

Alpha-Stim AID for anxiety disorders

Medical technologies guidance

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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.

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This guidance replaces MIB193.

1 Recommendations

1.1 Alpha-Stim AID shows promise for managing anxiety disorders. However, there is not enough good-quality evidence to support the case for routine adoption.

1.2 Research is recommended to address uncertainties about Alpha-Stim AID's:

- short- and long-term efficacy
- position in the care pathway for managing anxiety disorders and
- resource impact.

This research should include:

- a study to better understand how Alpha-Stim AID affects brain function in people with anxiety disorders
- a randomised controlled trial comparing Alpha-Stim AID with individual cognitive behavioural therapy (CBT), medication or both.

Find out details of the research recommended in [section 4.11](#).

Why the committee made these recommendations

Treatment for anxiety disorders usually includes CBT, medication or both. Alpha-Stim AID uses an electric current intended to generate calming brain waves, which may relieve anxiety symptoms.

Clinical trial evidence shows that Alpha-Stim AID can relieve anxiety symptoms in people with anxiety disorders. But it is not clear how this happens and how much benefit people get. Also, the evidence is of low quality. How long any benefit lasts is unclear because most of the trials lasted for only 5 or 6 weeks. There is also no evidence comparing Alpha-Stim AID with individual CBT or medication.

The effect of adopting Alpha-Stim AID on costs and resources is unclear because its clinical effectiveness and its position in the care pathway are uncertain. Alpha-Stim AID is not recommended for routine adoption and further research is needed.

2 The technology

Technology

- 2.1 Alpha-Stim AID is an electrotherapy device that uses a variable electric microcurrent to stimulate alpha wave activity. The current has a pulse repetition rate of 0.5 hertz, with a pattern of bipolar asymmetric rectangular waves which repeat at 10-second intervals.
- 2.2 Alpha-Stim AID is compact, about the size of a mobile phone, and delivers an electric current through a pair of small clips attached to the ear lobes. The clips have removable soft pads that are moistened to ensure electricity conduction. The strength of the current can be adjusted. Alpha-Stim AID is recommended to be used for between 20 and 60 minutes every day, every other day or as needed to treat symptoms of anxiety. Alpha-Stim AID is battery powered and portable. The company has 7 previous versions of the Alpha-Stim AID device and states that all versions are based on the same mechanism of action.

Innovative aspects

- 2.3 Alpha-Stim AID differs from other anxiety disorder treatments because it uses a patented electrical wave pattern that is transmitted to the brain to stimulate the production of alpha waves.

Intended use

- 2.4 Alpha-Stim AID is intended to be used to treat anxiety, insomnia and depression. This guidance focuses on the use of Alpha-Stim AID for treating anxiety disorders. The device can be self-administered at home, or by a healthcare professional in a hospital or clinic. Alpha-Stim AID may affect the functioning of implanted cardiac pacemakers and defibrillators. The instructions for use note that people should not operate potentially dangerous machinery or vehicles during treatment, and sometimes for several hours after treatment. The safety of cranial electrotherapy has

not been established during pregnancy. The device has a 5-year warranty.

Relevant pathway

- 2.5 [NICE's guideline on generalised anxiety disorder and panic disorder in adults: management](#) provides principles of care for people with generalised anxiety disorder. It recommends a stepped-care model to organise service provision and to help people with generalised anxiety disorder, their families, carers and practitioners choose the most effective intervention.
- 2.6 Improving Access to Psychological Therapies (IAPT) services provide evidence-based psychological therapies to people with anxiety disorders and depression. A clinical expert noted that IAPT teams are the standard structure of service provision for people with anxiety and depression in most regions of England. IAPT teams deliver the NICE-recommended stepped-care model for generalised anxiety disorder.
- 2.7 [NICE's guideline on social anxiety disorder: recognition, assessment and treatment](#) provides treatment principles for adults with social anxiety disorder. It recommends the use of individual cognitive behavioural therapy (CBT). If a person wants to have drug treatment, a selective serotonin reuptake inhibitor (escitalopram or sertraline) should be offered. For adults who decline CBT and drug treatment, short-term psychodynamic psychotherapy, that has been specifically developed to treat social anxiety disorder, should be considered.

