A practical guide to **STOPPING MEDICINES** in Older People

STOP

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Polypharmacy increases the risk of adverse effects and medicine interactions

The majority of older people have more than one medical condition, more than one prescriber and take more than one medicine.¹ Polypharmacy increases the risk of adverse effects and medicine interactions and the physiological changes that accompany ageing alter the handling and response to medicines. These factors make prescribing decisions, about both starting and stopping medicines in older people, difficult. The net result may be that the medicine regimen poses more risks than benefits.

The use of evidence based guidelines tends to increase the number of medicines required to meet specific targets, however this may not always be appropriate in older people because they are often poorly represented in clinical trials.^{2,3} Guidelines are population based and do not take into account individual variation, co-morbidities and patient preference. The clinical status of older people and the approach to decisions about the use of medicines for this population vary widely. There is often no clear consensus.

Individualised assessment that includes a review of the need for each drug can simplify treatment regimens and reduce the potential for harm. **Medicine withdrawal may be the best clinical decision and result in significant clinical benefits including a reduction in falls.** The key reasons for stopping medicines in older people include a decreased risk of adverse effects, a reduction in the potential for medicine interactions and to simplify a prescription regimen.

Key concepts

- The majority of older people who require drug therapy take multiple medicines
- Withdrawing medicines may be the best clinical decision
- Factors to consider when deciding if a medicine can be stopped include the wishes of the patient, clinical indication and benefit, appropriateness, duration of use, adherence and the prescribing cascade
- Only stop or reduce one medicine at a time
- Tapering the dose helps reduce the likelihood of an adverse withdrawal event

How do you decide which medicines can be stopped?

Reviewing the treatment needs of an older patient who is taking multiple medicines can be a complex and time consuming task. It can be difficult to know which medicine, if any, to stop. In some circumstances, the only way to know whether or not to stop a medicine is to actually stop it and see what happens.⁴

One way of considering if any medicines are able to be stopped is to group them into two categories – those that improve day-to-day quality of life and those that prevent future illness (see Box over page). Thinking about medicines in this way may provide a good starting point for talking with patients about the role and importance of each medicine. It may also allow a discussion about any variance between the goals of the doctor and those of the patient – the question is "what is the clinical and personal significance of this specific drug for this particular patient?"

Medicines can be grouped as:

- Those that keep the patient well and improve day-to-day quality of life e.g. analgesics, thyroxine or anti-anginals. In some cases, if these medicines are stopped, the patient may become ill or unable to function. However, some drugs may be able to be stepped down, stopped or used on an as required basis (prn) e.g. a protein pump inhibitor (PPI).
- 2. Those that are used for the prevention of illness in the future e.g. statins, aspirin, warfarin or bisphosphonates. A decision about whether to stop medicines such as these should include consideration of the risks and benefits of treatment for that particular patient, the length of time required for benefit and the life expectancy of the patient.

An estimation of life expectancy may be difficult and needs to take into account not only the person's age but also how many medical problems they have, how severe they are and how well they function.⁵ Diagnosis of a life-limiting illness may make the decision to stop long term medicines easier, but in reality, approaches range from stopping everything (except palliative medicine) to continuing all medicines until the patient is physically unable to take them.⁶

Best practice tip: Consider medicine regimens to have an expiry or "best before" date. Make sure that medicine reviews are carried out by this date unless there has been a change in the patient's clinical condition that prompts an earlier review. Use your PMS to make sure that reviews are done at least annually for older people. Factors to consider when deciding if a medicine can be stopped include:

- The wishes of the patient
- Clinical indication and benefit
- Appropriateness
- Duration of use
- Adherence
- The prescribing cascade

The wishes of the patient

The majority of people who take medicines would prefer not to, or at least to take only those that are really needed. Patients often ask if any of their pills can be stopped. It is easy to say "no" and continue on with the consultation but ideally this query should be viewed as a chance for a medicine review. Suggest a "brown bag review", where the patient brings in all their medicine, including overthe-counter and complementary/herbal medicines and also those that they are not actually taking but are still in their cupboard. Consider involving the practice nurse and pharmacist for a team approach.

See BPJ 11 (Feb, 2008) "Principles of prescribing for elderly people" for more information on a "brown bag review".

