

## Part II

### Summary of Product Characteristics

#### 1 NAME OF THE MEDICINAL PRODUCT

Surgam 300 mg Tablets

#### 2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 300 mg of tiaprofenic acid.

For excipients, see 6.1.

#### 3 PHARMACEUTICAL FORM

Tablets

White to cream-white, round, biconvex tablets with a breakline imprinted 'Surgam' and '300' on either side of the breakline and with the Roussel logo on the reverse side.

#### 4 CLINICAL PARTICULARS

##### 4.1 Therapeutic Indications

As an anti-inflammatory agent in the symptomatic management of rheumatoid arthritis; osteoarthritis; ankylosing spondylitis; low back pain; musculo-skeletal disorders such as fibrositis, capsulitis, epicondylitis and other sort tissue inflammatory conditions; sprains and strains, post-operative inflammation and pain, and other soft-tissue injuries.

##### 4.2 Posology and method of administration

Route of administration: Oral.

Adults: The usual total daily does is 600 mg divided in doses.

Children: There are insufficient data to recommend the use of Surgam in children.

Elderly: As for adults (see Section 4.4 Warning and Precaution). NSAIDs should be used with particular caution in older patients who generally are more prone to adverse reactions. Continuous use over prolonged periods is not recommended.

In cases of renal, cardiac or hepatic impairment, the does should be kept as low as possible. It is suggested that in such cases the dosage be reduced to 200mg twice daily.

Treatment should be reviewed at regular intervals and discontinued if no benefit is seen or if intolerance occurs.

##### 4.3 Contraindications

- Active gastroduodenal ulceration, history of gastroduodenal ulceration.
- Active bladder or prostatic disease or symptoms.
- History of recurrent urinary tract disorders.
- Hypersensitivity (e.g. bronchospasm, rhinitis, urticaria) to tiaprofenic acid, or any of the ingredients in the drug, aspirin or other NSAIDs.
- Severe renal or hepatic insufficiency.

- History of asthma, rhinitis or urticaria, whether or not induced by aspirin or other NSAIDs.
- Pregnancy (see section 4.6 Pregnancy and Lactation).

#### 4.4 Special warnings and precautions for use

Undesirable effects may be reduced by using the minimum effective dose for the shortest possible duration. Patients treated with NSAIDs long term should undergo regular medical supervision to monitor for adverse events.

As with other NSAIDs, Surgam should be used with care in the elderly and patients with a renal, cardiac or hepatic insufficiency, as the use of these drugs may result in the deterioration of renal function. The dose should be kept as low as possible and renal function should be monitored.

Patients over the age of 60 years for whom therapy with non-steroidal anti-inflammatory agents is intended should have an assessment of renal function prior to initiation of treatment. Patients taking Surgam for over a year in whom renal function has been monitored have shown no impairment in function. However, as with other non-steroidal anti-inflammatory agents, patients on prolonged therapy of more than one year should be regularly monitored as a precautionary measure. In the management of elderly patients with arthroses (e.g. osteoarthritis) continuous use over prolonged period of any non-steroidal anti-inflammatory drug should be avoided. Renal functions should also be monitored in patients on diuretics. Tiaprofenic acid should be used with caution in patients with arterial hypertension.

Tiaprofenic acid can cause cystitis which may become severe if the treatment is continued after the onset of urinary symptoms. If urinary symptoms such as frequency, urgency, dysuria, nocturia or haematuria occur, tiaprofenic acid should be stopped immediately, and urinalysis and urine culture performed. Patients should be warned about the onset of urinary symptoms which may suggest cystitis and advised to stop taking the drug and seek medical advice if these occur.

As NSAIDs can interfere with platelet function, they should be used with caution in patients with intracranial haemorrhage and bleeding diathesis.

Because of the risk of serious gastrointestinal side effects, especially in patients on anticoagulant treatment, special attention should be paid to the appearance of any gastrointestinal symptoms; treatment should be stopped immediately in the event of gastrointestinal haemorrhage.

