



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1399 – Percutaneous Tibial Nerve Stimulation administered through the Urgent PC Neuromodulation System

Applicant: Endotherapeutics Pty Ltd

Date of MSAC consideration: MSAC 68th Meeting, 24-25 November 2016

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, [visit the MSAC website](#)

1. Purpose of application and links to other applications

An application requesting new Medical Benefits Schedule (MBS) listings for Percutaneous Tibial Nerve Stimulation (PTNS) administered through the Urgent PC Neuromodulation System was received from Endotherapeutics Pty Ltd by the Department of Health.

2. MSAC's advice to the Minister

After considering the available evidence presented in relation to the safety, clinical effectiveness and cost-effectiveness, MSAC deferred its advice for public funding of PTNS in patients with idiopathic overactive bladder (OAB) due to the need for additional information regarding the proposed item descriptor, costing and implementation of the service. MSAC also considered that there was a need to substantially reduce the proposed fee.

MSAC requested the following information before it could finalise its advice:

- Justification of the proposed ongoing requirement for a specialist beyond confirming the initial diagnosis, with consideration of potential roles, with training, for general practitioners, incontinence nurses or patient self-administration.
- Clarification of the proposed frequency of treatment, particularly as the frequencies used in the trials appear to be at the upper limits, and the overall duration of treatment compared with other therapies.
- A more detailed cost breakdown and rationale for the proposed MBS fee, with further comparison to international prices, and inclusion of sensitivity analyses by the amount of the proposed fee, out-of-pocket payments and costs to other funding programs.
- Present economic modelling with comparison to sacral nerve stimulation (SNS) over a three-year time horizon (time to battery replacement).
- Present justification for the rates and extents of uptake and substitution for other later-line treatments in the financial analyses.

The response should be provided back to the next appropriate MSAC meeting via ESC.

3. Summary of consideration and rationale for MSAC's advice

MSAC noted that a single treatment consists of 30 minutes of continuous neurostimulation, performed once a week for 12 weeks. If successful, treatment is then tapered (over three months) to once a month. The treatment takes place in a consultation room and does not require admission to hospital, surgical intervention, or local anaesthetic.

MSAC noted that the proposed population is patients with idiopathic OAB that is refractory to conservative therapy (pharmaceutical therapy such as anticholinergic agents and behavioural therapy). The final protocol nominated SNS and botulinum toxin type A therapy as the comparators for PTNS, however, discussions with the applicant concluded that these treatments are unlikely to be used by patients who would adopt PTNS and therefore “best supportive care” was nominated as the most appropriate comparator. MSAC acknowledged the clinical need for PTNS therapy. However, MSAC considered that the place of PTNS in the clinical pathway is uncertain as it could be considered as a replacement for botulinum toxin type A and SNS in second line therapy or as third line therapy after these treatments have been ruled out as options for the patient.

After considering the clinical evidence provided to support the comparative safety of PTNS, MSAC acknowledged that PTNS appears to be well tolerated, with adverse events generally mild and transient in nature.

MSAC also considered the clinical evidence provided for the comparative effectiveness of PTNS and acknowledged that PTNS appears to be effective in reduction of OAB symptoms and improvement in patient quality of life compared with best supportive care. MSAC noted that there were no direct randomised comparisons of PTNS with botulinum toxin type A, nor with SNS. MSAC noted that based on an indirect comparison, PTNS appears to be more effective in reduction of OAB symptoms compared with botulinum toxin type A. It was not possible to conduct an indirect comparison between PTNS and SNS because the comparative evidence for SNS is limited to a single trial comparing botulinum toxin type A with SNS, available only in abstract form.

MSAC considered that there was uncertainty regarding the effect durability for PTNS beyond two years. MSAC requested that the applicant provide a rationale for the treatment frequency proposed and for ongoing treatment continuation. MSAC advised that, if listed, the Department may wish to consider the number of claims per patient over a 3–5 year period to assess the appropriateness of the treatment duration.

The economic model presented ICERs for each of the three treatments compared with best supportive care. PTNS had the highest ICER, despite having lower incremental costs than SNS. MSAC noted that this was because PTNS requires ongoing monthly treatment to maintain the treatment effect. MSAC considered that the base case ICER for PTNS is high and uncertain and is sensitive to the utilities and treatment costs used in the model.

MSAC was concerned that the equipment costs were poorly detailed in the application and that it was unclear whether the costs for the electrodes used in the procedure were included in the proposed item fee or would be billed separately. MSAC requested that the applicant provide a clear breakdown of all equipment costs associated with PTNS treatment, including clarification of how the cost of the electrodes will be funded. MSAC advised that the cost breakdown should include costs for:

- specialist supervision
- administration of the service by a continence nurse
- provision of room and facilities for 45 minutes to 60 minutes

- equipment costs, disaggregated and including the cost for electrodes.

