NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Evidence generation plan

Digitally enabled therapy for chronic tic disorders and Tourette syndrome: Neupulse

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1 Purpose of this document

NICE's assessment of digitally enabled therapy for chronic tic disorders and Tourette syndrome recommends that more evidence is generated while the Neupulse technology is being used in the NHS. A separate evidence generation plan has been produced for the Online Remote Behavioural Intervention for Tics (ORBIT) technology, which is the other technology that was assessed and is not covered in this plan.

This plan outlines the evidence gaps and what real-world data needs to be collected for a NICE review of the technology again in the future. It is not a study protocol but suggests an approach to generating the information needed to address the evidence gaps. For assessing comparative treatment effects, well-conducted randomised controlled trials are the preferred source of evidence if these are able to address the research gap.

The company is responsible for ensuring that data collection and analysis takes place.

Guidance on commissioning and procurement of the technology will be provided by NHS England, who are developing a digital health technology policy framework to further outline commissioning pathways.

NICE will withdraw the guidance if the company does not meet the conditions in section 4 on monitoring.

After the end of the evidence generation period (about 3 years), the company should submit the evidence to NICE in a form that can be used for decision making. NICE will review all the evidence and assess whether the technology can be routinely adopted in the NHS.

2 Evidence gaps

This section describes the evidence gaps, why they need to be addressed and their relative importance for future committee decision making.

The committee will not be able to make a positive recommendation without the essential evidence gaps (see section 2.1) being addressed. The company can strengthen the evidence base by also addressing as many other evidence gaps (see section 2.2) as possible. This will help the committee to make a recommendation by ensuring it has a better understanding of the patient or healthcare system benefits of the technology.

2.1 Essential evidence for future committee decision making

Clinical effectiveness compared with NHS standard care

There is limited evidence on the effectiveness of Neupulse in comparison to standard care. Further evidence should compare Neupulse to psychocoeducation, which the committee agreed should be delivered either through face-to-face or online appointments. Information about the impact that the technology has on people's symptoms should be recorded using the Yale Global Tic Severity Scale total scores.

Clinical impact of Neupulse in different subgroups

The anticipated use of Neupulse is not restricted to people with a clinical diagnosis of tic disorders or Tourettes. Due to the current unmet need for diagnosing these conditions, the technology is likely to be used without a formal diagnosis. Further evidence is needed about the clinical impact and potential adverse effects of the technology in people without a diagnosis. The committee heard that a risk of treating tics was increased anxiety. Further data on adverse events in this population would inform future decisions around the user population.

There is limited evidence on the clinical efficacy of Neupulse in people with severe tic disorders. The committee was advised that tic severity may be more stable in adults than in children and young people, enabling data analyses that could support future decisions around the user population.

Longer-term data on the clinical impact of Neupulse

It is unclear if the technology leads to a clinical benefit beyond 4 weeks. Follow-ups should be a minimum of 3 months after the intervention, and ideally at 6 months. This would improve the data available to populate future health-economic models and reduce uncertainty.

Impact of Neupulse on health-related quality of life

The impact of the technology on people's daily lives is uncertain. Further data should also be collected directly from the child, young person or adult with tics and their parents or carers if applicable. This should include the impact on daily life, for example on self-esteem, social interactions and school or work attendance and performance.

Resource use

More information on how using the technology would affect resource use in the NHS, during and after implementation is needed to help the committee understand the technology's cost effectiveness. Resource estimates should include training costs and the broader impact of the technology on services, for example those provided by local specialist clinics and carers. This could free up resources that could be used to increase access to treatment or reduce waiting times.

2.2 Evidence that further supports committee decision making

Clinical and cost effectiveness in people with comorbidities

There is limited evidence for people with diagnosed comorbidities, including:

- attention deficit hyperactivity disorder
- obsessive-compulsive disorder
- autism spectrum disorder

- mood disorders and
- anxiety.

More information about the impact of Neupulse in people with these conditions will support future committee decision making.

3 Approach to evidence generation

3.1 Evidence gaps and ongoing studies

Table 1 summarises the evidence gaps and ongoing studies that might address them. Information about evidence status is derived from the external assessment group's (EAG) report; evidence not meeting the scope and inclusion criteria is not included. The table shows the evidence available to the committee when the guidance was published. The EAG did not identify any ongoing studies that may address the evidence gaps.