Surgam should be used with caution in patients with history of peptic ulceration or inflammatory bowel disease.

There is a risk of cross-sensitivity among aspirin and NSAIDs, including the group to which tiaprofenic acid belongs. These pseudo-allergic reactions may include rash, urticaria, angio-oedema or more potentially severe manifestations (e.g. laryngeal oedema, bronchoconstriction and shock). The risk of pseudo-allergic reactions is greater in patients with recurrent rhino-sinusitis, nasal polyposis or chronic urticaria. Asthmatic patients are particularly at risk of dangerous reactions. Therefore tiaprofenic acid must not be administered to patients with a history of asthma (see section 4.3 Contraindications).

#### 4.5 Interaction with other medicinal products and other forms of interaction

Since Surgam is highly protein-bound, it is not recommended for co-administration with other highly protein bound drugs. Modification of the dosage may be necessary with hypoglycaemic agents, phentoin and diuretics. With oral hypoglycaemic agents, an inhibition of metabolism of sulphonylurea drugs, prolonged half-life and increased risk of hypoglycaemia has been reported.

It is considered unsafe to take NSAIDs in combination with warfarin or heparin unless under direct medical supervision.

Concomitant use of Surgam with corticosteroids and other NSAIDs (including high doses salicylates) should be avoided due to an increased risk of gastrointestinal disorder such as bleeding.

Caution should be exercised when Surgam is administered with cardiac glycosides and sulphonamides. With cardiac glycosides, NSAIDs may exacerbate cardiac failure, reduce GFR and increase cardiac glycoside levels.

Concomitant use of Surgam with methotrexate causes a decreased elimination of methotrexate. Concomitant use with high dose methotrexate should be avoided. Use with caution with low dose methotrexate.

The use of aspirin and other NSAIDs should be avoided for at least 8-12 days after mifepristone.

NSAIDs have been reported to increase steady state plasma levels of lithium and it is, therefore, recommended that these levels are monitored in patients receiving Surgam therapy.

NSAIDs may cause some sodium and fluid retention and may interfere with the natriuretic action of diuretic agents and reduce the effects of these. Diuretics can increase the risk of nephrotoxicity of NSAIDs.

NSAIDs also interact with anti-hypertensive drugs (e.g. beta-blockers, ACE inhibitors and angiotensin II receptor antagonists) which can cause a reduced anti-hypertensive effect. There may also be an increased risk of renal impairment and an increased risk of hyperkalaemia. This should be borne in mind in patients with incipient or actual congestive heart failure and/or hypertension.

The risk of nephrotoxicity may be increased if NSAIDs are given with cyclosporins. Convulsions may occur due to an interaction with quinolone antibiotics.

Care should also be taken if Surgam is concomitantly administered with aminoglycosides or probenecid. Aminoglycosides may interact with NSAIDs to cause a reduction in renal function in susceptible individuals, decreased elimination of aminoglycoside and increased plasma concentrations. A reduction in metabolism and elimination of NSAID and metabolites has been observed with probenecid.

## 4.6 Pregnancy and lactation

**Pregnancy:** Surgam should not be used in pregnancy unless considered essential by the physician. Tiaprofenic acid crosses the placental barrier and should not be prescribed during the first trimester, even though animal studies have not revealed a teratogenic effect. Tiaprofenic acid must not be prescribed during the final trimester, because of the possible risk of delayed parturition, premature closure of the ductus arteriosus and development of a bleeding tendency or renal risk in neonates.

**Lactation:** Since tiaprofenic acid is excreted in human breast milk, breast feeding or treatment of the mother therefore should be stopped as necessary.

## 4.7 Effects on ability to drive and use machines

None known.

## 4.8 Undesirable effects

**Gastro-intestinal tract:** Reported reactions include dyspepsia, nausea, vomiting, abdominal pain, anorexia, indigestion, heartburn, constipation, gastritis, flatulence and diarrhoea. In common with other NSAIDs, gastroduodenal ulcers, perforation and overt or occult gastrointestinal haemorrhage resulted in anaemia have occasionally been reported and in exceptional cases may have been associated with fatalities.