MSAC requested that the applicant provides justification for the proposed ongoing requirement for a specialist beyond confirming the initial diagnosis, with consideration of potential roles, with training, for general practitioners, continence nurses or patient self-administration. MSAC considered that the requested service fee was too high, particularly considering the potential for delivery of treatment by general practitioners and nurses. MSAC advised that as a requirement for recommendation for public funding of PTNS the item fee should be reduced by 50%. MSAC requested that the applicant provide a revised economic model using the reduced fee.

MSAC considered that the number of PTNS procedures completed per year is likely to be limited by the number of practitioners able to provide the service and that allowing general practitioners (GPs) and continence nurses or even patients to administer treatment would impact on utilisation. MSAC was concerned that there is potential for leakage with patients accessing PTNS without first being treated with botulinum toxin type A and SNS, particularly where there is a patient preference for PTNS. MSAC advised that if listed, the Department should consider monitoring the utilisation of botulinum toxin type A and SNS to assess whether there is use outside the third line population. MSAC considered that there is uncertainty regarding the likely rates and extent of uptake of PTNS and substitution of other later-line treatments and suggested that the uptake rates for PTNS are likely to be much higher than the estimates provided. MSAC requested that the applicant provides justification for the uptake and substitution rates used in the financial analyses including further information regarding GPs' and consumers' views about PTNS therapy to help inform these estimates.

MSAC advised that the wording of the item descriptor should be altered to clearly define the eligible patient population as those in whom botulinum toxin type A and SNS are contraindicated or who have previously failed these treatments. MSAC acknowledged that no age restriction had been included in the item descriptor and considered this to be appropriate. MSAC agreed with the ESC advice that it was not appropriate for the item descriptor to specify the device or brand name. MSAC also noted that there should be no co-claiming for the consultation in addition to the fee for supervision.

MSAC acknowledged the clinical need for PTNS and was satisfied on the basis of the evidence presented that it has acceptable safety and clinical effectiveness in the proposed population. However, MSAC was unable to support public funding at this time due to the need for additional information regarding the item descriptor, costing and implementation of the service. MSAC also considered that there was a need to substantially reduce the proposed fee.

4. Background

MSAC has not previously considered PTNS.

5. Prerequisites to implementation of any funding advice

The Urgent PC Neuromodulation System, the applicant's medical device required for the administration of PTNS, is currently registered with the Therapeutic Goods Administration (TGA) under the Australian Register of Therapeutic Goods (ARTG) identifier 152825. The product name is 'Incontinence-control electrical stimulation system, nonimplantable, percutaneous' and is categorised as Medical Device Included Class IIa.

6. Proposal for public funding

The proposed MBS item descriptors for PTNS are shown in Table 1 and Table 2.

Table 1: The proposed MBS item descriptor for PTNS initial treatment protocol

Category 3 – Therapeutic Procedures
<p>MBS [item number]</p> <p>Percutaneous Tibial Nerve Stimulation, neuromodulation initial treatment protocol, for the treatment of overactive bladder if:</p> <ul style="list-style-type: none">(a) the patient has been diagnosed with idiopathic OAB, and(b) the patient has been refractory to, or contraindicated/not suitable for, conservative treatments including anti-cholinergic agents, and(c) the patient is contraindicated or otherwise not suitable for botulinum toxin type A therapy, and(d) the patient is contraindicated or otherwise not suitable for sacral nerve stimulation, and(e) the patient is willing and able to comply with the protocol. <p>For each patient — applicable not more than once except if the patient achieves at least a 50% reduction in overactive bladder symptoms from baseline at any time during the treatment period.</p> <p>A session should last for a minimum of 45 minutes, of which neurostimulation should last for 30 minutes per session. These sessions are intended to be delivered one per week, for 12 weeks. Claims for this item may not exceed 12 sessions in a calendar year.</p> <p>Fee: \$425</p> <p>Explanatory note:</p> <p>N/A</p>

Table 2: The Proposed MBS item descriptor for PTNS (tapering and maintenance treatment)

Category 3 – Therapeutic Procedures
<p>MBS [item number]</p> <p>Percutaneous Tibial Nerve Stimulation, neuromodulation tapering and maintenance treatment, for the treatment of overactive bladder if:</p> <ul style="list-style-type: none">(a) The patient responded to neurostimulation initial treatment protocol and achieved at least a 50% reduction in OAB symptoms. <p>A session should last for a minimum of 45 minutes, of which neurostimulation should last for 30 minutes per session. The interval between sessions should be adjusted with the aim of sustaining therapeutic benefit and no more than XX sessions in a XX month period.</p> <p>Fee: \$425</p> <p>Explanatory note:</p> <p>N/A</p>

The applicant proposed fee is \$425 for each item.

