Depression... disturbed sleep...

Sinequan
brand of doxepin

lifts depression...
promotes restful sleep

■ SEDATIVE ANTIDEPRESSANT
■ ONCE NIGHTLY DOSAGE

Indications: depression with or without anxiety. Contraindications: glaucoma, urinary retention, hypersensitivity to the drug. Side effects: dry mouth and drowsiness are most commonly reported. Precautions: Sinequan may potentiate other compounds e.g. monoamine oxidase inhibitors; not recommended in pregnancy or children under 12 years age. Dosage: range 30 mg to 300 mg daily in divided doses, up to 100 mg may be given as a single dose at night. Packs and Basic N.H.S. Cost: 10 mg capsules (PL 57/5032), pack of 100, £2.96; 25 mg capsules (PL 57/5033), pack of 100, £4.24; 50 mg capsules (PL 57/5034), pack of 100, £7.01; 75 mg capsules (PL 57/0133), pack of 60, £6.64. Full information on request to the Company.
SINEM
Carbidopa and levodopa, MSD
A NEW START
'Sinemet-Plus' contains 100 mg of levodopa and 25 mg of carbidopa. 'Sinemet-Plus' provides a low dose of levodopa together with sufficient carbidopa to inhibit effectively peripheral dopa-decarboxylase in many patients. It retains the advantage of co-prescribing carbidopa and levodopa by reducing or eliminating certain levodopa side effects, e.g. GI upsets, etc.

Therefore 'Sinemet-Plus' is an effective low level introduction to levodopa therapy for:

☐ patients on anticholinergics requiring 'add on' levodopa therapy
☐ first-time patients requiring low levels of levodopa
☐ patients with a low levodopa tolerance to allow relatively higher levels of carbidopa

The addition of 'Sinemet-Plus' to the 'Sinemet' range means that Parkinsonian patients may benefit from levodopa therapy earlier and be eased more gradually into the full-scale therapy offered by Sinemet®110 and Sinemet®275.

**Sinemet-Plus™**

_A new start for many Parkinsonian patients_

For prescribing information, see overleaf.
PREScribing INFORMATION

INDICATIONS
For treatment of Parkinson's disease and syndrome.

DOSAGE AND ADMINISTRATION
The optimum daily dosage of 'Sinemet' must be determined by careful titration for each patient.

'Sinemet' Tablets are available as:
- Sinemet®110 containing 10 mg carbidopa and 100 mg levodopa.
- Sinemet®Plus containing 25 mg carbidopa and 100 mg levodopa.
- Sinemet®275 containing 25 mg carbidopa and 250 mg levodopa.

General considerations: Studies show that the peripheral enzyme dopa decarboxylase is fully inhibited (saturated) by carbidopa at doses between 70 and 100 mg a day. The formulations of 'Sinemet' are designed to provide a range of doses with sufficient carbidopa to inhibit peripheral dopa decarboxylase and thus prevent dyskinesia.

Patients who require less than 700 mg levodopa given as Sinemet®275 will theoretically not receive sufficient carbidopa to saturate peripheral dopa decarboxylase. 'Sinemet Plus' may be helpful, especially for patients with nausea and vomiting.

Most patients can be maintained on divided doses of three to six tablets of Sinemet®275 a day. Tablets are scored for easy division. The frequency of dosage should be increased. During the titration period, 'Sinemet Plus' may be more convenient.

Patients on Sinemet® Plus who need a higher dosage should be switched to Sinemet®275. Dosage with either form should not exceed eight tablets a day. If patients do show a need for higher doses, levodopa should be added.

Because both beneficial and adverse effects are seen more rapidly with 'Sinemet' than with levodopa, patients should be carefully monitored during the dosage adjustment period. Levodopa's toxicity, particularly parkinsonism, is a useful early sign of excess dosage in some patients.

Sinemet®110 can be used as an alternative to 'Sinemet Plus'.

Patients not receiving levodopa: Dosage may be initiated with one tablet of Sinemet® Plus three times a day, and adjusted as necessary by small increments to a maximum daily dosage of eight tablets. If patients need more levodopa, one additional tablet of Sinemet®275 should be substituted three or four times a day. If further titration is necessary, the dosage of Sinemet®275 may be increased gradually to a maximum of eight tablets a day.

Patients receiving levodopa: Discontinue levodopa at least twelve hours (24 hours for slow-release preparations) before starting therapy with Sinemet. The easiest way to do this is to give Sinemet as the first morning dose after a night without levodopa. The dose of Sinemet should be approximately 20% of the previous daily dosage of levodopa.

The suggested starting dose for most patients is one tablet of Sinemet®275 three or four times a day.

Patients requiring less than 1,500 mg levodopa a day should be started on one tablet of Sinemet® Plus three or four times a day.

The dosage may then be adjusted gradually but should not exceed eight tablets a day.

Patients receiving levodopa with another decarboxylase inhibitor: When transferring a patient to Sinemet from levodopa combined with another decarboxylase inhibitor, its dosage should be discontinued at least twelve hours before Sinemet is started. Begin with a dose of Sinemet that will provide the same amount of levodopa as contained in the other levodopa/decarboxylase inhibitor combination.

