# INDOCTO Mistriele kommitations chidosautiseuri.

Sandieresenter Dist

NSAIDs may cause as increased risk of senous cardiovascular thrombevents, invocardial infarction, and stroke, which can be flotal Phis risk may nerease with duration of use. Patients with cardiovascular disease or risk facors for cardiovascular disease may be at greater risk (See PRECAUTIONS) PODOCID is contemplicated for the treatment of very-enerative men in the set-

ting of coronary artery bypara goalt (CABG) surgery. (See PRECAL FIONS) Gastrointestinal Risk

NSATDE course on more cost tilly of serious asstraintestinal advance overel neluding 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 nationts are of greater risk for serious gastrointestinul events. (See PRECAUTIONS)

INDOCID<sup>®</sup> (indomethacin) is a highly effective non-steroidal anti-inflammatory drug with marked analysesic and antipyretic properties

Indomethacity is a potent inhibitor of prostaglandin synthesis in vitro. Concentrations are reached during therapy which have been demonstrated to have an afflow to sever as well

Indomethicin has been shown to be an effective anni-inflammatory agent, approminute for long-commune in rhammatesid arthettis, ankylosine enoughlitis, and esteroorthritta

Indomethican affords relief of symptoms; it has not been shown to aller the propreserve course of the underlying discuso.

INDOCID has been found effective in relieving the pain, reducing the reverswelling, rednets, and tenderness of acute gouty arthritis. The prostorlandin-inhibitory effect of INDOCID has been shown to be useful in

the relief of pain and associated symptoms of primary dysmenorrhoa.

INDOCID is indicated in active stages of

Rhoumstoul softettis: Moderate to severe juvenile (humestoid attentis-Disteourthatis, Degenerative joint disease of the hip: Ankyloxing sponovhitis As rate mounty arrivelya-

It is also indicated for. Acute musculoskeletal disorders, such as burnitis, tendinitis, synovins, tenosynovitis, consulitis of the shoulder, sprains and strains: Low back main (commonly referred to as lumbago); Peyer (as a short-term adjunct to specific therapy); Inflammation, pain, myrms and swelling following dental procedures, Inflammation, poin and swelling following orthopodic structual procedures and nonsurgical procedures associated with reflection and immubilization of fractures or distocations. Poin and associated contations of primary dysmens mea-

## DOSAGE AND ADMINISTRATION

INDOCID is available in the following dasage 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 dis-

solution and 50 mg of time-release coated pellets. Oral Suspension: Contaming 25 mg in each 5 mL

Suppositionies, 50 me and 100 mir.

Injection: 30 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 nationt'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 notent 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 ade-

quate period (up to one month is recommended) will produce maximum benefit and minimize adverse reactions. In nationts 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 INDO-

CID Retard are not recommended for use in acute courty arthritis.

In primary dysmenorrhea, the recommended dosage is 75 mg daily as a single or

divided close, starting at the auxer of craiges as blacking and continuing for as long as comptoms usually last.

INDRAMDISCULARIES. A dorage passe of 25 out to 150 mg daily may be administered. A maximum of three doses a day (150/ms) is recommended with a maximum single dose of 50 mg. The dose should be injected deeply into a large muscle mass. For multiple misetrone, each dose should be injected into a differ-

BEVENUE RHEUMATOID ARTHRITIS (PEDIATRIC URAGE). For children two years of age or older with weenile rheumatoid arthritis. INDO-

CID may be started at a docume of 1-2 marked day in dividual above hard, or tital and increased waesty as uneded to a maximum of 3 mg/kg/day. Maximum daily desage should not exceed 200 molday to 2 moltarities, whichever is less Limited data are available to support the use of a maximum daily nonues of 4 mg/kg/day. or 200 merday whichever is less. As symptomy aubuide, the total daily dosnieshould be reduced to the lowest level required to captrol symptomy, or the drugdecommod

### CONTRAD/DICATIONS

INDICATED should not be used in-

Patients who are hypersonalities to any component of this product

Patients in whom acute orthogonic attacks articarus or rhinds are receintated by acetylogicytic acid or other non-steroidal anti-inflammatory agents

As with other nati-ordanimatory ments, indomethacin may mask the signs and symptoms of peptic pices. Because indomethacin may cause peptic ulceration or irritation of the eastrointestinal tract, it should not be given to patients with active peptic ulcor or with a recurrent history of gastrointestinal alteration.

