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Clinical Commissioning Policy:

Levodopa-Carbidopa Intestinal Gel (LCIG) and LevodopaCarbidopa-Entacapone Intestinal Gel (LECIG) for Parkinson's Disease (adults) [2339]

Summary

NHS England will routinely commission treatment with levodopa-carbidopa intestinal gel (LCIG) and levodopa-carbidopa-entacapone intestinal gel (LECIG) for patients with advanced Parkinson's disease within the criteria set out in this document.

The policy is restricted to adults as this reflects the population affected by Parkinson's disease.

In creating this policy NHS England has reviewed this clinical condition and the options for its treatment. It has considered the place of this treatment in current clinical practice, whether scientific research has shown the treatment to be of benefit to patients, (including how any benefit is balanced against possible risks) and whether its use represents the best use of NHS resources.

This policy document outlines the arrangements for funding of this treatment for the population in England.

Our policies provide access on the basis that the prices of therapies will be at or below the prices and commercial terms submitted for consideration at the time evaluated. NHS England reserves the right to review policies where the supplier of an intervention is no longer willing to supply the treatment to the NHS at or below this price and to review policies where the supplier is unable or unwilling to match price reductions in alternative therapies.

What we have decided

NHS England have reviewed existing evidence and obtained policy working group (PWG) consensus to make the following treatments available for defined patients with advanced Parkinson's disease: LCIG or LECIG. We have concluded that there is enough evidence to make the treatment available.

The 2024 update to this clinical commissioning policy covering the use of LECIG is outside of the scope of the original independent evidence review conducted in 2015 and is based on PWG consensus.

Links and updates to other policies

This document updates and replaces policy D04/P/e Levodopa-Carbidopa Intestinal Gel (LCIG) (Clinical Commissioning Policy: LCIG).

Plain language summary

About Parkinson's disease

Parkinson's disease (PD) is a progressive neurodegenerative disorder that is one of the commonest causes of neurological disability in the UK. PD is a chronic disease of the brain characterised by gradually worsening tremor, muscle rigidity and difficulties with starting and stopping movements in addition to a complex range of non-movement (non-motor) problems. In advanced stages of the disease there can be severe fluctuations between almost total immobility, with or without tremor, and hypermobility with abnormal involuntary movements (dyskinesia) along with troublesome fluctuations in nonmotor symptoms. The estimated prevalence is about 160 per 100,000 population and the incidence rises with age. With progression of the disease physically disabling motor and non-motor complications occur with about 10% of patients estimated to have advanced disease.

Advanced PD is largely defined by motor problems when a patient has issues with balance, is usually taking over 4-5 doses of levodopa and experiencing troublesome off-periods of at least 2 hours and or troublesome dyskinesias for 1 hour that cannot be controlled by oral or transdermal therapies. The severe motor fluctuations and/or dyskinesias can significantly impair quality of life of patients and carers. Additionally, there are often sleep dysfunction, nonmotor fluctuations and pain. This is often further compounded by a range of gastric 'blocks' to absorption, which can occur in advanced PD. Eventually, these patients require transition to device-aided advanced therapies that can bypass the oral route and provide a steady and continuous dopaminergic stimulation or stimulation via deep brain electrodes as in deep brain stimulation (DBS).

About current treatment

Levodopa is the mainstay of treatment, supplemented with other therapies that include dopamine agonists, catechol-o-methyl transferase (COMT) inhibitors, monoamine oxidase type B (MAOB) inhibitors and other therapies. Motor complications include wearing-off effects and dyskinesia that do not adequately respond to oral medication manipulation. In such cases suitable patients are considered for a number of advanced therapies that include apomorphine subcutaneous infusions, DBS and Levodopa Carbidopa intestinal gel (LCIG). Recently, NICE have approved the use of subcutaneous foslevodopa–foscarbidopa infusion in advanced Parkinson's disease[1]. This is an alternative option to LCIG/LECIG in patients not suitable for apomorphine infusions or DBS.

If patients are not adequately controlled with the above therapies, patients are recommended for palliative care or continue with oral levodopa therapy.

About LCIG and LECIG

LCIG is a gel containing a combination of Levodopa (20mg/ml) and Carbidopa (5mg/ml). Levodopa is a precursor of dopamine, while carbidopa inhibits dopamine metabolism by dopamine decarboxylase and catechol-Omethyltransferase (COMT). LCIG is licensed for

[1] NICE TA934 | Foslevodopa–foscarbidopa for treating advanced Parkinson's with motor symptoms

the treatment of advanced levodopa-responsive PD with severe motor fluctuations and hyper/dyskinesia when available combinations of medicinal products are unsatisfactory.

