AWTTC
All Wales Therapeutics & Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

Evidence Status Report: opicapone (Ongentys®▼) as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations

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KEY FINDINGS

Report background
Opicapone (Ongentys®▼) was licensed in June 2016 as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations. Currently, opicapone has an All Wales Medicines Strategy Group (AWMSG) statement of advice issued, stating that it cannot be endorsed for use within Wales due to the absence of a health technology assessment (HTA) submission from the marketing authorisation holder. In NHS England, several clinical commissioning groups have accepted opicapone for restricted use within its licence as a second line catechol-O-methyltransferase (COMT) inhibitor, after entacapone. Clinicians in Wales consider there is an unmet need and have identified a cohort of patients who have failed, are intolerant to, or have concordance issues with entacapone and who could benefit from opicapone as a second line COMT inhibitor. Opicapone, restricted to second-line COMT inhibitor treatment, was considered suitable for assessment via the One Wales process and interim to HTA advice. If supported for use through the One Wales process, the marketing authorisation holder has committed to making a full HTA submission to AWMSG within 12 to 18 months. The data collected following the One Wales recommendation will be used to support the HTA submission.

Efficacy/Effectiveness
Data from two phase III studies showed that opicapone is superior to placebo, and non-inferior to entacapone, in reducing the time patients are in the off state. This reduction was maintained in open-label extension studies (one year of treatment in total).

Safety
No new safety signals have been observed for opicapone. The majority of adverse events are comparable with other COMT inhibitors.

Patient factors
- Opicapone enhances the effects of levodopa. Hence, it is often necessary to adjust levodopa dosage within the first days to first weeks after initiating treatment with opicapone to reduce levodopa-related dopaminergic reactions (e.g. dyskinesia, nausea, vomiting and orthostatic hypotension).
- Opicapone is taken once a day and may offer a simplified regimen when taken with levodopa compared to other available COMT inhibitors.
- Impulse control disorders can develop when taking dopaminergic medicines. Patients should be monitored regularly, and patients and carers should be made aware of what symptoms to look out for.

Cost effectiveness
There are no cost effectiveness data available. A health economics study is underway to support the HTA submission.

Budget impact
The addition of opicapone to the treatment pathway and subsequent delay in apomorphine treatment for an estimated 31.5 months would result in cost savings [commercial in confidence data removed]. This is based on 40 patients per year and assumes that all patients would receive treatment with apomorphine in the absence of opicapone.

Welsh commercial access agreements
The company has provided a commercial agreement to facilitate access within NHS Wales interim to HTA advice.

Impact on health and social care services
No significant changes in health and social care services are anticipated.

Innovation and/or advantages
Opicapone is being targeted as an oral treatment option after failure or intolerance to entacapone to delay treatment to more invasive, expensive and resource intensive non-oral treatment options including Duodopa®, apomorphine and deep brain stimulation.

BACKGROUND

Target group

The indication being considered is an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations. Opicapone is being positioned for use as a second-line catechol-O-methyltransferase (COMT) inhibitor after failure with entacapone, or in patients who cannot tolerate entacapone or have concordance issues.

Technology

Opicapone is a peripheral, selective and reversible COMT inhibitor[1]. In the presence of a DOPA decarboxylase inhibitor COMT becomes the major metabolising enzyme, and a considerable amount of levodopa is metabolised to 3-O-methyl-levodopa in the brain and periphery[1]. COMT inhibitors increase the plasma levels of levodopa when used with a DOPA decarboxylase inhibitor, thereby increasing the clinical response to levodopa[1,2].

Marketing authorisation date: 24 June 2016[3]

In June 2016, opicapone (Ongentys®▼) was licensed as an adjunctive therapy to preparations of levodopa/DOPA decarboxylase inhibitors in adult patients with Parkinson's disease and end-of-dose motor fluctuations who cannot be stabilised on those combinations[2].

Dosing

The recommended dose of opicapone is a 50 mg tablet taken once daily[2]. Opicapone should be taken at bedtime at least one hour before or after levodopa combinations. Dose adjustments to levodopa therapy within the first days to first weeks after starting treatment with opicapone are often necessary to reduce levodopa-related dopaminergic reactions (e.g. dyskinesia, nausea, vomiting and orthostatic hypotension)[2].