Clinical indication

Check that there is still a valid clinical indication and ongoing clinical benefit for each medicine. It may be necessary to review the patient notes to check what the original indication was. Consider if the benefit of the drug has already been achieved or if the clinical condition of the patient has changed.

Examples may include:

- A patient no longer taking a NSAID who now may not need a gastroprotective agent
- A patient with treated congestive heart failure who may be able to have their diuretic reduced or stopped

- A patient who has been successful with lifestyle modifications (such as a healthier diet, weight loss and smoking cessation) who may no longer require an antihypertensive
- A patient diagnosed with a terminal illness and a prognosis that makes the benefit of preventative medicines such as bisphosphonates and statins unlikely to be realised in that patient's lifetime

Appropriateness

Check that the medicine is appropriate for use in an older person (see sidebar "Defining inappropriate medicine use"). Two large studies have shown that approximately 21% of medicines used in older people may be inappropriate.^{7,8} Some medicines are less safe for use in older people and more likely to cause adverse effects or have an increased risk of medicine interactions.

Examples of medicines that may be inappropriate in older people include:

- Amitriptyline (particularly doses > 50mg), which is likely to cause sedation and also has strong anticholinergic actions - nortriptyline is recommended as a safer alternative if a tricyclic is required.
- Benzodiazepines, which can cause excessive sedation and increase the risk of falls.
- Dextropropoxyphene, which can cause confusion and excessive sedation particularly in older people. Evidence shows that it is no more effective for pain than regular paracetamol use.⁹ Due to this unfavourable risk-benefit balance, dextropropoxyphene is being withdrawn from the New Zealand market on 1 August 2010.

See BPJ 26 (Mar, 2010) "Dextropropoxyphene containing medicines to be withdrawn".

Consider if there are any other solutions that may be effective e.g. diet modification instead of a statin for reducing cholesterol, or non-pharmacological treatment instead of an antipsychotic for the behavioural and psychological symptoms of dementia.

Defining inappropriate medicine use

Several screening tools have been developed to help identify potentially inappropriate prescribing in older people such as the Beers' criteria and the more recent STOPP/START tools (Screening Tool of Older Person's Prescriptions and Screening Tool to Alert doctors to Right Treatment).¹⁰ Although widely used in research, these tools currently have limited value in primary care because they are not easy to use, time consuming and the Beers' criteria in particular includes medicines that in some situations may be appropriate e.g. dipyridamole, oxybutinin and doxazosin. These tools should not be used as a substitute for careful clinical judgement.¹¹



One way to "stop" medicines is not to start them in the first place

Prescribing for older people can be difficult. When considering any new medicine for an older person, check if it is appropriate by considering the following questions: (Adapted from Holmes, 2006)²

- Is there an indication for the drug?
- Is the medicine effective for the condition?
- Are there clinically significant drug-drug interactions?
- Are there clinically significant drug-disease/ condition interactions?
- Is there unnecessary duplication with other medicines?
- Is the likely duration of therapy known and acceptable to both doctor and patient?
- Will the patient take the medicine what are the likely adverse effects, is the dose correct, are the directions practical?
- Is this medicine the least expensive alternative compared with others of equal usefulness?

Georem See BPJ 11 (Feb, 2008) "Dilemmas in prescribing for older people"



Duration of use

Check how long the patient has been on the medicine. Some medicines are repeated for years as it can be quicker and simpler to maintain the status quo.

Check if there was a clear understanding at the time of initiation about the expected duration of use, particularly if the medicine was started in a secondary care setting. For example, a patient who was initiated on dipyridamole after a TIA, who has had no further ischaemic events, may be able to stop this medicine after two years.

Check whether there is still an indication for the use of the medicine and if so, that its use is still consistent with recommendations in current guidelines. Consider if there are more up-to-date drugs on the market that may be superior and safer.

Adherence

Check if the patient is taking all of their prescribed medicines. If not, ask them why? Did they understand the aims of treatment and did they experience any adverse effects? If the patient has remained well without the medicine, and is unlikely to suffer harm if it is not taken, consider stopping it e.g. corticosteroid inhalers for COPD.

The prescribing cascade

When a patient presents with new symptoms, consider an adverse medicine reaction as a possible cause. The aim is to avoid the prescribing cascade where additional medicines are initiated to treat adverse effects (both recognised and unrecognised) of other medicines.

