Early value assessment consultation document for HTE10056 Digital therapy for chronic tic disorders and Tourette syndrome

November 2024

Guidance development process

Early value assessment (EVA) guidance rapidly provides recommendations on promising health technologies that have the potential to address national unmet need. NICE has assessed early evidence on these technologies to determine if earlier patient and system access in the NHS is appropriate while more evidence is generated.

The medical technologies advisory committee has considered the evidence and the views of clinical and patient experts. EVA guidance recommendations are conditional while more evidence is generated to address uncertainty in their evidence base. NICE has included advice in this guidance on how to minimise any clinical or system risk of early access to treatment.

More evidence will be generated over the next 3 years to assess if the benefits of these technologies are realised in practice. NICE guidance will be reviewed to include this evidence and make a recommendation on the routine adoption of this technology across the NHS.

This document has been prepared for public consultation. It summarises the evidence and views that have been considered and sets out the recommendations made by the committee. NICE invites comments from registered stakeholders, healthcare professionals and the public. This document should be read along with the evidence (an EVA report).

The advisory committee is interested in receiving comments on the following:

Has all of the relevant evidence been taken into account?
Are the summaries of clinical and cost effectiveness reasonable interpretations of the evidence?

Are the recommendations sound, and a suitable basis for guidance to the NHS?

Equality issues

NICE is committed to promoting equality of opportunity, eliminating unlawful discrimination and fostering good relations between people with particular protected characteristics and others. Please let us know if you think that the recommendations may need changing to meet these aims. In particular, please tell us if the recommendations:

could have a different effect on people protected by the equality legislation than on the wider population, for example by making it more difficult in practice for a specific group to access the technology
could have any adverse effect on disabled people.

Please provide any relevant information or data you have about such effects and how they could be avoided or reduced.

Note that this document is not NICE's final guidance on digital therapy for chronic tic disorders and Tourette syndrome. The recommendations in section 1 may change after consultation.

After consultation, NICE will consider the comments received. The final recommendations will be the basis for NICE’s early value guidance.

Key dates:

Closing date for comments: 17 December 2024

1 Recommendations

Can be used while more evidence is generated

1.1 Two technologies can be used with standard care during the evidence generation period as options for treating chronic tic disorders and Tourette syndrome. The technologies are:

- Online Remote Behavioural Intervention for Tics (ORBIT; Mindtech) in children and young people 9 to 17 years
- Neupulse (Neurotherapeutics) in children and young people 12 years and over, and in adults.

  Neupulse is currently working towards CE and UKCA marking (expected 2026). Neupulse can be used once it has appropriate regulatory approval and meets the standards within NHS England's Digital Technology Assessment Criteria (DTAC).

  The technologies can only be used if the evidence outlined in the evidence generation plans is being generated.

1.2 The companies must confirm that agreements are in place to generate the evidence (as outlined in NICE's evidence generations plans). They must contact NICE annually to confirm that evidence is being generated and analysed as planned. NICE may withdraw the guidance for a technology if these conditions are not met.

1.3 At the end of the evidence generation period (about 3 years), the companies should submit the evidence to NICE in a form that can be used for decision making. NICE will review the evidence and assess if the technologies can be routinely adopted in the NHS.

What evidence generation is needed

1.4 More evidence generation in children, young people and adults is needed on:

- long-term clinical effectiveness
- the effect of the technologies on quality of life
- adherence
- how the conditions progress without the technologies
- adverse events
- the impact of long-term effectiveness on long-term costs
- long-term follow-up costs needed to maintain effectiveness
- clinical and cost effectiveness within subgroups
- views on the effects of the technologies from people with tic disorders or Tourette syndrome and their carers.

The evidence generation plans give further information on the prioritised evidence gaps and outcomes, ongoing studies and potential real-world data sources. They include how the evidence gaps could be resolved through real-world evidence studies.

