NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Single Technology Appraisal

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

Final scope

Final 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 uncontrolled motor symptoms.

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 145,000 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 34% of people have complex 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 (for example, 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 over 24 hours.

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)	Adults with Parkinson's disease that is responsive to levodopa, with motor symptoms uncontrolled by standard therapy

Comparators	• Best-medical therapy for treating Parkinson's disease, including:
	  ○ Levodopa plus the following adjunctive treatments:
	  ▪ Dopamine agonists
	  ▪ MAO-B inhibitors
	  ▪ COMT inhibitors
	  ○ Amantadine
	• 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 • sleep symptoms including daytime sleepiness and insomnia • 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, deep brain stimulation or levodopa-carbidopa intestinal gel 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.

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 (2018). The Incidence and Prevalence of Parkinson's in the UK. Accessed April 2021
4. Parkinson's UK. 2019 Audit Summary Report. Accessed April 2021.
5. Office for National Statistics (2019). Deaths from Parkinson's Disease, England and Wales, 2001 to 2018. Accessed January 2021