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Clinician and Patient Involvement Group (CAPIG) Summary of meeting held on 24 January 2018 Levodopa-carbidopa intestinal gel (Duodopa®) 20 mg/ml levodopa and 5 mg/ml carbidopa monohydrate

Marketing authorisation holder

AbbVie Ltd

Licensed indication

Levodopa-carbidopa intestinal gel (Duodopa®) for the treatment of advanced levodopa-responsive Parkinson's disease with severe motor fluctuations and hyper-/dyskinesia when available combinations of Parkinson medicinal products have not given satisfactory results.

Company's proposed positioning (if any)

For use in people with advanced Parkinson's disease who are not eligible for deep brain stimulation (DBS).

1. Severity of the condition

Parkinson's disease is a complex, progressive, neurodegenerative condition. There is no cure and current treatments can only manage the symptoms. Given that people can live with Parkinson's for many years, their quality of life is slowly and painfully eroded.

The disease is characterised by a slowness of movement, rigidity and rest tremor, which makes fine movements virtually impossible. People can experience 'freezing', where they are stuck to the spot unable to move. One person with Parkinson's described themselves as 'wooden', 'unable to perform the most menial of tasks'. Another described one occasion when they stabbed their cheek with a knife while trying to eat because their tremor left them unable to control their movements.

A person's balance is severely impacted and with that is a high propensity to fall, leading to frequent hospitalisation. Facial expression is lost having an effect on a person's ability to communicate, the voice softens and a person can have issues swallowing. Parkinson's also presents with a number of non-movement related symptoms: severe pain, sleep disturbance, chronic fatigue, digestive issues such as constipation (which in turn affects how medication is absorbed), urinary urgency, depression, hallucinations and dementia. These symptoms combine to make life very challenging and significantly impact on a person's quality of life over many years; one person with Parkinson's disease described their life as 'hell'.

'ON/OFF' responses to medication cause fluctuations from hour to hour and day to day. Someone is ON when their medication is working. But when someone is OFF, they can barely move and may become acutely anxious. Some people cycle between painful cramps (dystonia) when OFF and involuntary movements (dyskinesia) that can cause injury to themselves or others when they are ON. ON/OFF fluctuations can be unpredictable. One person with Parkinson's disease explained that from the time they woke up in the morning and before getting a chance to put their feet on the floor, they would be attacked with a bout of dyskinesia – 'excruciatingly painful'. Some people become reluctant to leave familiar surroundings in case they 'switch OFF' and are unable to move or communicate, which could leave them in a vulnerable or even

dangerous situation. Others are OFF for hours at a time, and become confined to their bed or chair. As the disease progresses, periods of OFF time become longer and more distressing. One person with Parkinson's disease described themselves being 'on the floor in agony' one minute, 'unable to move because of the cramps', and the next they would 'be up having violent, uncoordinated movements'.

People with advanced Parkinson's typically need 24–7 care and are often reliant upon their family to provide it. Caregivers may have to give up their job to provide round the clock care, and the unpredictable nature of the disease makes caring problematic. The disease can have a devastating impact on the physical, emotional and psychosocial aspects of a carer's life. One person caring for their partner with Parkinson's felt very strongly that their partner 'no longer existed', 'conversation was impossible', and they 'could no longer love' them 'or even like' them.

2. Unmet need

There is a small minority of people with advanced Parkinson's disease who have exhausted other treatment options. Some people have severe neuropsychiatric side effects from apomorphine and cannot tolerate it. Others with mental health symptoms, cognitive impairment and speech dysfunction caused by Parkinson's are not suitable for DBS. Therefore some people are not eligible for DBS or apomorphine infusion. Patient experts commented that Duodopa[®] can be an 'extremely valuable and important treatment option'. Continuous delivery of the medicine reduces the variability and unreliability of the medication, minimises the impact of time when the medication is not effective (OFF time) and maximises the time when it is effective (ON time).

Clinical and patient experts felt very strongly that there is an unmet need in Wales for people with advanced Parkinson's disease. One person in Wales with Parkinson's disease said that they were really frightened because at just 59 years of age they were told nothing more could be done for them, despite the fact that Duodopa[®] is available to people in England and Scotland. Duodopa[®] is available for use in Scotland for the treatment of advanced Parkinson's disease in those people deemed unsuitable for DBS. Duodopa[®] is also commissioned for use in NHS England, whose criteria state that eligible people should have advanced levodopa-responsive Parkinson's disease with severe motor fluctuations with at least 50% OFF periods and be ineligible for apomorphine or have failed, refused to consent to, or be unsuitable for DBS.