Use with other antiparkinsonian agents: Current evidence indicates that many antiparkinsonian agents such as anticholinergics and amantadine may be continued when Sinemet is introduced, although dosage may have to be adjusted.

CONTRA-INDICATIONS
Concurrent use with monoamine oxidase inhibitors (these must be discontinued at least two weeks before starting Sinemet), narrow-angle glaucoma, known hypersensitivity to this medication. Because levodopa may activate a malignant melanoma, it should not be used in patients with suspicious undiagnosed skin lesions or a history of melanoma.

See also 'Use in pregnancy and the nursing mother,' under Precautions.

PRECAUTIONS
Sinemet is not recommended for the treatment of drug-induced extrapyramidal reactions. Sinemet should be administered cautiously to patients with severe cardiovascular or pulmonary disease, bronchial asthma, renal, hepatic or endocrine disease. All patients should be monitored carefully for the development of mental changes, depression with suicidal tendencies, and other serious antipsychotic behaviour. Patients with current psychoses should be treated with caution. Patients with a history of severe involuntary movements or psychotic episodes when treated with levodopa alone should be observed carefully when Sinemet is substituted. These reactions are thought to be due to increased brain dopamine following administration of levodopa, and may be a complication of the patient's history. Concomitant administration of psycho-active drugs such as phenothiazines or butyrophenones is necessary, such drugs should be administered with caution, and patients carefully observed for loss of antiparkinsonian effect. Patients with a history of convulsions should be treated with caution. Both phenytoin and papaverine have been reported to reverse the beneficial effects of levodopa.

Patients with chronic wide-angle glaucoma may be treated cautiously with Sinemet, provided the intra-ocular pressure is well controlled and the patient monitored carefully for changes in intra-ocular pressure during therapy.

Care should be exercised when Sinemet is administered to patients with a history of myocardial infarction who have atrial, nodal, or ventricular arrhythmias. Cardiac function should be monitored with particular care in such patients during the period of initial dosage adjustment.

As symptoms of postural hypotension have occasionally been reported, Sinemet should be given with caution to patients receiving antihypertensive agents. Adjustment of the dosage of the antihypertensive agent may be required when Sinemet is started. (For patients on pargyline, see the contra-indication on monoamine oxidase inhibitors.

As with levodopa there is a possibility of upper gastro-intestinal haemorrhage in patients with a history of peptic ulcer.

If general anaesthesia is required, therapy with Sinemet may be continued as long as the patient is permitted to take fluids and medication by mouth. If therapy is interrupted temporarily, the usual daily dosage may be administered as soon as the patient is able to take oral medication.

Transient abnormalities in laboratory test results may occur, but have not been associated with clinical evidence of disease. These include elevated levels of blood urea, SGOT SGPT LDH, bilirubin, alkaline phosphatase, or protein-bound iodine.

Positive Coombs have been reported. Both with Sinemet and levodopa alone, but haemolytic anaemia is extremely rare.

Use in children: The safety of Sinemet in patients under eighteen years of age has not been established.

Use in pregnancy and the nursing mother: Although the effects of Sinemet on human pregnancy and lactation are unknown, both levodopa and combinations of carbidopa and levodopa have caused visceral and skeletal malformations in rabbits. Therefore, use of Sinemet in women of childbearing potential requires that the anticipated benefits of the drug be weighed against possible hazards should pregnancy occur. Sinemet should not be given to nursing mothers.

Drug interactions: Clinical experience with concurrent administration of Sinemet and other standard antiparkinsonian drugs, e.g. benztropine mesylate, benzhexol hydrochloride, is limited. To date, however, there has been no indication of interactions that would preclude concurrent use. No adverse reactions have been reported that do not occur with the various agents alone.

SIDE EFFECTS
Side effects that occur frequently with Sinemet are those due to the central neuropharmacological activity of dopamine. These reactions can usually be diminished by dosage reduction. The most common side effects are choreiform, dystonic and other involuntary movements. Muscle twitching and blepharospasm may be taken as early signs to consider dosage reduction. Less common are mental changes, including paranoid
ideation and psychotic episodes; depression, with or without development of suicidal tendencies; and dementia. Convulsions have occurred, but a causal relationship has not been established. Less frequent side effects are cardiac irregularities and/or palpitations, orthostatic hypotensive episodes, Bradykinetic episodes (the "on-off" phenomenon), anorexia, nausea, vomiting, and dizziness.

Gastro-intestinal bleeding: development of duodenal ulcer, hypertension, phlebitis, leucopenia, and agranulocytosis have occurred rarely. Positive Coombs tests have been reported both with 'Sinemet' and with levodopa alone, but haemolytic anaemia is extremely rare. Other side effects that have been reported include:

Psychiatric: euphoria, lethargy, sedation, stimulation, fatigue and malaise, confusion, insomnia, nightmares, hallucinations and delusions, agitation and anxiety.

Neurological: ataxia, faintness, headache, increased hand tremor, trismus, oculogyric crisis, weakness, numbness, bruxism.