Table 1 Evidence gaps and ongoing studies

Evidence gap	Neupulse
Clinical effectiveness compared with NHS standard care	Limited evidence
Clinical impact of Neupulse in different subgroups	No evidence
Longer term data on the clinical impact of Neupulse	No evidence
Impact of Neupulse on health-related quality of life	No evidence
Resource use	No evidence
Clinical and cost-effectiveness in people with comorbidities	No evidence

3.2 Data sources

Data could be collected using a combination of primary data collection, suitable real-world data sources, and data collected through the technology itself (for example, engagement data).

NICE's real-world evidence framework provides detailed guidance on assessing the suitability of a real-world data source to answer a specific research question.

The NHS England Secure Data Environment (SDE) service could potentially support this research. This platform provides access to high-standard NHS health and social care data that can be used for research and analysis. SDEs are data storage and access platforms that bring together many sources of data, such as from primary and secondary care, to enable research and analysis. They could be used to collect data to address the evidence gaps. The sub-national SDEs are designed to be agile and can be modified to suit the needs of new projects. Within an SDE, the data may be linked to other useful data such as that from primary care and could provide information on important confounders (for example, comorbidities).

The NHS Digital's Improving Access to Psychological Therapies data set (IAPT) and Mental Health Services Data Set (MHSD) are real-world data sets that could also be used to collect information about the impact that disorders have on mental health.

The quality and coverage of real-world data collections are of key importance when used in generating evidence. Active monitoring and follow up through a central coordinating point is an effective and viable approach to ensuring good-quality data with broad coverage.

3.3 Evidence collection plan

The suggested approach to addressing the evidence gaps for Neupulse is a longitudinal, parallel cohort study over 12 months. The study will follow 2 groups of people (intervention arm and a control arm) over 3 months (ideally 6 months), and compare their outcomes.

The studies should enrol a representative population, that is, people who would be offered standard care, including behavioural therapy, without digital technologies. This may include face-to-face appointments and monitoring. The studies should compare people with tic disorders or Tourette syndrome using digital technologies for self-management with a similar group having standard care. Eligibility for inclusion, and the point of starting follow up, should be clearly defined and consistent across comparison groups to avoid selection bias.

Data should be collected in all groups from the point at which a person would become eligible for standard care. The data from both the intervention and

comparison groups should be collected at appropriate time intervals and up to a minimum of 3 months. Data from people in different centres, with comparable standard care and patient population, but no access to digital technologies for self-management, should form the comparison group. Ideally, the studies should be run across multiple centres, aiming to recruit centres that represent the variety of care pathways in the NHS.

Despite consistent eligibility criteria, non-random assignment to interventions can lead to confounding bias, complicating interpretation of the treatment effect. So, approaches should be used that balance confounding factors across comparison groups, for example, using propensity score methods. To achieve this robustly, data collection will need to include prognostic factors related both to the intervention delivered and patient outcomes. These should be defined with input from clinical specialists. Also, analysis should be stratified according to the severity of the tic disorder. Incomplete records and demographically imbalanced groups can lead to bias if unaccounted for. Data collection should follow a predefined protocol and quality assurance processes should be put in place to ensure the integrity and consistency of data collection. See NICE's real-world evidence framework, which provides guidance on the planning, conduct, and reporting of real-world evidence studies. This document also provides best practice principles for robust design of real-world evidence when assessing comparative treatment effects using a prospective cohort study design.

3.4 Data to be collected

Study criteria

- At recruitment, eligibility criteria for suitability of using the digital technology and inclusion in the real-world study should be reported, and include:
  - a diagnosis status
  - position of the technology in the clinical pathway
  - the point that follow up starts
  - a detailed description of the standard care offered.

Baseline information and patient outcomes

- Information about individual characteristics at baseline, for example, sex, age, ethnicity, socioeconomic status, clinical diagnosis (and date of diagnosis), details of any comorbidities and treatments. Other important covariates should be chosen with input from clinical specialists
- Changes in tic severity using the Yale Global Tic Severity Rating Scale total score at baseline and during follow up (minimum of 3 months and ideally at 6 months).
- Changes in patient quality of life using the Gilles de la Tourette Syndrome-Quality of Life Scale at baseline and over follow up (for a minimum of 3 months).
- Information on healthcare resource use and exacerbation-related hospitalisation costs related to tic disorders and Tourette syndrome, including emergency department visits, hospital admissions and length of stay, and GP visits.
- Any changes in a person's medication and any referrals to other services.