Examples include:

 A patient taking 50 mg amitriptyline for pain presents with incontinence and/or constipation.
 Amitriptyline has anticholinergic actions which can cause urinary retention leading to overflow incontinence. If this is not recognised, oxybutynin may be prescribed, which aggravates the incontinence because it also has anticholinergic actions. In addition, the patient then becomes constipated and a laxative is prescribed. One medicine has led to the use of three others. Stopping the amitriptyline and finding an alternative medicine for the pain may be the best action

- A patient taking a calcium channel blocker presents with ankle swelling. Avoid prescribing a diuretic as they are not effective in this situation.
- For any patients taking NSAIDs who develop dyspepsia, hypertension or heart failure consider the NSAID as a potential cause.

What are the likely consequences of stopping medicines?

Stopping medicines may result in one or more of the following outcomes:

- 1. No adverse consequence for the patient
- Withdrawal events/symptoms that have a pharmacological or physiological basis, including rebound symptoms e.g. rebound hypertension after discontinuing therapy with a beta blocker
- Signs or symptoms of the pre-existing disease may re-appear e.g. increased blood pressure after stopping an antihypertensive.

How a medicine is stopped is likely to alter the risk of withdrawal symptoms

For some classes of medicine e.g. beta-blockers, corticosteroids and antidepressants, abrupt withdrawal can induce morbidity and even mortality as a result of rebound phenomena and specific withdrawal syndromes.¹² For many medicines, tapering the dose is likely to be safer and better tolerated by the patient than abrupt discontinuation.

For example, abrupt discontinuation of:

 A beta-blocker may result in rebound tachycardia, an increase in blood pressure and, in some circumstances, cardiac ischaemia.

- An antidepressant may result in withdrawal symptoms that are similar to those of depression, which may make it difficult to determine whether the original depression has returned, or if the symptoms are a result of the abrupt discontinuation.
- A PPI is more likely to result in rebound hyperacidity.

How to stop medicines

Take a stepwise approach to stopping medicines

A four step process can be used when stopping medicines:¹³

- 1. Recognise the need to stop
- 2. Reduce or stop one medicine at a time
- Consider if the medicine can be stopped abruptly or should be tapered
- 4. Check for benefit or harm after each medicine has been stopped

Recognise the need to stop a medicine

When the patient presents for a renewal of medicine ask if they have any new symptoms (including adverse effects) or any concerns about their medicine. Has the clinical condition of the patient changed? Consider the preferences of the patient.

Are there drugs that can be stopped? If more than one medicine can be stopped, which one should be stopped first? This relies on clinical judgement and consideration of factors such as medicines most likely to cause adverse effects or without clear indications.

Reduce or stop one medicine at a time

Try to reduce or stop only one medicine at one time. If problems develop it is then easier to know what the likely cause may be.

Taper medicines when appropriate

To reduce the likelihood of an adverse withdrawal event, many medicines should be tapered. It can be difficult to determine which can just be stopped and which should be tapered. Therefore if in doubt taper, as it is safer. For many medicines the first step in tapering is to halve the dose. The dose should then be tapered in a stepwise manner to establish if the patient's symptoms, conditions or risks can be managed with a lower dose or whether the medicine can be stopped completely.¹³ Generally there will be plenty of time to taper a medicine. If the medicine is being discontinued because toxicity is a concern, then a more ambitious taper can be undertaken or the medicine stopped abruptly. Once tapering has begun, ask the patient to note any symptoms that may suggest a more gradual withdrawal is required e.g. dyspepsia with reduced dose of PPI.

If intolerable symptoms occur following a decrease in the dose or after the medicine has been stopped, then it may be necessary to restart the previously prescribed dose and then try tapering again, but at a more gradual rate.

Check for benefit or harm after each medicine has been stopped

Ask the patient if any changes have occurred after a medicine has been stopped. Beneficial effects should be noted to reinforce that the decision to reduce or stop the medicine was correct. There is also evidence that the beneficial effects of some medicines may persist even after the medicine is stopped e.g. treatment with a bisphosphonate for five years, gives an ongoing reduction in risk of fracture for a further five years.¹⁴

If symptoms of the initial condition return and are troublesome, despite gradual tapering, then it may be that the medicine cannot be stopped completely. The patient may however be able to be managed on a reduced dose e.g. 10 mg PPI rather than 20 mg.

