INDOCID ®

Multiple Formulations (Indomethacin)

Cardiovascular Risk

. NSAIDs may cause an increased risk of serious cardiovascular thrombic events, myocardial infarction, and stroke, which can be fatal.This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. (See **PRECAUTIONS**).

. INDOCID is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. (See **PRECAUTIONS**).

Gastrointestinal Risk

. NSAIDs cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal.These events can occur at any time during use and without warning symptoms. Elderly patients are of greater risk for serious gastrointestinal events. (See **PRECAUTIONS**)

INDOCID® (indomethacin) is a highly effective non-steroidal anti-inflammatory drug with marked analgesic and antipyretic properties.
Indomethacin is a potent inhibitor of prostaglandin synthesis *in vitro*. Concentrations are reached during therapy which have been demonstrated to have an effect *in vivo* as well.
Indomethacin has been shown to be an effective anti-inflammatory agent, appropriate for long-term use in rheumatoid arthritis, ankylosing spondylitis, and osteoarthritis.
Indomethacin affords relief of symptoms; it has not been shown to alter the progressive course of the underlying disease.
INDOCID has been found effective in relieving the pain, reducing the fever, swelling, redness, and tenderness of acute gouty arthritis.
The prostaglandin-inhibitory effect of INDOCID has been shown to be useful in the relief of pain and associated symptoms of primary dysmenorrhea.

INDICATIONS

INDOCID is indicated in active stages of:
Rheumatoid arthritis; Moderate to severe juvenile rheumatoid arthritis; Osteoarthritis; Degenerative joint disease of the hip; Ankylosing spondylitis ; Acute gouty arthritis.
It is also indicated for:
Acute musculoskeletal disorders, such as bursitis, tendinitis, synovitis, tenosynovitis, capsulitis of the shoulder, sprains and strains; Low back pain (commonly referred to as lumbago); Fever (as a short-term adjunct to specific therapy); Inflammation, pain, trismus and swelling following dental procedures; Inflammation, pain and swelling following orthopedic surgical procedures and nonsurgical procedures associated with reduction and immobilization of fractures or dislocations; Pain and associated symptoms of primary dysmenorrhea.

DOSAGE AND ADMINISTRATION

INDOCID is available in the following dosage forms to provide maximum flexibility and interchangeability:
Capsules: 25 mg or 50 mg for oral administration.
Capsules-Retard: 75 mg provide 25 mg of free indomethacin for immediate dissolution and 50 mg of time-release coated pellets.
Oral Suspension: Containing 25 mg in each 5 mL.
Suppositories: 50 mg and 100 mg.
Injection: 50 mg/2 mL (25 mg per mL). Lyophilized powder to be reconstituted with 2 mL of sterile water to provide a solution of 50 mg (25 mg/mL).
The recommended dosage of INDOCID is 50 mg to 200 mg daily in divided doses and should be adjusted to the individual patient's response and tolerability to the drug. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.
Unlike some other potent antirheumatic agents, an initial high "loading" dose of INDOCID is not necessary. In chronic rheumatic disorders, initiating therapy with low doses, increasing gradually when necessary, and continuing for an adequate period (up to one month is recommended) will produce maximum benefit and minimize adverse reactions.
In patients with persistent night pain and/or morning stiffness, a dose of up to 100 mg at bedtime may be helpful in affording relief. It is rarely necessary to exceed a dosage of 200 mg per day.
In treatment of acute gouty arthritis, the recommended daily dosage is 150 mg to 200 mg in divided doses until all symptoms and signs subside. Capsules INDOCID Retard are not recommended for use in acute gouty arthritis.
In primary dysmenorrhea, the recommended dosage is 75 mg daily as a single or divided dose, starting at the onset of cramps or bleeding and continuing for as long as symptoms usually last..
INTRAMUSCULARLY: A dosage range of 25 mg to 150 mg daily may be administered. A maximum of three doses a day (150 mg) is recommended with a maximum single dose of 50 mg. The dose should be injected deeply into a large muscle mass. For multiple injections, each dose should be injected into a different site.
JUVENILE RHEUMATOID ARTHRITIS (PEDIATRIC USAGE)
For children two years of age or older with juvenile rheumatoid arthritis, INDOCID may be started at a dosage of 1-2 mg/kg/day in divided doses b.i.d. or t.i.d., and increased weekly as needed to a maximum of 3 mg/kg/day. Maximum daily dosage should not exceed 200 mg/day or 3 mg/kg/day, whichever is less. Limited data are available to support the use of a maximum daily dosage of 4 mg/kg/day or 200 mg/day whichever is less. As symptoms subside, the total daily dosage should be reduced to the lowest level required to control symptoms, or the drug discontinued.