**Muco-cutaneous:** Rash, urticaria, pruritis, purpura, alopecia and very rarely, erythema multiforme and bullous eruptions (Stevens Johnson Syndrome or, exceptionally, toxic epidermal necrolysis) have been reported. Very rarely, photosensitivity reactions and aphthous stomatitis.

**Hypersensitivity reactions:** Asthmatic attacks, especially in subjects allergic to aspirin and other NSAIDs, angio-oedema. Anaphylactic shock has also been reported.

**Haematological:** Thrombocytopenia, prolongation of bleeding time may occur.

Nervous system: Headaches, dizziness, tinnitus and drowsiness.

Urinary system: Bladder pain, dysuria, frequency and cystitis have been reported with tiaprofenic acid and other NSAIDs. On the basis of spontaneous reports, tiaprofenic acid appears to have a greater propensity than other non-steroidal anti-inflammatory drugs to cause urinary disorders.

Although generally reversible, in some cases where tiaprofenic acid has continued after the onset of urinary symptoms and an association with tiaprofenic acid not recognised, serious consequences requiring surgical intervention have resulted. Therefore, treatment with tiaprofenic acid should be discontinued immediately if urinary disorders develop.

Renal: Sodium and water retention (see Section 4.4 Special Warnings and Precautions).

Non-steroidal anti-inflammatory drugs have been reported to cause nephrotoxicity in various forms. As with other NSAIDs isolated case of acute interstitial nephritis, nephrotic syndrome and renal failure have also been reported with tiaprofenic acid.

Hepatic: Liver test abnormalities.

## 4.9 Overdose

In the event of overdosage with Surgam, supportive and symptomatic therapy is indicated.

## 5 PHARMACOLOGICAL PROPERTIES

### 5.1 Pharmacodynamic properties

Non-steroidal anti inflammatory drug.

### 5.2 Pharmacokinetic properties

Single dose studies: Following oral administration (max at 90 mins). Plasma level zero at 24 hours.  $t_{1/2} = 1.5$  to 2 hours.

Repeat dose studies: Surgam is rapidly eliminated and there is no accumulation after repeated doses of 600mg/day in divided doses. Steady state after first day. No impairment of absorption in patients with RA undergoing long term therapy. There is no evidence of different pharmacokinetics in the elderly.

Protein binding = 97 – 98%.

Plasma clearance = 6 litres/hour.

Elimination = 60% in urine remainder in bile.

Metabolites = there are two main metabolites which account for about 10% of urinary excretion and have low pharmacological activity. The parent compound is excreted mostly in the form of acylglucuronide.

### 5.3 Preclinical safety data

Not applicable.

## 6 PHARMACEUTICAL PARTICULARS

### 6.1 List of excipients

Maize starch  
Pluronic F68 (Poloxamer 188)

Magnesium stearate  
Talc

## **6.2 Incompatibilities**

Not applicable.

## **6.3 Shelf Life**

5 years.

## **6.4 Special precautions for storage**

Do not store above 25°C.

Bottles – Store in the original container.

Blister packs – Keep blister in the outer carton.

## **6.5 Nature and contents of container**

Polyethylene bottles with screw cap, amber glass bottles with polyethylene cap or blister packs sealed with aluminium foil in a cardboard carton in packs of 10, 12, 14, 20, 28, 30, 56 or 60.

Not all pack sizes may be marketed.

## **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**

Sanofi-aventis Ireland Ltd.  
Citywest Business Campus  
Dublin 24

## **8 MARKETING AUTHORISATION NUMBER**

PA 540/75/3

## **9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**

Date of first authorisation: 29 April 1982

Date of last renewal: 26 August 2004

## **10 DATE OF REVISION OF THE TEXT**

October 2006