INDOCID is contraindicated for the treatment of perisonerative pain in the settage of ouronary artery hypaus graft (CABG) surgery

Suppositiones PNDOCID are contraindicated in patients with a honory of practius or recept youth blooding.

### PRECAUTIONS

Carefully consider the petietral benefits and ricks of INDOCID and other treatment antique before decidion to use (NDOCID). Use the lowest effective dose for the shortest disustion containent with individual patient treatment eooks. As advancing years appear to increase the possibility of side effects, INDOCID

should be used with orester care in the alderly. CARDIOVASCULAR EFFECTS: Cardiovascular Thrombic Events: MSAIDs may cause an increased rick of serious cardiovascular throughic events, myocardial inflaction, and stroke, which can be fittel. All NSA(Ds; both COX-2 selective and apprelicative, more have a similar risk. This risk may increase with duratime of use. Patients with conflow requiar disease or risk factors for cardiovascular disease may be at greater task. To pumping the perential risk for an adverse cardiovascular event in outients treated with an NSAID, the lowest effective dose should be used for the shortest duration possible.

Hypertension: NSAIDs, including INDOCID: can lead to prive of new hypertension or worsening of pre-existing hypertencion, either of which may contribute to the increased incidence of CV events, Patients taking thiazides or loso diaretics. may have imperred response to these therapses when taking NSAIDs. NSAIDs. including INDOCTO, should be used with causion in patients with hypertension. Blood pressure (BP) should be mornlored closely turing the initiation of NSAID frestment and throughout the course of therapy.

Congestive Heart Fations, Fluid Retention and Edones. Congestive ligart failure. fluid refertion; and perinteral adema have been observed in some patients taking INDOCTO. Therefore, as with other NSAIDs, INDOCTO 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 INDO-CID 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 preexisting 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.

orgaterm administration of NSAIDs has resulted in renal monthery increase and other terral interv. In estients with reduced renal blood flow where renal provincianality may a major role in maritimizer usual neclinary, administration of a NSAID agent may precipitate overt renal decommensation. Patients at pressess risk of this reaction are those wills regal or heratic dyefunction, diabetes mellitus. advenced age, extracellular volume depletion, congestive heart failure, sensis, or concernitual use of any nephrotoxic desp. Caution should be used, when initiate the the rearmon with JKDOCID in nations will consciously debalwation live advisable or remodrate patients limit and then start therapy with INDOCTO. Continu is also recommended in onlinets with measuring kidney disease. A NSATE should be given with caution and most function should be premitted in any national who may have reduced renal reserve. Discontingation of non-sterroidal anti-information; therapy is usually followed by recovery to the metreatment

Increases in serim notatoirus concentration, including hypericalemia, have been reported, even in some patients without renal impairment. In patients with normal remail function, these effects have been attributed to a hyperenmemor hyposidosteremism state (see DRIVI INTERACTIONS)

Since INDOCID is climinated arimarily by the kidneys, nations with significants ly impaired renal function about the closely mentioned; a lower daily dosure should be used in avoid excessive ding accumulation Therefore treatment with INDOCID is not recommended in these patients with advanced repail discuse. If INDOCID therapy must be initiated, close magnitudes of the sument's repail function is advisable SKIN REACTIONS: NSAIDs, including INDOCTD, can more serious skin adverse exerts such as exclusive demostics. Species tobuson Syndrome (SIS)

and tone epidermal negrolysts (TEN), which can be fittal. These serious events

may accur without warming. Patients should be informed about the siens and symptoms of senous skin mamilestations and use of the drug should be discorting upd at the first appearance of skin rash or any other sign of hypersensitivity USE IN PRECINANCY: INDOCTO should be used during the first two trimestors of premisecy only if the intential benefit furtifies the noternal risk in the feter. The known effects of indomethacin and other draws of this class on the human fetus during the third trimester of pregnancy vaclade: constriction of the ducing arteriosus prenatally, tricuspid incompetence, and pulmonary hyportension; nonclosure of the ductus arteriosus postnatally which may be resistant to medical management; invocardial degenerative changes, plantlet dysfunction with resultare bleeding, intracrantal bleeding, renal dysfunction or failure, renal interviduapenesis which may result in prolonged as permanent renal fadure, oligolydram-

dies, gastrointestinal blooding or perforation and increased risk of necrotizing emerocolitis. Use of INDOCID during the food projector of preeminey is not me-NURSING MOTHERS: Administration of INDOCID is not recommended in musting mothers. Indomethicist is excreted in breast milk-