CONTRAINDICATIONS

INDOCID should not be used in:
Patients who are hypersensitive to any component of this product.
Patients in whom acute asthmatic attacks, urticaria, or rhinitis are precipitated by acetylsalicylic acid or other non-steroidal anti-inflammatory agents.
As with other anti-inflammatory agents, indomethacin may mask the signs and symptoms of peptic ulcer. Because indomethacin may cause peptic ulceration or irritation of the gastrointestinal tract, it should not be given to patients with active peptic ulcer or with a recurrent history of gastrointestinal ulceration.
INDOCID is contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.
Suppositories INDOCID are contraindicated in patients with a history of proctitis or recent rectal bleeding.

PRECAUTIONS

Carefully consider the potential benefits and risks of INDOCID and other treatment options before deciding to use INDOCID. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.
As advancing years appear to increase the possibility of side effects, INDOCID should be used with greater care in the elderly.
CARDIOVASCULAR EFFECTS: Cardiovascular Thrombic Events: NSAIDs may cause an increased risk of serious cardiovascular thrombic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs, both COX-2 selective and nonselective, may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk. To minimize the potential risk for an adverse cardiovascular event in patients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible.
Hypertension: NSAIDs, including INDOCID, can lead to onset of new hypertension or worsening of pre-existing hypertension, either of which may contribute to the increased incidence of CV events. Patients taking thiazides or loop diuretics may have impaired response to these therapies when taking NSAIDs. NSAIDs, including INDOCID, should be used with caution in patients with hypertension. Blood pressure (BP) should be monitored closely during the initiation of NSAID treatment and throughout the course of therapy.
Congestive Heart Failure, Fluid Retention and Edema: Congestive heart failure, fluid retention and peripheral edema have been observed in some patients taking INDOCID. Therefore, as with other NSAIDs, INDOCID should be used with caution in patients with cardiac dysfunction, hypertension, or other conditions predisposing to fluid retention.
GASTROINTESTINAL EFFECTS: Because of the occurrence and at times severity of gastrointestinal reactions the risks of continuing therapy with INDOCID in the face of such symptoms must be weighed against the possible benefits to the individual patient.
Single or multiple ulcerations, including perforation and hemorrhage of the esophagus, stomach, duodenum or small or large intestine have been reported to occur with INDOCID.These events can occur at any time during use and without warning symptoms. Fatalities have been reported in some instances. Rarely, intestinal ulceration has been associated with stenosis and obstruction.
Gastrointestinal bleeding without obvious ulcer formation and perforation of pre-existing sigmoid lesions (diverticulum, carcinoma, etc.) have occurred. Increased abdominal pain in ulcerative colitis patients or the development of ulcerative colitis and regional ileitis have been reported to occur rarely.
RENAL FUNCTION: As with other NSAIDs, there have been reports of acute interstitial nephritis with hematuria, proteinuria, and occasionally nephrotic syndrome in patients receiving long-term administration of indomethacin.
Long-term administration of NSAIDs has resulted in renal papillary necrosis and other renal injury. In patients with reduced renal blood flow where renal prostaglandins play a major role in maintaining renal perfusion, administration of a NSAID agent may precipitate overt renal decompensation. Patients at greatest risk of this reaction are those with renal or hepatic dysfunction, diabetes mellitus, advanced age, extracellular volume depletion, congestive heart failure, sepsis, or concomitant use of any nephrotoxic drug. Caution should be used when initiating the treatment with INDOCID in patients with considerable dehydration. It is advisable te rehydrate patients first and then start therapy with INDOCID. Caution is also recommended in patients with preexisting kidney disease. A NSAID should be given with caution and renal function should be monitored in any patient who may have reduced renal reserve. Discontinuation of non-steroidal anti-inflammatory therapy is usually followed by recovery to the pretreatment state.
Increases in serum potassium concentration, including hyperkalemia, have been reported, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninemic-hypoaldosteronism state (see DRUG INTERACTIONS).
Since INDOCID is eliminated primarily by the kidneys, patients with significantly impaired renal function should be closely monitored; a lower daily dosage should be used to avoid excessive drug accumulation.Therefore, treatment with INDOCID is not recommended in these patients with advanced renal disease. If INDOCID therapy must be initiated, close monitoring of the patient's renal function is advisable.