3. Added value of the medicine for the patient:

3a. How would this medicine be expected to add value to the patient's wellbeing and experience of care?

Clinical and patient experts were in strong agreement that Duodopa[®] should be made routinely available. They expressed concern for people with advanced Parkinson's disease who have very few treatment options available to them. Ensuring every person has access to the right medication at the right time is key to people with Parkinson's; delays can have significant consequences for treatment outcomes. Protecting the treatment options available becomes vitally important, which means ensuring that Duodopa[®] is readily offered as a treatment choice.

Duodopa[®] is delivered continuously. Not only can the continuous delivery improve the person's condition in a way periodic tablet doses cannot, it also removes the complicated timetable of numerous tablets having to be taken at many times throughout the day and night. This can restore a degree of control and consistency to a person's daily routine, a sense of greater normality, and an ability to participate in day to day and social activities. With this comes a significant improvement in quality of life not just for the patient but also their carer, family and friends.

Experts commented that for the few cases each year that would be suitable for Duodopa[®], 'it can be transformational'. One person with Parkinson's disease said that the difference Duodopa[®] has made to them 'is no less than a miracle...it takes effect quickly...I then have a day of what is fairly normal for me'. It has enabled them to continue living at home rather than being admitted to a care home. Another person said that they 'really could have done with [Duodopa[®]] long ago'. Before they couldn't walk around the room, but now they can move around the house, take a shower independently, and make short visits to see family or friends. One person said that they would tell anyone considering Duodopa[®] to 'go for it' and that 'the benefits far outweigh the negatives'. One clinician stated that Duodopa[®] treatment has allowed one of his patients to enjoy holidays twice a year in Tenerife. A patient expert described that for someone with Parkinson's disease being able to do simple things such as cooking, shaving with a razor, going outside and listening to the birds singing and children playing is so important. Having this ability makes them 'feel human'. Not being able to do these things and instead just sitting in a chair watching television all day makes them feel 'locked' in the house and they 'cease to exist'.

3b. How is this medicine better than current treatments?

Clinical and patient experts agreed that Duodopa[®] is a technically advanced treatment that provides significant benefits for people with advanced Parkinson's disease over other treatment options. Everyone with Parkinson's has a tailored medication regime, and most people with advanced Parkinson's take a number of different oral medications at specified times of the day; these can amount to tens of tablets each day. One person with Parkinson's described how taking medication every 90 minutes meant that sleep was practically impossible; their partner was up seven to eight times most nights to help and the strain on the family was almost unbearable. Duodopa[®] would allow people with Parkinson's to restore a sense of normality to their life and make a significant improvement in their quality of life.

According to patient experts, the current 'gold standard' treatment is levodopa, which is typically taken orally many times a day. The medication is effective with fewer side effects than alternative treatments for a period of time. However, this period of time reduces the longer the person lives with the disease, each dose taking longer to become effective. With time, the side effects of the medication become much more pronounced: severe cramping and dystonia, dyskinesia (uncontrolled writhing movements), chronic sleep disturbance, fatigue, balance issues (and increased risk of falls). As a Parkinson's advocate says: 'It's the tyranny of the drugs'. Another person described how standard treatments were not working for their partner: 'tablets do nothing to ease the symptoms [and] cause major problems with psychosis'. One clinical expert with 27 years of experience treating people with Parkinson's disease, said 'it's not rocket science', pointing out that Duodopa[®] is the same medicine, just delivered differently: 'we know it works'. Furthermore, because patients suitable for Duodopa[®] are levodopa responsive, a person already knows how they will respond to the drug. The expert described how for one of their patients, Duodopa[®] was 'transformational' and added that it would be 'criminal' if the patient had not been given access to Duodopa[®]; they would otherwise be in a care home. One patient said that if they had to go in to a care home 'shoot me and dig a hole'. Another patient, before being given Duodopa[®], had a fall and ended up in hospital for several weeks but since they had been given Duodopa[®] they were able to go out and about with confidence.

Clinical experts also highlighted that prior to treatment with Duodopa[®], one patient was having 300 NHS encounters per year but since receiving Duodopa[®], this was reduced to 10 a year; i.e. use of Duodopa[®] reduces the drain on NHS Wales resources. One patient confirmed that without Duodopa[®] his wife would have needed much more support from Social Services.

3c. Does this medicine have the potential to make a significant and substantial impact on health related benefits?