OCULAR EFFECTS: Corneal deposits and retinal disturbances, including those of the macula, have been observed in some nations who had received prolonyed therapy with INDOCID. The prescribing physician should be alert to the possible association of these changes and therapy with INDOCID; however, similar eye changes base been observed in parsents with meannatord arthritis who base not received indomethouse. It is advisable to discontinue therapy if such changes are observed. Blurget vision may be a somificant symptom and warrants a therough aphilipalinological examination. Since these changes may be asymptomatic, uppthalmological 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

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

controlled, infection.

DIURETICS: In some natients, the administration of INDOCID can reduce the

turions occur (e.g., cosinophilia, rash, etc.), therapy should be discontinued.

PLATELET AGGREGATION INDOCTO like other con-special appendium-

majory agenty, can inhibit platelet aggregation. This effect is of shorter denillan-

than then seen with approbaticable apid and usually disarrieses within 24 hours

after discontinuation of INDOCID. INDOCID has been shown to inclose bleed-

ing time that within the normal ranger in normal subjects. Because this effect

may be exaggerated in national with underlying hermostatic defects. INDOCTO

LABORATORY TESTS: Faiso-negative results in the dexamethasone approxi-

sion tost (DST) in patients being treated with INDOCID have been renormal

PETHATRIC USE: Safe conditions for one in children tender two years of new

have not been established. Children should be manifered closely and periodic

evaluations of liver function should be performed at appropriate intervals. Cases

SUPPOSITURA: Tenesmus and irritation of the rectal mucosa have been report-

ACRIVESALICYLIC ACID: The use of INDOCID in communion with accivi-

adjustic ació or other adjustates as not recommended. Committed clinical studies

have shown that the combined use of INDOCID and acetylealicylic acid does not

produce any greater therapeutic effect than the use of INDOCID along.

Furthermore, in one of these clinical studies, the meidence of gastromorrisal side

effects was agodicantly increased with combined therapy. In a study in normal

valentiers, it was found that eliminic concurrent administration of \$ 6 pm of

suggests allowly: sold per day decreases indomethacin blood levels approximately

DIFUNISAL: The combined use of INDOCID and diffunisal has been associat-

ed with fatal austrointestinal hemorrhage. The condministration of different and

INDOCTO results in an increase of about Vi-25% in indomethoric absent levels

and a concomitant decrease in renal classance of indomethacin and its conjugate.

OTHER NSAIDS: The concomitant use of INDOCID with other NSAIDs is not

recommended due to the increased possibility of astromastical toxicity, with lit-

ANTICOACULANTS: Clinical studies have shown for INDOCID did not influ-

ence the hypoprothrombinering orniqueed by arthrogonizates in patients and in por-

mal subjects. However, when any additional draw including INDOCID; is added

to the treatment of outients on anticoagulant therapy, the patient should be

observed closely for alterations of the proferombin time. In post marketing expo-

rience, bleeding has been reported in nations on concomitant treatment with utili-

congulants and INDOCID. Caution should be exercised when INDOCID and

PROSENECID: When INDEX ID is given to patients receiving pronuncial, the

has been associated with an increase in cyclosporine-induced toxicity, possibly

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

Therefore, INDOCID and different should not be used emographically

Thus, results of the DST should be interpreted with caution in these patients

should be used with gaution in nemons with quagulation defects.

of heretenneights including fatalities have been reported

ed accommally with the use of Supragitories INDOCTO.