LECIG is an intestinal gel combining levodopa (20 mg/ml), carbidopa (5 mg/ml) and entacapone (20 mg/ml). Entacapone also inhibits dopamine metabolism by dopamine decarboxylase and COMT. The combination of the three components ensures that high concentrations of levodopa are available to cross the blood-brain barrier, where it is converted to dopamine. LECIG is licenced for the treatment of advanced PD with severe motor fluctuations and hyperkinesia or dyskinesia when available oral combinations of Parkinson medicinal products have not given satisfactory results.

Both LCIG and LECIG are administered as a continuous infusion via an intestinal tube (percutaneous endoscopic gastronomy [PEG] / jejunostomy [PEJ] tube), using a portable pump. This enables the drugs to bypass parts of the gastrointestinal system which impair absorption of oral therapies in patients with advanced Parkinson's due to gastrointestinal dysfunction. Both LCIG and LECIG are given via a single use cassette and generally one cassette contains a single day's treatment. LCIG and LECIG have been determined as clinically equivalent treatment options (PWG consensus) and therefore the choice between the two treatment options should be patient and clinician driven.

Epidemiology and needs assessment

PD is a common, progressive neurological condition, estimated to affect 100–180 per 100,000 of the population (6–11 people per 6,000 of the general population in the UK) and has an annual incidence of 4–20 per 100,000. There is a rising prevalence with age and a higher prevalence and incidence of PD in males. It is estimated that about 10% of patients have advanced Parkinson's disease but many of these will suffer non-motor complications including neuropsychiatric and cognitive problems that will preclude them for many treatments including LCIG. The advanced PD patient pool potentially eligible for advanced therapies such as DBS, Apomorphine and LCIG/LECIG is uncertain. The specialised clinical commissioning policy for DBS in Movement Disorders reports a crude pro rata estimate of 300 patients per year would satisfy eligibility criteria for DBS 8 based on extrapolated data from the East Midlands Specialised Commissioning Group. Since it was licensed in 2006, about 200 patients have received treatment with LCIG in the UK and about 25 new patients per year start treatment in England. This small number is likely to reflect variability in commissioning and availability. With the introduction of this specialist commissioning policy and on the assumption that there will be no requirement for preapproval of funding it is estimated that between 75 and 100 new patients would be clinically appropriate to start LCIG/LECIG. Whilst this figure is an unsubstantiated estimate, it is in keeping with eligibility data in the Specialist Commissioning Policy for DBS in Movement Disorders.

Implementation

LCIG, LECIG and foslevodopa–foscarbidopa are all recommended treatment options at the same point in the treatment pathway for patients with advanced Parkinson's disease unsuitable for apomorphine infusions or DBS. PWG consensus is that there is clinical equipoise between LCIG and LECIG. The NICE technology appraisal for foslevodopa–foscarbidopa states "an indirect comparison suggests that foslevodopa–foscarbidopa works as well as levodopa–carbidopa intestinal gel, but the results are uncertain".

Therefore, the choice between starting a patient on LCIG vs LECIG vs foslevodopa–foscarbidopa should be a joint decision made between the patient and their movement disorders specialist after a discussion on the pros and cons of all therapies, subject to

the patient meeting all the relevant inclusion criteria and none of the exclusion criteria in this policy for LCIG/LECIG, or the NICE TA934 for foslevodopa–foscarbidopa.

Inclusion criteria

LCIG/LECIG will be available for all adult patients who satisfy **all** of the following criteria:

- Advanced levodopa-responsive PD with severe motor fluctuations, including significantly disabling off periods and/or dyskinesia that have not responded satisfactorily to available combinations of PD medications
- Have at least 50% 'off' periods
- The patient should not be disabled by symptoms unlikely to respond to levodopa
- Disease course of at least 5-years thereby reducing likelihood of atypical Parkinson's such as PSP or MSA
- Further reasonable drug therapeutic options are contraindicated due to comorbidities or late-PD disease complications
- Unable to tolerate or unsuitable for apomorphine
- Unsuitable for DBS, has refused to consent for DBS or DBS has failed

Exclusion criteria

The presence of one or more of the following would exclude both LCIG or LECIG therapy:

