Summary of Product Characteristics for Pharmaceutical Products

1. Name of the medicinal product

Synflex 550mg fIlm-coated tablet.

2. Qualitative and quantitative composition

Each film coated tablet contains 550 mg Naproxen sodium

Excipient with known effect: sodium 2,17 mmol (50 mg) per tablet.

For a full list of excipients, see section 6.1.

3. Pharmaceutical form

Film-coated tablet.

Blue colored oblong shaped, film coated tablet engraved 550 on one side and plain on other side

4. Clinical particulars

4.1 Therapeutic indications

Synflex is indicated for the treatment of rheumatoid arthritis, osteoarthrosis (degenerative arthritis), ankylosing spondylitis, juvenile rheumatoid arthritis, acute gout, and acute musculoskeletal disorders (such as sprains, strains, direct trauma, lumbosacral pain, cervical spondylitis, tenosynovitis and fibrositis), and in management of pain and primary dysmenorrhea.

4.2 Posology and method of administration

Posology:

General Dosing Instructions Carefully consider the potential benefits and risks of Synflex and other treatment options before deciding to use Synflex. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals. After observing the response to initial therapy with Synflex, the dose and frequency should be adjusted to suit an individual patient's needs Naproxen-containing products should not be used concomitantly since they all circulate in the plasma as the naproxen anion.

Rheumatoid Arthritis, Osteoarthritis and Ankylosing Spondylitis

The recommended dose of Synflex is 275 mg (one half tablet) twice daily. Alternatively,a single dose of 550 mg (naproxen 500 mg with 50 mg sodium) is given.

During long-term administration, the dose of naproxen may be adjusted up or down depending on the clinical response of the patient. A lower daily dose may suffice for long-term administration. The morning and evening doses do not have to be equal in size and administration of the drug more frequently than twice daily does not generally make a difference in response. In patients who tolerate lower doses well, the dose may be increased to naproxen 1500 mg/day for limited periods of

up to 6 months when a higher level of anti-inflammatory/analgesic activity is required in patients who;

1. Report severe night-time pain and/or morning stiffness.
2. Are being switched to naproxen from a high dose of another antirheumatic compound.
3. Have Osteoarthrosis where pain is the predominant symptom.

When treating such patients with naproxen 1500 mg/day, the physician should observe sufficient increased clinical benefits to offset the potential increased risk.

Acute Gout

Synflex may also be used at a starting dose of 825 mg (one- and one-half tablets) followed by 275 mg (one-half tablet) every 8 hours.

Management of Pain, Primary Dysmenorrhea, and Acute Tendonitis and Bursitis

The recommended starting dose of Synflex (naproxen sodium) tablets is 550 mg followed by 550 mg every 12 hours or 275 mg (one half of a 550 mg tablet) every 6 to 8 hours as required. The initial total daily dose should not exceed 1375 mg (two and one-half tablets) of naproxen sodium. Thereafter, the total daily dose should not exceed 1100 mg of naproxen sodium. Because the sodium salt of naproxen is more rapidly absorbed, Synflex is recommended for the management of acute painful conditions when prompt onset of pain relief is desired

Dysmenorrhea

The recommended initial dose is 550 mg of naproxen sodium taken as a single dose, followed by 275 mg of naproxen sodium every 6-8 hours if necessary.

Migraine headaches

The recommended initial dose is 825 mg of naproxen sodium taken as a single dose at the first symptoms, followed by 275 mg of naproxen sodium after half an hour.

Menorrhagia

The recommended first day daily dose is 825-1375 mg of naproxen sodium, divided into two doses, followed by a daily dose of 550-1100 mg of naproxen sodium for a maximum period of four days.

Special populations

Elderly

The dose should be reduced in elderly patients and the lowest effective dose should be used for the shortest possible duration.

Patients with renal and/or hepatic insufficiency

In patients with mild or moderate renal or hepatic failure the dose should be reduced, and the lowest effective dose should be used for the shortest possible duration. This medicinal product is not recommended in patients with a baseline creatinine clearance lower than 30 ml/min, since an accumulation of naproxen metabolites has been observed in patients with severe kidney failure and patients in dialysis.

Pediatric population

Synflex tablets are not recommended for use in children and adolescents under 16 years of age.
Method of administration This medicinal product is administered orally. The tablets should be swollen whole with some liquid and preferably during or after meals.

