NIHR | Innovation Observatory

Newcastle University

Health Technology Briefing
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Opicapone adjuvant for the treatment of idiopathic Parkinson's disease

Company/Developer	Bial Pharma UK Ltd

☐ New Active Substance ☒ Significant Licence Extension (SLE)

NIHRIO ID: 33698	NICE TSID: Not Available	UKPS ID: Not Available

Licensing and Market Availability Plans

Currently in phase II/III clinical trials.

Summary

Parkinson's disease (PD) is a chronic, progressive neurodegenerative condition resulting from the loss of dopamine nerve cells in the brain. This leads to a reduction in a chemical called dopamine in the brain, which plays a vital role in regulating movement of the body. The diagnosis and treatment of PD typically occur when the disease has already progressed to a relatively advanced stage in which motor symptoms are evident and substantial neurophysiological damage has already taken place. At this point, any possibility of delaying disease progression or, achieving neuroprotection may already be out of reach. There are currently no adjunct therapies recommended by the National Institute for Health and Care Excellence (NICE) for people with early-stage PD who have signs of treatable motor disability but have not developed dyskinesia or motor fluctuations. Catechol-O-Methyl transferase (COM-T) inhibitors such as opicapone as adjunct therapies have the potential to improve the clinical benefit of first-line treatment with levodopa (L-DOPA) - a precursor to dopamine that can be swallowed and can pass through the blood-brain barrier, allowing more L-DOPA to reach the brain.

Opicapone, a COM-T inhibitor inhibits (blocks) an enzyme (type of protein) that is involved in the breakdown of L-DOPA (a precursor of dopamine) in the body. As a result, L-DOPA remains active for longer, allowing more L-DOPA to reach the brain where it can restore the levels of dopamine in the parts of the brain that control movement and coordination. Administered orally, opicapone taken in combination with L-DOPA and another drug called a DOPA decarboxylase inhibitor (DCCI), helps to improve the symptoms of Parkinson's disease, such as stiffness and slowness of movement. If licensed, opicapone will offer the first adjunctive therapy in adult patients with early-stage PD with treatable motor disability.

Proposed Indication

For adjunctive treatment of adults, aged 30 to 80 years who are diagnosed with idiopathic Parkinson's disease (PD) between stages 1 to 2.5 and who are being treated with a combination of levodopa (L-DOPA) and a dopa decarboxylase inhibitor (DDCI) and show signs of treatable motor disability but no signs of motor complications (fluctuations in the motor response and/or involuntary movements or dyskinesias).[1]

Technology

Description

Opicapone (OPC, Ongentys, BIA 9-1067) is a selective and reversible third-generation catechol o-methyltransferase (COMT) inhibitor that increases L-DOPA plasma levels when co-administered with L-DOPA and a DDCI.[1,2] L-DOPA is a precursor of the neurotransmitter dopamine that can be taken by mouth. Opicapone inhibits an enzyme that is involved in the breakdown of L-DOPA in the body called COMT. As a result, L-DOPA remains active for longer, restoring the levels of dopamine in the parts of the brain that control movement and coordination. This helps to improve the symptoms of Parkinson's disease, such as stiffness and slowness of movement.[3] In the presence of a DDCI (carbidopa or benserazide), COMT becomes the major metabolising enzyme for L-DOPA catalysing its unwanted breakdown to 3-O-methyldopa (3-OMD) in the brain and periphery.[2] Opicapone therefore prevents peripheral breakdown of L-DOPA by inhibiting COMT allowing more L-DOPA to reach the brain.[4]

Opicapone is in development for adults diagnosed with early-stage idiopathic PD who are being treated with a combination of L-DOPA and DDCI, and who are without signs of any motor complications. In the ongoing phase III trial (EPSILON, NCT04978597), opicapone is administered orally as a 50 mg capsule taken once daily at least an hour after treatment with L-DOPA and DCCI for 24 weeks.[1]

Key Innovation

The diagnosis and treatment of PD typically occurs when the disease has already progressed to a relatively advanced stage in which motor symptoms are clearly evident and substantial neurophysiological damage has already taken place.[5] At this point, any possibility of delaying disease progression or, achieving neuroprotection may already be out of reach.[5]

First-line treatment with L-DOPA or dopamine agonist or monoamine oxidase-B (MAO-B) is recommended for people in the early stages of PD whose motor symptoms do not impact on their quality of life.[6] However, there are currently no adjunct therapies recommended by the National Institute for Health and Care Excellence (NICE) for people with early-stage PD who have signs of treatable motor disability but have not developed dyskinesia or motor fluctuations.[6] COMT inhibitors all have the potential to increase L-DOPA bioavailability, allowing more L-DOPA to reach the brain.[7-9]

In clinical trials, opicapone proved to be effective in the treatment of end-of-dose motor fluctuations in patients with PD. When opicapone is co-administered with L-DOPA and DDCI, peripheral COMT is inhibited, increasing L-DOPA bioavailability.[2,10-12] If licensed, opicapone will offer the first adjunctive therapy to preparations of L-DOPA/DDCI in adult patients with early-stage PD with treatable motor disability but without end-of-dose motor fluctuations.