- Abnormal upper gastro-intestinal anatomy causing difficulty with device implantation
- Significant dementia
- Significant PD related non transitory psychotic symptoms
- Significant co-morbidities that are likely to compromise the potential benefit of LCIG/LECIG (severe low body weight, severe skeletal or postural deformities)
- The presence of any contraindication as detailed in the LCIG/LECIG summary of product characteristics (SPC)
- Lack of social support / appropriate carer to administer the LCIG/LECIG if appropriate

The following criterion excludes the use of LECIG therapy only:

- Previous intolerance (severe resistant diarrhoea, dyskinesias) to oral entacapone

Starting criteria

Treatment with LCIG/LECIG may be delivered and managed through any acute provider trust which treats patients with Parkinson's disease under either neurology or elderly care services. Eligibility must be determined through a PD clinical network linked to a

specialised neurosciences centre or designated PD MDT at a specialised neurosciences centre.

Patients approved for LCIG/LECIG by MDT are referred to the local MDT pathway to initiate treatment following the approved local management pathway that will normally include:

- Pre-test dose clinical assessment and blood screening as per local pathway (Consider U&E, FBC, LFT, B12, B6, Vit D)
- Formal Rating scale scores to include Hoehn and Yahr, UPDRS, On-Off Diary or wearable sensor (e.g., 7 days recording of 24 hours Parkinson's kinetograph (PKG)) for 7 consecutive days, PDQ-39, NMSS or NMSQ[2].
- Test dose LCIG[3]/LECIG[3]
- Placement of PEJ
- Initiation of treatment
- Titration of LCIG/LECIG and withdrawal of PD therapies as clinically indicated.

The MDT managing patients being assessed for LCIG/LECIG should include a core membership of:

- At least one tertiary centre-based Consultant Neurologist specialising in Movement Disorders or PD and experienced in assessment of patients for DBS, apomorphine and LCIG/LECIG
- Movement Disorders or PD Specialist Nurse
- Consultant Gastroenterologist experienced in PEG/PEJ tube insertion
- Neurosciences Pharmacist

In addition to the core membership; referring secondary/tertiary care physicians can be invited to join the MDT to contribute to decisions relating to patients under their care or in the event of disagreement between patients/carers and clinicians, or between clinicians, with regard to interpretation of stopping criteria.

Stopping criteria

Patients will be treated as long as they continue to derive benefit as judged by discussions with patient, carers and after formal rating scale assessments or wearable sensor (if applicable). Patients who meet **any** of the following criteria must stop treatment with LCIG/LECIG:

- unacceptable adverse effects of the drug
- progressive loss of ambulation[4]

[2] Abbreviations - UPDRS: unified Parkinson disease rating scale; PDQ-39: Parkinson's disease questionnaire; NMSS: non-motor symptoms scale, NMSQ: non-motor symptoms questionnaire.
[3] The requirement for a test dose should be a clinical decision and is patient dependent.
[4] Unless there are other significant extenuating reasons for continuation such as severe painful dystonia unresponsive to other therapy. Other criteria will be at the treating clinician's discretion with decisions made in conjunction with other members of the MDT. Treatment will continue until the lead clinician judges that there is insufficient clinical improvement to justify on-going therapy.

- development of significant dementia, psychosis or other PD-related complications should prompt careful review of clinical utility of on-going treatment and discussion with other members of MDT
- development of progressive symptomatic peripheral neuropathy unresponsive to metabolic replacement
- patient choice
- hardware problems that can include recurrent PEJ tube displacement especially if related to patient compliance
- Severe weight loss, not responsive to nutritional and vitamin supplementation.

Patients who meet the following criterion must stop treatment with LECIG:

- severe gastrointestinal upset, specifically diarrhoea, or severe troublesome dyskinesia. A formal discussion should be had between the clinician and patient regarding the suitability of switching to LCIG therapy.
- progressive abnormal liver function tests

Treatment with LCIG/LECIG using a permanent tube can be discontinued at any time by withdrawing the tube and letting the wound heal.

Monitoring

After initial titration, the morning dose and maintenance dose are fine-tuned over the course of a few weeks.

LCIG/LECIG should initially be given as monotherapy[5]. If needed, other anti-Parkinsonian medicinal products can be taken concurrently. If treatment with other anti-Parkinsonian medicinal products is discontinued or changed, it may be necessary to adjust the doses of LCIG/LECIG.