Potential benefits of use in the NHS with evidence generation

- **Access:** Access to diagnosis and treatment options for people with chronic tic disorders and Tourette syndrome is limited because of variations in expertise, and access to and availability of services across the NHS. Digital therapies for chronic tic disorders and Tourette syndrome improve access and offer another treatment option. This could particularly benefit people who need more flexible access to treatment or prefer a digital therapy over face-to-face therapy.
- **Clinical benefit:** Clinical evidence suggests that digital therapies may reduce the severity of the symptoms of chronic tic disorders and Tourette syndrome and improve people's ability to function in everyday life.
- **Resources:** These technologies may reduce waiting lists and referrals to specialist services.

Considerations

- **Unmet need:** Provision of services for chronic tic disorders and Tourette syndrome varies across the NHS. There is a shortage of trained therapists and behavioural therapy is only available at a small number of specialist treatment centres. So, digital therapies could potentially increase access and treatment options and reduce waiting lists.
- **Costs:** There is considerable uncertainty associated with the early results from the economic modelling because of the limited evidence. This guidance will be reviewed after 3 years and the recommendations may change. This should be taken into account when negotiating the length of contracts and licence costs.
- **Patient outcomes:** Consistent quality-of-life measures should be used.
- **Equality:** Digital therapies may not be accessible to everyone. The following groups may be less likely to benefit and may prefer other treatment options:

- people with limited access to smart devices, laptops or an internet connection or an internet connection
- people less comfortable with or skilled at using digital technologies
- people who have difficulty reading or understanding health-related information in English.

2 The technologies

2.1 Digital therapy for chronic tic disorders and Tourette syndrome could allow people to have treatment for these conditions remotely.

2.2 NICE has assessed 2 digital technologies for chronic tic disorders and Tourette syndrome. The technologies have different features but both provide therapeutic intervention. The criteria for including technologies in this assessment are in the final scope on the NICE website. The included technologies are:

- Online Remote Behavioural Intervention for Tics (ORBIT; Mindtech): this is an online guided self-help intervention that delivers an evidence-based behaviour therapy for chronic tic disorders and Tourette syndrome. It is for children and young people 9 to 17 years and was developed from an existing research platform (BIP TIC) in Sweden. It was designed to be age-appropriate in appearance for use by children and young people 9 to 17 years and their parents or carers. It includes videos, animations and interactive scripts. ORBIT provides a form of behavioural therapy called an exposure with response-prevention intervention. It is supported by an online therapist across a 10-week programme. The programme is delivered alongside psychoeducation, parental support, reward and functional analyses through a secure internet platform. It includes self-help guided chapters that include tic psychoeducation. These are followed by exposure and response-prevention behavioural therapy tasks. It also includes separate chapters for parents and carers to further support them in their roles. The therapist has 10 to 20 minutes of contact with the family each

week, during which they promote engagement with the intervention and answer questions rather than delivering therapeutic content. The programme teaches children and young people to suppress their tics while tolerating the urges to tic. ORBIT has been studied as part of NIHR-funded UK-based trials. ORBIT does not require CE marking because it is not considered a medical device.

- Neupulse (Neurotherapeutics): this is a wearable wrist-worn neuromodulation device with a corresponding phone app. It is for treating chronic tic disorders and Tourette syndrome in children and young people 12 and over and in adults. The device addresses the imbalances in neural activity that are associated with tics and premonitory urges by modulating neural oscillations within the brain's sensorimotor networks. It delivers low-intensity electrical pulses to the median nerve (median nerve stimulation) to reduce tic frequency and severity. Neupulse produces low-intensity electrical stimulation up to a maximum of 14 mA. The device is currently under development for over-the-counter sale and will be supported by written and video-based guidance and a technical support helpline. Neupulse is working towards CE and UKCA marking, and it is estimated that it will be available in 2026.

See table 1 in the external assessment group's assessment report for details of the technologies.

Care pathway

2.3 The scope for this early value assessment included a targeted population of people with a diagnosed primary tic disorder who have had psychoeducation, but their tics continue to be bothersome. There is no comprehensive clinical guideline for the diagnosis and management of tic disorders in children and young people in the UK. NICE's guideline on suspected neurological conditions: recognition and referral contains some information on tic disorders. It recommends that children and young people with tic disorders that have a significant impact on their quality of

life, should be considered for referral to specialist mental health services, neurodevelopmental teams or for neurological assessment. Adults with tic disorders should be considered for neurological assessment if their symptoms are severe and the disorder continues to cause distress.

