that the external assessment centre (EAC) had rejected the study by Tsapas et al. (2014; a meta-analysis identified by the company) because of overlapping populations in the studies included and differences in the reference standards used, and had, instead, done its own meta-analysis. The results from the EAC's meta-analysis showed that Neuropad has a sensitivity of 89.4% (95% confidence interval [CI] 83.2 to 93.5) and a specificity of 60.3% (95% CI 50.9 to 69.0), when using a neuropathy disability score of 5 or more as a reference standard for the diagnosis of DPN. Based on this, the committee concluded that Neuropad demonstrates good sensitivity but poor specificity as a diagnostic test for DPN. Although no direct comparative data were available for 10 g monofilament, the committee and EAC agreed that it was appropriate to use the sensitivity (84%) and specificity (83%) estimates for 10 g monofilament that were used in NICE's healthtech guidance on VibraTip. The committee concluded, therefore, that the current evidence for Neuropad is insufficient to support its effectiveness as an alternative test to 10 g monofilament for detecting DPN.

Pathway positioning

4.2 The clinical experts advised the committee that patients with diabetes are offered foot checks every year, during which physical examination, 10 g monofilament testing and vibration testing are used to test for DPN and therefore the clinical risk of future complications. The clinical experts explained that patients who test positive for DPN at these foot checks (and who are therefore at moderate or high risk of foot complications) are referred to community podiatrists for ongoing foot care.

4.3 The clinical experts explained that Neuropad tests different nerve fibres and functions to a 10 g monofilament test: Neuropad tests sudomotor dysfunction, which is a feature of small fibre, preclinical DPN, whereas 10 g monofilaments are used to test for the loss of fine touch, which is a distinctive symptom of clinically apparent DPN. They explained that because it is uncertain how well autonomic testing (such as testing for sudomotor dysfunction) predicts progressive neuropathy or the development of complications, it is not included in current DPN scoring systems. This means that it would be difficult to understand, on the basis of current evidence, how Neuropad testing may affect diabetic foot risk assessment and referral practice. Specifically, the clinical experts advised that a positive Neuropad test alone would currently not lead to a change in management, because it would not alter the definition of risk status in a patient with diabetes. A patient diagnosed with preclinical DPN using Neuropad testing could be offered more attentive foot care, but it is unclear to what extent this would lead to beneficial clinical consequences.

Patient selection

4.4 The clinical experts explained that Neuropad has particular promise for patients who have difficulty in engaging with testing for DPN. Monofilament testing requires the patient to confirm when they feel a fine touch on their foot or toes, but for some people with cognitive impairment or communication difficulties, this may not be possible. The clinical experts estimated that between 5% and 10% of all patients with diabetes may have difficulty engaging with 10 g monofilament testing for these reasons. The committee acknowledged that because Neuropad testing does not need patient feedback, it may be of particular value for patients with cognitive impairment or communication difficulties if future evidence supports its case for adoption in the NHS.

4.5 The committee also heard that some patients, such as older and frailer people, may not be able to easily access foot clinics. The clinical experts explained that type 2 diabetes, which accounts for 90% of all diabetes, is much more common in older people. Many of these patients do not always attend their yearly foot checks and so do not have the benefit of foot care programmes. The clinical experts also explained that DPN progression may be prevented if it is detected early and appropriate treatment is started. Consequently, limited access to

regular testing may increase the risks of progressive DPN and its clinical complications in a vulnerable patient group. The committee acknowledged that a test such as Neuropad, which can be done easily in the community, may be of particular value to people with limited access to foot clinics but concluded that this has not been tested in clinical studies and cannot be inferred from the evidence available.

NHS considerations

4.6 The clinical experts stated that Neuropad might be considered as part of a community-delivered DPN detection and management service. However, they acknowledged that for this to be successful, changes would be needed to other important parts of the community package of care for people with diabetes. Having heard from the experts about the existing deficiencies in DPN detection and foot care services in the UK, the committee concluded that addressing these deficiencies in the current pathway would be needed before any potential benefits associated with detecting preclinical DPN could be realised.

4.7 The committee considered the importance of foot preparation before Neuropad testing in order to ensure a reliable result. It heard from the clinical experts that the foot needs to be completely dry and that the test strip should not be placed on calluses or dry skin for the result to be meaningful. It concluded that, were Neuropad introduced into the community, clear guidance on its use would be needed to avoid misleading results.

Cost savings

4.8 The committee noted the differences between the company's and EAC's revised cost models and their base-case estimates. It agreed with the EAC's changes and concluded that the revised model most accurately represented the cost consequences of adopting Neuropad.

4.9 The committee noted that Neuropad's low diagnostic specificity (based on the evidence presented and current diagnostic criteria) means that its use alone

would increase the rate of false-positive results for DPN. Because of the current uncertainty about whether patients with diagnosed preclinical DPN would benefit from referral to a foot care service, the committee concluded that a positive result with Neuropad would probably lead to further 10 g monofilament testing. The committee understood that the results of this dual-testing strategy in the EAC model should be treated with caution, because it assumed that the 2 tests are done completely independently (that is, the sensitivity and specificity of the 10 g monofilament test are not affected by the results of the Neuropad test). The committee was also aware there is no evidence to support the merits of such a dual-testing approach. It concluded that the cost modelling for Neuropad is uncertain, but that it is most likely that Neuropad testing alone would be cost incurring compared with conventional testing with a 10 g monofilament.

Potential research

4.10 In its assessment report, the EAC identified a number of possible priorities for future research on the comparative effectiveness of Neuropad and 10 g monofilament testing, and on the effectiveness of foot care programmes. The clinical experts also highlighted areas for future research that could be considered. They proposed a multicentre, longitudinal study with at least 5 years' follow up, comparing point-of-care testing strategies (including Neuropad) in predicting future diabetic complications, including DPN, using a reference standard (such as the neuropathy disability score). The experts also proposed a community-based study to explore the benefits of using Neuropad to detect preclinical DPN in populations that include vulnerable people, in whom 10 g monofilament testing is not possible. Such a study could also define the benefits to people with diabetes of improved access to DPN diagnostic and treatment services.

4.11 The committee considered that research into the wider benefits of detecting preclinical DPN and how to address the deficiencies in the current care pathway would be valuable but acknowledged that these are issues beyond the scope of this assessment. Such research would also help to clarify Neuropad's effectiveness in detecting preclinical DPN.

5 Committee members and NICE project team

Committee members

This topic was considered by NICE's medical technologies advisory committee, which is a standing advisory committee of NICE.

Committee members are asked to declare any interests in the technology to be appraised. If it is considered there is a conflict of interest, the member is excluded from participating further in that evaluation.

The minutes of the medical technologies advisory committee, which include the names of the members who attended and their declarations of interests, are posted on the NICE website.

NICE project team

Each medical technology appraisal is assigned to a team consisting of 1 or more health technology analysts (who act as technical leads for the topic) and a technical adviser.

2021 guidance review

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Update information

September 2022: We updated this guidance to reflect new evidence. These updates are marked **[2021]**. We also made editorial changes to section 1 to align with the current NICE editorial style. Details of the changes are explained in the review decision.

Minor changes since publication

December 2025: Medical technologies guidance 38 has been migrated to HealthTech guidance 486. The recommendations and accompanying content remain unchanged.

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