NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Health Technology Appraisal

Foslevodopa-foscarbidopa for treating Parkinson's disease with motor fluctuations

Draft scope

Draft remit/appraisal objective

To appraise the clinical and cost effectiveness of foslevodopa-foscarbidopa subcutaneous infusion within its marketing authorisation for treating Parkinson's disease with motor fluctuations.

Background

Parkinson's disease is a progressive chronic disorder of the central nervous system. It is caused by a loss of cells in the brain that are responsible for producing dopamine, which helps to control and coordinate body movements. In the early stages of Parkinson's disease, the 3 main symptoms are shaking (tremor), slowness of movement (bradykinesia) and muscle stiffness (rigidity). These develop gradually, in no particular order.[1] Other physical symptoms that can occur early on include balance problems, nerve pain and sleep disturbances. People with advanced Parkinson's disease have more complex symptoms that significantly impact daily living, including anxiety, depression and dementia.[2] Pharmacological treatment may also be less effective in later stages. Advanced Parkinson's disease has a severe negative impact on the quality of life of patients, their families and carers.

There are around 137,000 people living with Parkinson's disease in the UK.[3] Men are more likely to develop Parkinson's disease than women, and the risk of developing the disease increases sharply with age.[3] It is estimated that around 10% of patients have advanced disease.[4] In 2018 there were 6,505 deaths due to Parkinson's disease in England and Wales.[5]

NICE guideline [NG71] recommends levodopa as the first-line treatment for people in the early stages of Parkinson's disease whose motor symptoms impact their quality of life. However, people having long-term levodopa treatment develop motor complications. These include motor fluctuations, where the patient switches between being able to move ('on' phase) and being immobile ('off' phase), and involuntary movements (dyskinesias). Dopamine agonists, monoamine oxidase Type B (MAO-B) inhibitors or catechol-O-methyl transferase (COMT) inhibitors are offered as an add-on to levodopa for people who have developed dyskinesia or motor fluctuations despite optimal therapy. If the dyskinesia remains uncontrolled, amantadine can be considered. Best medical therapy for people with advanced Parkinson's disease may include intermittent apomorphine injection and/or continuous apomorphine infusion. Surgery (e.g. deep brain stimulation) can be considered in people whose disease has not responded adequately to best medical therapy. An NHS England Clinical Commissioning Policy recommends that levodopa-carbidopa intestinal gel can be considered in certain people with advanced levodopa-responsive Parkinson's disease, with severe motor fluctuations that have not responded to available medications.[4]

The technology

Foslevodopa-foscarbidopa (brand name unknown, Abbvie) is a prodrug combination of levodopa and carbidopa. Levodopa is metabolised to dopamine once it has reached the brain, improving nerve conduction and reducing the physical symptoms associated with Parkinson's disease. Carbidopa prevents metabolism of levodopa until it has crossed the blood-brain barrier. This means that a lower dose of levodopa is needed, reducing the risk of side effects. Foslevodopa-foscarbidopa is administered via subcutaneous infusion.

Foslevodopa-foscarbidopa does not currently have a marketing authorisation in the UK for any indication. It has been studied in a single-arm clinical trial and in a clinical trial compared with oral carbidopa-levodopa in people with Parkinson's disease experiencing motor fluctuations whose disease is responsive to levodopa, but uncontrolled by standard therapy.

Intervention(s)	Foslevodopa-foscarbidopa
Population(s)	People with Parkinson's disease that is responsive to levodopa, with motor fluctuations uncontrolled by standard therapy

Comparators	• Standard oral medication for treating Parkinson's disease, including levodopa plus the following adjunctive treatments:
	  ○ Dopamine agonists
	  ○ MAO-B inhibitors
	  ○ COMT inhibitors
	• Amantadine, with or without standard oral medication
	• Apomorphine, with or without standard oral medication
	• Deep brain stimulation
	• Levodopa-carbidopa intestinal gel

Outcomes	The outcome measures to be considered include: • 'on'/'off' time • dyskinesia • motor complications • cognitive functioning • mortality • adverse effects of treatment • health-related quality of life.
Economic analysis	The reference case stipulates that the cost effectiveness of treatments should be expressed in terms of incremental cost

