

Parkinson's disease

Prescribing at the end of life (including the last days / hours of life)

Parkinson's disease (PD) is common and may present across many specialties within secondary and primary care. This guidance is intended for use by healthcare professionals in any care setting. It highlights special considerations when prescribing for symptom management for patients with PD at the end of life who are in:

1. The last weeks/months of life.
2. The last hours/days of life.

General principles

- Symptoms of PD can be distressing and so it continues to be important to optimise symptom control as patients deteriorate.
- Common symptoms:
 - Tremor
 - Rigidity (stiffness)
 - Bradykinesia (slowness of movement)
 - Dyskinesia (involuntary movements)
 - Memory and cognitive problems, including hallucinations
 - Sleep problems
 - Pain
 - Constipation leading to exacerbations of other symptoms
 - Mental health problems, including anxiety and depression.
- Optimise non-pharmacological options where possible.
- It is important to continue PD drug treatment - particularly **dopaminergic therapy**, to maintain control of symptoms and avoid neuroleptic malignant syndrome.
 - Dopamine is crucial for the control of rigidity, bradykinesia, tremor, and pain.
 - This needs to be considered when patients are not able to take medicines orally, for example if the patient is nil by mouth, vomiting, acutely unwell or felt to be in the last days of life and too unwell to swallow (see below).
- Avoid centrally acting dopamine antagonists (e.g., metoclopramide and antipsychotics such as haloperidol, levomepromazine, amisulpride, risperidone, olanzapine, aripiprazole and fluphenazine) because they exacerbate PD symptoms, particularly rigidity and associated pain.

Assess the patient

Management will depend on the cause of symptoms and may be different for patients in the last days of life compared to those with a longer prognosis of weeks to months. Consider seeking specialist advice if unsure.

Symptom advice in the last weeks or months of life

Parkinson's disease symptoms

Dopaminergic drugs

Assess and optimise dopaminergic treatment as the patient deteriorates. In patients with well-controlled symptoms, dopaminergic drugs should generally be continued. However, in patients with advanced or end-stage Parkinson's disease, a gradual reduction of dopaminergic therapy may be appropriate due to reduced efficacy and/or increasing side effects such as agitation, delirium or hallucinations. Seek specialist advice, particularly if considering discontinuation of apomorphine.

If the patient has a **compromised swallow, is unable to swallow, or is nil by mouth**, management options include:

1. **If a viable enteral route is available**, switch dopaminergic medicines to dispersible preparations or crush and disperse suitable tablets in water; **or**
2. **Convert oral dopaminergic therapy to an equivalent rotigotine transdermal (TD) patch**, as outlined below.

Rotigotine transdermal (TD) patches (Available in 1 mg / 2 mg / 3 mg / 4 mg / 6 mg / 8 mg)

Rotigotine is an alternative dopaminergic medicine that can be administered via a transdermal patch.

3.3 mg of rotigotine is approximately equivalent to:

- Levodopa **100 mg**
- Levodopa/carbidopa/entacapone **75 / 18.75 / 200 mg**
- Ropinirole **5 mg**
- Pramipexole salt **1 mg**

To convert oral dopaminergic medicines to an equivalent rotigotine TD patch dose:

1. Add up the total dose of each oral dopaminergic medicine taken over 24 hours.
2. Multiply the 24-hour total dose (in mg) as follows:
 - Levodopa/benserazide (co-beneldopa; Madopar®) × **0.033**
 - Levodopa/carbidopa (co-careldopa; Sinemet®) × **0.033**
 - Levodopa/carbidopa/entacapone (Stalevo®, Stanek®, Sastravi®) × **0.04**
 - Ropinirole × **0.66**
 - Pramipexole salt × **3.3**
3. Select the nearest rotigotine TD patch dose, up to a maximum of **16 mg / 24 hours**.

Aim to convert back to the patient's usual oral regimen if and when they are able to resume oral medication.

For *Further Guidance*, refer to: [LTHT Parkinson's disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status \(Section 4 and 5\)](#) or seek Pharmacy advice.