Specific guidance on stopping medicines

Antidepressants

Antidepressants should be tapered rather than stopped abruptly, to reduce the risk of developing a discontinuation syndrome and to allow time to assess the possible re-emergence of depressive symptoms (Table 1). Antidepressant discontinuation syndrome (see over page) is more likely with a longer duration of treatment and a shorter half-life of the treatment drug.¹⁵

A general guide to tapering medicine:

Halve the dose. At the next scheduled visit review progress, then either:

- Maintain (at half dose)
- Continue to taper (e.g. quarter dose)
- Stop

Notes:

- View the discontinuation process as a trial
- Stop one medicine at a time so that any withdrawal event(s) can be easily attributed to the medicine that is being stopped
- Time taken to taper may vary from days to weeks to months

General tapering guide	Withdrawal effects
An antidepressant should not be stopped abruptly if it has been taken for six weeks or more The dose should be reduced gradually over at least four weeks, or longer if withdrawal symptoms emerge ¹⁷	Wide range of symptoms including anxiety, gastrointestinal disturbance, headache, insomnia, irritability, malaise, myalgia, recurrence of depression
Specific classes	Withdrawal effects
SSRIs and venlafaxine Taper slowly over several weeks or months e.g. reduce by 25% every four to six weeks for drugs with a shorter half-life ¹⁶ Fluoxetine at low doses may not need to be tapered, as it has a long half-life. ¹⁵	 Mild self limiting symptoms (above) may occur within a few days. There may be a delay before symptoms present for patients on higher doses of fluoxetine because of the longer half-life. Discontinuation syndrome appears to occur more frequently with paroxetine and venlafaxine. This may partly be due to the shorter half-life of these drugs.
TCAs Tricyclic and related antidepressants (e.g. mianserin) should be withdrawn slowly ¹⁸ e.g. reduce by 25% every four weeks	In addition to antidepressant discontinuation syndrome, rapid withdrawal may produce symptoms associated with cholinergic rebound (e.g. agitation, headache, sweating, gastrointestinal symptoms), parkinsonism and problems with balance. ¹⁵ This is more likely with the more potently anticholinergic TCAs such as amitriptyline.
MAOIs Withdraw slowly	Neuropsychiatric symptoms may be more prominent and include severe anxiety, agitation, altered sleep, hallucinations, delirium and paranoid psychosis ¹⁶

Table 1: A guide to discontinuing antidepressants

Antidepressants should normally be withdrawn over at least a four week period. Patients may experience withdrawal symptoms but usually these are mild and selflimiting. If these symptoms are not tolerated, it may be necessary to resume the previous dose and then reduce the antidepressant more slowly.¹⁶

Benzodiazepines

Regular and prolonged use of hypnotics should be avoided because of the risk of tolerance to effects, dependence and an increased risk of adverse events.^{19,20}

Patients who have taken benzodiazepines on a long term basis should be withdrawn gradually over a number of months (e.g. six months). The longer a patient has been taking a benzodiazepine, the more likely they are to develop dependence and tolerance.

There are a wide range of withdrawal symptoms (Table 2) and some may be similar to those for which the benzodiazepine was originally prescribed. Some patients may experience withdrawal symptoms such as rebound insomnia and anxiety after only two to four weeks of treatment. Withdrawal symptoms can continue for weeks or months after stopping a benzodiazepine.¹⁸ An awareness of this may help prevent additional medicines being prescribed for these symptoms.

Abrupt withdrawal may result in confusion, toxic psychosis, seizures or a condition termed benzodiazepine withdrawal syndrome which is similar to delirium tremens.¹⁸ Typical symptoms of this include insomnia, loss of appetite, weight loss, sweating, perspiration, tinnitus and disturbances of perception. Benzodiazepine withdrawal syndrome can occur within one day of stopping a short-acting benzodiazepine or up to three weeks after stopping a long-acting benzodiazepine.¹⁸

Successful discontinuation may result in improvements in cognitive and psychomotor function, particularly in older people. Patients may be more alert and have increased working memory, reaction times and balance.¹² Alternative strategies for insomnia (e.g. sleep compression, BPJ 14) may be required as improvements may not occur for some months after the benzodiazepine has been stopped.²¹

Antihypertensives

Beta-blockers are the cardiovascular medicine most often associated with adverse withdrawal events. Abrupt withdrawal may cause rebound hypertension, tachycardia, arrhythmia or angina. These events may be physiological withdrawal reactions or an exacerbation of the underlying condition.¹³ Gradual dose reduction is required (Table 3).