2.4 In the UK, people with chronic tic disorders and Tourette syndrome attend an initial appointment with a GP in primary care. When a tic disorder has a significant impact on a person's quality of life, they are usually referred to appropriate secondary or tertiary care services (depending on the presentation, comorbidities, and local specialist clinics). Children and young people may be referred to mental health services (including to the Children and Young People's Mental Health Services), neurodevelopmental teams, paediatric teams or paediatric neurology teams, depending on local services and pathways. Adults are usually referred to neurology services or to neuropsychiatry clinics. Because tics may improve with time, NICE's guideline on suspected neurological conditions: recognition and referral recommends a watch-and-wait approach for people presenting in primary care, especially if they do not have functional impairment. Current practice varies by location across the UK and by the availability of local services but, in general, treatment options for chronic tic disorders include:

- psychoeducation
- behavioural therapy
- pharmacological therapy
- deep brain stimulation and
- Botox.

2.5 Accepted evidence-based treatment options for diagnosed tic disorders are psychoeducation as a first line option and behavioural therapies for people who still have difficulties with their tics. For some people, behavioural approaches may not be as effective, feasible or accessible and other possible treatments (with or without behavioural therapies) will be discussed. Digital therapy for chronic tic disorders and Tourette

syndrome would be offered after clinical assessment and diagnosis. These interventions should only be considered if the person (and parent or carer where appropriate) has had access to a form of psychoeducation. If the tic disorder continues to cause difficulties, a healthcare professional may consider referring people for these interventions.

The comparator

2.6 The comparator is standard care for managing chronic tic disorders and Tourette syndrome, including psychoeducation and behavioural therapy. Standard care varies significantly across clinical practice. Digital therapy would be used in addition to standard care.

2.7 There was no evidence comparing any of the interventions with current standard care. The online psychoeducation may be a more active comparator than face-to-face psychoeducation in current UK clinical practice. In the economic modelling, the comparator for ORBIT is online psychoeducation in children and young people. The comparator for Neupulse is a waitlist control (that is, no stimulation) in children and young people 12 years and over, and in adults.

3 Committee discussion

NICE's medical technologies advisory committee considered evidence on digital therapy for chronic tic disorders and Tourette syndrome from several sources, including an early value assessment report by the external assessment group (EAG) and an overview of that report. Full details are in the project documents for this guidance on the NICE website.

Unmet need

3.1 Provision of services for chronic tic disorders and Tourette syndrome varies across the NHS. Barriers to access include a shortage of trained therapists and limited access to behavioural therapy, which is only available at a small number of specialist treatment centres. As a result, experts estimate that less than 20% of children and young people with

chronic tic disorders and Tourette syndrome currently have access to behavioural therapies (Marino et al. 2023). Clinical experts noted that there is often a long waiting list for referral to specialist services.

3.2 Because of variations in expertise, access and availability of services across the UK, many people are not getting the diagnosis, treatment and support they need. Digital therapies may improve access as well as equity of access to treatment options for people with chronic tic disorders and Tourette syndrome.

3.3 Clinical experts highlighted that providing any available resources to manage tics will help and support people living with tics. Both clinical and patient experts highlighted the great unmet need in this population. So, the committee recommended using Online Remote Behavioural Intervention for Tics (ORBIT) and Neupulse in the NHS while more evidence is being generated.

