SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

Indometacin capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each capsule contains 25mg Indometacin. Also contains lactose.
For the full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Ivory coloured, hard, gelatin capsules, size 3 overprinted ‘25’ and ‘PHARMVIT’ filled with a white powder.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Indometacin is a non-steroidal anti-inflammatory agent indicated for the active stages of rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, degenerative joint disease of the hip, acute musculoskeletal disorders, low back pain and acute gout. Also indicated in inflammation, pain and oedema following orthopaedic procedures and the treatment of pain and associated symptoms of primary dysmenorrhoea. Since indometacin is not a simple analgesic, its use should be limited to the above conditions.

4.2 Posology and method of administration

The dosage of indometacin should be carefully adjusted to suit the need of the individual patient.
In order to reduce the possibility of gastrointestinal disturbances, indometacin capsule should always be taken with food, milk or antacid and in chronic conditions start the therapy with a low dosage, increasing as required and continuing a trail of therapy for an adequate period (in some cases up to one month), will give the best results with a minimum of unwanted reactions.

Adult dosage : The recommended oral dosage range is 50-200mg daily in divided doses.
Acute rheumatoid arthritis: Initially 25mg two or three times a day.

Chronic rheumatic disorders: 25mg two or three times daily. (If response is inadequate, gradually increase by 25mg. Adequate response is usually achieved with not more than 150mg daily, rarely more than 200mg daily).
Sudden flare up of chronic condition: Increase if necessary, by 25mg daily until a satisfactory response is obtained, or a dosage of 150-200mg daily is reached. (If this causes any adverse effects, it should be reduced to a tolerable level for two or three days, then carefully increased, as tolerated).

Acute musculoskeletal disorders: Initially 50mg two or three times daily, according to severity for 10-14 days. Normally 150mg daily, rarely 200mg daily.

Lumbago: 50mg two or three times daily, according to severity. Duration of treatment is not normally more than five days, but may be continued for up to 10 days.

Gouty arthiritis: Acute attack: 50mg three or four times daily until symptoms subside.

Following orthopaedic procedures: Normally 100-150mg daily in divided doses until symptoms subside.

Additional considerations: In conditions where patients require a dosage of 150-200mg a day, it is often possible to reduce this gradually to a maintenance level of 75-100mg a day. In patients with persistent night pain and/or morning stiffness, a dose of up to 100mg at bed time may be helpful in affording relief. It is rarely necessary to exceed a dosage of 200mg a day.

Dosage in dysmenorrhoea : up to 75mg a day, starting with the onset of cramps or bleeding, and continuing for as the symptoms last.

Children : Paediatric dosage is not established.

Elderly : The elderly are at increased risk of the serious consequences of adverse reactions. If an NSAID is considered necessary, the lowest effective dose should be used and for the shortest possible duration. The patient should be monitored regularly for GI bleeding during NSAID therapy.

Undersirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4)

Method of Administration;
For oral administration.
To be taken preferably with or after food.

4.3 Contraindications

- Active peptic ulcer; a recurrent history of gastro-intestinal lesions; in patients who have nasal polyps associated with angioneurotic oedema.

- Safety for use in children has not been established.
- Hypersensitivity to indometacin or to any of the excipients (listed in section 6.1).
- NSAIDs are contraindicated in patients who have previously shown hypersentivity reactions (e.g. asthma, rhinitis, angioedema or urticaria) in response to ibuprofen, aspirin, or other non-steroidal anti-inflammatory drugs.
- Sever hepatic, renal and cardiac failure (see section 4.4-special warnings and precautions for use).
- During the last trimester of pregnancy (See section 4.6-Pregnancy and lactation)
- Active or history of recurrent peptic ulcer/haemorrhage (two or more distinct episodes of proven ulceration or bleeding).
- History of upper gastrointestinal bleeding or perforation, related to previous NSAIDs therapy.
- Use with concomitant NSAIDs including cyclo oxygenase 2 specific inhibitors (See section 4.5 Interactions).

4.4 Special warnings and precautions for use

Undersirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.2, and GI and cardiovascular risks below).

