PRECAUTIONS

Patients who require larger dosages of indomethacin must be observed more closely for the possible occurrence of toxic effects. The patient may accept the untoward effects of indomethacin if he is told of their possible occurrence. Indomethacin, like aspirin, should be administered on a regular schedule and not used indiscriminately in the treatment of rheumatoid arthritis.

Although there is no definite evidence that indomethacin causes peptic ulcers, *it is contraindicated in patients with active ulcers.* In addition, because of its potential for causing bleeding in the gastrointestinal tract, the drug should be used with caution if there is a history of ulcer, regional ileitis, gastritis, or ulcerative colitis. Patients with these conditions may tolerate the drug if small doses are used. Indomethacin also should be used with care in patients who have epilepsy, parkinsonism, or emotional or psychiatric problems. Since the drug may cause aggravation of these conditions.

Because of the possible occurrence of central nervous system effects, patients being given indomethacin should avoid activities requiring mental alertness, judgment, or physical coordination (e.g., driving a car, operating dangerous machinery), particularly during the early weeks of therapy.

No teratogenic effects have been demonstrated in annual studies. However, it has been shown that indomethacin does cross the placental barrier. Thus, the possibility of risk to the fetus must be weighed against the expected therapeutic benefits if indomethacin is considered for administration to a pregnant woman. Clinical studies have been insufficient to establish any recommendation for the use of indomethacin in *infants* and *children.*

PHARMACOLOGY

In man, indomethacin is absorbed promptly following oral administration, and peak plasma levels occur within two hours. About 90% of a single dose is excreted in 24 to 48 hours; approximately two thirds of this amount is excreted in the urine as the glucuronide and the remainder is excreted in the feces.

DOSAGE AND PREPARATIONS

Route of Administration.—Oral.

Dosage.—To minimize adverse reactions, small doses of indomethacin are given initially; when necessary, the size of the dose is then gradually increased until an effective level is reached.

In *rheumatoid arthritis, ankylosing spondylitis,* and *degenerative joint disease of the hip,* the initial dose is 25 mg. two or three times daily. If the patient does not respond, this dose is increased at weekly intervals by increments of 25 mg. a day until a satisfactory response is obtained or until a daily dose of 150 to 200 mg. is reached; larger doses are not recommended. If adverse reactions occur, the drug should be discontinued or successive adjustments in dosage should be made until the best possible response is obtained. After an acute phase or exacerbation of rheumatoid arthritis is controlled, the dose of indomethacin should be reduced to a satisfactory maintenance level. No reports on its occasional intermittent use for short periods are available.

When indomethacin is added to a regimen of corticosteroid therapy, it is often possible to reduce the dose of the steroid by as much as one half or to discontinue it entirely. However, this reduction should be made gradually in order to avoid the effects of steroid withdrawal.

Acute attacks of *gout* may be controlled with a dosage of 50 mg. three times a day until the attack subsides. During the intervals between attacks, a dose of 25 mg. twice a day may be sufficient.

Preparations.—Capsules 25 mg.

Supplied by.—Merck Sharp & Dohme [Indocin].

Year of introduction: 1965.

Evaluated for *N.D.* 1966.