4+1 the right balance in Parkinson's disease

Presentation
Madopar contains a combination of levodopa and the decarboxylase inhibitor benserazide in the ratio of 4:1. Madopar 62.5 capsules containing 50mg levodopa and 14.25mg benserazide hydrochloride (equivalent to 12.5mg of the base) Madopar 125 capsules containing 100mg levodopa and 28.5mg benserazide hydrochloride (equivalent to 25mg of the base) Madopar 250 capsules containing 200mg levodopa and 57mg benserazide hydrochloride (equivalent to 50mg of the base)

Indications
Parkinsonism — idiopathic, post-encephalitic

Dosage
Dosage is variable and the data sheet should be consulted for full details. The effective daily dose usually lies between four and eight capsules of Madopar 125 (two to four capsules of Madopar 250) daily in divided doses, most patients requiring no more than six capsules of Madopar 125 daily. In some elderly patients initial treatment with one capsule of Madopar 62.5 once or twice daily, increasing by one capsule every third or fourth day may suffice. Patients who experience fluctuations in response may also benefit from administration of smaller more frequent doses using Madopar 62.5

Contra-indications
Narrow-angle glaucoma, severe psychoneuroses or psychoses. It should not be given in conjunction with monoamine oxidase inhibitors or within two weeks of their withdrawal, to patients under 25 years of age, to pregnant women, or to patients who have a history of, or who may be suffering from, a malignant melanoma

Precautions
Drugs which interfere with central amine mechanisms should be avoided. Endocrine, renal, pulmonary or cardiovascular disease, hepatic disorder, peptic ulcer, osteoporosis, sympathomimetic drugs, antihypertensive drugs. Patients who improve on Madopar therapy should be advised to resume normal activities gradually as rapid mobilisation may increase the risk of injury.

Side-effects
Nausea and vomiting, cardiovascular disturbances, psychiatric disturbances, involuntary movements.

Packings
Madopar 62.5 capsules, Madopar 125 capsules and Madopar 250 capsules in packings of 100

Licence Numbers
0031/0125 (Madopar 62.5 capsules), 0031/0073 (Madopar 125 capsules), 0031/0074 (Madopar 250 capsules)

Basic NHS Cost
Madopar capsules 62.5
£4.01 per 100
Madopar capsules 125
£7.23 per 100
Madopar capsules 250
£12.94 per 100

ROCHE

Roche Products Limited
PO Box 8
Welwyn Garden City
Hertfordshire AL7 3AY

Madopar is a trade mark
J522191/382

Madopar

the original 4+1 combination in three dosage forms, 62·5, 125 *and* 250

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 exert optimal therapy.

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 should the frequency of daily dosage need to 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. Involuntary movements, particularly blepharospasm, 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 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 any 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 dosage 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 other 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 antisocial 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 bram dopamine following administration of levodopa, and use of 'Sinemet' may cause a recurrence. If 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 tests 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.

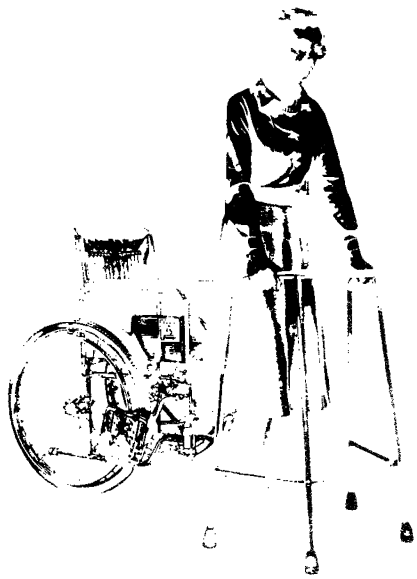
Drug interactions: Clinical experience with concurrent adminstration of 'Sinemet' and other standard antiparkinsonian drugs, e.g. benztropine mesylate, benzhexol hydrochloride, is limited. To date, however, there has been no indication of interactions that would preclude concurrent use. No adverse reactions 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 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

SPASTICITY FOLLOWING STROKE



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baclofen INN

Brings back a feeling of achievement

Prescribing notes: Indications Relief of spasticity of voluntary muscle arising from cerebrovascular accidents, cerebral palsy, meningitis, traumatic head injury, multiple sclerosis and other spinal lesions. **Dosage** Adults: Initially 15mg daily in three divided doses, increasing slowly at intervals of at least three days, until the optimum effect is achieved. Satisfactory control is usually obtained with doses up to 60mg daily, but careful adjustment is often necessary to meet the requirements of individual patients. A maximum daily dose of more than 100mg is not advised unless the patient is in hospital and under careful supervision. Children: Initially 5-10mg daily in divided doses, and a maximum dose of 60mg daily. There have been no reports of tolerance. **Side-effects** Nausea; vomiting; daytime sedation and confusion; muscle hypotonia and fatigue; visual hallucinations. **Precautions** Concurrent administration of antihypertensives; psychotic states; epilepsy; first three months of pregnancy. **Packs** Lioresal 10mg tablets in Securitainer packs of 100. **Basic NHS price** £11.66. PL0008/0053. ®denotes registered trademark.
Full prescribing information is available on request from CIBA Laboratories, Horsham, West Sussex.

