

Side Effects of Sinemet (carbidopa-levodopa)

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Does Sinemet (carbidopa-levodopa) cause side effects?

Sinemet (carbidopa-levodopa) is a combination of two drugs, levodopa and carbidopa. Carbidopa-levodopa is used in the treatment of Parkinson's disease.

Parkinson's disease is believed to be caused by low levels of dopamine in certain parts of the brain. When levodopa is taken orally, it crosses into the brain through the "blood- brain barrier." Once it crosses, it is converted to dopamine. The resulting increase in brain dopamine concentrations is believed to improve nerve conduction and assist the movement disorders in Parkinson disease.

Carbidopa does not cross the blood-brain barrier. Carbidopa is added to the levodopa to prevent the breakdown of levodopa before it crosses into the brain. The addition of carbidopa allows lower doses of levodopa to be used. This reduces the risk of side effects from levodopa such as nausea and vomiting.

Common side effects of Sinemet include

- gastrointestinal side effects (nausea, vomiting, loss of appetite, weight loss),
- dizziness on standing due to a drop in blood pressure,
- memory loss,
- anxiety,
- nervousness,
- agitation,
- restlessness,
- confusion,
- inability to sleep,
- nightmares,
- daytime tiredness,
- mental depression, and

- euphoria.

Serious side effects of Sinemet include

- occasional involuntary movements (muscle twitching, dizziness, muscle jerks during sleep, hand tremor, chewing, gnawing, twisting, tongue or mouth movements, head bobbing, and movements of the feet, hands, or shoulder which may respond to a reduction in the dose),
- and infrequently, a drop in white blood cell counts.

Drug interactions of Sinemet include amantadine, benztropine, procyclidine, and trihexyphenidyl because they can enhance the anti-Parkinson's effects of levodopa.

Droperidol, haloperidol, loxapine, metoclopramide, phenothiazines, and thioxanthenes can inhibit dopamine in the brain and shouldn't be used in combination with levodopa.

Methyldopa and reserpine also can interfere with the beneficial actions of Sinemet and can increase the risk of side effects.

The occurrence of postural hypotension (reduced blood pressure when standing from a sitting or lying down position) may increase when Sinemet is combined with drugs that reduce blood pressure.

Phenytoin can increase the break-down of Sinemet, reducing its effectiveness. Use of Sinemet with monoamine oxidase inhibitors (MAOI's) antidepressants can result in severe and dangerous elevations in blood pressure.

MAOI's should be stopped 2-4 weeks before starting carbidopa-levodopa therapy.

The side effects associated with levodopa, including dizziness upon rising, confusion, movement disorders, nausea, and hallucinations, all can be increased by selegiline.

There are no human studies that have examined the effects of Sinemet on a fetus. In prescribing Sinemet for a pregnant woman, the treating physician must weigh the potential risks to the fetus against the potential benefits to the mother.

Levodopa is distributed into breast milk. It also may inhibit production of milk. It is generally recommended that Sinemet should not be given to women who are breastfeeding.

What are the important side effects of Sinemet (carbidopa-levodopa)?

Most patients receiving carbidopa-levodopa experience side effects, but these usually are reversible.

Gastrointestinal side effects are common in patients receiving carbidopa-levodopa and these include:

- nausea,
- vomiting,
- loss of appetite, and
- weight loss.

Patients may experience dizziness upon standing up, associated with a drop in blood pressure.

Fortunately, the body develops tolerance to this side effect within a few months.

Other important side effects of carbidopa-levodopa therapy include:

- memory loss,
- anxiety,
- nervousness,
- agitation,
- restlessness,
- confusion,
- inability to sleep,
- nightmares,
- daytime tiredness,
- mental depression or
- euphoria.

Occasional involuntary movements are the most common of the serious side effects of carbidopa-levodopa therapy, and these are:

- muscle twitching,
- dizziness,
- muscle jerks during sleep,
- hand tremor,
- chewing,
- gnawing,

- twisting,
- tongue or
- mouth movements,
- head bobbing, or
- movements of the feet, hands, or shoulder which may respond to a reduction in the dose.

Infrequently, patients may develop a drop in white blood cell count during carbidopa-levodopa therapy. This is a significant reason to temporarily, if not permanently, stop treatment.