Antidepressant Discontinuation Syndrome^{16,22}

Antidepressant discontinuation syndrome can occur with rapid discontinuation of any antidepressant. Symptoms are variable.

Typical symptoms include – Flu-like symptoms, Insomnia, Nausea, Imbalance, Sensory disturbances and Hyperarousal (anxiety/agitation) (FINISH). Symptoms are likely to appear within one week of rapid dose reduction or abrupt discontinuation of an antidepressant. Symptoms are often mild and short lived and resolve without treatment in about ten days. For patients with more severe symptoms the pre-reduction dose may need to be restarted which usually results in resolution of symptoms within 24 hours. Subsequent tapering then needs to be at a slower rate.

Table 2: A guide to discontinuing benzodiazepines

Tapering guide	Withdrawal effects
Slowly taper the dose in steps of approximately one- eighth of the daily dose every two weeks ¹⁸ If withdrawal symptoms occur, maintain at the current dose until symptoms settle and then continue to taper, usually at a slower rate	Wide range of symptoms including anxiety, mood changes, insomnia, palpitations, tremor, headache, gastrointestinal disturbance, muscle stiffness and spasms Benzodiazepine withdrawal syndrome
Alternative withdrawal method ¹⁸	Dose equivalence ^{15,18,20}
 Transfer patient to an equivalent daily dose of diazepam, preferably taken at night Reduce the dose of diazepam every two to three weeks by 2 or 2.5 mg. If withdrawal symptoms occur, maintain this dose until there is improvement. Continue to reduce the dose, if necessary by smaller amounts. It is better to reduce too slowly rather than too quickly. Stop diazepam completely. The withdrawal period may vary from about four weeks to more than one year. 	Approximate equivalent doses for diazepam 5 mg: = lorazepam 0.5-1 mg = nitrazepam 2.5-5 mg = oxazepam 15 mg = temazepam 10 mg = triazolam 0.25 mg = zopiclone 7.5 mg

Table 3: A guide to discontinuing antihypertensives¹⁸

General tapering guide	Withdrawal effects
Most antihypertensives should be tapered. Taper dose at approximately monthly intervals, over three to six months.	Wide range depending on the specific medicine and the condition being treated. May include ankle oedema, weight gain, headache, tachycardia, increased blood pressure, worsening heart failure or angina, myocardial infarction.
Specific classes	Withdrawal effects
Beta-Blockers Gradual dose reduction necessary	Sudden withdrawal may cause or exacerbate angina
Calcium channel blockers Consider gradual reduction	Sudden withdrawal may exacerbate angina
Thiazides It may not be practical to cut tablets so either stop or consider alternate day dosing initially then twice weekly dosing	Possible exacerbation of the underlying condition
Angiotensin-converting enzyme inhibitors Consider gradual reduction	Possible exacerbation of the underlying condition

Table 4: A guide to discontinuing warfarin

Tapering guide	Withdrawal effects
Stop abruptly	A rebound
or Taper over several weeks	hypercoagulable state with a risk of thrombosis, has been reported in some patients but this can occur even if the dose is tapered and may reflect the initial pro-thrombotic state for which treatment was started ²⁴

Table 5: A guide to discontinuing NSAIDs

Tapering guide	Withdrawal effects
Consider prn use or	Recurrence of pain,
regular use at a lower	arthritis or gout
dose	symptoms
Can be stopped	
abruptly	
or	
Halve the dose for two	
to four weeks then	
stop	
Review the need for	
gastric protection	
therapy i.e. PPI or H ₂ RA	

Statins

The decision to stop a statin is based on an assessment of individual benefits and risks. For example, stopping may be justified in a person at relatively low risk of a cardiovascular event, who is also poorly compliant or experiencing troublesome adverse effects. In most cases statins can be stopped without the need for tapering.

Statins should not be stopped in patients admitted with (or with a history of) cardiovascular events including acute coronary syndrome, myocardial infarction and stroke.