Costs

- 2.8 The cost of Alpha-Stim AID is £450 (excluding VAT) per device. The device can be reused by multiple people. A per-person treatment cost of £70 is used in the cost modelling, which is based on a treatment time of 10 weeks and includes £40 to cover other costs such as staff time, postage and consumables.

For more details, see the [Alpha-Stim website for Alpha-Stim AID for](#)

anxiety disorders.

3 Evidence

Clinical evidence

The clinical evidence comprises 6 studies, of which 3 are randomised controlled trials

- 3.1 Six studies provided evidence relevant to the decision problem in the scope, including 2 published randomised controlled trials, 1 unpublished randomised controlled trial and 3 non-comparative observational studies. The studies included between 12 and 197 people. Only 1 study used the current model of the device, the others used older models. One study was done in the UK.

Evidence shows that using Alpha-Stim AID relieves anxiety symptoms

- 3.2 The 3 randomised controlled trials showed a statistically significant improvement in patient-reported anxiety scores with Alpha-Stim AID compared with drugs alone, a sham device or no treatment in people with anxiety disorders. The benefit of Alpha-Stim AID in relieving anxiety symptoms was also reported consistently in the observational studies.

There is no evidence of the long-term effect of Alpha-Stim AID

- 3.3 The studies were of short duration (usually 5 to 6 weeks) with only 1 observational study reporting longer-term outcomes at 24 weeks.

The published evidence on the effect of Alpha-Stim AID on quality of life is limited

- 3.4 Only 2 of the studies reported improvements in quality of life (Morriss et al. 2019, Lu and Hu 2014) using health questionnaire (EQ-5D-5L and WHOQOL BREF) scores. An improvement in quality of life was also

reported with Alpha-Stim AID in a patient survey run by NICE's Public Involvement Programme. For details, see the [assessment report overview in the supporting documents for this guidance](#).

Alpha-Stim AID is considered a safe device

- 3.5 Adverse events reported with Alpha-Stim AID in 2 studies included mild headache, dizziness, nausea and feeling strange. Similar symptoms were reported by people who used Alpha-Stim AID in the patient survey that was done as part of this assessment. Additional symptoms reported in this survey included ear discomfort and worsening of anxiety symptoms. All reported adverse events were mild. The instructions for use note that prolonged electrotherapy stimulation treatment at currents higher than necessary may cause dizziness or nausea that can last for hours to days. The clinical experts did not identify any specific safety concerns with Alpha-Stim AID.

Additional evidence on the mechanism of action of Alpha-Stim AID for treating anxiety disorders is uncertain

- 3.6 In response to consultation comments about the mechanism of action of Alpha-Stim AID, the external assessment centre (EAC) reviewed additional studies that were highlighted by the consultees. It concluded that 2 published studies (Kennerly 2004; Lande and Gragnani 2018), and 1 PhD thesis (Kennerly 2006) which reported electroencephalogram (EEG) parameters of brain activities after using the Alpha-Stim AID device, were potentially relevant. The EAC noted, however, that none of these studies examined the association between changes in brain wave activity and changes in anxiety symptoms. The EAC also reviewed a conference abstract and an unpublished single case report, which reported an increase in brain alpha waves and a reduction in perceived anxiety symptoms after using the Alpha-Stim AID device. But the EAC emphasised that these results should be treated with caution because of the small sample size and uncertainties around study details and the generalisability of the results.