Gastro-intestinal: constipation, diarrhoea, epigastric and abdominal distress and pain, flatulence, hiccup, salorrhoea, difficulty in swallowing, bitter taste, dry mouth, burning sensation of the tongue.

Dermatological: sweating, oedema, hair loss, rash, unpleasant odour, dark sweat.

Respiratory: hoarseness, bizarre breathing pattern.

Urogenital: urinary retention, incontinence, haematuria, dark urine, priapism.

Special senses: blurred vision, diplopia, dilated pupils, activation of latent Herpes zoster.

Other: hot flushes, weight gain or loss, flushing, abnormalities in laboratory tests (see Precautions).

PRESENTATION

There are three strengths of Sinemet: 25/100, 100/100, and 250/100. The standard strength is known as 'Sinemet 257' and is supplied as dappled yellow, half-scored, oval tablets, marked MSD 654, containing 25 mg carbipoda (as carbipoda monohydrate) and 100 mg levodopa BP in bottles of 100.

'Sinemet-Plus' is available as yellow, half-scored, oval tablets, marked 'SINEMET-PLUS', containing 25 mg carbipoda (as carbipoda monohydrate) and 100 mg levodopa BP in bottles of 100.

'Sinemet 100', supplied as dappled-blue, half-scored, oval tablets, marked MSD 647, containing 100 mg carbipoda (as carbipoda monohydrate) and 100 mg levodopa BP in bottles of 100.

Basic NHS costs:

'Sinemet 257 Tablets (100) £12.20.
'Sinemet-Plus Tablets (100) £10.70.
'Sinemet 100 Tablets (100) £5.50.

Product licence numbers:

'Sinemet 257 Tablets, 202591/0036.
'Sinemet-Plus Tablets, 202591/0150.
'Sinemet 100 Tablets, 202591/0004.

Product authorisation numbers:

'Sinemet 257 Tablets, 35/47.2.
'Sinemet-Plus Tablets, 35/47.3.
'Sinemet 100 Tablets, 35/47.4.

Agents in the Republic of Ireland:

Cahill May Roberts, P.O. Box 1090, Chapelizod, Dublin 20.

Additional information is available to the medical profession on request.

Issued September 1981.

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81S:SEM:61:GB:7952J

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Presentation
Madopar contains a combination of levodopa and the decarboxylase-inhibitor benzamide in the ratio of 4:1.

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Madopar 250 capsules containing 200mg levodopa and 125mg benzamide in hydrochloride equivalent, in a strength of 250mg of the base.

Indications
Parkinson's disease.

Dosage
Dosage should be by and the data sheet should be consulted for full details. The effective daily dosage range lies between four and eight capsules of Madopar 62.5 to four capsules of Madopar 125 daily. In the elderly, patients require treatment with the capsule of Madopar 62.5 once or twice daily increasing by one capsule every third or fourth day for a week may suffice. Patients who experience intestinal adverse reactions may also benefit from administration of an antacid three times a day before meals using Madopar 62.5.

Contra-indications
Not for use in patients with severe psychiatric or neuropsychiatric disorders. It should not be given to patients with endocarditis, prostatic hypertrophy, or glaucoma. In the elderly, patients under 75 years of age to prevent stroke due to patients with heart disease, who are on treatment with anti-thrombotics or hormone replacement therapy. Patients who have a history of, or who may be suffering from, a malignant tumour may also be excluded from this therapy.

Precautions
Patients with hypertension or a history of cardiovascular disease, or any other chronic or acute disorder, should be monitored closely.

Side-effects
Nausea and vomiting, cardiovascular disturbances, psychiatric disturbances, and somnolence may occur.

Packings
Madopar 62.5 capsules, Madopar 125 capsules and Madopar 250 capsules in packages of 100.

Licence Numbers
0001 (Madopar 62.5 capsules), 0002 (Madopar 125 capsules), 0003 (Madopar 250 capsules).

Basic NHS Cost
Madopar capsules 62.5 £3.49 per 100
Madopar capsules 125 £3.99 per 100
Madopar capsules 250 £11.25 per 100

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Presentation

Indications
Epilim is used in the treatment of epilepsy.

Dosage and Administration
To be taken with or after food. The dosage should be increased gradually over a period of 3 to 4 weeks until a satisfactory response is obtained. The maximum dosage is 1200mg/day in adults and 150mg/kg/day in children.

Contra-Indications, Warnings, etc.
Children under 3 years of age, pregnant women, and patients with liver disease should be given lower initial doses. The drug should be discontinued if signs of liver damage occur. Hyperammonemia, which may occur in children treated with valproate, can be severe and fatal. After discontinuation of the drug, the patient should be monitored for several days to be sure that the ammonia level has returned to normal. The drug should not be used in patients with known or suspected liver disease.

Further Information
When valproate is administered, a target serum concentration of 50-100mg/ml should be achieved. If the serum concentration is too low, the dose should be increased. The maximum dose should not exceed 2000mg/day. The drug should be administered in divided doses, usually two or three times daily.

Additional information is available from LABAZ: Sanofi U.K. Ltd., Regent House, Heaton Lane, Stockport SK4 1AG.
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