SKIN REACTIONS: NSAIDs, including INDOCID, can cause serious skin adverse events such as exfoliative dermatitis, Stevens-Johnson Syndrome (SJS), and toxic epidermal necrolysis (TEN), which can be fatal. These serious events may occur without warning. Patients should be informed about the signs and symptoms of serious skin manifestations and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.
USE IN PREGNANCY: INDOCID should be used during the first two trimesters of pregnancy only if the potential benefit justifies the potential risk to the fetus.
The known effects of indomethacin and other drugs of this class on the human fetus during the third trimester of pregnancy include: constriction of the ductus arteriosus prenatally, tricuspid incompetence, and pulmonary hypertension; non-closure of the ductus arteriosus postnatally which may be resistant to medical management; myocardial degenerative changes, platelet dysfunction with resultant bleeding, intracranial bleeding, renal dysfunction or failure, renal injury/dysgenesis which may result in prolonged or permanent renal failure, oligohydramnios, gastrointestinal bleeding or perforation and increased risk of necrotizing enterocolitis. Use of INDOCID during the third trimester of pregnancy is not recommended.
NURSING MOTHERS: Administration of INDOCID is not recommended in nursing mothers. Indomethacin is excreted in breast milk.
OCULAR EFFECTS: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some patients who had received prolonged therapy with INDOCID. The prescribing physician should be alert to the possible association of these changes and therapy with INDOCID; however, similar eye changes have been observed in patients with rheumatoid arthritis who have not received indomethacin. It is advisable to discontinue therapy if such changes are observed. Blurred vision may be a significant symptom and warrants a thorough ophthalmological examination. Since these changes may be asymptomatic, ophthalmological examination at periodic intervals is desirable in patients where therapy is prolonged.
CENTRAL NERVOUS SYSTEM EFFECTS: Headache, sometimes accompanied by dizziness or light-headedness, may occur usually early in treatment with indomethacin. Although the severity of these effects rarely requires discontinuing therapy, if headache persists despite dose reduction, indomethacin therapy should be discontinued. Patients should be warned that they may experience dizziness and in this event should not operate motor vehicles and should avoid potentially dangerous activities which require alertness.
Indomethacin should be used with caution in patients with psychiatric disturbances, epilepsy or parkinsonism, since it may, in some instances, tend to aggravate these conditions.
INFECTIONS: In common with other anti-inflammatory/analgesic/antipyretic drugs, indomethacin possesses the potential for masking the signs and symptoms which ordinarily accompany infectious disease. The physician should be alert to this possibility to avoid undue delay in initiating appropriate treatment of the infection. Indomethacin should be used with caution in patients with existing, but controlled, infection.
HEPATIC EFFECTS: As with other NSAIDs, borderline elevations of one or more liver tests may occur.
Significant (3 times the upper limit of normal) elevations of SGPT (ALAT) or SGOT (ASAT) occurred in controlled clinical trials in less than 1% of patients receiving therapy with NSAIDs. A patient with symptoms and/or signs suggesting liver dysfunction, or in whom an abnormal liver test has occurred, should be evaluated for evidence of the development of more severe hepatic reaction while on therapy with INDOCID. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations occur (e.g., eosinophilia, rash, etc.), therapy should be discontinued.
PLATELET AGGREGATION: INDOCID, like other non-steroidal anti-inflammatory agents, can inhibit platelet aggregation. This effect is of shorter duration than that seen with acetylsalicylic acid and usually disappears within 24 hours after discontinuation of INDOCID. INDOCID has been shown to prolong bleeding time (but within the normal range) in normal subjects. Because this effect may be exaggerated in patients with underlying hemostatic defects, INDOCID should be used with caution in persons with coagulation defects.
LABORATORY TESTS: False-negative results in the dexamethasone suppression test (DST) in patients being treated with INDOCID have been reported. Thus, results of the DST should be interpreted with caution in these patients.
PEDIATRIC USE: Safe conditions for use in children under two years of age have not been established. Children should be monitered closely and periodic evaluations of liver function should be performed at appropriate intervals. Cases of hepatotoxicity including fatalities have been reported.
SUPPOSITORY:Tenesmus and irritation of the rectal mucosa have been reported occasionally with the use of Suppositories INDOCID.