Warfarin

In older people taking warfarin, low initial and maintenance dosages are recommended (e.g. dose adjusted to maintain the INR at the lower end of the range of 2-3).²³ The optimum duration of warfarin therapy is determined by the condition being treated and its severity.²³

Some clinicians tail off long-term treatment over several weeks but the need for this is unclear. It is possible to stop abruptly rather than taper (Table 4).²⁴

NSAIDS

Consider stopping NSAID therapy when the risks associated with treatment outweigh the benefit. Risks associated with NSAIDs usually relate to declining renal function in the older age group and adverse gastrointestinal effects. NSAIDs may also reduce the effectiveness of antihypertensive therapy. Some patients may tolerate abrupt discontinuation but tapering the dose allows for other analgesics to be introduced or increased (Table 5).

Acid suppressants

Many people remain on acid suppressants despite there being no ongoing clinical indication e.g. NSAID stopped or *H. pylori* successfully treated. It is often possible to maintain symptom control on a lower dose or on an as needed basis rather than on long term high dose maintenance therapy.

Tapering the dose of an acid suppressant (both PPIs and H_2RAs) is recommended because of the risk of rebound

Table 6: A guide to discontinuing acid suppressants

General tapering guide	Withdrawal effects
Halve the dose for four to eight weeks then stop (or step down to a less potent agent)	Recurrence of oesophagitis and indigestion symptoms
Consider providing an antacid for dyspepsia symptoms	
Specific medicines	Withdrawal effects
 Proton pump inhibitors (PPI) Consider alternate day dosing. Capsules cannot be halved. Consider stepping down to an H₂RA if a more gradual taper is required 	Stopping PPIs suddenly can cause rebound hypersecretion of acid
Histamine receptor antagonists (H ₂ RA) Taper gradually	Rebound dyspepsia has also been described after stopping H ₂ RA therapy abruptly

Table 7: A guide to discontinuing oral corticosteroids

Table 8: A guide to discontinuing antiparkinsonian medicines

Tapering guide	Withdrawal effects
Antiparkinsonian medicines should not be stopped abruptly as there is a small risk of neuroleptic malignant syndrome ¹⁸	Hypotension, psychosis, pulmonary embolism, rigidity, tremor A symptom complex (resembling the neuroleptic
Reduce the dose gradually over about four weeks Sinemet CR tablets are scored and may be administered as half tablets	malignant syndrome) may occur. Symptoms include muscular rigidity, elevated body temperature, mental changes, diaphoresis, tachycardia, and tachypnea. There may be an increase in serum creatine kinase concentration. ²³

hypersecretion of gastric acid (Table 6).²⁵ If rebound hyperacidity is mistaken for a return of the underlying condition then acid suppressants may be restarted unnecessarily. Following discontinuance of omeprazole therapy, gastric acid secretion returns to baseline over a three to five day period.²³

Bisphosphonates

The beneficial effects (e.g. prevention of bone loss, improved bone mineral density [BMD], and reduced risk of both vertebral and non-vertebral fractures) are seen within one year of starting treatment. Beneficial effects on BMD persist after stopping the drug.²⁶ The half-life of bisphosphonates appears to be very long (probably up to several years) because of skeletal storage.²⁷ This may explain continued effectiveness after discontinuation.

Alendronate can be stopped abruptly without the need for tapering.

Oral Corticosteroids

Administration of oral corticosteroids for more than three weeks, or shorter courses at high doses (≥40mg prednisone), can lead to suppression of the hypothalamicpituitary-adrenal (HPA) axis.

Tapering may not be required for some patients who have received low to moderate doses (e.g. <40mg prednisone)

of corticosteroids for less than three weeks, however this will depend on the patient and the disease being treated.

Withdrawal should not be abrupt for the majority of patients who have been taking systemic corticosteroids for more than three weeks. These patients should generally have their corticosteroid slowly tapered to allow the HPA axis to recover (over weeks or months).^{23,26} The rate of dose reduction will vary depending on the original dose and duration of treatment, the disease and the response of the patient.²⁶ If the disease flares up during withdrawal, the dose may need to be increased and the subsequent withdrawal to be more gradual. An increase in dose may also be required during periods of stress e.g. infection, trauma or surgery. There are several methods for tapering oral corticosteroids (Table 7).

Antiparkinson agents

The majority of patients respond initially to levodopa and its use improves the quality of life. After two years or more, benefit is reduced as the disease progresses and late complications emerge.²⁶ The long term use of levodopa is limited by motor complications and drug induced dyskinesias.

If antiparkinsonian drug therapy is reduced abruptly, or discontinued, a symptom complex resembling neuroleptic malignant syndrome can occur (Table 8).²³

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