DRUG INTERACTIONS

the or no increase in officiery

combination drug treatment.

auticongulante are administrated concernitually

should be made continuely and in small increments.

lar secretion of methotrexate and to potentiate toxicity

SGOT (ASAT) occurred in controlled clinical trials to less than 1% of patients diaretic manurens, and authorienting effects of loop measure-sparing, and vation of blood pressure, technicardia, effect using arrhythmus, palintations, receiving therapy with NSATDs. A nations with symptoms and/or some suppositthingide direction. Therefore, when INDOCID and direction are used concomiing liver ductimetion, or in whom an algorithm layer but his accounted should be tandly, the national should be observed closely to determine of the desired effect of avaluated for evidence of the development of more severe henetic reaction while the diarctin is obtained on thereny with INDOCTO. If almormal liver tests percent or worsen, if clinical INDOCTO reduces based plasma regim activity (PRA), as well as those elevations. warns and symptoms consistent with liver disease develop, or if systemic manifes-

of PRA induced by furnsemide administration, or salt or volume depletion. These facts should be considered when exultating placess ronin activity in hypertension nations. If has been reported that the addition of trianteened to a maintaneous schedule at INDOCID resided in reversible scate repair follow in two of four healthy volunteers. (NDOCID and manteress should not be administered tage-

INDOCTO and notessium-marine denetics each may be associated with increased serior notaccion levels. The notential effects of INDOCTO and notate rism-sparing diagetics on parassium kinetics and renal function should be considered when these agents are administered concurrently.

Mad of the above effects concerning directics have been attributed at least in part, to mechanisms involving inhibition of prostaglindin synthesis by INDO.

DIGOXIN: INDOCID given concommantly with digorie has been reported to

increase the serior concentration and prolone the half-life of digotor. Therefore, when INDOCID and discount are used concountbuilty sensor discount tevels should be closely monitored.

ANTIHYPER TENSIVE MEDICATIONS. Condiminanturion of INDOCTO and some antihypertensive agents buy resulted in an attenuation of the latter's avponentive effect scattely, due to least in part to indomethactors inhibition of prosperlandin confluent. The prosperlier should, therefore, exercise contion when considering the addition of INDOCID to the regimen of a patient taking one of the following antibogertemove agency on alpho-advenerery blacking agent fouch as prazosin), an angiotenson converting operime inhibitor (such as cantopril or lisinomiil), a beta-salvenerus: blucking agent, a diuretic (sau DIURETICS). hydrollasine, or logartho (an approximate II recenter entagonist). In some authorswith compromised renal function, the co-administration of an NSAID and an ACF inhibitor or angittensin 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 phenylmpoanolamine alone and rurely to phenylpoonostiamine given with INDOCID. This additive effect is probably due at least in part to indomethacin's inhibition of prostagiancin synthesis. Caution should be exercised when INDO. CID and phonylpropanolamene are administered concornitantly

CENTRAL NERVOUS SYSTEM: Control nervous mention side effects associate oil with indomethacin are headache; dizzmiess, light-hendedness, denression, vertigo and fatigue (including malaise and listlessness), Reactions reported affremently include mental confusion anxiety, syncope, droweiness, convulsions, coma, peripheral neuropathy, muscle weakness, involuntary muscle movements. insornala, psychic disturbances such as depersonalization, psychotic episodes and rarely, paresthesias, dysarthria, averavation of endepsy and parkinsonism. These often are transient and disappear frequently with continued treatment or with a reduction of disage. However, the severity of these may, on occasion, require stonning therapy.

plannia levels of indonostrucin are likely to be increased. Therefore, a Inwer total GASTROINTESTINAL Castrongestinal reactions which occur most frequently daily design of INDOCTD may procuse a satisfactory therapeutic effect. When are smoter, motexia, vosolting, epigastric distress, abdominal print, constipation. increases in the date of INDOCID are made under these circumstances they and distrings. Others which may develop are identation a single in multiple of escribarus, stomach, duodersum ar smull or large intention, including perforation METHOTREXATE: Caution should be used if INDOCID is administered simuland hemorrhage with a few fatalities having been reported; gastrointestinal tract taneously with methotrexate. INDOCID has been reported to decrease the tububleeding without obvious ulcer formation; and increased abdominal pain when used in patients with preexisting ulcerative colitis. Reactions which occur infre-CYCLOSPORINE: Administration of NSAIDs concomitantly with cyclosporine quently are stomatitis, gastritis, flatulence, bleeding from the siemoid colon . occult or from a diverticulum, and perforation of preexisting sigmoid lesions due to decreased synthesis of renal prostacyclin. NSAIDs should be used with (diverticula, carcinoma). Rarely, intestinal strictures (diaphragms) and intestinal caution in patients taking cyclosporine, and renal function should be monitored ulceration followed by stenosis and obstruction has been reported. Other gastrointestinal side effects which may or may not be caused by indomethacin include LITHIUM: Indomethacin 50 mg Li.d. produced a clinically relevant elevation of 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