A sudden deterioration in treatment response with recurring motor fluctuations should lead to the suspicion that the duodenal/jejunal tube has been dislocated to the stomach. The location of the tube should be determined by X-ray. If the position is incorrect, the end of the tube is to be repositioned to the duodenum/upper jejunum. Tube blockage and or leakage may also occur and needs to be addressed by relevant gastroenterology team.

Patients treated with LECIG should be monitored for gastrointestinal side effects and emergent dyskinesia.

For patients who experience progressive anorexia, asthenia and weight loss within a relatively short period of time, a general medical evaluation including liver function assessment should be considered.

Dose

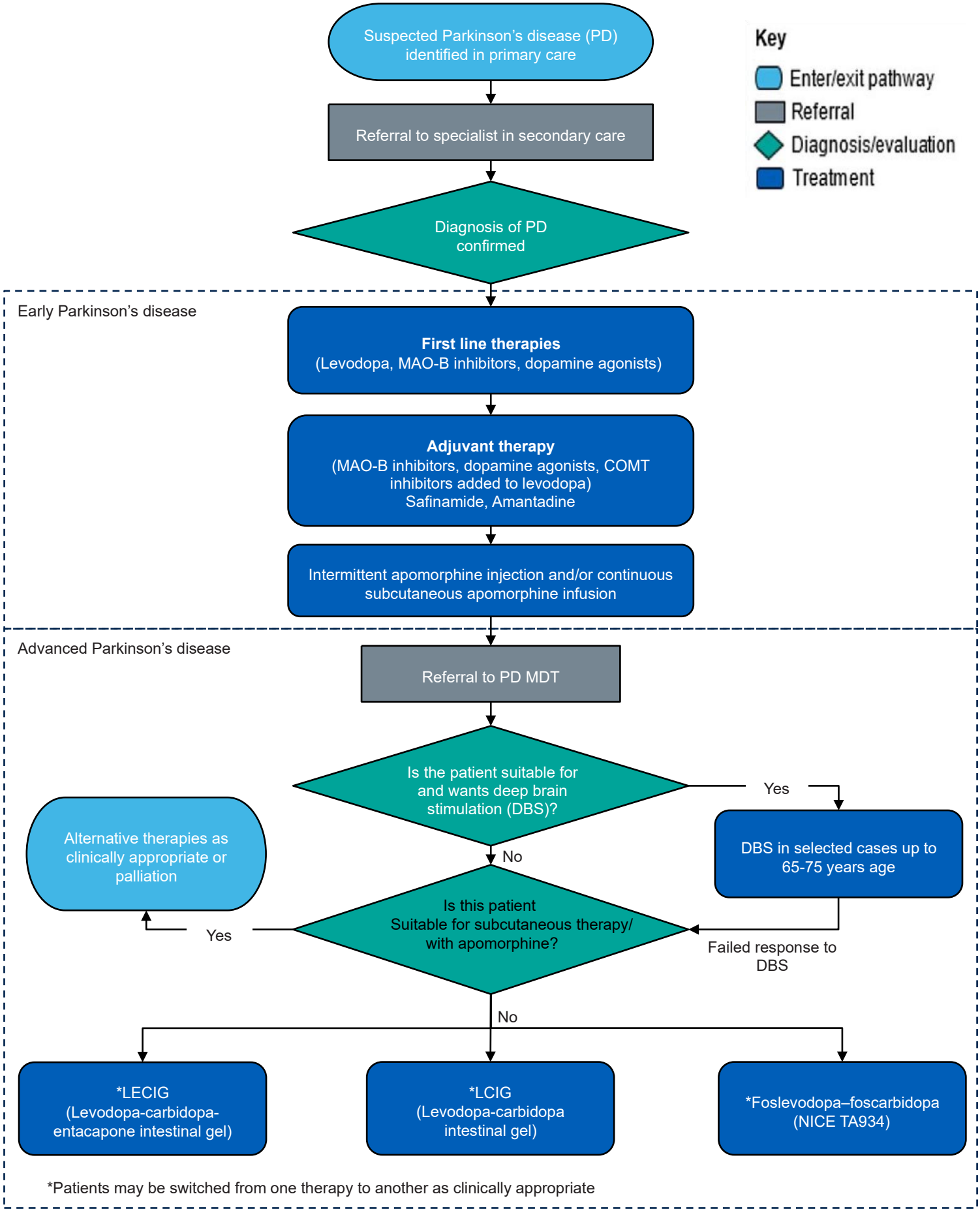
Under this policy, NHS England will commission the use of one intestinal gel cassette per patient per day.