Clinical effectiveness

3.4 The EAG prioritised 3 randomised controlled trials for assessment. Two studies compared ORBIT with psychoeducation; 1 was done in the UK and the other in Sweden. The third study was UK-based and compared Neupulse active stimulation with sham stimulation. The EAG noted that the overall risk of bias was low for the 3 trials. The EAG reported on evidence from the prioritised studies, which used the Yale Global Tic Severity Scale's (YGTSS) Total Tic Severity Score to assess tic severity. They showed that tic severity was lower in the intervention groups compared with the comparator groups at follow-up periods ranging from 4 weeks to 18 months. But, no significant improvements were observed between treatment groups in tic-related impairment and distress (measured using the impairment score of the YGTSS). Clinical experts noted that the YGTSS's impairment score is not used widely in the research framework. But they explained that it is helpful to understand how tics affect day-to-day participation and function by talking to people

with chronic tic disorders and Tourette syndrome, and their parents or carers.

3.5 The committee considered that ORBIT collected follow-up data for up to 18 months. Neupulse is still at an early stage of development, so there is no data beyond 4 weeks. Both companies mentioned that the clinical benefit will be sustained after using their technologies. Clinical experts explained that 18 months follow up in the ORBIT trial is more than enough and that it is common to treat lifelong neurological conditions where the evidence is in the shorter term. In clinical practice, the variability of treatment response in chronic tic disorders and Tourette syndrome is difficult to measure in a trial. It is unknown whether treatments continue to provide clinical benefits for years afterwards.

Managing risks

3.6 The committee carefully considered the safety of using digital therapy to treat chronic tic disorders and Tourette syndrome while further evidence is generated. Two ORBIT studies reported adverse events. Common adverse events reported in the UK ORBIT study were low mood, an increase in tics, and anger or irritability. Two serious adverse events were recorded, but both were deemed to be unrelated to participation. The company for ORBIT mentioned that there was no difference in the occurrence of adverse events in people with comorbidities in its post-hoc analysis. There were no adverse events reported in the Neupulse study. The company for Neupulse said that it had monitored and recorded adverse events but had not published this information. It mentioned that most adverse events are related to gel pads not being used correctly, which causes skin irritation. The committee noted concerns about the patient support for Neupulse because it is a self-administered device.

3.7 ORBIT has a potential escalation process for people who need more intensive treatment or referral to other services. The company for Nepulse stated that it does not yet have an escalation process. The committee

considered that services would need staff and resources to monitor and respond to unexpected events, and to escalate care when needed.

3.8 Clinical experts were concerned about the impact of using Neupulse in people with functional tics. The company for Neupulse indicated that it plans to provide the technology directly to people who have tics and that people can use Neupulse without a formal diagnosis. Clinical experts raised concerns about people using Neupulse outside of the healthcare professional's clinic. There is a possibility that it could have unintended effects for people with functional tics and comorbidities, such as suicidal thoughts, anxiety and attention deficit hyperactivity disorder. Clinical experts also suggested that people should continue working with healthcare professionals for their long-term care. The committee felt that more data is needed on the use of Neupulse in people with functional tics and comorbidities. The committee concluded that Neupulse should have a system in place that provides adequate and timely professional support in response to alerts and outputs from people using the technology.

Use of digital technologies

3.9 Clinical experts mentioned that it is important to take people's preference into account when considering treatment because people tolerate tics differently. Some people are happy to be discharged after a psychoeducation session. Both companies said that their technologies are not intended to replace psychoeducation, and ORBIT includes psychoeducation as one of its modules.

3.10 ORBIT has 'e-coaches' (not therapists), who are usually assistant psychologists, to support and motivate engagement throughout the programme.

3.11 The company stated that Neupulse does not need to be worn all the time because intermittent stimulation is sufficient to provide clinical benefits. The app for Neupulse can be used as a tracker for tics and a control for

the device. People with epilepsy are excluded from the Neupulse trial and are unlikely to be able to safely use the technology.

