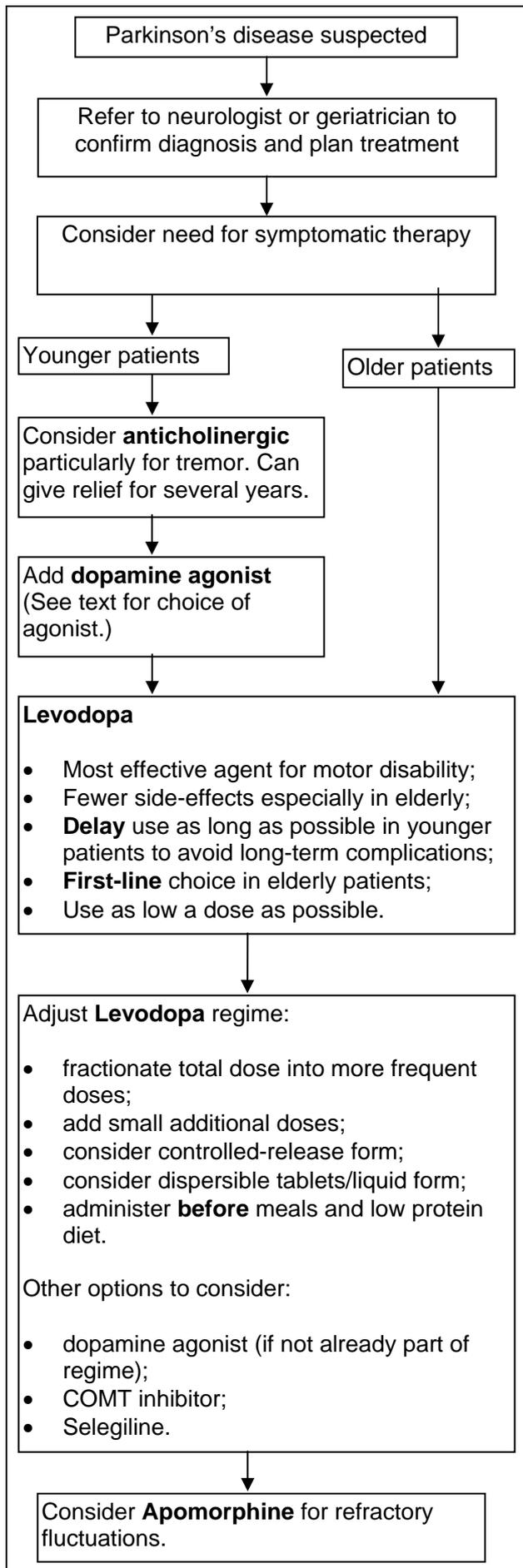


## PHARMACOLOGICAL MANAGEMENT OF PARKINSON'S DISEASE



### Principles of prescribing

- Non-specialists do not usually have enough experience of this disease to accurately diagnose the condition and plan treatment. The **younger** patient should be referred to a neurologist and specialist nurses. The **older** patient should be managed by geriatricians with a special interest in Parkinson's disease. There is no absolute age cut off. The decision should be based on biological age, co-morbidities, and patient wishes
- Pharmacological measures should **not** be initiated prior to specialist referral. Drugs that have been categorised as green or amber may be initiated by or on the recommendation of the consultant. Any necessary monitoring and titration of doses will be undertaken by the consultants or specialist nurses.
- Non-pharmacological measures are extremely important and must be considered before initiating or increasing drug treatment. Parkinson's disease nurses are particularly qualified to give this support.
- It is not possible to identify a universal first line choice drug therapy for PD. The choice of first line agent should take into account clinical and lifestyle characteristics, and patient preference.<sup>3</sup>
- Levodopa treatment should be delayed in younger patients if possible, as around 50% of patients will develop motor fluctuations (end-of-dose, on-off effects) and dyskinesias within six years.<sup>1</sup>
- Dopamine agonists have a useful role for early symptomatic treatment in younger patients to delay the need for levodopa. They may also be used for a levodopa-sparing effect in later disease to treat motor fluctuations. They are expensive drugs and are associated with serious side-effects. Impulse control disorders are an increasingly recognized problem (Hypersexuality, Gambling, compulsive spending etc) Visual hallucinations, psychosis and ankles oedema can also occur.

