Drugs for Parkinson's Disease

Drug	Pharmacokinetics	Uses	Side effect	Drug interaction	Contraindications
Levodopa + (Dopa Decarboxylase Inhibitor)	Absorbed from the small intestine by active transport. t½=2h	All types of parkinsonism **except** those associated with antipsychotic drug therapy.	Wearing-off effect, On-off effect. Dyskinesias. Anorexia, N & V → CRTZ. **Orthostatic hypotension**, cardiac arrhythmias occur in some patients. Vivid dreams, **delusions**, **hallucinations**, confusion & **sleep disturbances**.	**Proteins** ingested with **meals**. Nonselective MAO inhibitors (phenelzine, tranylcypromine). Pharmacologic doses of pyridoxine.	**Psychotic patient**. Angle closure glaucoma. Patients with **active ulcer**. Patients with history of melanoma.
Dopamine receptor agonists **Bromocriptine**	**Agonist** to D2-receptors & a partial D1-**antagonist**.	**Long duration of action**. Can be used with levodopa (with ↓ Levodopa dosage). Absorbed from the GIT; peak plasma levels are reached within 1–2 hours after an **oral** dose. Excreted →**bile & feces**.	**Used** for **hyperprolactinemia**.	**Less effective** than levodopa. Less likely to cause dyskinesias than levodopa. Postural **hypotension**, nausea, somnolence. Confusion, **hallucinations**, **delusions**. In order to minimize adverse effects, the dose is built up slowly over 2 or 3 months.	**Contraindications:** In **psychotic illness**. **Recent MI**. Active peptic ulceration. Peripheral **vascular disease**.
Amantadine (antiviral)	Affects dopamine release & reuptake. **Antagonist** at muscarinic & NMDA receptors.	Peak plasma concentrations of are reached 1–4 hrs after an oral dose. t½=2-4h. Excreted unchanged →**urine**.	**Useful** in the **early** stages of parkinsonism or as an adjunct to levodopa therapy. Modestly effective in treating symptoms of parkinsonism.	Nausea, dizziness, insomnia, confusion, hallucinations, ankle edema, and **livedo reticularis**. Amantadine & the anticholinergics may exert additive effects on mental functioning. Should be used with **caution** in patients with a history of **seizures or heart failure**.	
Selegiline (irreversible inhibitor of MAO-B)	Blocks the **metabolism** of dopa. It enhances the actions of endogenous dopamine.	**Uses:** Effective in the **newly** diagnosed patient with parkinsonism.	Selegiline +levodopa–carbidopa in **later-stage** parkinsonism to:- ↓levodopa dosage requirements & to ↓or delay the onset of dyskinesias & motor fluctuations that usually accompany long-term treatment with levodopa.	May **slow** the **progression** of disease → ↓ formation of **toxic free radicals** produced during the metabolism of dopamine. Metabolized to desmethylselegiline, which is antiapoptotic.	**Side effect:** Higher doses may inhibit MAO-A. May **cause insomnia** when taken later during the day. Effects of levodopa may be ↑by selegiline. Selegiline **shouldn't be** coadministered with **TCA**, **meperidine or SSRIs**. (may cause **hyperpyrexia**, agitation, delirium, coma).
Anticholinergic Drugs **Benztropine** **Trihexyphenidyl**	**Block muscarinic** receptors in the **striatum**.		**Uses:** They exert only **modest** antiparkinsonian actions, used during the **early** stages of the disease or as an adjunct to levodopa therapy.	**Side effect:** cycloplegia, dry mouth, urinary retention, and constipation. Confusion, **delirium**, & **hallucinations** may occur at higher doses. Trihexyphenidyl may cause withdrawal symptoms in patients receiving large doses.	