Further investigation of Alpha-Stim AID's mechanism of action is

needed

- 3.7 Three clinical experts, including 1 expert with extensive expertise in interpreting EEG recordings, also reviewed the additional evidence and agreed with the EAC's conclusions. The expert with EEG expertise considered that further investigation, preferably in studies that include a sham control, is justified to improve the understanding of Alpha-Stim AID's mechanism of action.

Cost evidence

One UK study is included in the economic modelling

- 3.8 The company identified 1 UK study (Morriss et al. 2019). This reported the cost impact of Alpha-Stim AID as a treatment option for people with anxiety disorders who were waiting for individual cognitive behavioural therapy (CBT) delivered by Improving Access to Psychological Therapies (IAPT) services. No additional economic analyses were identified by the EAC.

The company's IAPT model shows cost savings in treating anxiety disorders

- 3.9 The company developed a decision tree model with a time horizon of 6 months. The model compared the cost of using Alpha-Stim AID as an option for people waiting for individual CBT in IAPT services with that of individual CBT alone. The results showed that Alpha-Stim AID was cost saving by £817.68 per person.

The EAC changes the company's IAPT model to reflect the evidence and expert opinion

- 3.10 The EAC agreed with many of the assumptions in the company's IAPT model but found some limitations. In the UK observational study, a significant proportion of people who were offered Alpha-Stim AID chose not to use it and preferred to wait for individual CBT (Morriss et al. 2019). The EAC therefore revised the model to reflect the reduced uptake of

Alpha-Stim AID. The EAC also modified the structure of the model to better reflect the current care pathway as outlined by clinical experts. The EAC's base case included drug treatment as an option at the start of the pathway and for people whose anxiety symptoms did not respond to Alpha-Stim AID or individual CBT. The EAC excluded the second course of individual CBT for people whose anxiety symptoms did not respond to an initial course of treatment.

The EAC's updated analysis suggests that cost saving is influenced by response rate and assumptions about the treatment pathway

3.11 The EAC's base case showed that using Alpha-Stim AID saved £80.79 per person compared with individual CBT. This was based on a 47.2% response rate with Alpha-Stim AID (Morriss et al. 2019) and a 54.2% response rate with individual CBT (Gyani et al. 2013). The reported response rate for Alpha-Stim AID included everyone who used it in the Morriss et al. study. However, many people may also have had individual CBT alongside or after Alpha-Stim AID. The reported response rates for treatment combinations were more uncertain and varied. For instance, the response rate was 65.0% in people using Alpha-Stim AID alone and 13.0% in people having Alpha-Stim AID followed by individual CBT (Morriss et al. 2019). The EAC explored the effect of different response rates and treatment regimens. For details, see the [addendum to the EAC's assessment report in the supporting documents for this guidance](#).

Additional analysis suggests cost savings but uncertainties remain

3.12 In response to committee, clinical expert and consultation comments, the EAC revised the IAPT cost model to more closely reflect the current IAPT pathway. Results from this model suggested that introducing Alpha-Stim AID to the current pathway could be cost saving and result in fewer people being discharged from IAPT to primary care for further treatment. However, because of the limited data available and uncertainties in the modelling, the EAC concluded that the cost impact of using Alpha-Stim AID in the current IAPT care pathway remained

uncertain.

A primary care cost model shows that using Alpha-Stim AID could have additional savings but does not reflect clinical practice

- 3.13 During consultation, the company submitted a new model, which included Alpha-Stim AID in primary care as a first-line treatment for anxiety. The model was based on an unpublished study in the NHS and the results showed a cost saving of £285.00 per person when Alpha-Stim AID was included in the care pathway. However, the EAC considered that the proposed model did not reflect clinical practice because it did not capture medication use, possible variations in treatment options and repeat visits to a GP or nurse.

