SHARED CARE GUIDELINES FOR PRESCRIBING SELEGILINE OR RASAGILINE IN PARKINSON'S DISEASE

INDICATION

Selegiline and Rasagiline are monoamine-oxidase-B inhibitors used in conjunction with levodopa at the onset of motor fluctuations as an alternative to dopamine agonists or COMT inhibitors.

The evidence for any neuroprotective effect in early disease is **not** established and should not be offered.

NICE NG71 states:
Offer a choice of dopamine agonists, MAO-B inhibitors or catechol-O-methyl transferase (COMT) inhibitors as an adjunct to levodopa for people with Parkinson's disease who have developed dyskinesia or motor fluctuations despite optimal levodopa therapy, after discussing:

- the person's individual clinical circumstances, for example, their Parkinson's disease symptoms, comorbidities and risks from polypharmacy
- the person's individual lifestyle circumstances, preferences, needs and goals
- the potential benefits and harms of the different drug classes

AREAS OF RESPONSIBILITY FOR SHARED CARE

This shared care agreement outlines ways in which the responsibilities for managing the prescribing of selegiline or rasagiline can be shared between the specialist and general practitioner (GP). GPs are invited to participate. If the GP is not confident to undertake these roles, then he or she is under no obligation to do so. In such an event, the total clinical responsibility for the patient for the diagnosed condition remains with the specialist. If a specialist asks the GP to prescribe this drug, the GP should reply to this request as soon as practicable.

Sharing of care assumes communication between the specialist, GP and patient. The intention to share care is usually explained to the patient by the doctor initiating treatment. It is important that patients are consulted about treatment and are in agreement with it.

The doctor who prescribes the medication legally assumes clinical responsibility for the drug and the consequences of its use.

REFERRAL AND INITIATION

The diagnosis of Parkinson's disease will be undertaken by a consultant and their team. Pharmacological measures should not be initiated prior to specialist referral. In some cases, it may not be appropriate to initiate therapy with selegiline or rasagiline when the patient is seen by the specialist team. It may therefore be necessary for GPs to initiate therapy where a delay in initiation is required.

Specialist Responsibilities	
1	To assess the patient and establish the diagnosis, determine a management strategy and ensure appropriate follow-up in conjunction with the GP.
2	Where appropriate: ○ to initiate and stabilise treatment; ○ obtain consent from the patient's GP to continue prescribing once treatment has been stabilised (usually after 4 weeks) or if a delay in initiation is required to obtain their consent to start treatment when indicated, ○ monitor the patient and their therapy at six monthly intervals.
3	To provide the GP with appropriate prescribing information and any additional information requested.

4	To be available for advice if the patient's condition changes.
5	To ensure that procedures are in place for the rapid re-referral of the patient by the GP.
6	To ensure the patient has given informed consent to their treatment.
7	To liase with the GP on any suggested changes in prescribed therapy.

General Practitioner Responsibilities	
1	Initially, to refer the patient for specialist advice.
2	Where appropriate to continue to prescribe a selegiline as part of a shared care arrangement (usually after 4 weeks). If a decision has been made to delay initiation GPs may initiate therapy in accordance with the specialist's instructions.
3	To deal with general health issues of the patient.
4	Monitor concordance with therapy

Patient's role (or that of carer)	
1	Report to the specialist or GP if he or she does not have a clear understanding of the treatment.
2	Attend appropriate GP and other follow up appointments
3	Share any concerns in relation to treatment with the selegiline
4	Use written and other information on the medication.
5	Seek help urgently if suspect side effects, or otherwise unwell.

SUPPORTING INFORMATION

Dosage and Administration

The recommended dose of selegiline is 10 mg daily either alone or as an adjunct to levodopa or levodopa/peripheral decarboxylase inhibitor. When selegiline is added to a levodopa regimen it is possible to reduce the levodopa dosage by an average of 10 -30%. Reduction of the levodopa dose should be gradual in steps of 10% every 3 to 4 days.

The recommended dose of rasagiline is 1 mg once daily, to be taken with or without levodopa.

Monitoring

No specific monitoring is required.