Costs and resource use

3.12 The EAG developed a Markov cohort model to assess the cost effectiveness of different therapies for chronic tic disorders and Tourette syndrome in children and young people 12 years and over, and in adults. The EAG did not include any subgroup analyses in the economic model because there was not enough evidence to inform subgroup-specific transition probabilities. The EAG suggested that it was not possible to determine a definitive base-case incremental cost-effectiveness ratio (ICER). They explained that this is due to a lack of long-term follow-up data and uncertainty about the intervention costs that might be needed to maintain effectiveness in the long term. There is substantial uncertainty surrounding the estimated ICERs. While there is uncertainty for both technologies, the magnitude of uncertainty for Neupulse is greater than it is for ORBIT, driven by Neupulse's shorter follow up. Probabilistic ICERs ranged from £642 per quality-adjusted life year (QALY) gained to ORBIT being not cost-effective. The probability of ORBIT being cost-effective at a threshold value of £20,000 per QALY ranged from 52% to 89% across a range of explored scenarios. The EAG explained that the uncertainty is because of the extrapolation of the trial results from a short time horizon to a lifetime horizon.

3.13 Cost-effectiveness results for Neupulse were highly uncertain due to a lack of published transition probability data, the short 4-week follow up and uncertainty surrounding the intervention cost. The EAG assumed that there were no intervention costs assigned to the waiting list control arm of the model and no additional training or therapist support costs would be incurred. The company for Neupulse explained that Neupulse is intended to be a self-administered technology, with the company-provided materials containing all the training needed. The company is currently doing a usability study to assess how people follow the provided

information. The EAG noted that transition probabilities were based on small counts and longer follow up is needed to determine whether initially optimistic improvements can be sustained longer term.

3.14 The committee noted that the evidence informing the cost-effectiveness model was limited but there was plausibility of cost effectiveness. It concluded that it was appropriate to recommend both technologies for conditional use in the NHS while more evidence is being generated.

Patient considerations

3.15 Patient experts explained that chronic tic disorders and Tourette syndrome are lifelong conditions that affect all aspects of life, and it is often difficult to get a diagnosis and treatment. In some areas of the country, it is impossible to get access to services. People are often referred to multiple services but are told that the services cannot help them and that tics are out of their remit. A patient expert said that treatment relies heavily on people getting a diagnosis, but 56% of people waited more than a year for one. Even when they get a diagnosis, treatment and support are minimal in most areas. Many people are diagnosed and discharged in the same appointment with no offers of treatment. This may mean that they have to pay for private treatment. NICE surveyed people with chronic tic disorders and Tourette syndrome, and their parents or carers, about their experiences. NICE received 1,508 responses to the patient survey. People who completed the survey said that for most people it can take a long time to get a diagnosis (most people need to wait at least 6 months to 2 years). The acceptance of using digital technologies varied between people who completed the survey. The patient survey highlighted that the treatment options for chronic tic disorders and Tourette syndrome are limited.

3.16 Patient experts advised that any recommended digital therapy should only be offered when needed. They also suggested that digital therapy should be offered as a supplementary treatment after psychoeducation. Psychoeducation should be offered to everyone with a diagnosis. The

possibility of training education staff, social workers and support workers on the technology should be considered. A patient expert added that treatment will also have a wider therapeutic effect on carers, parents and families who are also negatively affected by the stigma surrounding tic disorders and Tourette syndrome. Patient experts expressed their concern that treatment may be shifting to digital therapy because it is cheaper and possibly easier to deliver than face-to-face care. They were concerned that this may be happening despite weak evidence of a clinical benefit compared with existing treatments.

Equality considerations

3.17 The committee acknowledged that access to diagnosis and treatment for people with chronic tic disorders and Tourette syndrome is limited. One clinical expert stated that there is a long wait for specialist assessment. The availability of behavioural therapy is extremely limited, particularly for adults. Digital therapies could increase access to treatment by providing another option for people with chronic tic disorders and Tourette syndrome. A submission from a patient organisation noted that chronic tic disorders and Tourette syndrome can have significant lifelong impacts on a person's ability to lead a normal life. These conditions can cause pain, stigma, isolation and anxiety. They can also have significant detrimental effects on education and employment, as well as on a person's physical, emotional and mental health. Patient experts also noted that people with chronic tic disorders and Tourette syndrome may experience stigma and discrimination, especially in childhood. So, it is important to carefully consider how treatments are presented and administered, because they could draw unwanted attention or further exacerbate social challenges for these people.