Key point for dementia and delirium:

Rotigotine may cause or exacerbate delirium, agitation, or hallucinations. Patients should be monitored closely, and the benefits of symptom control balanced against adverse effects.

Non dopaminergic drugs

The following can be omitted relatively safely but please seek Pharmacy advice as soon as possible: Amantadine (**Symmetrel®**), Entacapone (**Comtess®**), Opicapone (**Ongentys®**), Rasagiline (**Azilect®**), Safinamide (**Xadago®**), Selegiline (**Zelapar®** or **Eldepryl®**) and Tolcapone (**Tasmar®**).

Pain

Rigidity

- Usually controlled with dopaminergic drugs. Check:
 - Dopaminergic drugs are administered on time.
 - If there are any swallowing difficulties.
- With advance PD it may be challenging to relieve rigidity due to reduced efficacy as well as side effects of dopaminergic drugs such as delirium/hallucinations. Specialist advice is suggested.

Musculoskeletal pain

- Reduced mobility may be associated with joint stiffness and pain.
- Non-pharmacological management such as repositioning, physiotherapy and occupational therapy advice is suggested.
- Simple analgesia and TENS may be helpful.

Retained secretions / salivary management and drooling

- Inability to control oral secretions (sialorrhea/drooling) is a known complication of PD. This may be due to oro-facial rigidity, lingual bradykinesia and/or oro-pharyngeal dysphagia. It is not due to over production of saliva
- Ensure assessment for alternative source of secretions such as gastric reflux, fluid overload, chest infection. Seek advice on management, if unsure.

Non-pharmacological management

Optimise non-pharmacological management where possible, including:

- Attention to posture
- Support collars
- Consider suction for secretions not cleared by less invasive measures
- If antisecretory medication is used the mouth may feel dry which may be helped by frequent sipping of drinks such as dark grape juice / sage tea or any other fluids to prompt swallowing.
- Refer to **Further Guidance** below for *LTH Management of Drooling in Parkinson's Disease Guidance*.

Pharmacological management

1. **For excessive or retained saliva/'watery' airways secretions**

Consider an anti-cholinergic agent. This reduces secretion production but does not remove secretions already present. Medicines that do not cause central side effects are:

- First line - **Glycopyrronium bromide**
- Second line - **Hyoscine butylbromide**, if glycopyrronium bromide is unsuitable or ineffective.

Glycopyrronium bromide

- Has a long duration of action.
- Can be given orally.
- Monitor for anticholinergic effects.

Oral	Subcutaneous injection and infusion
Dose <ul style="list-style-type: none"> Glycopyrronium 400 micrograms to 1mg three times a day. 	Dose: <ul style="list-style-type: none"> Glycopyrronium 200micrograms subcutaneous injections (SC) can be given as needed, hourly. Total daily dose 1200micrograms in 24 hours. Consider starting a continuous subcutaneous infusion (CSCI), if 2 or more as needed doses are given and effective in 24 hours. Continue with 600micrograms to 1200micrograms (1.2mg) via CSCI over 24 hours and/ or 200micrograms SC hourly
Formulations: Glycopyrronium 400micrograms/mL (Sialanar®) oral solution, for use in patients with dysphagia and/or an enteral tube in situ.	Formulations: <ul style="list-style-type: none"> Glycopyrronium 200microgram/mL or 600microgram in 3mL ampoules

Xeomin (Clostridium Botulinum neurotoxin type A)

- Licensed for symptomatic treatment of chronic sialorrhea due to neurological disorders.
- Refer to **Further Guidance** below for *LTHT Management of Drooling in Parkinson's Disease Guidance*. Consider seeking specialist advice from PD team.

2. **For viscous secretions**, particularly when difficult to expectorate, consider:

- Mucolytics e.g., nebulised saline or carbocisteine.
- Thick secretions will not improve with anti-cholinergic agents.