4.3 Contraindications

Hypersensitivity to naproxen, naproxen sodium, or to any of the excipients listed in section 6.1.
Active or history of peptic ulceration or active gastrointestinal bleeding (two or more distinct episodes of proven ulceration or bleeding).
History of gastrointestinal bleeding or perforation related to previous NSAIDs therapy.
Since the potential exists for cross-sensitivity reactions, naproxen should not be given to patients in whom aspirin, ibuprofen or other non-steroidal anti-inflammatory/analgesic drugs induce the syndrome of asthma, rhinitis, nasal polyps or urticaria. These reactions have the potential of being fatal. Severe anaphylactic-like reactions to naproxen have been reported in such patients.
Severe heart failure, hepatic failure and renal failure.
Naproxen is contraindicated during the last trimester of pregnancy (see section 4.6).

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 symptoms (see section 4.2 and GI and cardiovascular risks below). Patients treated with NSAIDs long-term should undergo regular medical supervision to monitor for adverse events.

Elderly

The elderly and/or debilitated patients are particularly susceptible to the adverse effects of NSAIDs especially gastrointestinal bleeding and perforation, which may be fatal. Prolonged use of NSAIDs in these patients is not recommended. Where prolonged therapy is required, patients should be reviewed regularly.
The antipyretic and anti-inflammatory activities of naproxen may reduce fever and inflammation, thereby diminishing their utility as diagnostic signs.

Respiratory disorders

Bronchospasm may be precipitated in patients suffering from, or with a history of, bronchial asthma or allergic disease.

Hepatic effects

As with other non-steroidal anti-inflammatory drugs, elevations of one or more liver function tests may occur. Hepatic abnormalities may be the result of hypersensitivity rather than direct toxicity. Severe hepatic reactions, including jaundice and hepatitis (some cases of hepatitis have been fatal) have been reported with this drug as with other non-steroidal anti-inflammatory drugs. Cross reactivity has been reported.

Naproxen decreases platelet aggregation and prolongs bleeding time. This effect should be kept in mind when bleeding times are determined. Although sodium retention has not been reported in metabolic studies, it is possible that patients with questionable or compromised cardiac function may be at a greater risk when taking naproxen.

Gastrointestinal bleeding, ulceration and perforation

Gastrointestinal 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. 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 section 4.5).

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

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

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

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).

Renal effects

There have been reports of impaired renal function, renal failure, acute interstitial nephritis, haematuria proteinuria, renal papillary necrosis and occasionally nephritic syndrome associated with naproxen.

Renal failure linked to reduced prostaglandin production

The administration of an NSAID may cause a dose dependent reduction in prostaglandin formation and precipitate renal failure. Patients at greatest risk of this reaction are those with impaired renal function, cardiac impairment, liver dysfunction, those taking diuretics, angiotensin converting enzyme inhibitors, angiotensin-II receptor antagonists and the older people. Renal function should be monitored in these patients (see also section 4.3).

Use in patients with impaired renal function

As naproxen is eliminated to a large extent (95%) by urinary excretion via glomerular filtration, it should be used with great caution in patients with impaired renal function and the monitoring of serum creatinine and/or creatinine clearance is advised and patients should be adequately hydrated. Naproxen is contraindicated in patients having a

baseline creatinine clearance of less than 30 ml/minute (see section 4.3).
Haemodialysis does not decrease the plasma concentration of naproxen because of the high degree of protein binding.
Certain patients, specifically those whose renal blood flow is compromised, such as in extracellular volume depletion, cirrhosis of the liver, sodium restriction, congestive heart failure, and pre-existing renal disease, should have renal function assessed before and during naproxen therapy. Some elderly people in whom impaired renal function may be expected, as well as patients using diuretics, may also fall within this category. A reduction in daily dosage should be considered to avoid the possibility of excessive accumulation of naproxen metabolites in these patients.

Use in patients with impaired liver function

Chronic alcoholic liver disease and probably also other forms of cirrhosis reduce the total plasma concentration of naproxen, but the plasma concentration of unbound naproxen is increased. The implication of this finding for naproxen dosing is unknown but it is prudent to use the lowest effective dose.