Clinical and patient experts highlighted that clinical studies and patient stories provide conclusive evidence for Duodopa[®]'s effectiveness in patients with advanced Parkinson's disease. Many people with Parkinson's who have experience of using Duodopa[®] report significant improvements in speech, swallowing, sleep, pain and psychiatric issues. They are less likely to experience pressure sores or be extremely underweight and some report that they can reduce or stop using wheelchairs and mobility scooters. Furthermore, people with Parkinson's who are not receiving Duodopa[®] typically have longer stays in hospital than those who are receiving Duodopa[®]. One person with Parkinson's said that since receiving Duodopa[®] their health and ability to concentrate had vastly improved, such that they felt more than capable of taking up driving again.

People using Duodopa[®] typically talk about being able to 'engage in life again'; one person described Duodopa[®] as a 'miracle'. They are able to take on household chores, leave the house, and re-engage in exercise, social activities and hobbies. Some have reported being able to take on voluntary work and even paid employment, making them feel 'useful' and 'happier'. One person who has been living with Parkinson's for more than 13 years, summed up the difference Duodopa[®] has made as 'a bad day now is better than a good day before [Duodopa[®]]'. Once the pump is fitted it takes effect quickly and helps to maintain a consistent level throughout the day – the person then describes their day with Duodopa[®] as 'fairly normal'. Without Duodopa[®] some people have said that they would be in bed or in a wheelchair.

4. Added value of the medicine for the patient's family or carers

Most people with Parkinson's disease live at home and are cared for by family members. As the disease progresses, the burden of care becomes more demanding and the financial cost for a family can be significant. Carers 'do everything' for the person, from personal care to medication and constant supervision. They often have to give up their day jobs in order to provide round-the-clock care and give up activities outside the home, leading to a feeling of social isolation. Stress levels are high, and the burden of care has a significant impact on the physical, emotional and psychosocial aspects of a carer's life; their quality of life is poor.

Clinical experts considered Duodopa[®] as having the potential to not only significantly improve a patient's life, but also to reduce the burden and stress for carers by decreasing the severity of symptoms. A person using Duodopa[®] is typically able to do much more for themselves and participate in social activities, so less supervision is needed. One person with Parkinson's disease said that they were 'reasonably independent' with their administration of medication, thus reducing the pressure on their partner. One carer described how 'the effect of Duodopa[®] has been dramatic'; 'life has been 80% better', the patient is more independent and they feel 'so much less stressed'. Another carer said 'it's a relief' that their partner is on Duodopa[®]. Before Duodopa[®], it was 'impossible [for them] to do anything'. With Duodopa[®], they can go out for a couple of hours and it's no longer 'a strain'.

Some carers talk in terms of 'getting the person back' after Duodopa[®] is prescribed. One carer described how they felt about the difference Duodopa[®] has made for their partner, who started using Duodopa[®] over a year ago. They explained how they felt their partner of 51 years was instantly like the person they had been before their Parkinson's worsened – as soon as they started on Duodopa[®] they recognised them – they were back.

Duodopa® in some cases allows the carer to return to work. Without Duodopa® the patient would have to go to a care home.

5. What is the most appropriate position for the medicine in the pathway of care for the condition? Does this differ from the company's proposed positioning?

Duodopa® is licensed for use in patients with advanced Parkinson's disease who are levodopa-responsive but who are experiencing severe response fluctuations despite optimised treatment with available alternative medications. It is therefore licensed as a last available medical treatment for this rare disease. The company proposes that Duodopa® should be considered for use in people with advanced Parkinson's disease who also are not eligible for deep brain stimulation (i.e. older, less fit patients with advanced Parkinson's disease) and those who have failed or are not eligible for apomorphine infusion - which overall appears in line with clinical practice.

6. Are there specific patient groups for whom the medicine is particularly beneficial? If so, please specify

Clinical and patient experts do not expect the number of people receiving Duodopa® to increase significantly if it is made routinely available; there are currently six people in Wales using Duodopa® via Individual Patient Funding Requests (IPFRs). In Scotland there are 15 people using Duodopa®; however, Scotland has a larger population of people with Parkinson's disease and when it was made routinely available there was a backlog of people who had been waiting for Duodopa® to become available.

The clinical experts agreed that selection of patients for treatment with Duodopa® is done very carefully. Clinicians seek advice and discuss the decision with their colleagues.

7. Are there any important considerations in relation to treatment delivery (e.g. how treatment should be monitored, how long it should be continued etc.)?

