Parkinson's Australia

Parkinson's Disease Information Sheet 1.4
Medication Treatment Options

Parkinson's disease (Pd) is a progressive neurological condition which is related to a deficit of dopamine as a result of degeneration of dopamine producing neurons. Dopamine is a neurotransmitter which conveys messages between neurons to ensure effective movement and planning of movement.

As a consequence, most pharmaceutical treatment options focus on restoring the balance of dopamine and other neurotransmitters by several means:

- Dopamine replacement therapy
- Dopamine agonists
- COMT inhibition
- MAO Type B Inhibition
- Anticholinergic therapy
- Amantadine

Dopamine Replacement Therapy (Levodopa)

Replacement of dopamine using levodopa remains the gold standard treatment for Pd providing maximum symptom control, particularly for bradykinesia (slowness of movement), muscle rigidity and to a lesser extent tremor. A positive response to levodopa will assist in confirming the diagnosis of Pd.

As it is not possible to directly replace dopamine pharmaceutically, levodopa (a precursor) is used to cross the blood brain barrier where it is converted into dopamine and corrects the neurotransmitter imbalance.

Levodopa when taken orally is rapidly destroyed in the peripheral circulation resulting in a greatly reduced proportion passing the blood brain barrier. In order to reduce this breakdown and lessen the side effects of levodopa the addition of decarboxylase inhibitors is necessary. Sinemet® contains the decarboxylase inhibitor carbidopa. Kinson® is the generic form of Sinemet®. Madopar® contains the decarboxylase inhibitor benserazide.

Both of these medications are available in standard and controlled release forms and in varying dosages. Madopar® is available in a dispersible form where rapid action is required. Sinemet® may be dispensed in a liquid form which must be refrigerated and prepared freshly every 24 hours. These preparations are less frequently used than the standard tablet form.

Possible side effects of dopamine replacement therapy are:

- Nausea and vomiting
- Constipation
- Postural hypotension
- Increased dreams
- Hallucinations
- Dyskinesia (involuntary movements)

Nausea and vomiting may be experienced with the introduction of levodopa. On commencement of therapy it is important to take the medication with food however as the body adjusts this side effect may settle.

Constipation may be experienced with the introduction of and any change in medication regime. Extra fluids and a high fibre diet will address this problem.

Postural hypotension may present as dizziness and unsteadiness on standing and may result in falls. If this is experienced consult your doctor.

Increased dreams which may be vivid can occur with levodopa.

Hallucinations may occur as a result of long term levodopa therapy. In some cases this may require medication adjustment. If this is experienced consult your doctor. In some cases medication adjustment may be required.

Dyskinesia (involuntary movements) may develop with long term levodopa therapy. This can occur at various times in relation to the drug cycle e.g. peak dose or end of dose. Adjustment of medication may be necessary if the dyskinesia is problematic for PWP. Dyskinesia may be increased by stress.

Dopamine Agonists

Medications of the dopamine agonist family mimic dopamine and stimulate the dopamine receptors. Dopamine and levodopa are both taken up by the dopamine receptors of which there are several. Historically dopamine agonists were used in combination with levodopa however with ongoing development of drugs practice is changing to initiate treatment with dopamine agonists.

Currently, in Australia, the available dopamine agonists are:

- Cabaser® (cabergoline)
- Permax® (pergolide mesylate)
- Parlodel® (bromocriptine mesylate)
- Kripton® (bromocriptine mesylate)
- Apomine® (apomorphine hydrochloride) (subcutaneous injection or continuous subcutaneous infusion)

Possible side effects of dopamine agonist therapy are similar to those associated with levodopa with the additional rare side effects of pulmonary or peritoneal fibrosis and cardiac valve changes.

Apomine® requires the use of Motilium® prior to introduction because of nausea and vomiting. Localised skin reactions at the injection sites can occur.

COMT Inhibition

Catechol-o-methyl transferase (COMT) is an enzyme which metabolizes both levodopa and dopamine. By inhibiting the action of COMT availability of levodopa is maximised thus, in theory, providing an extended response to levodopa.

Currently, in Australia, the available COMT inhibitors are:

- Comtan® (entacapone) designed to be taken with a levodopa preparation. By itself Comtan® has no action.
- Stalevo® (levodopa/carbidopa/entacapone) a combination therapy of levodopa and Comtan® available in varying dosages.

The introduction of COMT inhibitors may exaggerate existing levodopa side effects. In addition a harmless side effect is a change in urine colour (bright yellow or a reddish hue). A rare side effect is diarrhoea which may commence several months after initiation of therapy.

MAO Type B Inhibition

Monoamine oxidase (MAO) is an enzyme responsible for the breakdown of dopamine. Type B is found in the brain. MAO type B inhibitors are reputed to scavenge the free radicals formed by the oxidative metabolism of dopamine hence the unproven theory that they may protect neurons from further damage.

Currently, in Australia, the available MAO type B inhibitors used in Pd are:

- Selgene® Eldepryl® (selegiline hydrochloride)

Possible side effects include sleep disturbance hence it is important to take this medication early in the day (preferable no later than 12 noon.

Drug interactions may occur when PWP taking selegiline are given Pethidine® and certain types of antidepressants. It is essential to check with your doctor before

taking any medication if you are prescribed selegiline.

Anticholinergic Therapy

Prior to the discovery of levodopa this group of medications was the first line treatment of Pd. The mode of action of the anticholinergic therapy is to correct the imbalance between dopamine and acetylcholine. They are useful in the treatment of tremor but may also address bradykinesia, rigidity and sialorrhea in the younger PWP.

Currently, in Australia, the available anticholinergics are:

- Artane® (benzhexol hydrochloride)
- Cogentin® (benztropine mesylate)
- Akineton® (biperiden hydrochloride)

Possible side effects (especially in the older PWP) include dry mouth, urinary retention, blurred vision and confusion.

Amantadine

Amantadine is an anti-viral agent that has anti-Parkinsonian effects. This is currently available, in Australia, as Symmetrel® (amantadine hydrochloride). Possible side effects are insomnia, confusion and a mottled rash on the lower limbs.

Summary

The previously discussed medications are those which may be prescribed in the treatment of Pd. The medical management of Pd is complex and ideally should be managed by a Consultant (Neurologist or Geriatrician). Just as the symptoms of Pd vary from person to person so to is the medication regime prescribed to control those symptoms.

Medication Warning

Pd is complex and often associated with other conditions. Many of the medications used in the treatment of other conditions have the potential to alter or interfere with the brain's dopamine system and maybe overlooked as having a detrimental effect on the symptoms of Pd.

It is imperative that PWP and health professionals involved in the care of PWP are aware of drug contraindications.

The most commonly prescribed medications which are contraindicated in Pd are:

- **Maxolon**® **Pramin**® (metoclopramide)
- **Stemetil**® (prochlorperazine)
- **Serenace**® **Haldol**® (haloperidol)

If treatment for nausea is required, Motilium at the minimum effective dose is a safe alternative.

For further information please contact your state organisation: FREECALL 1800 644 189

Parkinson's Australia **(08) 9346 7373**	New South Wales **(02) 9767 7881**	Victoria **(03) 9551 1122**	Queensland **(07) 3209 1588**
Australian Capital Territory **(02) 6290 1984**	South Australia **(08) 8357 8909**	Western Australia **(08) 9346 7373**	Tasmania **(03) 6224 4028**