Implementation

- Costs of digital technologies for supporting treatment of tic disorders and Tourette syndrome, including licence fees, healthcare professional staff time and training costs to support the service and integration with NHS systems
- access and uptake including the number and proportion of eligible people who were able to, or accepted an offer to, access the technology
- engagement and drop-out information, including reasons for refusal of treatment or stopping treatment
- acceptability of the technology to people using it

Safety monitoring outcomes

- Any adverse events arising from using digital technologies to support treatment of tic disorders and Tourette syndrome.

Data collection should follow a predefined protocol and quality assurance processes should be put in place to ensure the integrity and consistency of data collection. See NICE's real-world evidence framework, which provides guidance on the planning, conduct, and reporting of real-world evidence studies.

3.5 Evidence generation period

The evidence generation period should be 2 years (during which a minimum of 1 year of follow-up data will be collected). This will be enough time to implement the evidence generation study, collect the necessary information and analyse the collected data.

4 Monitoring

The company must contact NICE:

- within 6 months of publication of this plan to confirm agreements are in place to generate the evidence
- annually to confirm that the data is being collected and analysed as planned.

The company should tell NICE as soon as possible about anything that may affect ongoing evidence generation, including:

- any substantial risk that the evidence will not be collected as planned
- new safety concerns
- the technology significantly changing in a way that affects the evidence generation process.

If data collection is expected to end later than planned, the company should contact NICE to arrange an extension to the evidence generation period. NICE reserves the right to withdraw the guidance if data collection is delayed, or if it is unlikely to resolve the evidence gaps.

5 Minimum evidence standards

Neupulse has some clinical evidence suggesting that it may improve symptoms of tic disorders and Tourette syndrome in young people and adults. The technology did not report any safety concerns when using the digital technology to support treatment of tic disorders and Tourette syndrome.

In addition to the evidence above, the committee has indicated that it may in the future be able to recommend technologies in this topic area that have evidence for:

- a beneficial impact of the digital technologies compared with standard care for treating tic disorders and Tourette syndrome without digital technologies
- a clinical improvement in tic disorders and Tourette syndrome using the Yale Global Tic Severity Rating Scale total scoring
- resource use associated with the technologies and NHS standard care
- intervention acceptance, completion rates, patient preference, and uptake rates the safe use of the technology (including all adverse events).

The company can strengthen the evidence base by also having evidence for:

- effects on health-related quality of life measured through the EQ-5D
- effectiveness in different subgroups
- where the technology is used in the care pathway.

6 Implementation considerations

The following considerations around implementing the evidence generation process have been identified through working with system partners:

Technology

- Neupulse is still under development, and is anticipated to be ready for market in 2026. Modifications to the product in newer versions may impact clinical and cost effectiveness. The product will not be available to the NHS, but will be sold direct-to-customer.
- Training for health professionals and users is not provided by the company.
- The appropriateness of behavioural therapies or median nerve stimulation should be assessed on an individual basis.
- The app associated with the technology enables the user to modify frequency and strength of median nerve stimulation. Only evidence using the lowest setting was identified. The impact of changing these settings is unknown.

System considerations

- There is high variation in services available to the population. The contributing services or centres should be chosen to maximise the generalisability of evidence

generated, for example including groups of people with different socioeconomic status, or to improve data collection for any relevant subgroups. Developers should provide clear descriptions of the services and settings in which the study is done, and the characteristics of the people in the trial.

- The company does not provide training for staff to support use of the technology.
- The technology is intended for use on an ad-hoc basis to control tic symptoms. This should be considered in the study design.

Evidence generation

- Evidence generation should be overseen by a steering group including researchers, commissioners, healthcare professionals, and people with lived experience.
- The evidence generation process is most likely to succeed with dedicated research staff to reduce the burden on NHS staff, and by using suitable real-world data to collect information when possible.
- Careful planning of the approach to information governance is vital. The company should ensure that appropriate structures and policies are in place to ensure that the data is handled in a confidential and secure manner, and to appropriate ethical and quality standards.

Accessibility

- The technology may not be suitable for everyone, for example people without access to, or who cannot use, a smartphone or computer. People with cognitive impairment, problems with manual dexterity or learning disabilities may need additional help for carers or advocates.
- The technology could be more beneficial if it is set up to ensure that language and cultural considerations of its users are met, and the digital literacy of people using the technology is considered.
- The company intends to sell devices direct to customers in 2026. This could lead to socio-economic biases in future cohorts. It will be important to collect this data in the baseline information (see section 3.3).

Safety

- Neupulse offers several different settings for median nerve stimulation that can be adjusted by the user through the app. Evidence is needed to understand the clinical impact of the user switching between the settings.

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