Clinical background

Parkinson's disease is a progressive neurodegenerative condition resulting from the death of dopamine-containing cells in the substantia nigra of the brain[4]. Symptoms include bradykinesia (slow movements), rigidity, rest tremor (shaking) and postural instability (loss of balance). Alongside physical symptoms, people with Parkinson's can also suffer from depression, cognitive impairment and dementia[4]. Parkinson's disease usually presents later in life; it is rare before 50 years of age, with a mean age of onset of about 60 years[1].

Incidence/prevalence

In 2017, Parkinson's UK produced a research report estimating the incidence and prevalence rates for Parkinson's disease in the UK[5]. The estimated annual incidence rate of Parkinson's disease in Wales is 3 people per 10,000, with a higher incidence in men (4 in 10,000) compared with women (2 in 10,000). The report provided prevalence data for Wales in 2015 which estimated that 24 in every 10,000 people were living with Parkinson's disease. As with incidence rates, the prevalence of Parkinson's disease increases with age and is higher in men (28 in 10,000 men in 2015) compared with women (19 in 10,000 women in 2015)[5].

Current treatment options

Treatments for Parkinson's disease aim to control symptoms[4]. Symptom control is expressed as a decrease in 'off' time (when patients are symptomatic) and increase 'on' time (when symptoms are controlled). People in the early stages of disease receive levodopa as first-line treatment if motor symptoms impact on their quality of life. For people whose motor symptoms do not impact on their quality of a life, dopamine agonists, levodopa or monoamine oxidase B inhibitors should be considered. If dyskinesia or motor fluctuations develop despite optimal levodopa treatment, monoamine oxidase B inhibitors or COMT inhibitors are given as an adjunct to levodopa. For people with advanced disease, best medical therapy, which may include apomorphine injection or infusions, is recommended. For people whose symptoms are not adequately controlled by best medical therapy and have in the past responded well to levodopa based therapies, deep brain stimulation is recommended[4]. Levodopa-carbidopa intestinal gel (Duodopa®) is recommended by the All Wales Medicines Strategy Group (AWMSG) as an option for the treatment of advanced levodopa-responsive Parkinson's disease for patients not responding satisfactorily to Parkinson's medicines and who are not eligible for deep brain stimulation[6].

Guidance and related advice

- National Institute for Health and Care Excellence (NICE) quality standard (QS164; 2018) Parkinson's disease[7]
- NICE guideline (NG71; 2017) Parkinson's disease in adults[4]
- NICE evidence summary (ES9; 2017) Parkinson's disease with end-of-dose motor fluctuations: opicapone[8]

SUMMARY OF EVIDENCE ON CLINICAL EFFECTIVENESS

A comprehensive literature search conducted by the All Wales Therapeutics and Toxicology Centre (AWTTC), together with information provided by the manufacturer of opicapone, identified two phase III (BIPARK I and BIPARK II) studies investigating the efficacy and safety of opicapone as an adjunct to levodopa compared with entacapone and/or placebo in patients with Parkinson's disease[9,10]. Two open-label extension studies of these phase III studies were also identified[10,11]. These studies are briefly described below.

Efficacy

The BIPARK I multicentre study evaluated the superiority of opicapone compared with placebo and the non-inferiority of opicapone to entacapone in 600 patients with Parkinson's disease and motor fluctuations[9]. Patients were randomised (1:1:1:1:1) to receive oral opicapone (5 mg, 25 mg or 50mg), placebo, or entacapone (200 mg with every levodopa intake) for 14–15 weeks[9]. After completing the double-blind period, patients could enter an additional 52-week, open-label extension period in which all patients received opicapone treatment[11].

The BIPARK II multicentre study investigated the efficacy of two doses of opicapone (25 mg and 50 mg once daily) compared with placebo in 427 patients with Parkinson's disease and motor fluctuations[10]. Patients were randomised (1:1:1) to receive opicapone (25 mg or 50 mg) or placebo for 14–15 weeks. A day after completing the end of the double-blind period, patients entered the 1-year open label phase and received opicapone treatment[10].