The use of Indometacin capsules with concomitant NSAIDs including cyclooxygenase-2 selective inhibitors, should be avoided (see section 4.5)

Cardiovascular and cerebrovascular effects
Clinical trail and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with a small increased risk of arterial thrombotic events (for example myocardial infarction or stroke). There are insufficient data to exclude such a risk for Indometacin.

Patients with uncontrolled hypertension, congestive heart failure, established ischaemic heart disease, peripheral arterial disease, and / or cerebrovascular disease should only be treated with Indometacin after careful consideration. Similar consideration should be made before initiating longer-term treatment of patients with risk factors for cardiovascular disease (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking).

Indometacin should be used with caution in patients with psychiatric disorders, epilepsy, or Parkinsonism, as it may tend to aggravate these disorders.

Gastro-intestinal disorders may be minimised by giving indometacin with food, milk or with an antacid. If gastro-intestinal bleeding occurs, indometacin should be immediately discontinued.

Indometacin may mask the signs and symptoms of infection, so antibiotic therapy should be initiated promptly if an infection occurs during therapy with indometacin. It should be used cautiously in patients with existing but controlled infection. Caution is advised with concomitant use of live vaccines.
In patients with rheumatoid arthiris, eye changes may occur which may be related to the underlying disease or to the therapy. Therefore, in chronic rheumatoid disease, opthalmological examination at periodic intervals are recommended. Therapy should be discontinued if eye changes are observed for any unwanted effects on peripheral blood (anaemia), liver function or gastro-intestinal tract.

Cardiovascular, Renal and Hepatic Impairment:
The administration of NSAIDs may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at great risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics, the elderly, diabetes mellitus, extracellular volume depletion, congestive heart failure, sepsis, or concomitant use of any nephrotoxic drug. Renal function should be monitored in these patients (See also section 4.3-Contraindication)

Caution in patient with a history of hypertension and/or heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Acute interstitial nephritis with haematuria, and occasionally nephritic syndrome has been reported in patients receiving long term administration of indometacin. In patients, with a reduced renal blood flow where renal prostaglandins play a major role in maintaining renal perfusion, administration of a NSAID may precipitate overt renal decompensation.

Indometacin should be given with caution and renal function should be monitored in any patient who may have reduced renal reserve, a lower daily dosage should be used to avoid excessive drug accumulation. Discontinuation of indometacin is usually followed by recovery to the pre-treatment state.

Increase in plasma potassium concentration, including hyperkalaemia, have been reported, even in some patients without renal impairment (attributed to hyporenin-anaemic hypo aldosteronism state).

Elderly :
The elderly have an increased frequency of adverse reactions to NSAIDs especially gastrointestinal bleeding and perforation, which may be fatal (See section 4.2-Posology and administration)

Respiratory disorders :
Caution is required if administered to patients suffering from, or with a previous history of, bronchial asthma since NSAIDs have been reported to precipitate bronchospasm in such patients.

Caution is advised in patients with pre-existing sigmoid lesions (such as diverticulum or carcinoma) (or the development of these conditions) as indometacin can aggravate these conditions.

Gastrointestinal bleeding, ulceration and perforation:
GI bleeding, ulceration or perforation, which can be fatal, has been reported with all NSAIDs at any time during treatment, with or without warning symptoms or a previous history of serious GI events.

When GI bleeding or ulceration occurs in patients receiving Indometacin, the treatment should be withdrawn.

The risk of GI bleeding, ulceration or perforation is higher with increasing NSAID doses, in patients with a history of ulcer, particularly if complicated with haemorrhage or perforation (see section 4.3), and in the elderly. These patients should commence treatment on the lowest dose available.

Combination therapy with protective agents (e.g. misoprostol or proton pump inhibitors) should be considered for these patients, and also for patients requiring concomitant low dose aspirin, or other drugs likely to increase gastrointestinal risk (see below and section 4.5).

Patients with a history of GI toxicity, particular when elderly, should report any unusual abdominal symptoms (especially GI bleeding) particularly in the initial stages of treatment.

Caution should be advised in patients receiving concomitant medications, which could increase the risk of gastroxicity or bleeding, such as oral corticosteroids, or anticoagulants such as warfarin, selective serotonin reuptake inhibitors or anti-platelet agents such as aspirin (see section 4.5).