3.18 The committee considered that most participants in at least one of the ORBIT studies (the UK study) were white. A clinical expert explained that it reflects the cohort of people with chronic tic disorders and Tourette syndrome in NHS practice.

3.19 A patient expert advised that digital therapy may not be accessible to all socio-economic groups. Additional support and resources may also be needed for people with visual or hearing impairments, cognitive impairment, problems with manual dexterity, learning disabilities or who have difficulty reading or understanding health-related information in English. People's ethnic, religious, and cultural backgrounds may affect their views of digital health technologies. Healthcare professionals should discuss the language and cultural content of the technologies with people before use.

3.20 Digital therapies may not be suitable for everyone. They are delivered using a smartphone, tablet or computer. People need regular access to a device with internet access to use the technologies. Additional support and resources may be needed for people who are unfamiliar with digital technologies or do not have access to smart devices or the internet. People with limited access to these technologies or who are less comfortable or skilled at using digital technologies may be less likely to benefit.

Implementation

3.21 Neither of the technologies included in this assessment are currently used in the NHS. Both technologies function differently. The company for Neupulse stated that it is a self-administered device, but the committee suggested that both technologies should involve supervision from healthcare professionals.

3.22 There is limited evidence on the acceptance and adherence of using digital therapies in people with chronic tic disorders and Tourette syndrome. There were also uncertainties around whether people would need to use the ORBIT platform for the longer term after finishing the sessions and the effectiveness of repeated interventions after relapse.

Evidence gap review

3.23 For both technologies, there were evidence gaps related to population, intervention, comparators and outcomes. The committee concluded that there is potential benefit and some evidence to support recommending both digital therapies for people with chronic tic disorders and Tourette syndrome in the NHS with evidence generation, once appropriate regulatory approval is in place. The key evidence gaps were:

- Population: the relevant evidence for both technologies was around children and young people. There was limited evidence of the effects of using the technologies in adults. To get access to a diagnosis and treatment for adults with tic disorders is extremely difficult. The symptoms of tic disorders often fluctuate. Certain life events, such as periods of increased stress, can cause some adults with mild tics to experience severe symptoms if they cannot access treatment. So, more research is needed on the benefits and risks of using digital therapies in adults. The clinical experts also mentioned that people with attention deficit hyperactivity disorder, obsessive-compulsive disorder and autism spectrum disorder are under-represented in the trial compared with clinical practice. This difference might be due to the measures used to assess comorbidities in the trial, rather than the population itself. People with these conditions could be disadvantaged by using digital technologies. More evidence is needed on using the technologies in people with comorbidities.
- Intervention: there was limited evidence particularly for Neupulse. The clinical experts suggested that evidence for Neupulse is required for a minimum of 6 months, with 12 months being the ideal duration. For ORBIT, the EAG stated that having data from additional timepoints would support extrapolation of the effectiveness beyond 18 months. The clinical experts advised that a minimum of 3 months of data is collected, with 6 months being the ideal. This is in addition to the 18 months of ORBIT data. But, securing sufficient funding for a 2-year data collection period may present challenges.

- Outcomes: evidence is lacking on the effect of digital therapies on quality of life. The EAG would like evidence that captures how a reduction in severity impacts quality of life or activity in daily life. The clinical experts explained that the connection between the objective measure of tics and quality of life is difficult. The EAG stated that the CHU-9D (Child Health Utility 9D) reported in the ORBIT trial is the only available utility score for the modelled health states. The clinical experts suggested that considering outcome measures such as school and employment attendance, interviews with families and a qualitative survey may be beneficial. The process-evaluation study used during the ORBIT trial included both children and parents and carers. But, more children's reported response for their own health state is needed. It will be useful to have views from people with chronic tic disorders and Tourette syndrome and their parents and carers.
- Adverse events: more information related to the tolerability and comfort of using Neupulse is needed. The clinical experts also advised that more research is needed on the effects of stopping Neupulse.
- Cost and resource use: more evidence is needed on long-term costs needed to maintain long-term effectiveness. It would also be useful to know the training requirements, staff and resource use for Neupulse.

4 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 evaluated. 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.

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NICE project team

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

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