

apomorphine is associated with a relatively high frequency of oropharyngeal side effects, which are generally mild and resolve either spontaneously or with treatment withdrawal.

MAO-B INHIBITORS

Inhibitors of monoamine oxidase type B (MAO-B) block central dopamine metabolism and increase synaptic concentrations of the neurotransmitter. Selegiline and rasagiline are relatively selective suicide inhibitors of the MAO-B isoform of the enzyme. Clinically, these agents provide antiparkinsonian benefits when used as monotherapy in early disease stages and reduced “off” time when used as an adjunct to levodopa in patients with motor fluctuations. MAO-B inhibitors are generally safe and well tolerated. They may increase dyskinesia in levodopa-treated patients, but this can usually be controlled by down-titrating the dose of levodopa.

Inhibition of the MAO-A isoform prevents metabolism of tyramine in the gut, leading to a potentially fatal hypertensive reaction known as a “cheese effect” because it can be precipitated by foods rich in tyramine such as some cheeses, aged meats, and red wine.

Selegiline and rasagiline do not functionally inhibit MAO-A and are not associated with a cheese effect with doses used in clinical practice. There are theoretical risks of a serotonin reaction in patients receiving concomitant selective serotonin reuptake inhibitor (SSRI) antidepressants, but these are rarely encountered.

Safinamide (Xadago) is a reversible MAO-B inhibitor that has been approved as an adjunct to levodopa for treating advanced PD patients with motor fluctuations. The drug also acts to block activated sodium channels and inhibit glutamate release, and therefore has the potential to provide antidyskinetic as well as anti-parkinsonian effects.

Interest in MAO-B inhibitors has also focused on their potential to have disease-modifying effects. MPTP toxicity can be prevented experimentally by coadministration of a MAO-B inhibitor that blocks its oxidative conversion to the toxic pyridinium ion MPP⁺ that is taken up by and selectively damages dopamine neurons. MAO-B inhibitors also have the potential to block the oxidative metabolism of dopamine and prevent oxidative stress. In addition, both