Haematological

Patients who have coagulation disorders or are receiving drug therapy that interferes with haemostasis should be carefully observed if naproxen-containing products are administered.
Patients at high risk of bleeding or those on full anti-coagulation therapy (e.g. dicoumarol derivatives) may be at increased risk of bleeding if given naproxen containing products concurrently.

Anaphylactic (anaphylactoid) reactions

Hypersensitivity reactions may occur in susceptible individuals. Anaphylactic (anaphylactoid) reactions may occur both in patients with and without a history of hypersensitivity or exposure to aspirin, other non-steroidal anti-inflammatory drugs or naproxen-containing products. They may also occur in individuals with a history of angio-oedema, bronchospastic reactivity (e.g. asthma), rhinitis and nasal polyps.
Anaphylactoid reactions, like anaphylaxis, may have a fatal outcome.

Steroids

If steroid dosage is reduced or eliminated during therapy, the steroid dosage should be reduced slowly and the patients must be observed closely for any evidence of adverse effects, including adrenal insufficiency and exacerbation of symptoms of arthritis.

Ocular effects

Studies have not shown changes in the eye attributable to naproxen administration. In rare cases, adverse ocular disorders including papillitis, retrobulbar optic neuritis and papilloedema, have been reported in users of NSAIDs including naproxen, although a cause-and-effect relationship cannot be established; accordingly, patients who develop visual disturbances during treatment with naproxen-containing products should have an ophthalmological examination**.**

Cardiovascular and cerebrovascular effects

Appropriate monitoring and advice are required for patients with a history of hypertension and/or mild to moderate congestive heart failure as fluid retention and oedema have been reported in association with NSAID therapy.

Clinical trial and epidemiological data suggest that use of coxibs and 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). Although data suggest that the use of naproxen (1000 mg daily) may be associated with a lower risk, some risk cannot be excluded.

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

SLE and mixed connective tissue disease:

In patients with systemic lupus erythematosus (SLE) and mixed connective tissue disorders there may be an increased risk of aseptic meningitis (see section 4.8).

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 reactions occurring in the majority of cases within the first month of treatment. Naproxen should be discontinued at the first appearance of skin rash, mucosal lesions, or any other sign of hypersensitivity.

Combination with other NSAIDs

The combination of naproxen-containing products and other NSAIDs, including cyclooxygenase-2 selective inhibitors, is not recommended, because of the cumulative risks of inducing serious NSAID-related adverse events.

4.5 Interaction with other medicinal products and other forms of interaction

Antacid or colestyramine: Concomitant administration of antacid or colestyramine can delay the absorption of naproxen but does not affect its extent.

***With food*:** Concomitant administration of food can delay the absorption of naproxen, but does not affect its extent.

Anti-coagulants: It is considered unsafe to take NSAIDs in combination with anticoagulants such as warfarin or heparin unless under direct medical supervision, as NSAIDs may enhance the effects of anti-coagulants (see section 4.4).

Other analgesics including cyclooxygenase-2 selective inhibitors: Avoid concomitant use of two or more NSAIDs (including

aspirin) as this may increase the risks of adverse effects (see section 4.4).

Acetylsalicylic acid: Clinical pharmacodynamic data suggest that concomitant naproxen usage for more than one day consecutively may inhibit the effect of low-dose acetylsalicylic acid on platelet activity and this inhibition may persist for up to several days after stopping naproxen therapy. The clinical relevance of this interaction is not known**.**

Effect of high plasma protein binding of naproxen on other drugs: Due to the high plasma protein binding of naproxen, patients simultaneously receiving hydantoins, anticoagulants, other NSAIDs, aspirin or a highly protein bound sulfonamide should be observed for signs of over dosage of these drugs. Patients simultaneously receiving naproxen and a hydantoin, sulfonamide or sulfonylurea should be observed for adjustment of dose if required. No interactions have been observed in clinical studies with naproxen and anticoagulants or sulfonylureas, but caution is nevertheless advised since interaction has been seen with other non-steroidal agents of this class.

Diuretics: Caution is advised when naproxen is co-administered with diuretics as there can be a decreased diuretic effect. The natriuretic effect of furosemide has been reported to be inhibited by some drugs of this class. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

Lithium: Inhibition of renal lithium clearance leading to increases in plasma lithium concentrations has also been reported.