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Epilim

sodium valproate

200 enteric-coated, 500 enteric-coated tablets; syrup.

Epilim is a powerful anticonvulsant capable of providing control for the majority of adults with tonic-clonic seizures or other epilepsies, including those not well controlled on previous treatments. Because it controls without sedation, Epilim allows many patients to lead full, normal lives.

Presentation
1. Epilim 200 enteric-coated. A lilac-coloured enteric-coated tablet containing 200mg sodium valproate.
2. Epilim tablets. A white scored tablet containing 200mg sodium valproate.
3. Epilim 500 enteric-coated. A lilac-coloured enteric-coated tablet containing 500mg sodium valproate.
4. Epilim Syrup. A red cherry-flavoured syrup containing 200mg sodium valproate per 5ml.

Indications
Epilepsy. In women of childbearing age, Epilim should be used only in severe cases or in those resistant to other treatment.

Dosage and Administration
To be taken with or after food; enteric-coated and plain tablets should be swallowed whole. Optimum dosage should be established using the 200mg enteric-coated tablet. Epilim 500 enteric-coated is recommended for patients requiring high dosages.
Adults: Dosage should start at 600mg/day, in divided doses, increasing by 200mg/day at three-day intervals until control is achieved. (Maximum Dose 2600mg/day).
In patients already receiving other therapy the same pattern should be followed.
Dosage of barbiturates should be reduced as that of Epilim is increased; the respective dosages should be adjusted, during the stabilisation period, to give optimum control at the lowest possible combined-dose level, and it may be found possible to maintain control with Epilim alone.
Once known enzyme-inducers have been withdrawn, it may be possible to maintain seizure control on a reduced dose of Epilim. Although a method of measuring plasma levels is available, optimum dosage must ultimately be determined by seizure-control.
Children over 20kg: Initially 400mg/day in divided doses with spaced increases until control is achieved (usually in the range of 20-30mg/kg/day).
Children under 20kg: 20mg/kg of body weight per day; in severe cases, this may be increased up to 50mg/kg/day but should be undertaken only in patients in whom plasma valproate levels, clinical chemistry and haematological parameters can be monitored.

Contra-Indications, Warnings, etc.
Liver dysfunction, including hepatic failure resulting in fatalities has occurred in patients whose treatment included valproic acid or sodium valproate. The incidents occurred during the first six months of therapy, the period of maximum risk being 2-12 weeks. No deaths have occurred in patients receiving the drug continuously for more than 6 months.
Biochemical tests may not always become abnormal early in the evolution of hepatic failure; non specific findings such as loss of seizure control, malaise, anorexia and vomiting, developing after a period of satisfactory Epilim treatment may alert the clinician to the possibility of hepatic damage.
Epilim should not be administered to patients with pre-existing hepatic dysfunction.
All patients for whom treatment with Epilim is contemplated should have base line liver function assessed (including serum fibrinogen and albumin levels) prior to commencement of therapy. Liver function should be carefully monitored, particularly during the first six months of therapy, and when dosage is being titrated upwards.
Patients with a prior history of liver disease or with severe or unusual seizure disorders, e.g. those accompanied by mental retardation and/or organic brain disease, should be followed particularly carefully. Transient elevations of liver enzymes are not uncommon during early treatment with Epilim, but, if elevations are accompanied by other evidence of hepatic dysfunction, especially raised serum bilirubin or lowered serum fibrinogen, then the drug should be immediately withdrawn.
Hyperammonaemia without hepatic damage can occur in patients during treatment with valproic acid or sodium valproate. This may manifest clinically as vomiting, ataxia and increasing clouding of consciousness. Should these symptoms occur, Epilim should be discontinued.
Valproic acid inhibits second stage of platelet aggregation. Reversible prolongation of bleeding time and thrombocytopenia have been reported. Spontaneous bruising or bleeding is an indication for withdrawal of medication pending investigations. Patients receiving Epilim should be monitored for platelet function before major surgery. Red cell hypoplasia and leucopenia have been reported. The blood picture returned to normal when the drug was discontinued. Pancreatitis has occurred in patients receiving valproic acid or sodium valproate. Patients experiencing acute abdominal pain should have serum amylase estimated.
Minor gastric irritation and, less frequently, nausea may occur at the start of treatment, but these problems can usually be overcome by administering Epilim tablets or syrup with or after food, or by transferring the patient to the Epilim enteric-coated formulations. Transient hair loss has been noted in some patients. Regrowth normally begins within six months. Tremor has occasionally been observed at high dosage. Oedema has been reported. Increase in alertness, appetite and weight may occur.
Combined medication: Epilim is generally well tolerated in combination with other anti-epileptic agents; however, as interaction occurs between these compounds, it may sometimes be necessary to reduce the dosage of other drugs when adding Epilim to existing anti-convulsant therapy. Epilim may also potentiate the effect of monoamine oxidase inhibitors and other anti-depressants, and dosage of such compounds should be reduced.
Diabetic patients: Epilim may give false positives in urine testing for ketones. Care should be taken when treating diabetic patients with Epilim Syrup which contains 3.6g sucrose per 5ml.
Women of childbearing age: Valproic acid or sodium valproate, like certain other anti-convulsants, have been shown to be teratogenic in animals. In women of childbearing age, the benefits of these compounds should be weighed against the possible hazard suggested by these findings.

