SUMMARY OF PRODUCT CHARACTERISTICS (SmPC)

SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets / Paracetamol &Diclofenac Sodium Tablets

1 NAME OF THE MEDICINAL PRODUCT

SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each uncoated tablet contains:

- Paracetamol BP (325 mg)
- Diclofenac Sodium BP (50 mg)
- Colour: Approved colour used. (In House) (-)
- Excipients (In House) (- QS)

Batch Size: 7,50,000 Tablets

Sr. No.	Ingredients	Specification	Label Claim (In mg)	% Overages	Qty / Batch in (Kg)	Reason for inclusion
Mixing Material						
1.	Paracetamol	BP	325		375.000	Medicament
2.	Diclofenac Sodium	BP	50		37.500	Medicament
3.	Maize Starch	BP			115.000	Diluent, Disintegrating Agent or Binder
4.	Dibasic Calcium Phosphate	BP			85.000	Filler and Diluent
Paste Material						
5.	Maize Starch	BP			22.500	Diluent, Disintegrating Agent or Binder
6.	P.V.P.K -30	BP			6.250	Binder
7.	Methyl Paraben	BP			0.825	Preservative
8.	Propyl Paraben	BP			0.080	Preservative
9.	Col Brilliant Blue Supra	BP			0.440	Colorant
10.	Colour Tartrazine Supra	BP			0.095	Colorant
11.	Purified Water	BP			150.000	Solvent
Lubrication						

12.	Purified Talcum	BP			12.460	Lubricant
13.	Magnesium Stearate	BP			6.620	Lubricant
14.	Sodium Starch Glycolate	BP			6.180	Lubricant
15.	Sodium Lauryl Sulphate	BP			2.540	Lubricant

3 PHARMACEUTICAL FORM

Green coloured, oval shape, uncoated tablet having break line on one side of each tablet.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

Due to its anti-inflammatory and analgesic effects, SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablet is indicated for the treatment of:

- Rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, cervical spondylosis, intervertebral disc syndrome, and sciatica.
- Non-articular rheumatic conditions such as fibrositis, myositis, bursitis, low back pain etc.
- Soft tissue injuries such as sprains, strains, and sports injuries.
- Painful inflammatory conditions in gynaecology.
- Post-operative and post-traumatic inflammation and swelling.
- Pain and inflammation following surgery.
- Acute attacks of gout.

4.2 Posology and method of administration

Posology

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control symptoms (see section 4.4 Special warnings and precautions for use).

Adults: 1 tablet 2-3 times daily.

If the symptoms are more important by night or in the morning, the tablets should be taken in the evening.

Children: the pharmaceutical form and dosage are not indicated for children.

Method of administration

SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets should be swallowed with adrink, preferably while eating.

Elderly patients: the dosage should be reduced and monitoring of biological parameters is recommended.

The daily dose of paracetamol cannot exceed 2 g in the following situations:

Liver failure

Gilbert's syndrome

Chronic alcoholism

Impaired renal function:
The dose should be reduced in terms of the creatinine clearance:

Glomerular filtration rate	Dose (paracetamol)
10 - 50 mL/min	325 mg every 6 hours
< 10 mL/min	325mg every 8 hours

4.3 Contraindications

- Established congestive heart failure (NYHA II-IV), ischemic heart disease, peripheral arterial disease and/or cerebrovascular disease.
- Gastrointestinal ulcer
- Known hypersensitivity to the active ingredients or any of the excipients
- Severe hepatic failure
- Moderate to severe renal failure
- Due to cross-allergy, diclofenac should not be given to patients, especially asthmatics, who have experienced symptoms of asthma, urticaria or acute rhinitis after taking aspirin or other non-steroidal anti-inflammatory drugs (prostaglandin-synthetase inhibitors).
- Severe heart failure
- Third term of pregnancy

4.4 Special warnings and precautions for use

Undesirable effects may be minimised by using the lowest effective dose for the shortest duration necessary to control the symptoms (see Section 4.2 and Gastrointestinal and cardiovascular risks, hereunder).