Nausea and vomiting

- Identify the cause of symptoms and address reversible causes.
- Note in PD delayed gastric emptying and constipation are often contributing factors.
 - Review current medication and reduce constipating medicines if possible.
 - Ensure well hydrated.
- Ensure good mouth care – refer to **Further Guidance** below for *LTHT Oral Hygiene (Adult) Management Guidance*.

Pharmacological management

- Choice of antiemetic is challenging as many antiemetics block dopamine receptors and can exacerbate PD symptoms and increase the risk of neuroleptic malignant syndrome. Dopamine antagonists to avoid are metoclopramide, levomepromazine, prochlorperazine and haloperidol. Seek specialist advice if unsure.
- Safer options:
 - Domperidone** (a dopamine antagonist which does not cross the blood brain barrier)
 - Prokinetic and may be of benefit when reduced gastrointestinal motility / constipation are main problems.
 - Cannot be given parentally (IV/SC).
 - Can be given rectally but may not be well tolerated.
 - Can prolong QT interval.
 - 5HT₃ antagonists such as **ondansetron** or **granisetron**.
 - Do not use in conjunction with apomorphine (dopamine agonist injections and infusion) can cause severe hypotension.**
 - Note constipation is a significant side effect.**
 - Cyclizine**
 - Causes constipation and delayed gastric emptying.
 - Can increase confusion.
 - Can exacerbate PD symptoms but can be considered if benefits outweigh risks.
- When absorption or tablet burden are an issue, consider the non-oral route.

Commonly used antiemetics and doses:

Antiemetic	Oral (PO)	Subcutaneous Cutaneous (SC) 1:1 conversion PO: SC	Continuous Subcutaneous Infusion (CSCI) over 24 hours	Transdermal patch
Ondansetron	4 to 8mg up to three times a day Oro dispersible tablets and liquid available.	4 to 8mg up to three times a day*	Informed by 'as needed' doses in the previous 24 hours. Usual range 8 to 16mg* CSCI over 24 hours. Dose reduction in moderate to severe liver impairment to maximum 8mg over 24hrs or consider granisetron.	3.1mg in 24 hours. Apply one patch every 7 days.
Granisetron	1 to 2mg once daily up to a maximum of 9mg in 24 hours	1 to 2mg once daily up to a maximum of 9mg in 24 hours	3 to 9mg CSCI over 24 hours. CSCI may not be needed, as SC dose is long acting.	
Domperidone	Tablets or liquid (can be used via enteral feeding tube) 10mg up to three times a day			
Cyclizine	50mg up to three times a day.	50mg up to three times a day.	100mg CSCI, can be increased to 150mg over 24hours.	
<ul style="list-style-type: none"> *Doses may require amendment for patients who are frail/ elderly and / or have liver or renal impairment. <i>Refer to further guidance below for liver failure and renal impairment guidance.</i> Start at the lower end of the range. Consider seeking specialist advice early if symptoms persist, anti-emetic doses are rapidly escalating, you are concerned about side effects or unsure what to do. 				

Delirium

- Refer to **Further Guidance** below *LTHT Delirium - Clinical Guideline for Diagnosis and Management of Delirium in Adults*.
- Review dopaminergic medicines as these may cause delirium/hallucinations. Consider seeking specialist advice from PD team, if unsure.

Non-pharmacological management is important

- Environment: calm and reassuring, repositioning, reorientation by familiar people, personalised bed space.
- Spiritual and emotional distress: consider support mechanisms e.g., spiritual advisor, wishes and preferences.
- Carer support: provide explanation of symptoms and address concerns.

Pharmacological management:

- Consider only if non-pharmacological approaches are ineffective.
- Avoid dopamine antagonists as they will exacerbate PD symptoms e.g., haloperidol, levomepromazine.
- Benzodiazepines (sublingual lorazepam) can be used where benefits outweigh the risks.
 - Dependence occurs so aim for short term use.
 - 0.5 to 1 mg '**When Required**'. Initially a maximum of 2 mg in 24 hours.

