In two instances transient jaundice, probably analogous to that seen previously with chlorpromazine and (infrequently) with imipramine, has been noted; liver function studies in suspect cases, prior to and during prolonged designamine hydrochloride therapy are thus advised.

In patients suspected of having glaucoma or urinary or gastric retention, the

anticholinergic nature of the drug may be deleterious.

Patients receiving thyroid hormone, or sympathomimetic drugs may experience potentiation of the effects of these drugs, resulting in behavioral and/or cardiovascular toxicity. Patients receiving desipramine hydrochloride and anticholinergic drugs simultaneously are known to experience enhanced atropine-like side effects.

Animal teratology studies have proved negative. However, the drug is new and there is little clinical information about its use during pregnancy. Consideration of the possible risks relative to benefits should guide the decision to use Norpramin (desigramine hydrochloride) in women who are pregnant or who may be an-

ticipated to become so.

Precautions: (1) Norpramin treatment should not be substituted for hospitalization or restraint if the risk of homicide or suicide is considered grave. (2) In patients with manic depressive illness, Norpramin may induce a hypomanic state after the depressive phase terminates. (3) As with any drug, death may ensue from the suicidal ingestion of large doses of desigramine hydrochloride. (4) Discontinue therapy prior to elective surgery. (5) Use with caution in patients receiving sympathomimetic drugs or thyroid hormone as potentiation of the action of these drugs may occur. (6) Reduce dosage, or alter treatment, if serious adverse effects occur.

Adverse Effects: Undesired side effects in the desigramine hydrochloride treated patients were usually well tolerated; only occasionally did therapy have to be discontinued because of them. The side effects of desigramine hydrochloride were considered to be similar to those of imipramine; in general, these can be

expected in about one of four patients.

The following side effects have been encountered: dry mouth, constipation, dizziness, palpitation, delayed urination, agitation and stimulation ("jumpiness", "nervousness", "anxiety", "insomnia"), bad taste, sensory illusion, tinnitus, sweating, drowsiness, headache, hypotension (orthostatic), flushing, nausea, cramps, weakness, blurred vision and mydriasis, rash, tremor, allergy (general), altered liver function, ataxia and extrapyramidal signs, agranulocytosis.

Additional side effects more recently reported include: seizures, eosinophilia, confusional states with hallucinations, purpura, photosensitivity, galactorrhea, gynecomastia, and impotence. Side effects which could occur (analogy to related drugs) include weight gain, hearburn, anoresia, and hand and arm parasthesias.

Dosage and Administration: Optimal results are obtained at about 150 mg./day. Dosage over 200-225 mg./day increases incidence of side effects. Norpramin may be administered as follows: two tablets (50 mg.) t.i.d. (150 mg./day). Partial response may be expected within 2-5 days; optimal response 70 100 mg./day. After optimal results are achieved a maintenance dose . . . 50-100 mg./day . . . should be sought.

An alternate method of giving Norpramin (desipramine hydrochloride) which may, however, delay the rapid onset of therapeutic respones is: One tablet (25 mg.) three or four times a day= 75 or 100 mg. with a 25 mg. increment every few

days, if needed, to a maximum dose of 200 mg. per day.

Overdosage: (1) Prevention: Keep out of reach of children. (2) Treatment: Gastric lavage, catharsis. For coma and circulatory collapse: adequate fluids, oxygen, assisted respiration, assisted cardiac impulse. Do not hesitate to digitalize. Use sympathomimetic drugs with caution. For seizures: parenteral barbiturates or diphenylhydantoin (note: diphenylhydantoin, though having an antiarrhythmic effect, has not been fully defined in respect of its effect on the heart or its rhythm.)

Blood dialysis is of little avail; continuous gastric lavage has been advocated on the basis of desipramine resecretion in gastric juice.

Supplied: Norpramin (designamine hydrochloride) tablets of 25 mg., in bottles of 50, 500, and 1000; and tablets of 50 mg., in bottles of 30, 250, and 1000.