

information

MEDICAL OPTIONS FOR PARKINSON'S

Parkinson's is a progressive neurological condition, which is characterised by both motor (movement) and non-motor symptoms.

It is primarily related to a lack of dopamine as a result of degeneration of dopamine producing neurons within the mid-brain.

Dopamine is a neurotransmitter which conveys messages between neurons to ensure effective planning, initiation and maintenance of movement. 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)

The use of levodopa to replace dopamine remains the gold standard treatment for Parkinson's and a positive response to levodopa will assist in confirming the diagnosis. Levodopa is efficient in managing the symptoms of bradykinesia and muscle rigidity. Tremor is the least responsive symptom to levodopa.

Levodopa (a precursor to dopamine) crosses the blood brain barrier where it is converted to dopamine and corrects the imbalance of neurotransmitters. In order to prevent the breakdown of levodopa and to ensure it passes the blood brain barrier the addition of decarboxylase inhibitors is necessary.

Currently, in Australia, levodopa is available as:

- Duodopa®
- Kinson®
- Madopar®
- Sinemet®
- Stalevo®

Duodopa® is a gel form of levodopa and carbidopa (decarboxylase inhibitor) which is delivered directly into the duodenum via a PEGJ tube.

Kinson® is a generic form of Sinemet® and is available in one dose only.

Madopar® is available in standard, controlled release and a dispersible form when more rapid action is required. Several dosages are available.

Sinemet® is available in standard and controlled release forms with several dosages available. It may be prescribed as a liquid which must be prepared freshly every 24 hours and refrigerated.

Stalevo® is levodopa with carbidopa and an additional ingredient and will be discussed under COMT inhibition.

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Possible early side effects of dopamine replacement therapy are:

- Nausea and vomiting
- Constipation
- Postural hypotension
- Increased dreams

Possible side effects after prolonged use are:

- Hallucinations
- Dyskinesia (involuntary movements)

Nausea and vomiting may be experienced with the early introduction of levodopa and therefore initially it is recommended to take this medication with food. This side effect usually passes as the body adjusts.

Constipation is a common side effect of levodopa therapy in addition to being a symptom of Parkinson's. Additional fluids and a high fibre diet are recommended.

Postural hypotension is the lowering of blood pressure on standing. It may present as dizziness and unsteadiness and can result in falls. If these side effects occur they should be discussed with your doctor.

Increased dreams, which may be vivid, can occur. These may also be related to Parkinson's but can also be exacerbated or occur due to levodopa.

Hallucinations which are usually visual may or may not be frightening. Medication adjustment may be necessary. Apart from being related to levodopa, hallucinations may occur if a chest or urinary tract infection is present. Medical review is recommended.

Dyskinesia (involuntary movements) may develop with long term levodopa therapy. This can occur at various times in the drug cycle, for example, peak dose or end of dose. Adjustment of medication may be made by your treating specialist if dyskinesia is problematic.

Dopamine Agonists

These medications mimic dopamine and stimulate the dopamine receptors. They may be prescribed as initial therapy or in conjunction with levodopa.

The side effects listed above may also occur with dyskinesia being less likely.

Currently, in Australia, the available dopamine agonists are:

- Apomine® (apomorphine hydrochloride)
- Cabaser® (cabergoline)
- Neupro® (rotigotine)
- Parlodel® (bromocriptine mesylate)
- Permax® (pergolide mesylate)
- Sifrol® (pramipexole)

Apomine® is given by subcutaneous injection or a subcutaneous pump infusion. It is necessary to give Motilium® prior to and during its use to prevent nausea and vomiting. Localised skin nodules may occur at the site of injection.

Cabaser® is an ergot derived dopamine agonist therefore cardiac valve changes and pulmonary fibrosis may occur. This is a long acting medication and is taken once daily.

Neupro® is a transdermal patch which is applied to different skin areas each day. To avoid skin irritation the patch should not be applied to the same area of skin within 14 days. It is important to hold the patch firmly in place for 60 seconds to ensure fixation.