Cardiovascular and cerebrovascular effects

- As fluid retention and oedema have been reported in association with non-steroidal antiinflammatory drugs (NSAIDs) therapy, caution is required in patients with history of high blood pressure and/or heart failure.
- Clinical studies and epidemiologic data suggest that diclofenac use, especially at high dose (150 mg daily) and prolonged use can be associated to a slight increase in arterial thrombotic events (such as cardiac infarction or stroke).
- Patients with significant risk factors for cardiovascular events (e.g. hypertension, hyperlipidaemia, diabetes mellitus, smoking) should only be treated with diclofenac after careful consideration.
- As the cardiovascular risks of diclofenac may increase with dose and duration of exposure, the shortest duration possible and the lowest effective daily dose should be used. The patient's need for symptomatic relief and response to therapy should be reevaluated periodically.

Gastrointestinal effects

- Gastrointestinal (GI) bleeding, ulceration or perforation have been reported with all NSAIDs at any time during treatment, with or without warning symptoms or in patients without any history of GI events. In elderly patients these events are usually more severe.
- Should GI bleeding or ulceration occur in patients receiving diclofenac, treatment should be discontinued.

- As with others anti-inflammatory drugs, allergic reactions including anaphylactic reactions can occur, even without prior exposure to the drug.
- NSAIDs can mask the signs or symptoms of infection (due to antalgic and antipyretic effects) resulting in delayed diagnosis and treatment.
- Patients with GI disorders or with a history ulcer as well as patients with ulcerous colitis, Crohn's disease, impaired hepatic function should be closely monitored.
- During diclofenac treatment, increase in several hepatic enzymes levels can occur.
- Hepatic function monitoring is recommended, as a preventive measure, during long term treatment. SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets treatment should be discontinued if hepatic function tests remain abnormal or worsen, if clinical symptoms of hepatic affections occur, or in case of other signs (such as eosinophilia, rash, …). Hepatitis can appear without prodromal symptoms. Risk of hepatic toxicity significantly increases in case of chronic alcoholism. Dosage reduction is required in alcoholic patients. Special care is recommended in case of observed hepatic failure. The same recommendation is applicable forpatients treated by hepatic enzymes inductors (alcohol, barbiturates and anti-epileptics). In those cases, paracetamol toxic metabolites accumulation may lead to or worse hepatic lesions.
- In patient with hepatic porphyria, special care is recommended as diclofenac can induce an attack.
- Due to the role of prostaglandins in maintaining renal blood flow, particular monitoring is required when diclofenac is used in patients with impaired heart, hepatic or renal function, in elderly patients, in patients treated by diuretics and in patients who have lost large extracellular volumes (for example during the peri-operative or post-operative phase of major surgical procedures). The effect is reversible upon discontinuation of the treatment.
- In case of prolonged use, blood analysis, including haematocrit, transaminase levels, total proteins and serum albumin, should be performed regularly.
- As with others NSAIDs, SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets may temporarily inhibit platelets aggregation.
- Special care is required in patients with haemostasis disorders.
- Special attention should be paid in elderly patients, especially regarding gastro-intestinal and renal undesirable effects. It is recommended to administer the lowest effective dose, particularly in debilitated patients.
- Administration of SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets to patients with bronchial asthma should be carefully considered because of the risk of worsening symptoms.
- As with others NSAIDs, increase in uraemia and creatininaemia can occur.
- Prostaglandins synthesis inhibitors can modify the renal function especially if this function is already affected for example in case of sodium depletion, cardiac decompensation or severe liver affection.
- As with others prostaglandins synthesis inhibitors, the following renal abnormalities can occur: glomerulonephritis, interstitial nephritis, papillary necrosis, nephrotic syndrome, acute renal failure.

Paracetamol

- A frequent or time extended use is unadvised. A time extended use, unless controlled by a medical professional, can harm the health.

- The maximal dose should not be exceeded. In order to prevent the risk of overdose, no othermedical product containing paracetamol should be taken simultaneously.
- Taking at once a dose corresponding to several times the daily dose can seriously damage the liver; there might not be any conscious loss. Despite, it is recommended to call a doctor in regard to the risk of irreversible liver damage.
- Caution should be given if the following risk factors, lowering the liver toxicity threshold, are present: liver failure (including Gilbert's syndrome), acute hepatitis, kidney failure, chronic alcoholism and very meagre adults (< 50 kg). In those cases, the posology should be adapted (see 4.2).
- A concomitant treatment with drugs influencing the liver function, dehydration, chronic malnutrition (low glutathione liver stock) are as well regarded as risk factors for the emergence of liver toxicity and that can lower the liver toxicity threshold. The maximal daily dose should certainly not be exceeded in these patients.
- Caution should be given in case of paracetamol administration to patients with glucose6-phosphate dehydrogenase deficiency and with haemolytic anaemia.
- In case of acute fever, signs of secondary infection or persistency of the complaints, the patients should be referred to the doctor.
- Paracetamol administration in patients with moderate to severe renal failure may lead to accumulation of conjugated derivatives.