Further Information
When plasma valproic acid is within the recommended range of 50-120mg/litre (350-840m mol/litre) and serum albumin levels are normal, about 90% of the drug is bound to albumin. If the total plasma valproic acid rises above the upper range of normal, or if there is hypoalbuminaemia, the percentage of free valproic acid may rise markedly in disproportion to any dosage increase and may be associated with a higher incidence of adverse effects.

Product Licence Numbers, Names and Addresses
Epilim 200 enteric-coated tablets 0623/0006
Epilim Tablets 0623/0001
Epilim 500 enteric-coated tablets 0623/0005
Epilim Syrup 0623/0004

NHS Cost
Epilim 200 enteric-coated tablets: 100, £7.04
Epilim 500 enteric-coated tablets: 100, £17.60
Epilim Syrup: 200ml, £4.03
Epilim 200mg tablets: 100, £5.45

LABAZ: Sanofi UK Ltd
Regent House, Heaton Lane,
Stockport SK4 1AG, Cheshire
Telephone: 061-480 0895/6/7/8
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For many grand mal patients

a full, normal life under the protection of

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SEPTEMBER 23-25, 1982

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The Second Congress on Laser Neurosurgery will be held in Chicago, Illinois September 23-25, 1982. International in scope and clinical in orientation, the Congress will be preceded by a one half day tutorial session on laser biophysics.

World experts on each of the applications of laser in Neurosurgery will present their techniques and experience with CO_2, Argon, and Nd: YAG instruments. Governmental and legal representatives will discuss the issues of control and regulation. Laser safety, anesthesiologic considerations, and nursing aspects will be specifically addressed. Basic Science and free paper sessions will round out this comprehensive update on the state of the art of laser neurosurgery. The Congress will be useful to those already employing the instrument as well as those contemplating its use.

For further information contact: The Alumni Center for Continuing Education, Northwestern University Medical School, 301 E. Chicago Ave., Chicago, Illinois. Telephone (312) 649-8533.

CME Credits: 15

Sponsored by: The Alumni Center for Continuing Education, Northwestern University Medical School; the Division of Neurological Surgery, Northwestern University Medical School; The Midwest Bio-Laser Institute; The American Society for Laser Medicine and Surgery.

AMERICAN ASSOCIATION OF ELECTROMYOGRAPHY AND ELECTRODIAGNOSIS

ANNOUNCES

Fifth Annual AAEE CME Course in Electromyography — **October 7, 1982**
Twenty-ninth AAEE Annual Meeting — **October 8-9, 1982**
AAEE International Symposium on Central EMG — **October 10, 1982**
in St. Paul, Minnesota

October 10, 1982: **INTERNATIONAL SYMPOSIUM ON CENTRAL EMG** *(New This Year!)*
Faculty: Drs. P. Delwaide (Belgium), M. Dimitrijevic (Houston), H. Freund (Germany), K.-E. Hagbarth (Sweden), J. Lance (Australia), D. Marsden (England), B. Shahani (Boston), A. Struppler (Germany) and R. Young (Boston).

October 7, 1982: **COURSE I - FUNDAMENTALS OF EMG**
Faculty: Drs. J. Albers (Ann Arbor), J. Daube (Rochester, MN), C. Jablecki (San Diego), J. Kimura (Iowa City) and W. Stolov (Seattle).

COURSE II - SPECIAL TOPICS IN EMG: **A. Pediatric EMG** **B. Somatosensory Evoked Potentials**
Faculty: **A.** Drs. G. Eng (D.C.), R. Miller (San Francisco) and A. Sumner (Philadelphia).
B. Drs. E. Baran (Philadelphia), K. Chiappa (Boston), R. Cracco (Brooklyn), A. Eisen (Vancouver), P. Maccabee (New York), W. Wiederholt (San Diego) and R. Young (Boston).