- Entacapone (a COMT inhibitor) may be used as an alternative to a dopamine agonist, in conjunction with levodopa, in late disease to reduce end-of-dose fluctuations. With disease progression, it is very likely that patients will be on a cocktail of antiparkinsonian drugs that commonly include all three drugs
- Neuroprotection with selegiline and dopamine agonists is unproven. Coenzyme Q10 and vitamin E have no effect and should **not** be offered.
- Excessive daytime sleepiness and sudden onset of sleep can occur with co-beneldopa, co-careldopa and the dopamine agonists. Patients should be advised accordingly.

## Formulary

### 4.9.1 Dopaminergic drugs used in parkinsonism

#### Levodopa

#### Co-beneldopa (Madopar) Co-careldopa (Sinemet)

Most effective treatment for motor disability and side effects are milder compared with some other treatments. May be considered as a **first-line** choice for elderly patients but delay treatment for as long as practicable in younger patients to **delay** long-term complications.

A modified-release form is useful for motor fluctuations and nocturnal akinesia. Due to decreased bioavailability, it is necessary to increase the dose by 30-50%. Absorption can be unpredictable and it may also be necessary to supplement the regimen with conventional tablets, particularly in the morning, to offset their slower onset of action. As a general rule, patients find the standard formulation preferable during the day.

Modified release levodopa should not be used to delay motor complications.

Nausea and vomiting are rarely dose-limiting but domperidone may be useful in controlling these effects. Taking levodopa with food can limit this, but later in the disease, mealtimes are best avoided to aid absorption.

N.B. Duodopa® is an intestinal gel licensed for administration via an enteral tube. It is extremely expensive, but effective and should be considered as a therapeutic option for a small minority of patients. Where its use is being considered an application should be made to the relevant PCT's individual patient request scheme.

## Dopamine agonists

#### Pramipexole (Mirapexin) Ropinirole (Requip) Rotigotine (Neupro) Cabergoline (Cabaser) Pergolide (Celance)

A dopamine agonist may be used for early **symptomatic** treatment in younger patients to delay the need for levodopa and for elderly patients in later disease to treat motor fluctuations.

Choice:

- **first-line** choices are the non-ergoline agonists ropinirole or pramipexole. Rotigotine is available in a patch formulation which may be used for those patients who cannot tolerate the first-line oral agents. Pramipexole and ropinirole are available in once daily oral formulation which provide improved night time cover. Initial choice of agent should include consideration of the cost-effectiveness.
- If side effects occur with one agonist it is worth trying another. If an agonist is tolerated in full dosage but without sufficient efficacy it is unlikely that an alternative agonist will be of more benefit.
- excessive daytime sleepiness and sudden onset of sleep can occur with **all** dopamine agonists;
- Patients and their partners should be carefully counseled regarding the risk of impulse control disorders and hallucinations

**Note:** The ergot-derived dopamine agonists, bromocriptine, cabergoline, and pergolide are associated with pulmonary, retroperitoneal and pericardial fibrotic reactions.

Ergot derived dopamine agonists should only be used for patients with informed choice. They should be the last option, where all other options have been exhausted. GPs will

be prompted by the Parkinson's specialist nurses to carry out the required monitoring of patients taking these drugs. These include yearly ESR and renal function with bi-annual echocardiography and chest Xray.

## COMT inhibitors

### Entacapone

By inhibiting metabolism of levodopa, entacapone allows a reduction in dose of levodopa and reduces end-of-dose deterioration.