In order to offer PTNS, a physician must be adequately qualified to first diagnose OAB and be capable of prescribing anticholinergic agents to treat the condition. The physician must be a specialist in the field of urology, continence and/or gynaecology.

The applicant suggests that the ability to prescribe PTNS as a treatment should be restricted to urologists and urogynaecologists. The service can be administered by a practice nurse acting under the supervision of a qualified urologist or urogynaecologist.

7. Summary of Public Consultation Feedback/Consumer Issues

Following public consultation, eight responses were received from: five specialists, one general practitioner, one consumer and one peak body.

Overall, the responses supported the proposed intervention as it will have a positive impact on a patient's quality of life. Other benefits of PTNS noted in the responses included the following:

- it is a minimally invasive and low risk procedure compared to SNS
- it is less likely to cause side-effects, unlike some anticholinergics
- MBS listing of the treatment will reduce the out-of-pocket costs for patients.

Disadvantages noted included:

- the need to have ongoing treatments and complying with the protocol, which could pose a burden to some patients
- restricting who can deliver PTNS could result in access issues for patients – it was suggested that it should be moved to mainstream general practice.

8. Proposed intervention's place in clinical management

The current approach to treating patients with idiopathic OAB involves, in the first instance, providing conservative therapies including behavioural therapy and pharmacological therapy. Second line treatment includes botulinum toxin type A injected into the bladder wall (botulinum toxin type A therapy) or SNS. Third line treatment includes best supportive care.

Under the proposed clinical management algorithm, PTNS would be used as a second line treatment for those that are unsuitable for botulinum toxin type A therapy or SNS, or a third line therapy when botulinum toxin type A therapy or SNS have proved ineffective. Third line treatment involves best supportive care.

PTNS is administered through an Urgent PC Neuromodulation System to treat OAB symptoms by administering a proprietary pre-programmed treatment protocol which provides electrical stimulation to the sacral nerve complex via the posterior tibial nerve. The treatment protocol produces an inhibitory effect on overactive bladder activity thereby providing symptom relief to patients.

The service is intended for patients who have been diagnosed with OAB and their condition has been shown to be refractory to conservative therapy. A single treatment session lasts for 30 minutes of continuous neurostimulation. Ongoing treatments are required in order for the patient to maintain symptom relief.

It is expected that PTNS services will be provided in private clinics specialising in urology and/or continence services. The expected PTNS service providers are likely already offering the proposed comparator treatment/s to OAB patients. It is expected that these specialist clinics will offer PTNS as a treatment option for OAB in addition to the comparator services. PTNS is expected to be offered to patients who may not be suitable and/or are ineligible for botulinum toxin type A therapy or SNS.

9. Comparator

The current treatment pathway for OAB involves botulinum toxin type A injections and SNS therapy.

SNS is a two-stage process of testing and permanent treatment. Permanent treatment involves the surgical implantation of a pulse generator and sacral leads for continuous electrical stimulation to the sacral nerve complex. In some cases, devices need to be explanted due to treatment becoming ineffective, adverse events requiring removal, or other reasons. A re-operation to replace the simulator battery is also required every 3-7 years.

While the final protocol identified SNS and botulinum toxin type A therapy as the comparator for PTNS, discussions with the applicant concluded that 'best supportive care' is the appropriate comparator, because SNS and botulinum toxin type A therapy would typically not be used by patients that would adopt PTNS, whose only other option would be best supportive care.

The economic assessment has compared the three, second line therapies (PTNS, SNS and botulinum toxin type A therapy) to best supportive care. This has allowed the cost effectiveness comparison between PTNS and the MBS listed second line treatments to be conducted.

10. Comparative safety

PTNS is a minimally invasive intervention which has been associated with few adverse events, side-effects and risks. PTNS does not require a surgical procedure in order for the patient to receive the treatment.

A meta-analysis of 16 clinical studies of PTNS found no serious adverse events and showed that PTNS was associated with occasional transient side-effects occurring in approximately 8.5% of the patients. Side-effects included pain, bruising, tingling and/or bleeding at the needle electrode insertion site and leg cramp and numbness/pain under the sole of the foot.