October 8-9, 1982: **TWENTY-NINTH AAEE ANNUAL MEETING - Didactic Program: Disorders of Neuromuscular Function**
Faculty: Drs. D. Drachman (Baltimore), G. Fischbach (St. Louis), E. Lambert (Rochester, MN) and E. Stålberg (Sweden). **Lambert Lecturer:** Dr. E. Henneman (Boston).

Register for one or any combination of the above by requesting registration material from
Ella M. VanLaningham, AAEE Executive Secretary, 732 Marquette Bank Building, Rochester, MN 55901 (507/288-0100).

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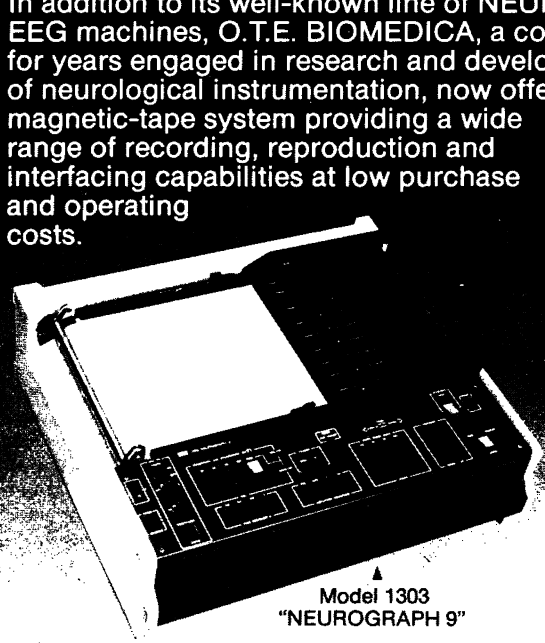

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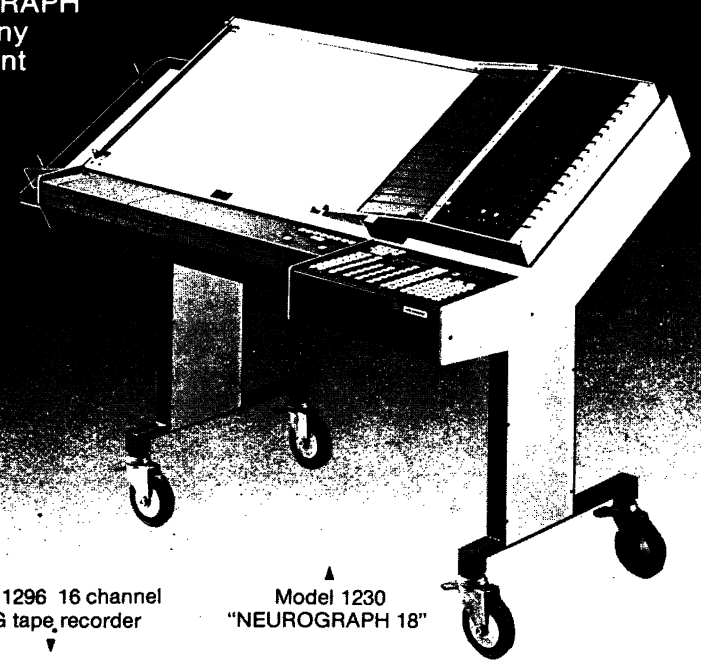

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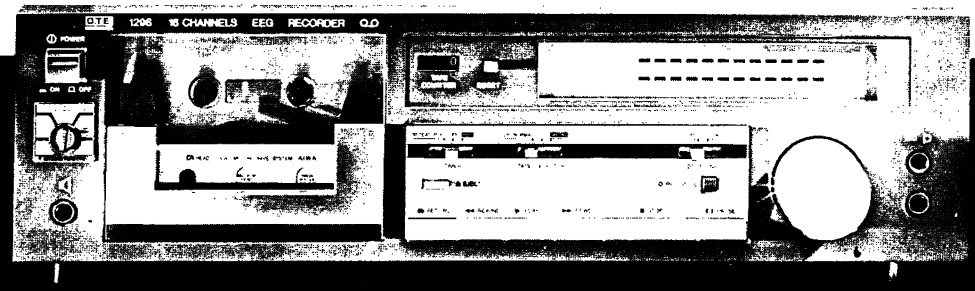

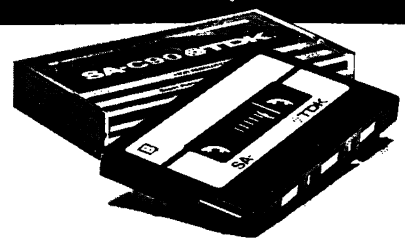

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