DRUG INTERACTIONS

ACETYLSALICYLIC ACID: The use of INDOCID in conjunction with acetylsalicylic acid or other salicylates is not recommended. Controlled clinical studies have shown that the combined use of INDOCID and acetylsalicylic acid does not produce any greater therapeutic effect than the use of INDOCID alone. Furthermore, in one of these clinical studies, the incidence of gastrointestinal side effects was significantly increased with combined therapy. In a study in normal volunteers, it was found that chronic concurrent administration of 3.6 gm of acetylsalicylic acid per day decreases indomethacin blood levels approximately 20%.
DIFUNISAL: The combined use of INDOCID and diflunisal has been associated with fatal gastrointestinal hemorrhage. The coadministration of diflunisal and INDOCID results in an increase of about 30-35% in indomethacin plasma levels and a concomitant decrease in renal clearance of indomethacin and its conjugate. Therefore, INDOCID and diflunisal should not be used concomitantly.
OTHER NSAIDS: The concomitant use of INDOCID with other NSAIDs is not recommended due to the increased possibility of gastrointestinal toxicity, with little or no increase in efficacy.
ANTICOAGULANTS: Clinical studies have shown that INDOCID did not influence the hypoprothrombinemia produced by anticoagulants in patients and in normal subjects. However, when any additional drug, including INDOCID, is added to the treatment of patients on anticoagulant therapy, the patient should be observed closely for alterations of the prothrombin time. In post marketing experience, bleeding has been reported in patients on concomitant treatment with anticoagulants and INDOCID. Caution should be exercised when INDOCID and anticoagulants are administrated concomitantly.
PROBENECID: When INDOCID is given to patients receiving probenecid, the plasma levels of indomethacin are likely to be increased. Therefore, a lower total daily dosage of INDOCID may produce a satisfactory therapeutic effect. When increases in the dose of INDOCID are made under these circumstances they should be made cautiously and in small increments.
METHOTREXATE: Caution should be used if INDOCID is administered simultaneously with methotrexate. INDOCID has been reported to decrease the tubular secretion of methotrexate and to potentiate toxicity.
CYCLOSPORINE: Administration of NSAIDs concomitantly with cyclosporine has been associated with an increase in cyclosporine-induced toxicity, possibly due to decreased synthesis of renal prostacyclin. NSAIDs should be used with caution in patients taking cyclosporine, and renal function should be monitored carefully.
LITHIUM: Indomethacin 50 mg t.i.d. produced a clinically relevant elevation of plasma lithium and reduction in renal lithium clearance in psychiatric patients and normal subjects with steady state plasma lithium concentrations. This effect has been attributed to inhibition of prostaglandin synthesis. As a consequence, when indomethacin and lithium are given concomitantly, the patient should be observed carefully for signs of lithium toxicity. (Read circulars for lithium preparations before use of such concomitant therapy). In addition, the frequency of monitoring serum lithium concentrations should be increased at the outset of such combination drug treatment.
DIURETICS: In some patients, the administration of INDOCID can reduce the diuretic, natriuretic, and antihypertensive effects of loop, potassium-sparing, and thiazide diuretics. Therefore, when INDOCID and diuretics are used concomitantly, the patient should be observed closely to determine if the desired effect of the diuretic is obtained.
INDOCID reduces basal plasma renin activity (PRA), as well as those elevations of PRA induced by furosemide administration, or salt or volume depletion. These facts should be considered when evaluating plasma renin activity in hypertensive patients. It has been reported that the addition of triamterene to a maintenance schedule of INDOCID resulted in reversible acute renal failure in two of four healthy volunteers. INDOCID and triamterene should not be administered together.
INDOCID and potassium-sparing diuretics each may be associated with increased serum potassium levels. The potential effects of INDOCID and potassium-sparing diuretics on potassium kinetics and renal function should be considered when these agents are administered concurrently.
Most of the above effects concerning diuretics have been attributed, at least in part, to mechanisms involving inhibition of prostaglandin synthesis by INDOCID.
DIGOXIN: INDOCID given concomitantly with digoxin has been reported to increase the serum concentration and prolong the half-life of digoxin. Therefore, when INDOCID and digoxin are used concomitantly, serum digoxin levels should be closely monitored.
ANTIHYPERTENSIVE MEDICATIONS: Co-administration of INDOCID and some antihypertensive agents has resulted in an attenuation of the latter's hypotensive effect acutely, due at least in part to indomethacin's inhibition of prostaglandin synthesis. The prescriber should, therefore, exercise caution when considering the addition of INDOCID to the regimen of a patient taking one of the following antihypertensive agents: an alpha-adrenergic blocking agent (such as prazosin), an angiotensin converting enzyme inhibitor (such as captopril or lisinopril), a beta-adrenergic blocking agent, a diuretic (see DIURETICS), hydralazine, or losartan (an angiotensin II receptor antagonist). In some patients with compromised renal function, the co-administration of an NSAID and an ACE inhibitor or angiotensin II antagonist may result in further deterioration of renal function, including possible acute renal failure, which is usually reversible.
PHENYLPROPANOLAMINE: Hypertensive crises have been reported due to oral phenylpropanolamine alone and rarely to phenylpropanolamine given with INDOCID. This additive effect is probably due at least in part to indomethacin's inhibition of prostaglandin synthesis. Caution should be exercised when INDOCID and phenylpropanolamine are administered concomitantly.