In both studies, patients had a clinical diagnosis of Parkinson's disease for at least three years, a Hoehn-Yahr stage of 1–3 (during the on state), indicating mild to mid-stage disease but patients are fully independent in their daily living activities[12], and were on a stable dose of levodopa and other medicines for Parkinson's disease (mainly dopamine agonists)[9,10]. Patients had to have signs of end-of-dose motor fluctuations for at least four weeks before screening, with a mean total awake time in the off state of at least 1.5 hours, excluding morning akinesia[9,10]. Only data for the licensed (50 mg) dose of opicapone are presented below.

In both studies, the primary endpoint was the change in absolute time in the off state from baseline to the end of the double-blind phase, assessed by daily patient diaries[9,10]. Overall, the results showed that the licensed dose of opicapone (50 mg) was statistically significantly superior to placebo in reducing the time patients are in the off state (Table 1 and Table 2)[9,10]. Based on the predefined non-inferiority margin of 30 minutes, opicapone 50 mg was found to be non-inferior to entacapone (Table 1)[9].

Table 1. Primary endpoint results from the BIPARK I study[9]

	Placebo	Entacapone	Opicapone 50 mg
Change in absolute time in the off state from baseline*			
Least-squares mean change (minutes)	−56.0	−96.3	−116.8
95% CI	−82.3 to −29.7	−122.6 to −70.0	−144.2 to −89.4
Change in absolute time in the off state compared with placebo*			
Mean difference (minutes)	-	−40.3	−60.8
95% CI	-	−76.2 to −4.3	−97.2 to −24.4
p value	-	0.014	0.002
Change in absolute time in the off state compared with entacapone†			
Mean difference (minutes)	-	-	−26.2
95% CI	-	-	−63.8 to 11.4
p value	-	-	0.005

* Full analysis set, n = 590; † Per protocol set, n = 537
CI: confidence interval

Table 2. Primary endpoint results from the BIPARK II study[10]

	Placebo	Opicapone 50 mg
Change in absolute time in the off state from baseline*		
Least-squares mean change in minutes (SD)	−64.5 (14.4)	−118.8 (13.8)
Difference in least-squares mean (SE) compared with placebo (minutes)	-	−54.3 (18.9)
95% CI for difference with placebo	-	−96.2 to −12.4
p value	-	0.008

* Analysis of covariance full analysis set, n = 407
CI: confidence interval; SD: standard deviation; SE: standard error

The key secondary efficacy endpoint results for the licensed dose are shown in Table 3. In the BIPARK I study, the time patients were in the on state with troublesome dyskinesia was not statistically significant between the opicapone (50 mg), entacapone and placebo groups[9]. A statistically significantly higher proportion of patients in the opicapone (50 mg) group of the BIPARK I study showed improvements from baseline in Clinician's and Patient's Global Impression of Change scores compared with patients in the placebo and entacapone groups[9]. In the BIPARK II study there was no statistical difference in these scores between

the opicapone and placebo groups[10]. Other scale-based secondary efficacy outcomes measured were the change from baseline to the end of study treatment in Unified Parkinson's Disease Rating Scale (UPDRS), Parkinson's Disease Sleep Scale (PDSS), Non-Motor Symptoms Scale (NMSS) and the quality of life measure, 39-item Parkinson's Disease Questionnaire (PDQ-39)[9,10]. There was no statistically significant difference in these scores between the opicapone (50 mg) or entacapone and placebo groups in both studies[9,10].

Table 3. Key secondary efficacy endpoint results from BIPARK I and BIPARK II studies in the full analysis sets[9,10]