observed carefully for signs of lithium toxicity. (Read circulars for lithium prepa-HEPATIC: Hepatic reactions reported on rare occasions in conjunction with rations before use of such concomitant therapy). In addition, the frequency of indomethacin therapy are jaundice and hepstitis and some fatal cases have been monitoring serum lithium concentrations should be increased at the outset of such

CARDIOVASCULAR-RENAL: Cardiovascular - renal reactions which may occur infrequently in conjunction with indomethacin therapy include edema, elehypotension, congestive heart failure. BUS elevation, and hematuria.

HYPERSENSITIVITY: Hypersensitivity seartions required informatily are now ritus, urticaria, angiitis, erythema podosum, skin rathes, exfoliative dermatitis, Stevensolohnoon syndrome, erotisma multiforms, toxic enidernal merrilysis tors of heir, scute respiratory distress, a rapid fell in blood pressure resembling a shock-like state, acute anaphylaxis, angionetrotar odensa, sudden dyapnes, asfaone and malmovistry address.

HEMATOLOGIC Hematologic reactions which may develop infrequently in commercian with indemedian a thorany are legislaterial refer has an vectorousis manufacture and detection and hemolytic angeling and throughout toponia, and discommented infratyracular equalitation. Rately, agranulucylesis and hone marrow depression have been reported, but a definite relationship to indomethacin has not been

established. Some nationity may manifest apernia accondary to obvious or occol) sustrictions nai bleeding. Therefore, appropriate blood determinations are recommended. EYE: Blurred viscon diplopia and orbital and persorbital pain hazy occur infrecountly. Corneal departs and retinal disturbuscus, including those of the maci-

In have been reported in some patients with thousastoid arthritis on irrelenged factors with INDOCTO. Similar eve changes have been absenved in some partitions with this disease who have not received INDOVID. HAR! Tinnitus, hearing disturbances, and deatness rarely, have been reported for

GENITOURINARY Reported rarely, proteinura, nephrotic syndrome, interstistial nephritis and renal insufficiency, including renal failure

MISCRULANEOUS Miscollaneous adverse tractions reported rately in conjunction with indomethacin therapy include vaginal bleeding, hyperelycenia and alvensoria, hyperkalemia. Hashing and executing mistoria, alternative domentitis, and broast changes, including milargement and tendencess, or gynocomastia. The following local adverse reactions have been associated with the use of Sourcestories INDOCTO resessors amenitic rectal blooding; humane must dis-

The following additional total side effects have been associated with the use of Injection INDOCID: pain tenderness; indiration.

OVERDOSAGE: The following symmoms may be observed following overcooper national vomitime interne besidence dizziness mental confusion distroentation, or lethorey. There have been reports of paresthesias, numbress, and convolicious. Treatment in symptometric and supportion. The stomach should be erunted as quickly as possible if the operation is recent. If vorniture has not accurred approximationally, the patient should be induced to vurnit with symm of theore. If the eatlett is unable to venue, eastly layage should be not formed. Gove the stomach has been emetted, 25 in 50 em of activated charcoal may be given Depending on the condition of the purient, slowe medical observation and mursing care may be someted. The nation absolid he followed for several days necessstastrointestinal 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 35 mg are supplied in packages of 30, 100 and 1000 capsales, Suppositories INDOCID 100 mg are supplied in packages of 5 and 10 sup-Storage Conditions: Store in a dry place below 30°C, protected from facts. Go-

not retrigente.

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.

Suppositories are Manufactured in Zouk Mosbeh, Lebanon, by ALGORITHM S.A.L. Capsules are Packaged in Zouk Mosbeh, Lebanon, by ALGORITHM S.A.L.

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