Regulatory & Development Status

Opicapone currently has marketing authorisation in the UK for use as adjunctive therapy to preparations of L-DOPA/DCCI in adult patients with PD and end-of-dose motor fluctuations who cannot be stabilised on those combinations.[13]

Opicapone is not in phase II/III clinical development for any other indications.[14]

Patient Group

Disease Area and Clinical Need

PD is a chronic, progressive neurodegenerative condition resulting from the loss of dopamine nerve cells in the substantia nigra.[15] This leads to a reduction in a chemical called dopamine in the brain, which plays a vital role in regulating movement of the body.[16] Idiopathic PD is the most common form of PD.[17,18] Idiopathic means the cause is unknown, but it may involve changes in brain cells and neurotransmitters such as dopamine, norepinephrine and/or a combination of genetic and environmental causes.[18,19] The main symptoms of idiopathic PD are tremors, rigidity, slowness of movement, balance and speech problems.[17,18] PD is not clinically apparent until at least 50% of dopaminergic cell activity has been lost.[15] When symptoms occur, PD progression can be clinically classified into stages between 1and 5 using the modified Hoehn and Yahr staging tool. Stages 1 to 2.5 are classified as early-stage PD.[20] Age is the biggest risk factor for PD.[19] Men are more likely to develop the disease than women, and individuals with a parent or sibling who is affected have approximately two times the chance of developing PD. Head trauma and environmental causes such as exposure to chemicals are also risk factors.[19]

In 2015, prevalence rates for PD in England for all ages was 174.1 females per 100,000 population and 245 males per 100,000 population. Among people aged 20 to 29, PD prevalence in the UK in 2015 was 1 or 2 people in every 100,000. Among those aged 30 – 39, it was 4 or 5 people in every 100,000. Prevalence increases sharply with age with the prevalence for those aged 80-84 being 1,696 per 100,000 people.[21] The incidence rate for PD per 100,000 population of all ages in England is 20.3 among females and 32.8 among males each year.[21] In England, 2021-22, there were 11,820 finished consultant episodes (FCE) and 5,631 admissions for Parkinson disease (ICD-10 code G20) which resulted in 96,212 FCE bed days and 1,178 day cases.[22]

Recommended Treatment Options

Treatment of PD aims to relieve symptoms and maintain quality of life for patients and may include medications to improve symptoms such as tremors and movement problems, and supportive therapies such as physiotherapy, occupational therapy, and surgery..[16]

NICE recommends dopamine agonists, MAO-B inhibitors or COMT inhibitors as an adjunct to L-DOPA for people with PD who have developed dyskinesia or motor fluctuations despite optimal L-DOPA therapy.[6] There are currently no adjunct therapies recommended for people with early-stage PD who have signs of treatable motor disability but have not developed dyskinesia or motor fluctuations.[6]

Clinical Trial Information

Trial	**EPSILON**, NCT04978597, EudraCT 2020-005011-52; A Phase III, Double-Blind, Randomized, Placebo-Controlled and Parallel-Group Study to Evaluate the Efficacy and Safety of Opicapone, as Add-on to Stable Levodopa (L-DOPA) Plus a Dopa Decarboxylase Inhibitor (DDCI) Therapy in Early Idiopathic Parkinson's Disease Patients, With an Open-Label Extension. **Phase III** – Active, not recruiting. **Location**: Bulgaria. **Primary completion date**: January 2024.

Trial Design	Randomised, parallel assignment, quadruple-blind
Population	N = 410 (actual); Subjects with early idiopathic PD; aged 30 to 80 years old.
Intervention(s)	Opicapone 50 mg oral capsules
Comparator(s)	Matched Placebo
Outcome(s)	• Change from baseline (Visit 2) to the end of the double-blind period (Visit 9) in Movement Disorder Society-Unified PD Rating Scale (MDS-UPDRS) Part III total score [Time Frame: Up to 24 weeks] • Change from open-label baseline (Visit 9) to the end of the open-label period (Visit 15) in MDS-UPDRS Part IV total score. [Time Frame: Up to 1-year]
Results (efficacy)	--
Results (safety)	--

Estimated Cost

Opicapone is already marketed in the UK. A pack of thirty 50 mg capsules of opicapone cost £93.90. Therefore, treatment with 50 mg of opicapone once daily for 24 weeks would cost £525.84.[23]

Relevant Guidance

NICE Guidance

- NICE technology appraisal in development. Istradefylline with levodopa for treating motor fluctuations in Parkinson's disease [GID-TA10773]. Expected publication date: TBC
- NICE technology appraisal in development. Foslevodopa-foscarbidopa for treating Parkinson's disease with motor symptoms (GID-TA10772). Expected November 2023.
- NICE guideline. Parkinson's Disease in adults (NG71). July 2017
- NICE Quality Standard. Parkinson's disease (QS164). February 2018
- NICE Interventional Procedures Guidance Deep brain stimulation for Parkinson's disease. [IPG19]. November 2003

NHS England (Policy/Commissioning) Guidance

- NHS England. 2013/14 NHS Standard Contract for Neurosciences: Specialised Neurology (Adult). D04/Sa. 2013.
- NHS England. Clinical Commissioning Policy: Levodopa-carbidopa intestinal gel (LCIG). D04/P/E. July 2015.
- NHS England. Commissioning Policy: Stereotactic Radiosurgery (SRS) for adults with Parkinson's Tremor and Familial Essential Tremor. 16007/P. July 2016.
- NHS England. Clinical Commissioning Policy: Deep Brain Stimulation (DBS) In Movement Disorders. NHSCB/D03/P/b. April 2013

Other Guidance

- Fox, S.H et al. International Parkinson and Movement Disorder Society Evidence-Based Medicine Review: Update on Treatments for the Motor Symptoms of Parkinson's Disease. 2018.[24]
- Parkinson's UK. Best practice pathway for non-oral treatments in Parkinson's. 2021.[25]

- National Collaborating Centre for Chronic Conditions (UK). Parkinson's Disease: National Clinical Guideline for Diagnosis and Management in Primary and Secondary Care. 2006.[26]

Additional Information

Bial Pharma UK Ltd did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development.

As a result, the NIHR Innovation Observatory has had to obtain data from other sources.

UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision-making and faster uptake of innovative new medicines for patients who could benefit.

We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate, and comprehensive information on new medicines.

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