	BIPARK I			BIPARK II	
	Placebo	Entacapone	Opicapone (50 mg)	Placebo	Opicapone (50 mg)
Responder rate of ≥ 1 hour reduction in time in the off state at the end of treatment					
Number of patients (%)	57 (48)	70 (58)	80 (70)	68 (50.4)	97 (66.0)
Comparison with placebo					
OR 95% CI p value	- - -	1.6 0.9 to 2.6 0.094	2.5 1.5 to 4.3 0.001	- - -	1.9 1.2 to 3.1 0.009
Comparison with entacapone					
OR 95% CI p value	- - -	- - -	1.6 1.0 to 2.8 0.063	- - -	- - -
Responder rate of ≥ 1 hour increase in time in the on state at the end of treatment					
Number of patients (%)	55 (46)	69 (58)	75 (65)	61 (45.2)	91 (61.9)
Comparison with placebo					
OR 95% CI p value	- - -	1.6 1.0 to 2.7 0.067	2.2 1.3 to 3.8 0.003	- - -	2.0 1.2 to 3.2 0.006
Comparison with entacapone					
OR 95% CI p value	- - -	- - -	1.4 0.8 to 2.4 0.15	- - -	- - -
Total time in the on state at end of study treatment (minutes)					
Least-squares mean change (SE)	47.1 (13.6)	99.7 (13.6)	119.0 (14.1)	58.7 (14.2)	111.3 (13.7)
Comparison with placebo					
Least-squares mean difference 95% CI p value	- - -	52.6 16.1 to 89.1 0.005	71.9 35.0 to 108.8 0.0001	- - -	52.6 15.8 to 89.3 0.005
Comparison with entacapone					
Least-squares mean difference 95% CI p value	- - -	- - -	19.3 −17.6 to 56.2 0.30	- - -	- - -
Time in the on state without troublesome dyskinesia (minutes)					
Least-squares mean change (SE)	46.5 (14.2)	94.1 (14.3)	109.1 (14.9)	NR	NR
Comparison with placebo					
Least-squares mean difference 95% CI p value	- - -	47.6 9.3 to 86.0 0.02	62.6 23.8 to 101.4 0.002	NR	NR
Comparison with entacapone					
Least-squares mean difference 95% CI p value	- - -	- - -	15.0 −23.8 to 53.7 0.45	- - -	- - -
CI: confidence interval; OR: odds ratio; NR: not reported; SE: standard error					

In the open-label extension studies, the reduction in the time patients were in the off state was sustained[10,11]. In the BIPARK I open-label phase (full analysis set included 494 patients, and 432 patients completed the study), the median reductions in off time were 33.8 minutes compared with the open-label baseline, and 126.9 minutes compared with the double-blind baseline[11]. Decreases in off time were associated with increases in absolute on time without

dyskinesia, but no relevant changes were observed in the median on times with troublesome or non-troublesome dyskinesia during the open-label phase. The changes in on and off time from open-label baseline to visit 14 based on previous double-blind treatment are shown in Table 4. In the BIPARK II open-label phase (367 patients entered, and 286 completed, the open label phase), the adjusted mean reduction in off time from the start to the end of this phase was 18.31 minutes[10]. Mean total on time increased by 24.9 (standard deviation 156.4) minutes and the mean on time with troublesome dyskinesia increased by 6.0 (standard deviation 129.1) minutes[10].

Table 4. Key endpoints from BIPARK I open label extension study[11]

	Double blind placebo	Double blind entacapone	Double blind opicapone 50 mg
Change in off time from open-label baseline to visit 14 by previous double-blind treatment (minutes)			
Least-squares mean change (SE)	−64.9 (14.8)	−39.3 (14.4)	−1.8 (14.6)
95% CI	−93.9 to −35.9	−67.6 to −11.1	−30.5 to 26.9
p value	<0.0001	0.0060	0.9007
Change in total on time from open-label baseline to visit 14 by previous double-blind treatment (minutes)			
Least-squares mean change (SE)	66.9 (14.8)	30.1 (14.5)	−6.1 (14.7)
95% CI	37.7 to 96.0	1.7 to 58.5	−35.0 to 22.8
p value	<0.0001	0.0370	0.6823
Change in on time without dyskinesia from open-label baseline to visit 14 by previous double-blind treatment (minutes)			
Least-squares mean change (SE)	43.1 (19.2)	45.7 (18.7)	21.1 (19.0)
95% CI	5.4 to 80.7	8.9 to 82.4	−16.2 to 58.4
p value	0.0247	0.0148	0.2659
Change in on time with troublesome dyskinesia from open-label baseline to visit 14 by previous double-blind treatment (minutes)			
Least-squares mean change (SE)	7.0 (6.1)	−7.3 (6.0)	−11.6 (6.0)
95% CI	−5.1 to 19.1	−19.0 to 4.4	−23.5 to 0.2
p value	0.2546	0.2186	0.0538

* Full analysis set, n = 494
CI: confidence interval; SE: standard error

Safety

The summary of product characteristics (SPC) lists adverse events associated with opicapone[2]. The most common of which is dyskinesia. Other events include, but are not limited to, vascular disorders (hypotension and hypertension), psychiatric disorders (such as anxiety and depression) and gastrointestinal disorders. Impulse control disorders can occur in people treated with dopamine agonists and/or other dopaminergic treatments. The SPC advocates regular monitoring for the development of impulse control disorders and review of treatment if symptoms develop. People taking dopaminergic treatments and their carers should be made aware of the behavioural symptoms of impulse control disorders including pathological gambling, increased libido, hypersexuality, compulsive spending or buying, binge eating and compulsive eating[2].