NSAIDs should be given with care to patients with a history of gastrointestinal disease (ulcerative colitis, crohn's disease) as these conditions may be exacerbated (See section 4.8 – Undersirable effects)

Indometacin can inhibit platelet aggregation. The effect usually disappears within 24 hours of discontinuting indometacin. Indometacin should be used cautiously in patient with coagulation defects.

Caution is required in post-operative patients as bleeding time is prolonged (but within normal range) in normal adults.

Headache, dizziness and light-headedness may occur. Starting therapy with a low dosage and increasing it gradually will usually minimise the incidence of headache. Symptoms frequently disappear on continuting therapy or reducing the dosage, but if headache persists indometacin should be withdrawn.

SLE and mixed connective tissue disease:
In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders. There may been increased risk of aseptic meningitis (See section 4.8 – Undersirable effects).

Female fertility:
The use of indometacin may impair female fertility and is not recommended in woman attempting to conceive. In women who have difficulties conceiving or who are undergoing investigation of infertility, withdrawl of indometacin should be considered.

Dermatological:
Serious skin reactions, some of them fatal, including exfoliative dermatitis, Stevens-Johnson syndrome, and toxic epidermal necrolysis, have been reported very rarely in association with the use of NSAIDs (see section
4.8). Patients appear to be at highest risk for these reactions early in the course of therapy: the onset of the reaction occurring in the majority of cases within the first month of treatment. Indometacin capsules should be discontinued at the first appearance of skin rash, mucosal lesions, and any other sign of hypersensitivity.
Increases in plasma potassium concentration, including hyperkalaemia have been reported, even in some patients without renal impairment. In patients with normal renal function, these effects have been attributed to a hyporeninaemic-hypoaldosteronism state.

Borderline elevations of certain liver tests may occur, and significant elevations of ALT(SGPT) or AST(SGOT) have been seen in less than 1% of patients receiving indometacin in controlled trials.
False negative tests results in the dexamethasone suppression test (DSI) in patients being treated with indometacin have been reported.

4.5 Interaction with other medicinal products and other forms of interaction

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including aspirin) as this may increase the risk the adverse effects (See section 4.3 Contraindications). Clinical studies have shown no enhanced therapeutic effect and an increase in the incidence of gastro-intestinal side effects.

Anti-coagulants : NSAIDs may enhance the effects of anti-coagulants, such as warfarin (See section 4.4-special warnings and precautions for use). Patients also receiving anticoagulants should be closely observed for alterations of the prothrombin time.

Antidiabetics : the effect of sulphonylureas may be increased by NSAIDs.

Anti-hypertensives : Reduced anti-hypertensive effect. Indometacin may acutely reduce the antihypertensive effect of beta-blockers due partly to indometacin's inhibition of prostaglandin synthesis. Patients receiving dual therapy should have the antihypertensive effect of their therapy reassessed. Therefore, caution should be exercised when considering the addition of indometacin to the regimen of a patient taking any of the following antihypertensive agents: alpha-adrenergic blocking agents, ACE inhibitors, beta-adrenergic blocking agents, angiotensin-2-receptor antagonists, hydralazine or nifedipine. An increased risk of hyperkalaemia has also been reported when NSAIDs are taken with ACE inhibitors.

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs) : Increased risk of gastrointestinal bleeding (see section 4.4).

Antipsychotics : Increased drowsiness with indometacin and haloperidol.

Antivirals : Risk of indometacin toxicity with ritonavir, avoid concomitant use.

Cardiac glycosides : NSAIDs may exacerbate cardiac failure, reduced GFR and increase plasma glycoside levels.

Ciclosporin : Incresed risk of nephrotoxicity. Administration of NSAIDs concomitantly with ciclosporin has been associated with an increase in ciclosporin-induced toxicity, possibly due to decreased synthesis of renal prostacyclin. NSAIDs should be used with caution in patients taking ciclosporin, and renal function should be monitored carefully.

Corticosteroids : Increased risk of GI ulceration or bleeding (See section 4.4-special warnings and precautions for use).

Cytotoxics : Indometacin may decrease the tubular secretion of methotrexate thus potentiating toxicity; simultaneous use should be undertaken with caution.

Desmopressin : Effect potentiated by indometacin.

Diflunisal : Avoid concomitant use. Increases plasma levels of indometacin by about a third with a concomitant decrease in renal clearance. Fatal gastro-intestinal haemorrhage has occurred.

