OVERDOSAGE
The highest dose of 'Tasmar' (tolcapone) administered to humans was 800 mg t.i.d., with and without levodopa coadministration. This was in a one week study in elderly, healthy volunteers. The peak plasma concentrations of tolcapone at this dose were on average 30 µg/ml (compared to 3 and 6 µg/ml with the 100 mg and 200 mg t.i.d. doses of tolcapone, respectively). Nausea, vomiting and dizziness were observed, particularly in combination with levodopa. The threshold for the lethal plasma concentration for tolcapone based on animal data is >100 µg/ml. Respiratory difficulties were observed in rats at high oral (gavage) and intravenous doses and in dogs with rapidly injected intravenous doses. Management of overdose: Hospitalisation is advised. General supportive care is indicated. Based on the physicochemical properties of the compound, hemodialysis is unlikely to be of benefit.

DOSAGE AND ADMINISTRATION
METHOD OF ADMINISTRATION 'Tasmar' (tolcapone) is administered orally three times a day, as an adjunct to levodopa/AADC-I (carbidopa or benserazide) therapy. The first dose of the day of 'Tasmar' should be taken together with the first dose of the day of a levodopa/AADC-I preparation, and the subsequent doses of 'Tasmar' should be given approximately 6 and 12 hours later. 'Tasmar' may be taken with or without food (see ACTIONS AND CLINICAL PHARMACOLOGY, PHARMACOKINETICS AND METABOLISM OF TOLCAPONE). 'Tasmar' can be combined with all pharmaceutical formulations of levodopa/carbidopa and levodopa/benserazide. Dosage: Therapy with 'Tasmar' should be initiated with 100 mg t.i.d. In clinical trials, the majority of patients required a decrease in daily levodopa dose if their daily dose of levodopa was >600 mg or if patients had moderate or severe dyskinesias

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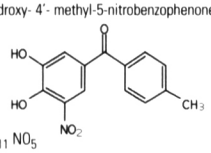
been evaluated in patients whose creatinine clearance was < 30 ml/min.

DISCONTINUATION OF 'TASMAR' Due to the possibility for the occurrence of Neuroleptic Malignant Syndrome (NMS) upon a sudden decrease in the dose of dopaminergic drugs, including 'Tasmar' (see PRECAUTIONS), physicians should consider increasing the patient's levodopa dose if 'Tasmar' is discontinued.

PHARMACEUTICAL INFORMATION Proper Name: Tolcapone
Chemical Name: 3, 4 dihydroxy- 4'- methyl-5-nitrobenzophenone
Structural Formula:



Molecular Formula: $C_{14}H_{11}NO_5$
Molecular Weight: 273.24

Description: Tolcapone is a yellow, odourless, non-hygroscopic, crystalline powder. It is practically insoluble in water and in acidic aqueous medium, but easily soluble in most organic solvents. The partition coefficient in n-octanol/phosphate buffer pH 7.5 is 6.1. Its dissociation constant (pKa) is 4.3. Its melting point is 143.0 to 146.0°C.
Composition: 'Tasmar' 100 mg and 200 mg film coated tablets contain 100 mg and 200 mg tolcapone, respectively. The non-medicinal ingredients are (in alphabetical order): calcium hydrogen phosphate, ethylcellulose, hydroxypropyl methylcellulose, iron oxide, lactose, magnesium stearate, microcrystalline cellulose, povidone K30, sodium lauryl sulfate, sodium starch glycolate, talc, titanium dioxide, triacetin.

Storage: 'Tasmar' tablets should be stored at room temperature (15-30°C).

AVAILABILITY OF DOSAGE FORMS 'Tasmar' (tolcapone) 100 mg is a pale to light yellow, hexagonal, biconvex film-coated tablet, with "Roche" and "100" engraved on one side. 'Tasmar' tablets are available in blisters (30 and 60 tablets) and in glass bottles of 100 tablets. 'Tasmar' (tolcapone) 200 mg is a brown to orange yellow, hexagonal, biconvex film-coated tablet, with "Roche" and "200" engraved on one side. 'Tasmar' tablets are available in blisters (30 and 60 tablets) and in glass bottles of 100 tablets.

PM available on request.
References: 6. Tasmar product monograph, 1997. 9. Rajput AH et al. Tolcapone 200 mg t.i.d. improves motor function in parkinsonian patients with "wearing-off" phenomenon: a double-blind, placebo-controlled, multicenter trial. Neurology 1997. 10. Waters CH et al. Tolcapone in stable Parkinson's disease: Efficacy and safety of long-term treatment. Neurology 1997; 49:1-7. 12. Agid Y et al. Tolcapone, bromocriptine, and Parkinson's disease. The Lancet, 1997

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For further information about the scientific program, registration and abstracts (DEADLINE for abstracts: JULY 15, 1998), please contact:
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