Anti-hypertensives: Naproxen and other non-steroidal anti-inflammatory drugs can reduce the anti-hypertensive effect of anti-hypertensives. Concomitant use of NSAIDs with ACE inhibitors or angiotensin-II receptor antagonists may increase the risk of renal impairment, especially in patients with pre-existing poor renal function (See Section 4.4).

Probenecid**:** Probenecid given concurrently increases naproxen plasma levels and extends its plasma half-life considerably.

Methotrexate: Caution is advised where methotrexate is administered concurrently because of possible enhancement of its toxicity, since naproxen, among other non-steroidal anti-inflammatory drugs, has been reported to reduce the tubular secretion of methotrexate in an animal model.

Cardiac glycosides: NSAIDs may exacerbate cardiac failure, reduce GFR and increase plasma cardiac glycoside levels when co-administered with cardiac glycosides.

Ciclosporin: As with all NSAIDs caution is advised when ciclosporin is co-administered because of the increased risk of nephrotoxicity.

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

Corticosteroids**:** As with all NSAIDs, caution should be taken when co-administering with corticosteroids because of the increased risk of gastrointestinal ulceration or bleeding.

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

Anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs): There is an increased risk of gastrointestinal bleeding (see section 4.4) when anti-platelet agents and selective serotonin reuptake inhibitors (SSRIs) are combined with NSAIDs.

Tacrolimus: There is a possible risk of nephrotoxicity when NSAIDs are given with tacrolimus.

Zidovudine: There is an 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 zidovudine and ibuprofen.

Interference with laboratory tests: It is suggested that naproxen therapy be temporarily discontinued 48 hours before adrenal function tests are performed because naproxen may artifactually interfere with some tests for 17-ketogenic steroids. Similarly, naproxen may interfere with some assays of urinary 5-hydroxyindoleacetic acid**.**

4.6 Fertility, pregnancy, and lactation

Pregnancy:

Congenital abnormalities have been reported in association with NSAID administration in man; however, these are low in frequency and do not appear to follow any discernible pattern. As with other drugs of this type, naproxen produces delay in parturition in animals and also affects the human foetal cardiovascular system (closure of ductus arteriosus). Use of naproxen in the last trimester of pregnancy is contraindicated (see section 4.3). From the 20th week of pregnancy onward, naproxen use may cause oligohydramnios resulting from foetal renal dysfunction. This may occur shortly after treatment initiation and is usually reversible upon discontinuation. In addition, there have been reports of ductus arteriosus constriction following treatment in the second trimester, most of which resolved after treatment cessation. Therefore, during the first and second trimester of pregnancy, naproxen should not be given unless clearly necessary. If naproxen is used by a woman attempting to conceive, or during the first and second trimester of pregnancy, the dose should be kept as low and duration of treatment as short as possible. Antenatal monitoring for oligohydramnios and ductus arteriosus constriction should be considered after exposure to naproxen for several days from gestational week 20 onward. naproxen should be discontinued if oligohydramnios or ductus arteriosus constriction are found.

During the third trimester of pregnancy, all prostaglandin synthesis inhibitors may expose the foetus to:

- cardiopulmonary toxicity (premature constriction/closure of the ductus arteriosus and pulmonary hypertension);
- renal dysfunction (see above);

the mother and the neonate, at the end of pregnancy, to:
- possible prolongation of bleeding time, an anti-aggregating effect which may occur even at very low doses;
- inhibition of uterine contractions resulting in delayed or prolonged labour.
Consequently, naproxen is contraindicated during the third trimester of pregnancy (see sections 4.3 and 5.3).

Labour and delivery

Naproxen containing products are not recommended in labour and delivery because, through its prostaglandin synthesis inhibitory effect, naproxen may adversely affect foetal circulation and inhibit contractions, with an increased bleeding tendency in both mother and child.

Breast-feeding

Naproxen has been found in the milk of lactating women. The use of naproxen should be avoided in patients who are breast-feeding.

Fertility:

The use of naproxen, as with any drug known to inhibit cyclooxygenase/prostaglandin synthesis may impair fertility and is not recommended in women attempting to conceive. In women who have difficulty conceiving or are undergoing investigation of infertility, withdrawal of naproxen should be considered.