4 Committee discussion

Clinical-effectiveness overview

A better understanding of how Alpha-Stim AID works in people with anxiety disorders is needed

4.1 The committee considered that Alpha-Stim AID's mode of action was uncertain although the clinical experts explained the physiological role of alpha brain waves in mediating feelings of calmness. The clinical experts and the external assessment centre (EAC) reviewed the evidence submitted at consultation. They concluded that there was no robust evidence showing the effect of regular use of Alpha-Stim AID on the brain waves of people with anxiety disorders. The committee considered that a clear understanding of the therapeutic effect of this technology is important. It proposed that further evidence is generated to investigate any acute or longer-term changes in brain activity after using Alpha-Stim AID in people with anxiety disorders. Potential studies could involve using a sham device as a control and recording brain activity, for example by electroencephalography or functional imaging.

Alpha-Stim AID is a promising treatment option for managing anxiety disorders, but the evidence is weak

4.2 The randomised controlled trial evidence showed short-term relief of anxiety symptoms with Alpha-Stim AID in people with anxiety disorders. However, the committee noted that the quality of the evidence was low because of a high risk of bias. The committee was concerned about the possibility of a significant placebo effect with Alpha-Stim AID. But it also acknowledged that reducing anxiety symptoms was the most important outcome regardless of how this was achieved. The committee concluded that a well-planned and well-conducted trial is needed to be certain about Alpha-Stim AID's clinical benefit.

Evidence on the long-term benefit of using Alpha-Stim AID is needed

- 4.3 The evidence consisted of relatively short-term studies, mostly with follow-up periods of 6 to 12 weeks. In 1 study follow up was 24 weeks. The clinical experts advised that anxiety disorders are long-term conditions and many people have relapses in symptoms. No convincing evidence was available on the longer-term benefits of Alpha-Stim AID and the committee concluded that further research was needed to explore this.

More evidence is needed to assess the effect of Alpha-Stim AID compared with other options in the care pathway

- 4.4 The clinical experts explained that there are several different treatments offered to people with anxiety disorders in the NHS. The committee considered that Morriss et al. (2019) provided information about the use of Alpha-Stim AID in people waiting for individual cognitive behavioural therapy (CBT). But aside from this, there is a lack of evidence to support the use of Alpha-Stim AID at specific points in the pathway. Also, there is uncertainty about how the clinical effect of Alpha-Stim AID compares with other treatments. The committee noted, for example, that there was no evidence for the effect of Alpha-Stim AID compared with medication in people with anxiety disorders. It recognised that Alpha-Stim AID may not replace other options in the treatment pathway, but it could be an additional option (see [section 4.7](#) and [section 4.8](#)). The committee proposed that further evidence would be helpful to understand Alpha-Stim AID's benefit compared with established treatments for anxiety disorders, such as individual CBT or medication, or both.

Side effects and adverse events

Alpha-Stim AID is a low-risk device with no serious side effects

- 4.5 The evidence suggested that adverse events with Alpha-Stim AID were mild. The clinical experts explained that people may have vertigo or dizziness when Alpha-Stim AID is first used, particularly at a high electric

current, but these symptoms tend to lessen when the current is reduced. Data from the patient survey confirmed that the device is generally well tolerated. The committee concluded that people using Alpha-Stim AID have a low risk of side effects. Also, the device might be a treatment option for some people for whom conventional treatments are unsuitable or who would prefer to avoid them.

NHS considerations overview

Training and ongoing support is important for people using Alpha-Stim AID at home

- 4.6 The clinical experts advised that training on the correct use of Alpha-Stim AID is important and this is offered to people before treatment starts. This involves explaining technical issues such as ensuring correct connections and setting appropriate currents. The patient expert also noted that people may need ongoing support while using Alpha-Stim AID at home. The committee concluded that providing information and support was essential to ensure that the technology is used correctly.