Single adverse events were reported in one study including headache, hematuria, generalised swelling, worsening incontinence, and vaso-vagal response to needle placement. There has been no risk of serious of harm and/or death relating to PTNS reported in the currently available literature. The SUmIT trial reported 5.5% (6/110) of patients had nine mild to moderate treatment related adverse events including ankle bruising, discomfort at the needle site and tingling in the leg. The ORBIT trial reported 16% (8/49) of patients had reported moderate adverse events including generalised swelling, worsening incontinence, headache, haematuria, inability to tolerate stimulation, leg cramps, intermittent foot/toe pain, vaso-vagal response to needle placement.

The potential side-effects of PTNS are usually transient in nature and typically only present during the procedure. Based on the limited reporting of adverse events in randomised controlled studies, PTNS appears to be a well-tolerated procedure, with adverse events being of a mild nature. No significant harms have been reported.

11. Comparative effectiveness

The clinical evaluation suggests that, relative to the comparator (best supportive care); PTNS has minimally inferior safety and superior effectiveness. PTNS is more effective than sham treatment in reducing urinary urgency, urinary urge incontinence, urinary frequency and nocturia (although estimates for these secondary outcomes are less reliable). PTNS also results in clinically meaningful changes in quality of life compared with sham treatment.

The estimate of effect (relative risk of responding to treatment) of PTNS vs sham for overall bladder symptoms is RR 6.91 (95% CI 2.05, 23.25).

For PTNS vs botulinum toxin type A, the overall indirect estimate of effect is RR 5.19 (95% CI 1.53, 17.64).

Based on a single study comparing SNS and botulinum toxin type A, SNS appears effective as a treatment option for patients with idiopathic overactive bladder. Further studies, including randomised sham controlled studies are required to confirm its effectiveness in this setting.

Overall, botulinum toxin type A therapy appears to be effective for treatment of patients with idiopathic overactive bladder. It produces a larger proportion of responders compared to placebo and had good quality evidence to suggest it improves urinary urge incontinence, urinary frequency, nocturia and quality of life.

12. Economic evaluation

The cost utility analysis presented used a time horizon of 25 years with the median age of OAB patients being approximately 60 years of age and life expectancy of around 25 years. Shortening this time horizon will reduce the cost effectiveness of PTNS.

PTNS has a higher ICER than both SNS and botulinum toxin type A therapy, despite SNS having higher incremental costs (Table 3). This is due to SNS having significant upfront costs, but delivering benefits over a longer period. In contrast, PTNS treatments must be repeated every month in order to maintain the treatment effect. This indicates that PTNS is the least cost effective second line treatment for OAB.

Table 3: Incremental cost effectiveness ratio, present value

	Cost (\$mn)	Incremental cost	Effectiveness	Incremental effectiveness	ICER
	\$m	\$m	QALYs	QALYs	\$
PTNS	4.253	3.842	1 583	73	52 748
SNS	5.665	4.222	1 766	256	16 522
Botulinum toxin type A therapy	3.595	2.004	1 788	277	7 225

Comparing PTNS to SNS and botulinum toxin type A therapy does not reflect the trade off in OAB treatment; PTNS is expected to be used by patients who are contraindicated or refractory to existing MBS listed second line treatments.

A sensitivity analysis was conducted, with the conclusions remaining unchanged under a number of alternative assumptions.

13. Financial/budgetary impacts

There is no precise consensus around the prevalence of OAB in the literature, partly due to different population bases, but also differing definitions of OAB. For the purposes of this analysis, prevalence was assumed to be 16 per cent for males and 16.8 percent for females, which indicates that over 3 million Australians experience OAB symptoms.

The numbers of potential users of PTNS, however, is likely to be significantly lower, as a large proportion of patients do not seek any medical treatment or are treated using first and second line therapies. For instance, of the 3.4 million OAB sufferers in 2015, 40 per cent are believed to not seek treatment. There were 772,007 people that adopted first line therapies, but only 468 that were treated with existing second line treatments.

This leaves 514,203 OAB patients that are currently receiving ‘usual care’, only a small proportion of which would be possible (second or third line) PTNS adopters.

The expected use of PTNS treatments depends on the stock of potential patients, new patients that are diagnosed each year, and the suitability of PTNS to their condition. Not all people with OAB in Australia need to be counted in the model as being potentially eligible for PTNS. For instance:

- not all patients with OAB seek medical advice for their condition, and
- for those that do, most are happy to manage symptoms without adoption of the clinical management algorithm, through the use of incontinence pads etc.

The estimated potential patient population for people who are eligible for PTNS today is around 80,000, which increases over time. Forecasts change in line with expected population growth and changes in the stage of the disease for each person.