In the double-blind phase III studies, the most common adverse events occurring in the opicapone (50 mg) groups compared with placebo were dyskinesia, constipation, insomnia and dry mouth[9,10]. Most of the dyskinesia events happened in patients who were already experiencing dyskinesia at baseline[9,10]. In the BIPARK I extension study dyskinesia was most prevalent in the first few weeks of treatment, after which it reduced to < 1%[11]. This timeline coincided with the majority of levodopa dose adjustments, suggesting that dyskinesia could be managed in part by reducing the opicapone or levodopa dose[11]. The incidence of serious treatment-emergent adverse events in both studies was low across all groups (≤ 7%)[9,10]. In

the open-label extension studies, dyskinesia was the most commonly reported adverse event (≤ 21.5% in both studies)[10,11].

A common adverse event of entacapone and tolcapone is diarrhoea[13,14]. In BIPARK I and II no patients discontinued opicapone treatment due to diarrhoea[9,10] . In BIPARK I, two patients discontinued treatment with entacapone due to diarrhoea[9]. The Committee for Human Medicinal Products concluded that the safety and tolerability of opicapone is generally good and the majority of adverse events are comparable to other COMT inhibitors[1].

Clinical effectiveness issues

- Opicapone has been shown to be non-inferior to entacapone based on a short-term (14–15 weeks) study (BIPARK I). Due to the double-blind nature of this study, patients took the same number of tablets irrespective of the treatment they were randomised to. Therefore, tablet burden could not be assessed. Patients who had previously taken entacapone were excluded from BIPARK I and entacapone had to be withdrawn for at least one month before screening in the BIPARK II study. In the open-label extension phase of BIPARK I, patients who switched from entacapone to opicapone had a significant improvement in response. However, these patients were not failing, or intolerant of, entacapone. Overall, there are limited data for the target group under consideration in this assessment.
- In the double-blind studies, opicapone was investigated in people taking a stable optimised regimen of levodopa and other medicines for Parkinson's disease. Some patients were taking anticholinergics (8%) which is not recommended in the NICE guideline for patients with later Parkinson's disease. Patients who had severe dyskinesia, or severe and/or unpredictable periods in the off state were excluded from both studies. The BIPARK I study excluded centres in the UK; participants may not reflect the UK population and routine clinical practice.
- There are no long-term data to support the duration patients would receive treatment with opicapone, and consequently the delay in receiving more invasive, non-oral therapies.
- There are three COMT inhibitors currently marketed in the UK: entacapone, tolcapone and opicapone[2,13,14]. Tolcapone has an increased risk of hepatic toxicity and is limited to patients with motor fluctuations who have failed or are intolerant to other COMT inhibitors[13]. Tolcapone is prescribed under specialist supervision only and requires regular liver function tests[13]. Opicapone and entacapone do not require routine liver function monitoring[2,14].
- Entacapone is the most prescribed COMT inhibitor and may be taken up to 10 times a day with each levodopa dose to manage end-of-dose motor fluctuations[14]. Opicapone is given as a once daily dose[2], which offers a simplified regimen when compared with entacapone, but entacapone is commonly prescribed as a combination tablet with levodopa/carbidopa in a variety of strengths[15]. Specialists who reviewed the NICE evidence summary highlighted that a combination product of entacapone may be difficult for some people who are on differing levodopa doses at different times of the day[8]. Some people taking complicated dosing regimens may find it easier to add in a single tablet like opicapone and keep their familiar levodopa doses over the day. In addition, using once-daily opicapone enables flexible dosing of levodopa without altering the opicapone dose, unlike when using entacapone[8].
- Clinical expert opinion from Wales suggests that the availability of opicapone would delay switching to non-oral therapies by at least 12–18 months. In addition, quality of life would be maintained, drug concordance improved and some patients may be stabilised in the long term.
- A phase IV open-label study (OPTIPARK) (completed but results not yet available) is looking at the efficacy of three months on treatment with opicapone in patients experiencing wearing off motor fluctuations whilst taking levodopa, and a decarboxylase inhibitor with or without entacapone. The results of this study, together with outcome data

collected from Welsh patients if an interim One Wales decision is recommended, will form part of the company's health technology assessment submission.