COMT inhibitors can be used as an adjunct to levodopa therapy in patients who cannot be stabilised, particularly those with "end-of-dose" fluctuations.

Use of tolcapone is not routinely recommended (red) due to the risk of adverse effects and requirement for rigorous liver function tests on a continual basis. It is however more effective than entacapone.

### Stalevo®

Stalevo® is a combination preparation containing levodopa, carbidopa and entacapone. It reduces the number of tablets that patients need to take and ensures levodopa and entacapone are taken together. May be considered for patients:

- receiving levodopa and entacapone for whom compliance is a problem;
- receiving treatment with levodopa at the point at which entacapone would have been introduced;
- who have difficulty swallowing larger tablets.

## Others

### Selegiline

Selegiline can be useful at the onset of motor fluctuations as an alternative to dopamine agonists or COMT inhibition.

It can be used as monotherapy but the evidence for any neuroprotective effect in early disease is **not** established.<sup>2</sup>

There is a risk of **potentially hazardous** interactions with antidepressants and selegiline taken concomitantly although this is very rare. Specialist advice should be sought.

### Amantadine

May be used for dyskinesias in advanced disease. Tolerance to its effects may develop and confusion and hallucinations may occasionally occur. Withdrawal of amantadine should be gradual irrespective of the patient's response to treatment.

### Rasagiline

Rasagiline is licensed for use as monotherapy (TEMPO ADAGIO) or as adjunct therapy with levodopa for patients with end of dose fluctuations (LARGO PRESTO). Rasagiline is "not recommended". Where selegiline is not suitable or not tolerated an application could be made through an individual patient request to the relevant PCT for rasagiline if required

### Apomorphine

Apomorphine may be considered for refractory motor fluctuations **not** controlled by levodopa or other dopaminergic drugs.

Treatment is managed by the Parkinson's disease specialist nurses. Given subcutaneously either by injection (in young patients with short off-periods) or by infusion in more disabled patients.

## 4.9.2 Anticholinergic drugs used in parkinsonism

### Trihexiphenidyl Orphenadrine

Useful **first-line** therapy in occasional younger patients for symptomatic relief of tremor, when other agents ineffective.

Side effects limit their use particularly for elderly patients for whom they should be **avoided**. They are **contra-indicated** in cognitive decline, prostatism and glaucoma.

Different preparations have similar efficacy and are all inexpensive. There may be patient variation in how well they are

tolerated. Trihexiphenidyl and orphenadrine are **first-line** choices.

### Drug Costs

Comparative costs of one year's treatment (based on MIMS/Drug Tariff May 2010)

Drug	Dose	Annual Cost
Co-careldopa	275 qds	£490
Pramipexole (salt)	0.75mg tds	£2,092
Pramipexole (prolonged release)	1.57mg od	£2,091
Ropinirole	3mg tds	£1,981
Ropinirole (modified release)	12mg od	£2,190
Rotigotine	6mg/24 hrs	£1,861
Entacapone	200mg qds (doses administered with levodopa)	£839
Stalevo®	150mg qds	£1,012
Selegiline	10mg od	£86
Rasagiline	1mg od	£922
Apomorphine	(based on 5mg 5xdaily sc via multidose pen)	£5,338

### Contact names and numbers for Parkinson's Disease specialist nurses:

Name	Trust	Phone number
Sharon Atkins	NHS Dorset (covering Christchurch/St Leonards)	01202 705393
Alison Bush	Poole Hospital NHS FT	01202 442401
Cindy Thompson	Royal Bournemouth & Christchurch Hospitals NHS FT	01202 705320
Liza Villanueva	Dorset County Hospital NHS FT	01305 254789

### References

1. National Prescribing Centre. MeReC Bulletin 1996; **7**: (11) 41-44
2. Drug and Therapeutics Bulletin 1999; **37**:(5) 36-40
3. NICE Clinical Guideline no. 35, Parkinson's Disease, June 2006.

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