Symptom management for patients in the last days of life

Parkinson's disease symptoms

Dopaminergic medicines (last days / hours of life)

It is important to avoid abrupt withdrawal of dopaminergic treatment, as this can lead to severe rigidity, pain and significant distress.

If the patient is approaching the last days of life and is **unable to swallow**, but an **enteral route remains viable**, continue dopaminergic therapy via that route (e.g. dispersible preparations or crushed medicines where suitable). Seek Pharmacy advice as needed. The [LTHT Parkinson's disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status \(Section 4\)](#) may be used to support administration decisions.

If **oral or enteral administration is not possible**, consider use of a **rotigotine transdermal (TD) patch** using the following **emergency prescribing approach**, rather than the detailed dose-conversion calculations used for patients with a prognosis of weeks to months. There is no longer a rotigotine patch calculator.

Prescribe ONE rotigotine transdermal patch as follows:

- **Patients with dementia, delirium, or frailty:**
 - Rotigotine **6 mg / 24 hours**
- **Patients without cognitive impairment:**
 - Rotigotine **10 mg / 24 hours**

This approach aims to maintain dopaminergic therapy, reduce the risk of distress from abrupt withdrawal, and minimise prescribing error. Detailed dose conversion is not required in the last days or hours of life. Refer to [Emergency admissions for Parkinson's disease and related disorders in the LTHT Parkinson's disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status](#)

Review regularly for benefit and adverse effects, particularly **delirium, agitation and hallucinations**, as rotigotine may cause or exacerbate these symptoms. Adjust treatment in line with the patient's goals of care.

Key point:

In patients with a longer prognosis (weeks to months), rotigotine conversion should follow the detailed LTHT Parkinson's disease conversion guidance within [LTHT Parkinson's disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status \(Section 5\)](#)

Non dopaminergic drugs

The following can be omitted relatively safely but please seek Pharmacy advice as soon as possible: Amantadine (**Symmetrel®**), Entacapone (**Comtess®**), Opicapone (**Ongentys®**), Rasagiline (**Azilect®**), Safinamide (**Xadago®**), Selegiline (**Zelapar®** or **Eldepryl®**) and Tolcapone (**Tasmar®**).

Pain

- Rigidity
 - Continue dopaminergic drugs as discussed above.
 - Consider midazolam for associated distress ensuring the risk of sedation has been considered and discussed with the patient if possible/ those important to them.
- Other causes of pain
 - Management is unlikely to be directly affected by PD.
 - Refer below to **Further Guidance** for the *LTHT Care of the Dying Person Symptom Management guidance: Pain or LCH Symptom Management Guidance in the Last Days of Life*.

Retained secretions / salivary management and drooling

- Patients in the last days or hours of life may not be able to clear secretions by coughing or swallowing.
- If the patient has reduced consciousness reassure the family that the patient is likely to be unaware of the secretions.
- Assess the source of the secretions (e.g., salivary, bronchial, gastric reflux or fluid overload) as this can affect management (Note. Bronchial secretions are less likely to respond to anti-secretory drugs and they will not affect secretions where fluid overload or reflux is the cause).
- **Non-pharmacological management** such as positioning is the most important component of treatment.
- **Pharmacological Management:**
 - Avoid hyoscine hydrobromide because of its central effects.
 - **Hyoscine butylbromide** is non-sedating.
 - Hyoscine butylbromide (20mg/mL) 20mg SC **'When Required'**: minimum dosage interval of 1 hour (in LTHT) or (30 minutes the community).
 - *Note* it is short-acting therefore if effective consider a continuous subcutaneous infusion (typical starting dose 60mg SC over 24 hours).
 - Ensure good mouth care as dry mouth is a side effect.
- For patient already using subcutaneous **glycopyrronium** this can be continued.
- Refer below to **Further Guidance** for the *LTHT Care of the Dying Person Symptom Management guidance: retained secretions or LCH Symptom Management Guidance in the Last Days of Life*.