SIDE EFFECTS

CENTRAL NERVOUS SYSTEM: Central nervous system side effects associated with indomethacin are headache, dizziness, light-headedness, depression, vertigo and fatigue (including malaise and listlessness). Reactions reported infrequently include mental confusion, anxiety, syncope, drowsiness, convulsions, coma, peripheral neuropathy, muscle weakness, involuntary muscle movements, insomnia, psychic disturbances such as depersonalization, psychotic episodes and rarely, paresthesias, dysarthria, aggravation of epilepsy and parkinsonism. These often are transient and disappear frequently with continued treatment or with a reduction of dosage. However, the severity of these may, on occasion, require stopping therapy.
GASTROINTESTINAL: Gastrointestinal reactions which occur most frequently are nausea, anorexia, vomiting, epigastric distress, abdominal pain, constipation, and diarrhea. Others which may develop are ulceration - single or multiple of esophagus, stomach, duodenum or small or large intestine, including perforation and hemorrhage with a few fatalities having been reported; gastrointestinal tract bleeding without obvious ulcer formation; and increased abdominal pain when used in patients with preexisting ulcerative colitis. Reactions which occur infrequently are stomatitis, gastritis, flatulence, bleeding from the sigmoid colon - occult or from a diverticulum, and perforation of preexisting sigmoid lesions (diverticula, carcinoma). Rarely, intestinal strictures (diaphragms) and intestinal ulceration followed by stenosis and obstruction has been reported. Other gastrointestinal side effects which may or may not be caused by indomethacin include ulcerative colitis and regional ileitis.
Studies in man with radioactive chromate tagged red blood cells indicate that the highest recommended oral dosage of indomethacin (50 mg, 4 times a day) produces less fecal blood loss than average doses of acetylsalicylic acid (600 mg, 4 times a day).
HEPATIC: Hepatic reactions reported on rare occasions in conjunction with indomethacin therapy are jaundice and hepatitis and some fatal cases have been reported.
CARDIOVASCULAR-RENAL: Cardiovascular - renal reactions which may occur infrequently in conjunction with indomethacin therapy include edema, elevation of blood pressure, tachycardia, chest pain, arrhythmia, palpitations, hypotension, congestive heart failure, BUN elevation, and hematuria.
HYPERSENSITIVITY: Hypersensitivity reactions reported infrequently are pruritus, urticaria, angiitis, erythema nodosum, skin rashes, exfoliative dermatitis, Stevens-Johnson syndrome, erythema multiforme, toxic epidermal necrolysis, loss of hair, acute respiratory distress, a rapid fall in blood pressure resembling a shock-like state, acute anaphylaxis, angioneurotic edema, sudden dyspnea, asthma and pulmonary edema.
HEMATOLOGIC: Hematologic reactions which may develop infrequently in conjunction with indomethacin therapy are leukopenia, petechiae or ecchymosis, purpura, aplastic and hemolytic anemia and thrombocytopenia, and disseminated intravascular coagulation. Rarely, agranulocytosis and bone marrow depression have been reported, but a definite relationship to indomethacin has not been established.