Sinemet (carbidopa-levodopa) side effects list for healthcare professionals

The most common adverse reactions reported with Sinemet have included dyskinesias, such as choreiform, dystonic, and other involuntary movements, and nausea.

The following other adverse reactions have been reported with Sinemet:

Body As A Whole

Chest pain, asthenia.

Cardiovascular

Cardiac irregularities, hypotension, orthostatic effects including orthostatic hypotension, hypertension, syncope, phlebitis, palpitation.

Gastrointestinal

Dark saliva, gastrointestinal bleeding, development of duodenal ulcer, anorexia, vomiting, diarrhea, constipation, dyspepsia, dry mouth, taste alterations.

Hematologic

Agranulocytosis, hemolytic and non-hemolytic anemia, thrombocytopenia, leukopenia.

Hypersensitivity

Angioedema, urticaria, pruritus, Henoch-Schönlein purpura, bullous lesions (including pemphigus-like reactions).

Musculoskeletal

Back pain, shoulder pain, muscle cramps.

Nervous System/Psychiatric

Psychotic episodes including delusions, hallucinations, and paranoid ideation, bradykinetic episodes ("on-off" phenomenon), confusion, agitation, dizziness, somnolence, dream abnormalities including nightmares, insomnia, paresthesia, headache, depression with or without development of suicidal tendencies, dementia, pathological gambling, increased libido including hypersexuality, impulse control symptoms.

Convulsions also have occurred; however, a causal relationship with Sinemet has not been established.

Respiratory

Dyspnea, upper respiratory infection.

Skin

Rash, increased sweating, alopecia, dark sweat.

Urogenital

Urinary tract infection, urinary frequency, dark urine.

Laboratory Tests

Decreased hemoglobin and hematocrit; abnormalities in alkaline phosphatase, SGOT (AST), SGPT (ALT), LDH, bilirubin, BUN, Coombs test; elevated serum glucose; white blood cells, bacteria, and blood in the urine.

What drugs interact with Sinemet (carbidopa-levodopa)?

Caution should be exercised when the following drugs are administered concomitantly with Sinemet.

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- Symptomatic postural hypotension occurred when Sinemet was added to the treatment of a patient receiving antihypertensive drugs. Therefore, when therapy with Sinemet is started, dosage adjustment of the antihypertensive drug may be required.
- For patients receiving MAO inhibitors (Type A or B). Concomitant therapy with selegiline and carbidopa levodopa may be associated with severe orthostatic hypotension not attributable to carbidopa levodopa alone.
- There have been rare reports of adverse reactions, including hypertension and dyskinesia, resulting from the concomitant use of tricyclic antidepressants and Sinemet.
- Dopamine D₂ receptor antagonists (e.g., phenothiazines, butyrophenones, risperidone) and isoniazid may reduce the therapeutic effects of levodopa. In addition, the beneficial effects of levodopa in Parkinson's disease have been reported to be reversed by phenytoin and papaverine. Patients taking these drugs with Sinemet should be carefully observed for loss of therapeutic response.
- Use of Sinemet with dopamine-depleting agents (e.g., reserpine and tetrabenazine) or other drugs known to deplete monoamine stores is not recommended.
- Sinemet and iron salts or multivitamins containing iron salts should be coadministered with caution. Iron salts can form chelates with levodopa and carbidopa and consequently reduce the bioavailability of carbidopa and levodopa.
- Although metoclopramide may increase the bioavailability of levodopa by increasing gastric emptying, metoclopramide may also adversely affect disease control by its dopamine receptor antagonistic properties.

Summary

Sinemet (carbidopa-levodopa) is a combination of two drugs, levodopa and carbidopa. Carbidopa-levodopa is used in the treatment of Parkinson's disease. Common side effects of Sinemet include gastrointestinal side effects (nausea, vomiting, loss of appetite, weight loss), dizziness on standing due to a drop in blood pressure, memory loss, anxiety, nervousness, agitation, restlessness, confusion, inability to sleep, nightmares, daytime tiredness, mental depression, and euphoria. There are no human studies that have examined the effects of Sinemet on a fetus. Levodopa is distributed into breast milk. It also may inhibit production of milk.