4.5 Interaction with other medicinal products and other forms of interaction

The anticoagulant effect of warfarin and other coumarins may be enhanced by prolonged regular daily use of paracetamol with increased risk of bleeding; occasional doses have no significant effect. As with other NSAIDs, caution should be exercised in patients receiving oral anticoagulants, heparin via parenteral route and ticlopidine, thiazide diuretics, moclobemide, lithium, sulphonamide hypoglycemiant, methotrexate, pentoxifylline, zidovudine and baclofen. Take into account interactions with antihypertensives (beta-blockers, conversion enzyme inhibitors, and diuretics), digoxin, and thrombrolytics.

4.6 Fertility, pregnancy and lactation

Paracetamol crosses the placental barrier and is excreted in breast milk. Diclofenac appears in the breast milk in very low concentrations and is likely to affect the breast-fed infant adversely. Whilst, human and animal studies have not identified any risk to pregnancy or embryofoetal development, the use of SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets during pregnancy should, if possible, be avoided. Human studies have not identified any risk to lactation or the breast-fed offspring.

4.7 Effects on ability to drive and use machines

Vertigo or central nervous system effects can occur during treatment with SOCOMOL Paracetamol325 mg & Diclofenac Sodium 50 mg Tablets. If these effects appear while using SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets, driving a car and using machines are not recommended.

4.8 Undesirable effects

At recommended doses SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablet is generally well tolerated. At the start of treatment, however, patients may sometimes complain

of epigastric pain, nausea, diarrhoea, dizziness or headache. These unwanted effects are normally of a mild nature. Peripheral oedema and skin reactions such as drug rash, urticaria, and eczema, have also been reported.
The following side-effects have seldom been reported with SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets, although there are reported cases:
- CNS side-effects, such as tiredness, insomnia, and irritability.
- Gastrointestinal effects such as ulceration and haemorrhage, hypersensitivity reactions such as bronchospasm, elevated transaminase levels, hepatitis, renal failure and nephrotic syndrome; isolated cases of leucopenia, and thrombocytopenia have also been observed.

4.9 Overdose

- **Diclofenac**

Symptoms:
Diclofenac overdose symptoms include headache, motor agitation, muscular spasm, irritability, ataxia, vertigo sensations, and convulsions especially in small children, epigastric pain, nausea, vomiting, haematemesis, diarrhoea, gastrointestinal ulcer, hepatic function disorders and oliguria.

Therapeutic measure:
NSAIDs acute intoxication treatment essentially consists in symptomatic treatment such as:
- As early as possible after (within one hour) ingestion of potentially toxic amount, activated charcoal and gastric lavage should be considered.
- Supportive and symptomatic treatment in case of complications such as hypotonia, renal failure, convulsions, gastrointestinal irritation and respiratory depression.
As NSAIDs are highly bound to plasma proteins and mainly biotransformed, measures for NSAIDs elimination such as accelerated excretion, dialysis or hemoperfusion are ineffective.

- **Paracetamol**

In adults with normal hepatic function, paracetamol toxic dose is 150 mg/kg (in one intake), i.e. around 10 grams for a 70kg adult.
A risk of liver toxicity exists, in particular in elderly people, young children, in case of liver and kidney failure, chronic alcoholism, chronic malnutrition, enzyme inducing agents and very meagre adults (< 50 kg).
It has to be kept in mind that a massive overdose with a glutathione depletion exceeding 70% (which theoretically requires that an adult absorb 15 g paracetamol and a child a dose equal or higher than 150 mg/kg body weight) leads to an increased quantity of reactive metabolite which, as it cannot be detoxified, causes hepatic cytolysis potentially leading to a complete and irreversible necrosis. Paracetamol accumulation due to metabolism impairment has not been observed at therapeutic doses.
Glutathione depletion, which could increase the toxicity risk, does not usually occur.

Symptoms:
Early symptoms, that can occur only 12 hours after ingesting a potentially toxic dose, might include: nausea, vomiting, anorexia, abdominal pain and sweating. Clinical and biological proofs of liver disorder can appear later (48 to 72 hours).