Some patients may manifest anemia secondary to obvious or occult gastrointestinal bleeding. Therefore, appropriate blood determinations are recommended.
EYE: Blurred vision, diplopia and orbital and periorbital pain may occur infrequently. Corneal deposits and retinal disturbances, including those of the macula, have been reported in some patients with rheumatoid arthritis on prolonged therapy with INDOCID. Similar eye changes have been observed in some patients with this disease who have not received INDOCID.
EAR: Tinnitus, hearing disturbances, and deafness rarely, have been reported to occur.
GENITOURINARY: Reported rarely: proteinuria, nephrotic syndrome, interstitial nephritis and renal insufficiency, including renal failure.
MISCELLANEOUS: Miscellaneous adverse reactions reported rarely in conjunction with indomethacin therapy include vaginal bleeding, hyperglycemia and glycosuria, hyperkalemia, flushing and sweating, epistaxis, ulcerative stomatitis, and breast changes, including enlargement and tenderness, or gynecomastia.
The following local adverse reactions have been associated with the use of Suppositories INDOCID: tenesmus; proctitis; rectal bleeding; burning; pain; discomfort; itching.
The following additional local side effects have been associated with the use of Injection INDOCID: pain; tenderness; induration.

OVERDOSAGE: The following symptoms may be observed following overdosage: nausea, vomiting, intense headache, dizziness, mental confusion, disorientation, or lethargy. There have been reports of paresthesias, numbness, and convulsions. Treatment is symptomatic and supportive. The stomach should be emptied as quickly as possible if the ingestion is recent. If vomiting has not occurred spontaneously, the patient should be induced to vomit with syrup of ipecac. If the patient is unable to vomit, gastric lavage should be performed. Once the stomach has been emptied, 25 or 50 gm of activated charcoal may be given. Depending on the condition of the patient, close medical observation and nursing care may be required. The patient should be followed for several days because gastrointestinal ulceration and hemorrhage have been reported as adverse reactions of indomethacin. Use of antacids may be helpful.

AVAILABILITY: INDOCID is available in capsules and suppositories. Capsules INDOCID 25 mg are supplied in packages of 30, 100 and 1000 capsules. Suppositories INDOCID 100 mg are supplied in packages of 5 and 10 suppositories.
Storage Conditions: Store in a dry place below 30˚C, protected from light. Do not refrigerate.

This is a medicament

- A medicament is a product which affects your health, and its consumption contrary to instructions is dangerous for you.
- Follow strictly the doctor's prescription, the method of use and the instructions of the pharmacist who sold you the medicament.
- The doctor and the pharmacist are experts in medicine, its benefits and risks.
- Do not by yourself interrupt the period of treatment prescribed.
- Do not repeat the same prescription without consulting your doctor.

Do not use after expiry date.

Keep Medicament out of reach of children.

Manufactured in Zouk Mosbeh, Lebanon, by
ALGORITHM S.A.L.
Formulated / packaged using know-how obtained from Merck & Co. Inc.

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