The estimate of patients who will receive PTNS over the next 25 years is based on the evidence around progression of the disease following diagnosis, the distribution of disease severity in the relevant literature, and suitability of alternative treatments including SNS.

The financial implications to the MBS resulting from the proposed listing of PTNS are summarised in Table 4 and Table 5. The estimated lower and upper bound cost to the MBS of PTNS is shown below.

Using lower bound patient estimates, the predicted cost to the MBS of PTNS is \$7.1 million in the first year and \$12.5 million by year 5. Using upper bound patient estimates, the predicted cost to the MBS of PTNS is \$27.6 million in the first year and \$48.4 million by year 5. This cost is not reduced by substitution of alternative services.

It is noted that these costs assume very low uptake rates of PTNS, in line with experience in the US and UK, and in line with access patterns to existing second line treatments. The potentially eligible population is many times higher than that modelled to produce these estimates.

Table 4: Total costs to the MBS associated with PTNS - lower bound

	2016-2017	2017-2018	2018-2019	2019-2020	2020-2021
	\$m	\$m	\$m	\$m	\$m
Cost of treatment for initial protocol and first 12 months of treatment	6.47	6.60	6.72	6.84	6.96
Cost of treatment for initial protocol and 8 weeks treatment only	0.65	0.66	0.68	0.69	0.70
Cost of treatment for ongoing full year treatment	-	1.59	2.90	3.97	4.85
Total cost to the MBS	7.12	8.85	10.29	11.49	12.51

Table 5: Total costs to the MBS associated with PTNS - upper bound

	2016-2017	2017-2018	2018-2019	2019-2020	2020-2021
	\$m	\$m	\$m	\$m	\$m
Cost of treatment for initial protocol and first 12 months of treatment	25.05	25.53	26.01	26.48	26.94
Cost of treatment for initial protocol and 8 weeks treatment only	2.52	2.57	2.62	2.66	2.71
Cost of treatment for ongoing full year treatment	-	6.17	11.21	15.35	18.78
Total cost to the MBS	27.57	34.27	39.84	44.49	48.44

14. Key issues from ESC for MSAC

PTNS appears to be a well-tolerated procedure, with mild adverse events transient in nature and typically only present during the procedure. No significant harms have been reported.

PTNS has a higher ICER than SNS and botulinum toxin type A therapy, despite SNS having higher incremental costs. SNS has significant upfront costs, but delivers benefits over a longer period.

A cost utility analysis was assessed over 25 years: median age of the idiopathic OAB patient is ~ 60 years of age; life expectancy is around 25 years. However the data provided only spanned two years and so concern was expressed as to the stability of outcomes beyond this period.

Costs savings for PTNS would be relatively small where patients have difficulties in attending 12 appointments per year or the benefits are not consistent with expectation.

The estimated cost is at full MBS price and the fee appears high, particularly where the service is delivered by a nurse.

There were no randomised control trials identified that compared PTNS with botulinum toxin type A treatment or SNS or SNS with sham treatment. However, an indirect comparison of PTNS with botulinum toxin type A was undertaken.

Concern that the PTNS high average risk of 6.7 claimed to be safer than botulinum toxin type A risk data led to the agreement that the high effect size was potentially confounded by publication bias.

Concern was raised over the need for a specialist to deliver the therapy which would affect patient accessibility and it was recommended that once a diagnosis is made a GP be able to perform the therapy personally or oversee a trained nurse.

The applicant's suggested item descriptor included a proprietary request regarding the machine used to deliver the treatment due to 'safety purposes'. It was agreed that this was inappropriate.

PTNS is a reasonable treatment option due to its minimal invasiveness and should not necessarily be considered as a last resort therapy. Its place in the clinical pathway is uncertain, but could be considered as a replacement for botulinum toxin type A and SNS as

an initial second line therapy or after botulinum toxin type A and SNS have been ruled out as treatment options.

15. Other significant factors

Nil

16. Applicant's comments on MSAC's Public Summary Document

The applicant thanks MSAC for their consideration and the issues raised in the PSD. We wish to comment on the estimated uptake figures for the PTNS procedure, should the service be included on the MBS. We believe the potential rate of uptake of PTNS in Australia is likely being overestimated. There are a number of extraneous factors which will inhibit the uptake of the procedure, even if PTNS were made available for GPs to perform. These factors include the availability of clinician training, the willingness of clinicians to adopt the procedure, and the availability of equipment required to perform the procedure. We submit that factors such as these would likely result in lower rates of uptake for the PTNS procedure, as has been experienced in the UK and USA.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website:
[visit the MSAC website](#)