As a consequence, in case of any suspicion of paracetamol overdose, the patient should be immediately hospitalized and serum levels should be determined at the earliest from the 4th hour post-ingestion on.
Values exceeding 200 µg/ml at the 4th hour or 50 µg/ml at the 12th hour let suspect a high risk of hepatic necrosis. The usual liver function tests should be performed early and regularly repeated (every 24 hours).
Treatment:
The overdose treatment in a specialized environment includes administering at the earliest the N-acetylcysteine antidote.
Early treatment can result in a total functional recovery.
N-acetylcysteine proposed posology: initial dose 150 mg/kg in 30 minutes, then 50 mg/kg in 4 hours and 100 mg/kg during the following 16 hours. A close monitoring of hepatic function is recommended (every 24 hours).

5 PHARMACOLOGICAL PROPERTIES

In postoperative pain treatment, the doses of morphinic analgesics can be significantly reduced when SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablet is associated to the treatment.

5.1 Pharmacodynamic properties

Diclofenac is a potent anti-inflammatory with analgesic and antipyretic action. Its analgesic and antipyretic effects are further reinforced by paracetamol. The mode of action can best be understood by looking at each active constituent of SOCOMOL Paracetamol 325 mg & DiclofenacSodium 50 mg Tablets separately.
Diclofenac sodium: It is an NSAID which has been demonstrated to inhibit prostaglandin biosynthesis, thus exerting a pronounced anti-inflammatory, analgesic and antipyretic action.
Paracetamol: The analgesic and antipyretic actions of paracetamol are similar to those of the salicylates. Analgesia is mediated peripherally and also centrally whereas antipyresis is produced by a central action on the hypothalamic regulatory centre.

5.2 Pharmacokinetic properties

Absorption
Diclofenac sodium is well absorbed after oral administration, and peak concentrations are usually attained after 1-4 hours. Absorption occurs more rapidly when ingested on an empty stomach than when administered after a meal.
Paracetamol is rapidly and almost completely absorbed from the Gastrointestinal tract. Both diclofenac sodium and paracetamol in SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablets are well absorbed from the Gastrointestinal tract.

Distribution
Plasma concentrations show a linear relationship with the size of the dose. Doses are maintained at higher levels in the synovial fluid rather than in plasma.
However, paracetamol achieves peak plasma concentration much faster than diclofenac sodium, as the latter is enteric coated. This ensures rapid action and at the same time minimises the chances of gastric irritation.

Metabolism

A large proportion of diclofenac sodium is metabolised in the liver and about 30% of the ingested dose undergoes first pass metabolism.

The complete ingested dose is extensively metabolised in the liver and excreted in the urine as inactive metabolites.

SOCOMOL Paracetamol 325 mg & Diclofenac Sodium 50 mg Tablet is metabolised in the liverand excreted mainly in the urine.

Excretion

Approximately 60% of the dose is excreted through the kidney and the remainder in the faeces, in the form of metabolites. Less than 1% is excreted via the kidneys in an unchanged form. The plasma half-life to the terminal elimination phase is about 1-2 hours. More than 99% is protein bound.

5.3 Preclinical safety data

Not data available.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Maize Starch
Dibasic Calcium Phosphate
P.V.P.K -30
Methyl Paraben
Propyl Paraben
Col Brilliant Blue Supra
Colour Tartrazine Supra
Purified Talcum
Magnesium Stearate
Sodium Starch Glycolate
Sodium Lauryl Sulphate
Purified Water

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

3 years.

6.4 Special precautions for storage

Do not store above 30°C.

Store in the original package.

6.5 Nature and contents of container

1X10 Tablets.

6.6 Special precautions for disposal of a used medicinal product or waste materials derived from such medicinal product and other handling of the product
No special requirements.

7 MARKETING AUTHORISATION HOLDER

Importer
MOREHOPE PHARMA NIGERIA LIMITED
NO. 1 OMOLABAKEADEOTI STREET,
AJAO ESTATE, ISOLO, LAGOS STATE , NIGERIA

Manufacturing Site
MCW HEALTHCARE PVT LTD.
286, 287-A, 287-B, SECTOR-E
INDUSTRIAL AREA SANWAR ROAD,
INDORE, INDIA.

8 MARKETING AUTHORISATION NUMBER

NAFDAC Registration Number B4-9193