[5] Patients might be treated with nighttime dopamine replacement therapy as judged by the clinician.

Each cassette is for single use only and should not be used for more than 24 hours. Once opened, a cassette may be used into the next day, i.e., up to 24 hours after it was first opened. The cassette is removed from the pump after 24 hours of use or when used up, whichever occurs first.

When switching between LCIG and LECIG, the titrations recommended in the SmPC should be followed.

Patient pathway



Governance arrangements

LCIG/LECIG may be delivered and managed through any acute provider trust which treats patients with Parkinson's disease under either neurology or elderly care services that agree to publish their results using established PD-related outcome measures. This should include complication rates related to PEJ tube placement and subsequent PEJ management.

Eligibility must be determined through a PD clinical network linked to a specialised neurosciences centre or designated PD MDT at a specialised neurosciences centre.

For other governance arrangements see Neurosciences: Specialised Neurology (Adults) service specification.

Mechanism for funding

This policy has been agreed on the basis of NHS England's understanding of the likely price of care associated with enacting the policy for all patients for whom NHS England has funding responsibility, as at the time of the policy's adoption. Should these prices materially change, and in particular should they increase, NHS England may need to review whether the policy remains affordable and may need to make revisions to the published policy. Where all three treatment options are equally clinically suitable (LCIG, LECIG or foslevodopa–foscarbidopa), the treatment option with the lowest acquisition cost should be used.

Where an individual's clinician believes that there may be exceptional clinical circumstances that might warrant consideration of funding outside of this policy, an application can be made under NHS England's Individual Funding Request (IFR) procedure. This includes cases that may be considered clinically critically urgent. Please see NHS England's website for more details.

LCIG/LECIG is commissioned by NHS England in line with the scope and manual for specialised neurology. It is recommended that LCIG/LECIG be funded only within the remit of this policy document.

Audit requirements

Providers will be expected to provide information on activity and outcomes on request.

Core data to include:

- Annual activity figures:
- Hospital length of stay
- Therapy complications

Baseline severity and annual progression based on:

- UPDRS
- PDQ39
- On-off diary or wearable sensor over 7 consecutive days
- Hoehn and Yahr status

- NMSS or NMSQ

Policy review date

This document will be reviewed when information is received which indicates that the policy requires revision. If a review is needed due to a new evidence base then a new Preliminary Policy Proposal needs to be submitted by contacting england.CET@nhs.net.

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Equality statement

Promoting equality and addressing health inequalities are at the heart of NHS England's values. Throughout the development of the policies and processes cited in this document, we have:

- Given due regard to the need to eliminate discrimination, harassment and victimisation, to advance equality of opportunity, and to foster good relations between people who share a relevant protected characteristic (as cited under the Equality Act 2010) and those who do not share it; and
- Given regard to the need to reduce inequalities between patients in access to, and outcomes from healthcare services and to ensure services are provided in an integrated way where this might reduce health inequalities.

Definitions

Deep Brain Stimulation (DBS)	This is a procedure in which stimulating electrodes are placed stereotactically into the deep structures of the brain. The electrodes are connected to an implanted pulse generator which is battery powered.
Dyskinesia	Abnormal involuntary movements that in the context of Parkinson's Disease often take the form of chorea and are a complication of long-term levodopa-based medication and PD progression.
Levodopa Carbidopa Intestinal Gel (LCIG)	LCIG, otherwise known as Duodopa, is a gel formulation of levodopa-carbidopa that is given by infusion directly into the distal duodenum or proximal jejunum.
Levodopa Carbidopa Entacapone Intestinal Gel (LECIG)	LECIG, otherwise known as Lecigon, is a gel formulation of levodopa-carbidopaentacapone that is given by infusion directly into the distal duodenum or proximal jejunum.

Off-period	A type of motor fluctuation that occurs in advanced PD that is characterised by a slowing or reduction in movement that
	leads to immobility, increasing tremor and disabling stiffness. They typically occur prior to the onset of action of PD medication (typically levodopa) or towards the end of its duration of action as it wears off.
Percutaneous Endoscopic Jejunostomy (PEJ)	A surgical procedure guided by endoscopy that allows the placement of a tube in the jejunum for feeding or in the context LCIG, to administer delivery of the drug for optimal intestinal absorption.

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