| Drug | Uses & MOA | Pharmacokinetics | ADRs | Drug Interactions | Contraindications |
|---|---|---|---|---|---|
| **1-Levodopa**<br>**Carbidopa is used to:**<br>**-To inhibit peripheral conversion of L-dopa to dopamine**<br>**-To decrease metabolism of L-dopa in GIT and peripheral tissues, Thus,increasing tl/2.**<br>**-To increase LD availability**<br>**-To reduce dose of levodopa and side effects.**<br>**-Do not cross BBB.** | -Precursor of **dopamine**(it's a prodrug , converted to its active form (dopamine) in the body )<br>-First line treatment<br>-used combined with **carbidopa( peripheral dopa decarboxylase inhibitor)** | **-L-dopa** is absorbed from the small intestine by active transport<br>**-Ingestion of meal** especially high protein meal interferes with absorption and transport into CNS *(taken on an empty stomach).*<br>**-Short duration** of action t½= 1-2 h *(fluctuation of plasma concentration).* | **-Wearing-off effect.**<br>**-On-Off) phenomenon**<br>**- Dyskinesia**<br>**-Peripheral effects:**<br>1-anorexia, nausea, and vomiting<br>2- Mydriasis, orthostatic hypotension,and cardiac arrhythmias.<br>**-CNS effects**<br>(Psychological disorders) mainly psychosis, delusions, hallucinations, confusion, sleep disturbances and depression. | **-Proteins ingested with meals (Decrease absorption)**<br>**-Pyridoxine (Vitamin B6)(Increase its breakdown)**<br>**-Nonselective MAO inhibitors (phenelzine). (can produce a hypertensive crisis)** | • **Psychotic patient.**<br>• **Closed angle glaucoma** (due to mydriatic effect)<br>• **Patients with history of melanoma**.(levodopa is also a Precursor of melanin) |

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| **2-Dopamine receptor agonists**<br>**Ergot derivatives Bromocriptine**<br>**Non ergot derivatives Pramipexole:**<br>**-Non Ergot dopamine agonist**<br>**-Used alone (in Mild cases) or in combination with L-Dopa.**<br>**-Has the advantage of** being free radicals scavenger.<br>**-Side effects: similar to L-Dopa, but less dyskinesias.** | **-Have longer duration of action than L-dopa** (less likely to cause dyskinesias than levodopa)<br>**-Dopamine agonists are used in advanced Parkinson's disease with fluctuation and dyskinesia. However, less effective if the patins could not respond to L-Dopa.**<br>Bromocriptine is:<br>**-Used in advanced Parkinson's disease with fluctuation and dyskinesia.**<br>**-Rx of hyperprolactinemia (galactorrhea)**<br>**-Rx of infertility in women.**<br>**-is an agonist at D2-receptors.** | • Is given orally, short tl/2 | • Nausea, vomiting & postural hypotension ,<br>• Confusion, hallucinations, delusions.<br>• Dyskinesia (less prominent) | **-Patients with a history of psychotic illness.**<br>**-Avoided in patients with peripheral vascular disease**<br>-Recent myocardial infarction<br>-Active peptic ulceration. |
| **3-Drugs that release Dopamine (Amantadine)** | -**Originally introduced** as an antiviral.<br>-**modestly** effective in treating symptoms of Parkinsonism but last only for short period (few weeks) and only used for L-Dopa resistance<br>**-Amantadine increases dopamine release and inhibit uptake.**<br>**-Also acts as an antagonist at muscarinic and NMDA *(N-methyl-D-aspartate)* receptors,which is type of glutamate Receptor** | -**Given** orally with short half-life.<br>**-Most of the drug being excreted unchanged in the urine.** | -**Nausea**, anxiety, insomnia, confusion, hallucinations **(dopamine like side effects).**<br>-**Dry mouth, urinary** retention **(anticholinergic effects).**<br>-**Restlessness and** hallucinations **(NMDA antagonist).** | |

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| **4- MAO-B inhibitors (Selegiline also called deprenyl) reduces the formation of *toxic free radicals* produced during dopamine metabolism (*antioxidant*).** | -Selegiline is an irreversible inhibitor **of MAO-B (selective inhibitor).**<br>-As monotherapy, may be effective in the newly diagnosed patient with parkinsonism.<br>-Combined with levodopa / carbidopa in later-stage parkinsonism to: **Reduce the required dose of levodopa, and delay the onset of dyskinesias and motor fluctuations that usually accompany long-term treatment with levodopa.** | -Selegiline is metabolized **to desmethylselegiline**, Which is an anti-apoptotic. | -At high doses, selegiline may inhibit MAO-A *(hypertensive crises).*<br>-May cause insomnia when taken later during the day | |
| **5- COMT Inhibitors (Catechol-O-methyl transferase) Inhibitors (Entacapone and Tolcapone)** | -It is used: **as adjuvant to L-Dopa to:**<br>1) **Decrease fluctuations**<br>2) **Improve response**<br>3) **Prolong the ON-Time**<br>-Acts **peripherally and centrally to inhibit COMT enzyme required for dopamine degradation** | | • L-Dopa side effects.<br>• Orange discoloration of urine. | |
| **6- Anticholinergic Drugs: e.g. Benztropine, Trihexyphenidyl** | • Used during the early stages of the disease or as an adjunct to levodopa therapy.<br>• Provide benefit in drug-induced parkinsonism.(caused by **antipsychotics**)<br>• **Act by blocking muscarinic receptors in the striatum.**<br>• **Have modest antiparkinsonian actions. (effective in treating tremors)** | **Cycloplegia (**paralysis of the ciliary muscle; paralysis of accommodation)**, dry mouth, urinary retention, and constipation.**<br>**Confusion, delirium, and hallucinations may occur at higher doses.** | | • **Prostatic hypertrophy** (this drug cause urinary retention)<br>• **Glaucoma**<br>• **Intestinal obstruction** |