SUMMARY OF EVIDENCE ON COST-EFFECTIVENESS

There are currently no cost effectiveness data available. A health economics study is underway to support the health technology assessment submission.

BUDGET IMPACT

Based on population estimates for Wales, the company estimates an incidence of 977 people in the first year, with a prevalent population of 7,692. Nine percent of the UK population with Parkinson's disease are estimated by the company to be receiving a COMT inhibitor plus levodopa/carbidopa, which equates to 733 people in Wales in the first year. Based on expert opinion from two clinicians in Wales, the company estimates that 27.5% of these patients (n = 202) would receive entacapone, and after two to three months of treatment 20% (n = 40) of patients would go on to receive opicapone due to intolerance, compliance issues or lack of response to entacapone. Based on expert opinion from two clinicians in Wales, the company has assumed that all 40 patients would remain on treatment with opicapone for 31.5 months before progressing to apomorphine. This represents a mid-point between the two estimates for duration of opicapone treatment (36-60 months and 12-18 months, respectively). The company has assumed that 40 patients receive opicapone each year, plateauing at 120 patients per year by Year 3. Table 5 details AWTTC's estimated budget impact based on medicine acquisition costs only, assuming that opicapone displaces and delays treatment with apomorphine by 31.5 months. The commercial arrangement price for opicapone has been applied [commercial in confidence figure removed], VAT and any local contracting agreements are excluded.

The commercial agreement price of opicapone is [commercial in confidence figure removed] per patient per year. The annual cost of apomorphine based on a daily dose of 20 mg is £2,771. As both groups of patients would remain on treatment with levodopa/carbidopa these costs have been excluded for simplification.

Table 5. Net medicine acquisition costs for 31.5 months of opicapone followed by apomorphine

	Year 1	Year 2	Year 3
Patient numbers	40	80	120
Medicine acquisition costs for opicapone	¶¶	¶¶	¶¶
Medicine expenditure of the displaced medicine*	£110,843.20	£221,686.40	£332,529.60
Net medicine acquisition costs	¶¶	¶¶	¶¶

* Apomorphine 20 mg per day, as per WHO Collaborating Centre for Drug Statistics Methodology[16]
¶¶ commercial in confidence figure removed

Assuming the upper bound of the lower estimate of duration of opicapone treatment (i.e. 18 months), the estimated cost saving would be [commercial in confidence data removed].

Budget impact issues

- Based on data provided by clinical experts, there are approximately 127–190 patients in Wales eligible for treatment with opicapone annually. This is higher than the company's Year 3 estimate of 120 patients.

- The duration of treatment with opicapone has been based on estimates from two clinical experts in Wales. The estimates were 36–60 months and 12–18 months, and the company used a mid-point of 31.5 months. There are no long term studies published to inform the average duration of opicapone treatment. It has been assumed that all patients receive 100% of their dose for the full duration of treatment.
- It has been assumed that the number of patients failing on entacapone will remain constant for the next three years. This is a simplified approach and does not take in to consideration incidence and mortality rates.
- Administration and monitoring costs associated with apomorphine treatment have not been included in the budget impact which would incur an additional cost to the service.
- On advice from clinical experts, where opicapone is not available to prescribe then patients failing or intolerant of entacapone are likely to be candidates for apomorphine treatment. Patients are estimated to be treated for 2–5 years with apomorphine before progressing to Duodopa® or deep brain stimulation. As the budget impact considers the first three years of treatment only, Duodopa® or deep brain stimulation have not been included.
- There is no clinical trial evidence to support the use of opicapone after long-term entacapone treatment. One clinical expert suggested that opicapone could be a treatment option for these patients. A second clinical expert indicated that whilst this may be an option, the percentage of patients offered opicapone at this stage in their treatment would be very small. Therefore this option has not been included in the budget impact calculations.

Welsh commercial access agreement

As this is a licensed indication, the company has provided a commercial agreement to facilitate access within NHS Wales interim to HTA advice.

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