4.7 Effects on ability to drive and use machines.

Some patients may experience drowsiness, dizziness, vertigo, insomnia, fatigue, visual disturbances or depression with the use of naproxen. If patients experience these or similar undesirable effects, they should not drive or operate machinery.

4.8 Undesirable effects

The following adverse events have been reported with NSAIDs and with naproxen.

Gastrointestinal disorders: The most commonly observed adverse events are gastrointestinal in nature. Heartburn, nausea, vomiting, constipation, diarrhoea, flatulence, dyspepsia, abdominal discomfort and epigastric distress. More serious reactions which may occur are gastro-intestinal bleeding, which is sometimes fatal, particularly in older people (see section 4.4), inflammation, ulceration, perforation, and obstruction of the upper and lower gastrointestinal tract, melaena, haematemesis, stomatitis, exacerbation of ulcerative colitis and Crohn's disease (see section 4.4), oesophagitis, gastritis and pancreatitis.

Blood and lymphatic system disorders: Neutropenia, thrombocytopenia, granulocytopenia including agranulocytosis, eosinophilia, leucopenia, aplastic anaemia and haemolytic anaemia.

***Immune system disorders*:** Hypersensitivity reactions have been reported following treatment with NSAIDs in patients with, or without, a history of previous hypersensitivity reactions to NSAIDs. These may consist of (a) non-specific allergic reactions 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, angio-oedema and more rarely exfoliative and bullous dermatoses (including epidermal necrolysis and erythema multiforme).

***Metabolic and nutrition disorders*:** hyperkalaemia. *Psychiatric disorders*: Insomnia, dream abnormalities, depression, confusion and hallucinations.

Nervous system disorders: Convulsions, dizziness, headache, lightheadedness, drowsiness, paraesthesia, retrobulbar optic neuritis, inability to concentrate and cognitive dysfunction have been reported. Aseptic meningitis (especially in patients with existing auto-immune disorders, such as systemic lupus erythematosus, mixed connective tissue disease), with symptoms such as stiff neck, headache, nausea, vomiting, fever or disorientation (see section 4.4).

Eye Disorders: Visual disturbances, corneal opacity, papillitis and papilloedema.

Ear and Labyrinth disorders: Tinnitus, hearing disturbances including impairment and vertigo.

Cardiac disorders: Oedema, palpitations, cardiac failure and congestive heart failure have been reported.

Clinical trial and epidemiological data suggest that use of coxibs and 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) (see section 4.4).

Vascular disorders: Hypertension, vasculitis.

Respiratory, thoracic and mediastinal disorders: Dyspnoea, asthma, eosinophilic pneumonitis and pulmonary oedema.

***Hepatobiliary disorders*:** Jaundice, fatal hepatitis and abnormal liver function tests.

***Skin and subcutaneous tissue disorders**:* Skin rashes including fixed drug eruption, itching (pruritus), urticaria, ecchymoses, purpura, sweating. Alopecia, erythema multiforme, Stevens Johnson syndrome, erythema nodosum, lichen planus, pustular reaction, SLE, epidermal necrolysis, very rarely toxic epidermal necrolysis, photosensitivity reactions (including cases in which skin resembles porphyria cutanea tarda “pseudoporphyria”) or epidermolysis bullosa-like reactions which may occur rarely.

If skin fragility, blistering or other symptoms suggestive of pseudoporphyria occur, treatment should be discontinued and the patient monitored.

***Musculoskeletal and connective tissue disorders*:** Myalgia and muscle weakness.

Renal and urinary disorders: Including, but not limited to, glomerular nephritis, interstitial nephritis, nephrotic syndrome, haematuria, raised serum creatinine, renal papillary necrosis and renal failure.

Reproductive system and breast disorders: Female infertility.

General disorders and administration site conditions: Thirst, pyrexia, fatigue and malaise.

Reporting of suspected adverse reactions: Healthcare professionals are asked to report any suspected adverse reactions via pharmacy and poisons board, Pharmacovigilance Electronic Reporting System (PvERS) https://pv.pharmacyboardkenya.org

4.9 Overdose

Symptoms

Symptoms include headache, heartburn, nausea, vomiting, epigastric pain, gastrointestinal bleeding, rarely diarrhoea, disorientation, excitation, drowsiness, dizziness, tinnitus, fainting. In cases of significant poisoning, acute renal failure and liver damage are possible. Respiratory depression and coma may occur after the ingestion of NSAIDs but are rare.