	per quality-adjusted life year. The reference case stipulates that the time horizon for estimating clinical and cost effectiveness should be sufficiently long to reflect any differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. The availability of any commercial arrangements for the intervention, comparator and subsequent treatment technologies will be taken into account. The availability of any managed access arrangement for the intervention will be taken into account.
Other considerations	If the evidence allows the following subgroups will be considered: • subgroups based on the proportion of time spent in the 'off' state • People for whom apomorphine is not suitable • People for whom deep brain stimulation is not suitable. The available and cost of biosimilar and generic products should be taken into account. Guidance will only be issued in accordance with the marketing authorisation. Where the wording of the therapeutic indication does not include specific treatment combinations, guidance will be issued only in the context of the evidence that has underpinned the marketing authorisation granted by the regulator.
Related NICE recommendations and NICE Pathways	**Related Technology Appraisals:** None **Terminated appraisals:** None **Appraisals in development (including suspended appraisals):** Istradefylline with levodopa for treating motor fluctuations in Parkinson's disease NICE technology appraisals guidance [ID3868]. Publication date to be confirmed. **Related Guidelines:** Parkinson's disease in adults (2017) NICE guideline NG71 Suspected neurological conditions: recognition and referral (2019) NICE guideline NG127. Review date July 2019 **Related Interventional Procedures:** Deep brain stimulation for Parkinson's disease (2003). NICE

	interventional procedures guidance 19 Unilateral MRI-guided focused ultrasound thalamotomy for moderate to severe tremor in Parkinson's disease (2018). NICE interventional procedures guidance 606 Unilateral MRI-guided focused ultrasound thalamotomy for treatment-resistant essential tremor (2018). NICE interventional procedures guidance 617 Subthalamotomy for Parkinson's disease (2004). NICE interventional procedures guidance 65 **Related Quality Standards:** Parkinson's disease (2018). NICE quality standard 164 **Related NICE Pathways:** Parkinson's Disease (2020) NICE pathway
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan NHS England (2016) Clinical Commissioning Policy: Stereotactic Radiosurgery (SRS) for adults with Parkinson's tremor and Familial Essential Tremor NHS England (2015) Clinical Commissioning Policy: Levodopa-Carbidopa Intestinal Gel (LCIG) Department of Health and Social Care, NHS Outcomes Framework 2016-2017: Domains 1 and 2. https://www.gov.uk/government/publications/nhs-outcomes-framework-2016-to-2017 NHS England. 2013/14 NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/S/a.

Questions for consultation

Would foslevodopa-foscarbidopa only be offered to people with advanced Parkinson's disease?

Which treatments are considered to be established clinical practice in the NHS for treating Parkinson's disease that is responsive to levodopa, with motor fluctuations uncontrolled by standard therapy?

Have all relevant comparators for foslevodopa-foscarbidopa been included in the scope? In particular:

- Is levodopa-carbidopa intestinal gel a relevant comparator?
- Is deep brain stimulation a relevant comparator?
- Are other forms of surgery for Parkinson's disease (e.g. ultrasound thalamotomy, subthalamotomy) relevant comparators?

Which other treatments for Parkinson's disease (if any) will foslevodopa-foscarbidopa be used in combination with?

Are the outcomes listed appropriate?

Are the subgroups suggested in 'other considerations appropriate? Are there any other subgroups of people in whom foslevodopa-foscarbidopa is expected to be more clinically effective and cost effective or other groups that should be examined separately?

Where do you consider foslevodopa-foscarbidopa will fit into the existing NICE pathway, Parkinson's disease?

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 proposed remit and scope may need changing in order to meet these aims. In particular, please tell us if the proposed remit and scope:

- could exclude from full consideration any people protected by the equality legislation who fall within the patient population for which foslevodopa-foscarbidopa will be licensed;

- could lead to recommendations that have a different impact on people protected by the equality legislation than on the wider population, e.g. by making it more difficult in practice for a specific group to access the technology;

- could have any adverse impact on people with a particular disability or disabilities.

Please tell us what evidence should be obtained to enable the Committee to identify and consider such impacts.

Do you consider foslevodopa-foscarbidopa to be innovative in its potential to make a significant and substantial impact on health-related benefits and how it might improve the way that current need is met (is this a 'step-change' in the management of the condition)?

Do you consider that the use of foslevodopa-foscarbidopa can result in any potential significant and substantial health-related benefits that are unlikely to be included in the QALY calculation?

Please identify the nature of the data which you understand to be available to enable the Appraisal Committee to take account of these benefits.

To help NICE prioritise topics for additional adoption support, do you consider that there will be any barriers to adoption of this technology into practice? If yes, please describe briefly.

NICE intends to appraise this technology through its Single Technology Appraisal (STA) Process. We welcome comments on the appropriateness of appraising this topic through this process. (Information on the Institute's Technology Appraisal processes is available at http://www.nice.org.uk/article/pmg19/chapter/1-Introduction).

References

1. NHS (2019) Parkinson's disease symptoms. Accessed January 2021

2. Parkinson's UK. Advanced Parkinson's. Accessed January 2021

3. Parkinson's UK (2017). The Incidence and Prevalence of Parkinson's in the UK. Accessed January 2021

4. NHS England (2015). Clinical Commissioning Policy: Levodopa-Carbidopa Intestinal Gel (LCIG). Accessed January 2021

5. Office for National Statistics (2019). Deaths from Parkinson's Disease, England and Wales, 2001 to 2018. Accessed January 2021