The position of Alpha-Stim AID in the treatment pathway is not clear

- 4.7 The clinical experts explained that because of the number of people with anxiety disorders there is huge pressure on individual CBT services. They also explained that individual CBT is not suitable for everyone and some people may have to wait a long time to have it. So, easy access to self-administered treatment such as Alpha-Stim AID that can be used at home is a potentially attractive option for people waiting for individual CBT. The committee also considered that a range of different options for anxiety disorders was needed in the NHS so that treatment can be tailored to the person's needs. The clinical experts explained that Alpha-Stim AID can be offered early in the care pathway (see [section 4.8](#)) and it may help people engage better with subsequent individual CBT if it is still needed. The clinical experts also suggested that Alpha-Stim AID may particularly benefit people who want to avoid taking

medication or when medication is unsuitable for them. The committee understood the importance of choice in treating anxiety in primary care and that this technology could be used to complement existing treatments for anxiety disorders. It concluded that Alpha-Stim AID has the potential to be a useful addition to the care pathway if evidence showing its clinical benefits is generated (see [sections 4.2 to 4.4](#)).

There is potential for Alpha-Stim AID to be used in primary care to help people manage anxiety disorders

4.8 The clinical experts explained about the potential role of Alpha-Stim AID in primary care, where there is an unmet clinical need for people with anxiety disorders. The committee noted that the EAC has reviewed the results of a study exploring the use of Alpha-Stim AID as a first-line treatment for anxiety in primary care. A clinical expert who is a GP described the use of Alpha-Stim AID within social prescribing in his practice. Initial results suggested that uptake of Alpha-Stim AID and feedback from people using it was good. The clinical experts advised that people who do not want to have medication or psychological therapy often prefer to use Alpha-Stim AID. The committee concluded that Alpha-Stim AID may fit better in primary care where a range of treatment options is needed and this should be explored in further studies.

Cost modelling overview

The EAC's updated IAPT model is acceptable but uncertainties remain

4.9 The committee considered that the Improving Access to Psychological Therapies (IAPT) model reflects current care but there was limited data available to populate the uptake and response rates in this complex pathway. The primary care model reflected an alternative position for the technology in the care pathway, but the committee again noted that limited data was available to populate the model. So, it was difficult to draw firm conclusions from either model about the cost benefits of using Alpha-Stim AID. The committee concluded that further clinical efficacy

evidence was needed to accurately assess whether using Alpha-Stim AID alone or as an add-on treatment would lead to cost savings compared with standard care.

Further information about resource use would be valuable

- 4.10 In the EAC's base-case analysis for the IAPT model, the main drivers in the cost model were the uptake rate and response rates for the different treatments. The clinical experts explained that the uptake rates were likely to vary across services and people's preferences. They considered that the uptake rate of 22% used in the EAC's model did not reflect the much higher rates found in their own clinical practice. The clinical experts also commented that people may stop treatment early with Alpha-Stim AID if their symptoms improved and this may have confounded the calculated response rates. The committee concluded that more robust data was needed to understand the potential resource impact of using Alpha-Stim AID in the NHS.

Further research

Further good-quality research is needed to address uncertainties about the clinical efficacy of Alpha-Stim AID

- 4.11 The committee noted the mostly positive patient experience described in the response to the patient survey and in patients' consultation comments. It considered that Alpha-Stim AID shows significant promise for managing anxiety disorders, but further studies are needed to address uncertainties about its clinical efficacy. A fundamental understanding of the effect of Alpha-Stim AID on brain function in people with anxiety disorders would be helpful. For example, from a study using electroencephalography or functional imaging in treatment and sham groups. The committee considered that a well-conducted randomised controlled trial should be done to evaluate the short- and long-term effects of Alpha-Stim AID compared with established treatment options such as medication and individual CBT. Such a study should include an assessment of patient-reported outcome measures and resource use to inform a future assessment of the cost consequence of using

Alpha-Stim AID in the NHS.

Collecting real-world data is encouraged

4.12 The committee considered that collecting real-world data on the use of Alpha-Stim AID would be helpful to understand issues in different clinical scenarios, such as:

- people's treatment preferences
- the uptake of the device and
- the response rates and treatment completion rates.

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

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