Diuretics : Reduced diuretics effect. When indomethacin and diuretics are used comcomitantly, the patient should be observed to determine whether the desired effect of the diuretic is obtained, as indomethacin can reduced the diuretic and anti-hypertensive effects of loop, potassium-sparing, and thiazide diuretics. Indometacin may cause blocking of the furosemide -induced increase in plasma renin activity. Diuretics can increase the risk of nephrotoxicity of NSAIDs. Indometacin reduces the basal plasma renin activity (PRA), as well as those elevations of PRA induced by frusemide administration, or salt or volume depletion. Indometacin and traimterene should not be administered together as reversible acute renal failure has been reported. Indometacin and potassium sparing diuretics each may be associated with increased plasama potassium levels. The potential effects on potassium kinetics and renal function should be considered when these agents are administered concurrently.

Lithium : Decreased elimination of lithium. Indometacin is an inhibitor of prostaglandin synthesis and therefore the following drug interactions may occur; indometacin may raise plasma lithium levels and reduce lithium clearance in subjects with steady state plasma lithium concentrations. At the onset of such combined therapy, plasma lithium concentration should be monitored more frequently.

Methotrexate : Caution should be exercised with the simultaneous use of indometacin with methotrexate, as it has been reported to decrease the tubular secretion of methotrexate and to potentiate toxicity.

Mifepristone : NSAID should not be used for 8-12 days after mifepristone administration as NSAIDs can reduce the effect of mifepristone.

Muscle Relaxants : Increased risk of baclofen toxicity due to reduced rate of excretion.

Pentoxifylline : Possible increased risk of bleeding when taken with NSAIDs.
Probenecid : Co-administration of probenecid may increase indometacin plasma levels. When increases in the dose of indometacin are made under these circumstances, they should be made cautiously and in small increments.

Quinolone antibiotics : Animal data indicate that NSAIDs can increase the risk of convulsion associated with quinolone antibiotics. Patients taking NSAIDs and quinolones may have an increased risk of developing convulsions.

Salicylates : Use of indometacin with aspirin or other salicylates is not recommended because there is no enhancement of therapeutic effect while the incidence of gastro-intestinal side-effects is increased. Moreover, co-administration of aspirin may decrease the blood concentration of indometacin.

Tacrolimus : Possible increased risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Tiludronic acid : The bioavailability of tiludronic acid is increased by indometacin.

Triamterene- **i**ndometacin and triamterene should not be administered together since reversible renal failure may be induced.

Zidovudine : Increased risk of haematological toxicity when NSAIDs are given with zidovudine There is evidence of an increased risk of haemarthroses and haematoma in HIV(+) haemophiliacs receiving concurrent treatment with zidouvdine and ibuprofen.

Laboratory tests*:* False-negative results in the dexamethasone suppression test (DST) in patients being treated with indometacin have been reported. Thus, results of this test should be used with caution in these patients.

4.6 Fertility, pregnancy and lactation

Pregnancy :

Congenital abnormalities have been reported in association with NSAIDs administration in man, however, these are low in frequency and do not appear to follow any discernible pattern.
In view of the known effects of NSAIDs on the foetal cardiovascular system (risk of the closure of the ductus arteriosus and possibly persistant pulmonary hypertension of the new born), use in the last trimester of pregnancy in contraindicated. The onset of labour may be delayed and the duration increased with an increase bleeding tendency in both mother and child (See section 4.3 Contarindications). NSAIDs should not used during the first two trimesters of preganancy or labour unless the potential benefit to the patients outweigh the potential risk to the foetus.

Lactation :

In limited studies so far available, NSAIDs can appear in breast milk in very low concentrations to be harmful, however, convulsions have been reported in one infant. NSAIDs should, if possible, be avoided when breastfeeding. It is advisable only to administer indometacin during lactataion, if essential. See section 4.4 Special warnings and precautions for use, regarding female fertility.

4.7 Effects on ability to drive and use machines

Patients should be warned that they may experience dizziness and, if they do, should not drive a car or operate machinery.

