NICE National Institute for Health and Care Excellence

Evidence generation plan for digital therapy for chronic tic disorders and Tourette syndrome: Neupulse

Implementation support

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1 Purpose of this document

NICE's assessment of digitally enabled therapy for chronic tic disorders and Tourette syndrome considered the Neupulse technology. This plan outlines the evidence gaps and what data needs to be collected for a future NICE recommendation about the use of the technology in the NHS. It is important that evidence generation is aligned with how the technology could be used in the NHS in the future: under the supervision of a healthcare professional following a formal diagnosis.

NICE has produced a separate evidence generation plan for the Online Remote Behavioural Intervention for Tics (ORBIT) technology.

This plan 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 developer is responsible for ensuring that data collection and analysis takes place.

Neupulse is included in this early value assessment but is awaiting CE and UKCA marking approval. It is estimated that it will be available in 2026, so it cannot be used or included in the NICE recommendations at this time. NICE is publishing the evidence generation plan before regulatory approval has been granted and a NICE recommendation is made. This is to support the planning and design for further evidence generation in anticipation of regulatory approval. NICE will withdraw any subsequent recommendation in the guidance if the developer does not meet the conditions in section 4 on monitoring.

After the end of the evidence generation period (3 years), the developer 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 developer can strengthen the evidence base by addressing the other evidence gaps (see section 2.2). 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 with standard care. Further evidence should compare Neupulse with 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, the Clinical Global Impression Score – Improvement, and ideally the Goal Based Outcomes scale. Also, information about the impact of the technology on daily life, for example on self-esteem, social interactions and school or work attendance and performance should be collected.

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 recorded at 3 and 6 months after commencing or ongoing use of the intervention, and ideally at 12 and 18 months. This would improve the data available to populate future health-economic models and reduce uncertainty.

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 clinical assessment.

2.2 Evidence that further supports committee decision making

Clinical and cost effectiveness in different subgroups

There is limited evidence for people in different subgroups, such as those with severe tic disorders and those with diagnosed comorbidities, including:

- attention deficit hyperactivity disorder (ADHD)
- 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
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 impact of Neupulse in different subgroups	Limited 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 Talking Therapies, for anxiety and depression 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

It is important that evidence generation is aligned with how the technology could be used in the NHS in the future: under the supervision of a healthcare professional following a formal diagnosis.

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

Statistically robust data about the effectiveness of the technology in different subgroups requires very large study populations that are not feasible in this context. Analysis of any data that is available at the end of the evidence generation period will nevertheless support future NICE decision making, so relevant characteristics should be recorded.

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. The technology is indicated for use with or without a formal diagnosis. It is likely that people participating in future multi-centre trials will have a formal diagnosis. Further evidence on the clinical impact of Neupulse and potential adverse events in people without a diagnosis should also be collected if it is being used in this way.

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 6 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, the Clinical Global Impression Score – Improvement, and ideally the Goal Based Outcomes scale, at baseline and during follow up (minimum of 6 months and ideally at 12 and 18 months).
- Information about the impact of the technology on daily life, for example on self-esteem, social interactions and school or work attendance and performance.
- 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 stopping treatment.

Safety monitoring outcomes

- Any adverse events arising from the technology 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 3 years. This will be enough time to implement the evidence generation study, collect the necessary information and analyse the collected data.

4 Monitoring

The developer 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 developer 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 developer 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, the Clinical Global Impression Score – Improvement and, ideally the Goal Based Outcomes scale
- improvements in overall patient quality of life
- 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).

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 initially be sold direct-to-customer.
- 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.
- There is an unmet need for diagnosing and treating tic disorders and Tourette syndrome, and access to treatment also varies across the NHS. This will bias which centres or services are selected for data collection. This could also bias which centres adopt the technology and increase health inequalities.
- 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 developer 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.
- Once the evidence generation period has concluded, ideally further data about the clinical impact of the digitally enabled therapy for chronic tic disorders and Tourette syndrome could be collected to support planning and decision making.

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.
- People from ethnic minority backgrounds are underrepresented in terms of accessing the appropriate services for tic disorders and Tourette's syndrome. This could impact study recruitment and access to the technology.

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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