In one case of naproxen overdose, transient-prolongation of the prothrombin time due to hypothrombinaemia may have been due to selective inhibition of the synthesis of vitamin-K dependent clotting factors.

A few patients have experienced seizures, but it is not known whether these were naproxen-related or not. It is not known what dose of the drug would be life-threatening.

Management

Patients should be treated symptomatically as required. Within one hour of ingestion of a potentially toxic amount, activated charcoal should be considered. Alternatively, in adults, gastric lavage should be considered within one hour of ingestion of a potentially life-threatening overdose.

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 prolonged convulsions should be treated with intravenous diazepam. Other measures may be indicated by the patient's clinical condition.

Haemodialysis does not decrease the plasma concentration of naproxen because of the high degree of its protein binding. However, haemodialysis may still be appropriate in a patient with renal failure who has taken naproxen.

5. Pharmacological properties

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Anti-inflammatory and antirheumatic products, nonsteroids. ATC code: M01AE02

Naproxen is a non-steroidal anti-inflammatory analgesic compound with antipyretic properties as has been demonstrated in classical animal test systems. Naproxen exhibits its anti-inflammatory effect even in adrenalectomised animals, indicating that its action is not mediated through the pituitary-adrenal axis.

Naproxen inhibits prostaglandin synthetase (as do other NSAIDs). As with other NSAIDs, however, the exact mechanism of its anti-inflammatory action is not known.

5.2 Pharmacokinetic properties

Naproxen is completely absorbed from the gastro-intestinal tract, and peak plasma levels are reached in 2 to 4 hours. Naproxen is present in the blood mainly as unchanged drug, extensively bound to plasma proteins. The plasma half-life is between 12 and 15 hours, enabling a steady state to be achieved within 3 days of initiation of therapy on a twice daily dose regimen. The degree of absorption is not significantly affected by either foods or most antacids.
Excretion is almost entirely via the urine, mainly as conjugated naproxen, with some unchanged drug. Metabolism in children is similar to that in adults. Chronic alcoholic liver disease reduces the total plasma concentration of naproxen but the concentration of unbound naproxen increases. In the elderly, the unbound plasma concentration of naproxen is increased although total plasma concentration is unchanged**.**

5.3 Preclinical safety data

In animals, the administration of a prostaglandin synthesis inhibitor has shown an increase in pre- and post-implantation losses and embryo-foetal mortality. Furthermore, an increase in the incidence of various malformations, including cardiovascular malformations, has been reported in animals that received a prostaglandin synthesis inhibitor during the organogenesis period.

6. Pharmaceutical particulars

6.1 List of excipients

Synflex 550mg Tablets:
Tablet core:
Microcrystalline Cellulose PH-102
Povidone K-30
Talc
Magnesium Stearate
Coating material
Opadry II Blue 85 F205034

6.2 Incompatibilities

Not Applicable

6.3 Shelf life

36 months

6.4 Special precautions for storage:

Do not store above 30°C.
Keep the blister in the outer carton in order to protect from light.

6.5 Nature and contents of container

Commercial Presentation: 20's and 30's
3 x 10's (10 tablets are packed in one Alu-Alu blister and 3 such Alu-Alu blisters are kept in one cartonalong with package insert).

6.6 Special precautions for disposal and other handling:

No special requirements.

Any unused medicinal product or waste material should be disposed of in accordance with local requirements.

7. Marketing authorization holder and manufacturing site addresses

Marketing authorization holder:

Company Name:	CINTANA HEALTHCARE LTD
Address:	P. O. BOX 45214 – 00100 NAIROBI
Country:	KENYA
Telephone:	+254733338478
E-Mail:	cintanahealthcare@gmail.com

Manufacturing site address:

Company Name:	Martin Dow Limited.
Address:	Plot # 37, Sector 19, Korangi Industrial Area, Karachi-74900, Pakistan.Country: Pakistan
Telephone:	+92-21-111-111-637 (Ext: 267)
E-Mail:	ahsan.raees@martindow.com

8. Marketing authorization number

CTD9846

9. Date of first registration

10/02/2023

10. Date of revision of the text:

14/09/2023

11. Dosimetry:

Not Applicable

12. Instructions for Preparation of Radiopharmaceuticals:

Not Applicable