Nausea and vomiting

- The principals of guidance are the same as for patients with longer prognosis. See above guidance for nausea and vomiting for a patient with a prognosis of months to weeks.
- As patients deteriorate and lose the oral route the optimal antiemetics are likely to be SC:
 - 5HT₃ antagonist such as **ondansetron** or **granisetron** e.g., ondansetron **4 to 8 mg SC 'When Required'**: minimum dosage interval 8 hours or
 - **Cyclizine** (50mg/mL) 50mg SC **'When Required'**: Do not repeat within 4 hours; maximum THREE doses in 24 hours; (depending on concentrations may be incompatible with hyoscine butylbromide).
- Refer below to **Further Guidance** for the *LTHT Care of the Dying Person Symptom Management guidance: Nausea and Vomiting or LCH Symptom Management Guidance in the Last Days of Life or LCH Symptom Management Guidance in the Last Days of Life*.

Agitation/delirium

- Consider reversible causes.
- **Non-pharmacological management** is the most important strategy.

- **Pharmacological management:**
 - For persistent symptoms despite addressing reversible causes and /or severe distress associated with agitation.
 - Avoid dopamine antagonists as they will exacerbate PD symptoms e.g., haloperidol, levomepromazine.
 - If able to take oral medication see agitation /delirium advice for longer prognosis above.
 - If unable to take oral medication, consider:
 - **Midazolam** (10mg/2mL) (a benzodiazepine and likely to be sedative), particularly if the patient seems frightened or anxious.
 - Dose 1.25 to 5mg SC '**When Required**' (minimum dosage interval of 30 minutes). It is suggested that '**When Required**' dose range is prescribed.
 - Request clinical review if TWO '**When Required**' doses have been given in the last 24 hours.
 - Consider commencing a CSCI if two or more SC doses are given with good effect within 24 hours. Some patients require a CSCI sooner than 24 hours if they have received two or more effective doses within a few hours.
 - For prominent psychotic symptoms or if the dying person remains distressed despite midazolam seek specialist advice.
- Refer below to **Further Guidance** for the *LTHT Care of the Dying Person Symptom Management guidance: Agitation or LCH Symptom Management Guidance in the Last Days of Life*.

Further Guidance

- [LTHT Oral Hygiene \(Adult\) Management Guidance](#)
- [LTHT Parkinson's disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status.](#)
- [LTHT Delirium - Clinical Guideline for Diagnosis and Management of Delirium in Adults](#)
- [LPCN Renal Impairment - prescribing at the end of life \(including last days and hours of life\)](#)
- [LPCN Liver Failure - prescribing at the end of life \(including last days and hours of life\)](#)
- [LTHT Care of the Dying Person Symptom Management guidance: retained secretions](#)
- [LTHT Care of the Dying Person Symptom Management guidance: Nausea and Vomiting](#)
- [LTHT Care of the Dying Person Symptom Management guidance: Agitation](#)
- [LTHT Management of Drooling in Parkinson's disease Guidance](#)
- [LCH Symptom Management Guidance in the Last Days of Life](#)

Please also see - [Prescribing Guidance & Medicines Management](#) (LTHT Intranet)

Bibliography

- [LTHT Parkinson's Disease: Acute management of patients with Parkinson's disease who cannot take their usual medications, due to compromised swallow or nil by mouth status.](#)

Drug conversion rates based on:

- Tomlinson *et al.* Systematic review of levodopa dose equivalency reporting in Parkinson's disease. *Movement Disorders* Vol 25 No 15, 2010. P 2649-2653.

Medicines administration references:

- White R *et al.* Handbook of drug administration via enteral feeding tubes; 2007.
- Smyth J *et al.* The NEWT guidelines for administration of medication to patients with enteral feeding tubes or swallowing difficulties; 2010.
- Alty J, Robson J, Duggan-Carter P, Jamieson S. What to do when people with Parkinson's disease cannot take their usual oral medications: *Pract Neurol.* 2016 Apr;16(2):122-8.

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