Duodopa® is administered as a continuous infusion using a portable pump via a permanent percutaneous gastrojejunostomy tube. This is an invasive treatment which presents ongoing risks, including discomfort and potential infection; although the number of infections is small. However, patient and clinical experts report that people with severe advanced Parkinson's are willing to accept these risks for the benefits of the treatment.

Clinical experts highlighted that the disadvantages of Duodopa® can be compared to the downsides of current standard treatments, even though these treatments would always be considered before Duodopa® were recommended. For example, DBS surgery is much more invasive than a gastrojejunostomy tube.

Clinical experts stated that ideally, Duodopa® should be administered in specialist centres as part of a complex therapy service delivery plan. Managing Duodopa® treatment can be difficult, with particular issues related to the tube as well as the pump, and there should be available support for patients and carers to help them through it. The company highlighted that there is already a service in place that provides nurses that can educate patients, carers and other nursing staff, on the use of the pump, and care of the tube. The nurses can make home visits to patients receiving Duodopa® giving them one-to-one support and there is also a 24-hour phone call centre for advice.

8. Other considerations

At the moment the only way that patients in Wales can access Duodopa[®] is via the IPFR process. Clinical and patient experts highlighted that the IPFR process is causing unnecessary delays in treatment. Because NHS Wales is paying the list price, Duodopa[®] costs more than if it was routinely available with the Patient Access Scheme.

Parkinson's is a progressive disease and the window of opportunity for treating people with advanced Parkinson's is small; the delay in access due to the IPFR process is harming people with the disease. The current situation leaves individuals without effective treatment while the process takes effect. One clinical expert commented that the process can take so long that by the time the patient is given Duodopa[®], they have already deteriorated to the point that they are no longer suitable for the treatment. It places significant extra burden on carers and family members in the meantime, and there is the added stress and anxiety for all concerned as to whether the treatment will be approved and if so, when. Patient experts highlighted that this situation is not in line with principles of Prudent Health Care; they feel they are being 'short-changed', yet they, and clinicians, are only asking for what is needed.

This frustration was one of the drivers for the company submitting Duodopa[®] for appraisal in Wales. The company submitted an application to AWMSG so that clinicians would not have to undertake burdensome and lengthy IPFRs, and Welsh patients would have equity of access and not face uncertainty.

Clinical and patient experts also highlighted the lack of equity for patients with neurodegenerative conditions. They felt strongly that priority is given to people with conditions that receive more public attention such as cancer and that there is a general lack of understanding about Parkinson's disease..

9. Is there a key factor, or combination of factors, that would justify this medicine being available in NHS Wales?

- Duodopa[®] is routinely available in England and Scotland. People with advanced Parkinson's disease should have access to Duodopa[®] regardless of where they live.
- The only way that patients in Wales can access Duodopa[®] is via IPFR. This process causes unnecessary delays leaving people without effective treatment. This is not in line with the principles of prudent healthcare. Furthermore, it costs NHS Wales more for Duodopa[®] via the IPFR process than if it was routinely available.
- Patients in Wales currently receive Duodopa[®] via the IPFR scheme (at list price). Since the medicine is associated with a Wales Patient Access Scheme and assuming the number of patients receiving Duodopa[®] does not change, a positive recommendation by AWMSG is anticipated to result in an effective net saving to NHS Wales.
- For people who are eligible for Duodopa[®] there is no alternative treatment option. Without Duodopa[®] their Parkinson's will not be managed, quality of life will be severely impacted, and their need for carer and nursing support will increase.
- Duodopa[®] contains levodopa, the 'gold standard' treatment for Parkinson's disease. Clinicians know Duodopa[®] works in patients who are levodopa-responsive.
- A clinical expert estimates that if it were approved 4–5 people per year would receive Duodopa[®] in Wales.
- Clinical experts support each other in deciding who is suitable for Duodopa[®].

- Through a home care scheme dedicated nursing resource is available to educate patients, carers and other nursing staff, on the use of the pump, and care of the tube. In addition nurses make home visits to patients receiving Duodopa® giving them one-to-one support.
- Introduction of Duodopa® will release NHS resource as patients transferring to Duodopa® need less care and support.
- Consistent delivery of Duodopa® helps restore a degree of control and enables people to regain significant independence and greater consistency in their daily routine. It gives people with Parkinson's a sense of greater normality and an ability to participate in everyday and social activities which they would otherwise be unable to do.
- Duodopa® has the potential to not only significantly improve a patient's life, but also to reduce the burden and stress for carers by decreasing the severity of symptoms.

One expert involved in compiling this response declared a personal specific interest, and two other experts had no conflicting interests, in relation to Duodopa®.