4.8 Undesirable effects

Blood and lymphatic disorders: Infrequently, blood dyscrasias may occur including leucopenia, neutropenia, petechiae or ecchymosis, purpura, apalastic or haemolytic anaemia, agranulocytosis, bone-marrow depression, disseminated intra-vascular coagulation, and particularly thrombocytopenia. Because some patients may develop anaemia secondary to obvious or occult gastro-intestinal bleeding, appropriate blood determinations are recommended. Epistaxis has been reported rarely.

Hypersensitivity : Hypersensitivity reactions have been reported following treatment with NSAIDs. These may consists of (a) non specific allergic reaction and anaphylaxis (b) respiratory tract reactivity comprising asthma, aggravated asthma, bronchospasm or dyspnoea, or (c) assorted skin disorders including rashes of various types, pruritus, urticaria, purpura, angiodema and, more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

Metabolism and nutrition disorders: Hyperglycaemia, glycosuria, hyperkalaemia, sweating has been reported rarely.

Nervous system disorders : Visual disturbances, headaches, paraesthesia, dizziness and lightheadedness are common side effects**.** Starting therapy with a low dose and increasing gradually minimises the incidence of headache. These symptoms frequently disappear on continued therapy or reducing the dosage, but if headache persists despite dosage reduction, indometacin should be withdrawn.

Other CNS effects include aspetic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus mixed connective tissue disease), with symptoms such as stiff neck, nausea, vomiting, fever or disorientation (See section 4.4), depression, confusion, vertigo, malaise, fatigue, dysarthria, syncope, coma, cerebral oedema, nervousness**,** mental confusion, anxiety and other psychiatric disturbances, muscle weakness, involuntary muscle movements, depersonalisation, hallucinations**,** drowsiness, convulsions and aggravation of epilepsy and parkinsonism, peripheral neuropathy, involuntary movements and insomnia. These effects are often transient and abate or disappear frequently on reduced or stopping treatment. However, the severity of these may, on occasion, require cessation of therapy**.**

Eye disorders : Infrequently blurred vision, diplopia, optic neuritis and orbital and peri-orbital pain. Corneal deposits and retinal or macular disturbances have been reported in patients with rheumatoid arthritis on prolonged therapy; but similar changes may be expected in such patients who have not received indometacin. Ophthalmic examinations are desirable in patients given prolonged treatment.

Ear and labyrinth disorders : Tinnitus, hearing disturbance (rarely deafness).

Cardiac disorders: Oedema has been reported in association with NSAID treatment. Other adverse events reported less commonly include increased blood pressure, tachycardia, chest pain, arrhythmia, palpitation, hypotension, congestive heart failure (all infrequent).

Vascular disorders : Flushing has been reported rarely

Respiratory, thoracic and mediastinal disorders : Pulmonary eosinophilia. Bronchospasm may be precipitated in patient suffering from or with a history of bronchial asthma or allergic disease.

Gastrointestinal disorders: The most commonly-observed adverse events are gastrointestinal in nature. Anorexia, epigastric discomfort,ulceration at any point in the gastro-intestinal tract (even with resultant stenosis and obstruction), bleeding (even without obvious ulceration or from a diverticulum) and perforation of preexisting sigmoid lesions (such as diverticulum or carcinoma), increased abdominal pain or exacerbation of the condition in patients with ulcerative colitis or Crohns disease (or the development of this condition), intestinal strictures and regional ileitis have been rarely reported. Occasionally severe reactions stopping therapy, ulceration

of the oesophagus, stomach or duodenum, sometimes with haemorrhage and perforation; gastro-intestinal tract bleeding. Rarely intestinal ulceration followed by stensis and obstruction has been reported.
Peptic ulcers, perforation or GI bleeding, sometimes fatal, particularly in the elderly, may occur (see section 4.4 Special warnings and precautions for use). If gastro-intestinal bleeding does occur treatment with indometacin should be discontinued. Gastro-intestinal disorders which occur can be reduced by giving indometacin with food, milk or antacids. Nausea, vomiting, diarrhoea, flatulence, constipation, dyspepsia, abdominal pain, melaena, haematemesis, ulcerative stomatitis, exacerbation of colitis and Crohn's disease (see section 4.4) have been reported following administration. Less frequently, gastric has been observed. Pancreatitis has been reported very rarely.