Contraindications

- Hypersensitivity to the active ingredients or excipients of the preparation
- Pregnancy or Breastfeeding
- Concomitant treatment with other monoamine oxidase (MAO) inhibitors (including medicinal and natural products without prescription e.g. St. John's Wort) or pethidine, At least 14 days must elapse between discontinuation of rasagiline and initiation of treatment with MAO inhibitors or pethidine.
- Severe hepatic impairment.
- Selegiline is contra-indicated in patients receiving treatment with serotonin-agonists (e.g. sumatriptan, naratriptan, zolmitriptan and rizatriptan).
- Selegiline should not be used in patients who are being treated with antidepressant drugs, including MAO inhibitors, tricyclic antidepressants, serotonin noradrenaline reuptake inhibitors (SNRI) (venlafaxine) and selective serotonin reuptake inhibitors (e.g. citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline.
- Selegiline should also not be used with other drugs which are also monoamine oxidase inhibitors, e.g. linezolid.
- Selegiline should not be used in combination with sympathomimetics
- Selegiline should not be used in patients with active duodenal or gastric ulcer.
- Selegiline should not be used in patients with other extrapyramidal disorders not related to dopamine deficiency.
- Selegiline in combination with levodopa is contra-indicated in severe cardiovascular disease, arterial hypertension, hyperthyroidism, phaeochromocytoma, narrow-angle glaucoma,

prostatic adenoma with appearance of residual urine, tachycardia, arrhythmias, severe angina pectoris, psychoses, advanced dementia and thyrotoxicosis.

Special Warnings

Dopaminergic effects

Excessive daytime sleepiness (EDS) and sudden sleep onset (SOS) episodes

Selegiline and rasagiline may cause daytime drowsiness, somnolence, and, occasionally, especially if used with other dopaminergic medicinal products - falling asleep during activities of daily living. Patients must be informed of this and advised to exercise caution while driving or operating machines during treatment. Patients who have experienced somnolence and/or an episode of sudden sleep onset must refrain from driving or operating machines.

Impulse control disorders (ICDs)

ICDs can occur in patients treated with dopamine agonists and/or dopaminergic treatments. Similar reports of ICDs have also been received post-marketing with rasagiline and also rarely with selegiline. Patients should be regularly monitored for the development of impulse control disorders. Patients and carers should be made aware of the behavioural symptoms of impulse control disorders, including cases of compulsions, obsessive thoughts, pathological gambling, increased libido, hypersexuality, impulsive behaviour and compulsive spending or buying.

Common Side Effects

Nausea, constipation, diarrhoea, dry mouth, postural hypotension, abnormal movements (such as dyskinesias), vertigo, sleeping disorders, confusion, hallucinations.

Drug Interactions

- Tramadol may also potentially interact with Selegiline.
- Dopamine should be used with caution in patients receiving Selegiline.
- The concomitant use of rasagiline and dextromethorphan or sympathomimetics such as those present in nasal and oral decongestants or cold medicinal product containing ephedrine or pseudoephedrine is not recommended
- Concomitant use of oral contraceptives (tablets containing the combination of gestodene/ethinylestradiol or levonorgestrel/ethinylestradiol) and selegiline may cause an increase in the oral bioavailability of selegiline. Thus appropriate caution during the concomitant administration of selegiline and oral contraceptives should be applied.
- There have been reports of medicinal product interactions with the concomitant use of dextromethorphan and non-selective MAO inhibitors. Therefore, in view of the MAO inhibitory activity of rasagiline, the concomitant administration of rasagiline and dextromethorphan is not recommended.

Cost of selegiline 10mg od = £9.02 (28 days)
Cost of rasagiline 1mg od = £2.55 (28 days)

The manufacturer's summary of product characteristics (SPC) and the most current edition of the British National Formulary should be consulted for full information on contra-indications, warnings, side-effects and drug interactions.

References

1. Pharmacological Management of Parkinson's disease. Updated by the neurology working group of Dorset Medicines Advisory Group. March 2018
2. British National Formulary online.
3. Summaries of product characteristics for selegiline and rasagiline, accessed March 2018
4. Drug Tariff Online. March 2018

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