Neupro® must not be worn during an MRI scan or cardioversion.

Parlodel® is an ergot derived dopamine agonist, therefore cardiac valve changes and pulmonary fibrosis may occur. This medication is taken three times a day.

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Permax® is an ergot derived dopamine agonist, therefore cardiac valve changes and pulmonary fibrosis may occur. This medication is taken three times a day.

Sifrol® is a non-ergot derived dopamine agonist which means the cardiac and pulmonary side effects are not an issue. Sifrol® is available in extended release formulation (ER) which is taken once daily, and normal release which is taken three times a day.

There is a risk of obsessive compulsive behaviour with all of these medications. This may take the form of gambling, excessive shopping, eating, increased libido or interest in pornography. This must be discussed with your treating specialist if any of these behaviours occur.

COMT Inhibition

Catechol-o-methyl transferase (COMT) is a naturally occurring enzyme which metabolizes both levodopa and dopamine. By inhibiting the action of COMT more levodopa is available - in theory, providing a more prolonged response to each dose.

Currently, in Australia, the available COMT inhibitors are:

- Comtan® (entacapone)
- Stalevo® (levodopa/carbidopa/entacapone)

Comtan® is taken with each dose of levodopa (by itself, Comtan® has no therapeutic action).

Stalevo® is a combination of levodopa and Comtan®, and is available in several doses.

COMT inhibitors may exaggerate existing levodopa side effects. Discoloration of urine is a side effect which is not harmful. Some people with Parkinson's may experience diarrhoea with these medications. This may occur after extended periods.

MAO Type B Inhibition

Monoamine oxidase (MAO) is a naturally occurring enzyme which is responsible for the breakdown of dopamine. MAO Type B inhibitors are reputed to scavenge free radicals formed by oxidative metabolism of dopamine hence the unproven theory that they may be neuro-protective.

Currently, in Australia, the available MAO Type B inhibitors are:

- Azilect® (rasagiline mesylate)
- Eldepryl® (selegiline hydrochloride)
- Selgene® (selegiline hydrochloride)

Azilect® is taken once a day.

Eldepryl® and Selgene® are taken twice a day with the second dose no later than noon, otherwise sleep disturbances may occur.

Drug interactions may occur with these medications. Pethidine® and some forms of antidepressants must be treated with caution. It is essential to discuss this with your treating specialist.

Anticholinergic Therapy

Prior to the development of levodopa, anticholinergics were the only treatment option available. Anticholinergics correct the imbalance between dopamine and acetylcholine. They are useful in the treatment of tremor.

Currently in Australia the available anticholinergics are:

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

These are rarely used due to commonly occurring side effects such as dry mouth, urinary retention, blurred vision and confusion.

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Amantadine

Amantadine is an antiviral agent and its mode of action is not clear but it is reported as giving improvement to symptoms and more recently it has been used to reduce dyskinesia.

Currently in Australia amantadine is available as **Symmetrel®** (amantadine hydrochloride).

Possible side effects are insomnia, confusion, swollen ankles and a mottled rash on the lower limbs.

Medication Warning

Many medications used in the treatment of other medical conditions have the potential to alter the dopamine system. It is important to consider the possibility that treatment of other conditions may cause or worsen existing Parkinson's symptoms.

The most commonly prescribed medications which are contraindicated in Parkinson's are:

- **Maxolon® Pramin®** (metoclopramide)
- **Stemetil® Stemizine®** (prochlorperazine)
- **Serenance®** (haloperidol)

If treatment for nausea is required **Motilium®** is a safe alternative.

Summary

The medications described in this information sheet are used in the management of Parkinson's in Australia. The pharmaceutical management of this condition is complex and should be prescribed by a specialist (neurologist, geriatrician or physician) with an interest in Parkinson's.

As each person with Parkinson's presents differently, it is essential that the medical management be prescribed on an individual basis bearing in mind potential side effects.

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