Hepatobiliary disorders : Cholestasis, borderline elevations of one or more liver tests may occur, and significant elevations of ALT (SGPT) or AST (SGOT) have been seen in less than 1% of patients receiving therapy with NSAIDs in controlled clinical trials. If abnormal liver tests persist or worsen, if clinical signs and symptoms consistent with liver disease develop, or if systemic manifestations such as rash or eosinophilia occur, indometacin should be stopped. Abnormal liver function, hepatitis and jaundice are infrequent.

Skin and subcutaneous tissue disorders : Pruritus, urticaria, angioneurotic oedema angitis, erythema nod sum, skin rash, photosensitivity, exfoliative dermatitis. Bullous reactions including Steven Johnson syndrome, erythema multiform, toxic epidermal necrolysis, loss of hair, rapid fall in blood pressure resembling a shock like state, acute respiratory distress including sudden dyspnoea, asthma and pulmonary oedema (all infrequent).

Musculoskeletal and connective tissue disorders : Muscle weakness and acceleration of cartilage degeneration.

Renal and urinary disorders : Blood urea elevation, haematuria, nephrotoxicity in various forms, including interstitial nephritis, nephrotic syndrome and renal failure, renal insufficiency, proteinuria have all been reported. In patients with renal, cardiac or hepatic impairment, caution is required since the use of non-steroidal anti-inflammatory drugs may result in deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored.

Reproductive system and breast disorders : Rarely vaginal bleeding, breast changes (enlargement, tenderness, gynaecomastia).

Clinical trail and epidemiological data suggest that use of some NSAIDs (particularly at high doses and in long term treatment) may be associated with an increased risk of arterial thrombotic events (for example myocardial infarction or stroke) (See section 4.4).

4.9 Overdose

a) **Symptoms:** include headache, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, epigastric pain, gastrointestinal bleeding, disorientation, excitation, coma, drowsiness, dizziness, tinnitus, fainting, mental

confusion, lethargy, paraesthesiae, numbness and convulsion. In cases of significant poisoning acute renal failure and liver damage are possible.

b) Therapeutic measure:

Patients should be treated symptomatically as required.
The stomach should be emptied as quickly as possible if ingestion is recent. If vomiting has not occurred spontaneously, the patient should be induced to vomit with syrup of ipecac. Within one hour of ingestion of a potentially toxic amount, 25 or 50g activated charcoal should be considered. Alternatively, in adults gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.
Ulceration and haemorrhage have been reported as adverse reaction of indometacin, use of antacid may be helpful.
Good urine output should be ensured.
Renal and liver function should be closely monitored.
Patients should be observed for at least four hours after ingestion of potentially toxic amounts. Frequent or pronged convulsions should be treated with intravenous diazepam.
Other measures may be indicated by the patient's clinical condition.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

ATC CODE: M01A B01
Indometacin has an analgesic, anti-inflammatory, and antipyretic properties: it is an inhibitor of prostaglandin synthetase.

5.2 Pharmacokinetic properties

Indometacin is readily absorbed from the gastro-intestinal tract with peak plasma concentrations being reached about 2 hours after a dose. Indometacin has a half life of about 4.5 hours and about 99% is bound to plasma proteins. It is metabolised and undergoes enterohepatic circulation. Excretion of indometacin and metabolites, as glucuronide conjugates, is predominantly in the urine with lesser amount appearing in the faeces.

5.3 Preclinical safety data

N/A

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose 212mg
Sodium lauryl sulphate 002mg
Colloidal silicon dioxide 001mg
Hard gelatin capsule

6.2 Incompatibilities
None known

6.3 Shelf life
5 years

6.4 Special precautions for storage
Store under 30°C, in a cool dry condition

6.5 Nature and contents of container

Plastic securitainer with polypropylene lids with double security closure containing indometacin capsule (material of the container complies to EEC directives for plastic in contact with food stuff and drugs)
Blister packs of 0.25mm thick PVC and Aluminium foil of thickness 20 microns.
Pack Sizes : 28, 56, 84, & 500 Capsules.
Not all pack sizes may be marketed.

6.6 Special precautions for disposal

None

7 MARKETING AUTHORISATION HOLDER

Pharmvit Limited

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UB6 7HQ

8 MARKETING AUTHORISATION NUMBER(S)

PL 4556/0002

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

10/11/2014