APPROVED PROFESSIONAL INFORMATION

SCHEDULING STATUS: S4

PROPRIETARY NAME (AND DOSAGE FORM):

SUROGRAN 50 mg (tablet)

SUROGRAN 100 mg (tablet)

COMPOSITION:

SUROGRAN 50 mg: Each uncoated tablet contains Sumatriptan Succinate equivalent to Sumatriptan Anhydrous 50 mg.

SUROGRAN 100 mg: Each uncoated tablet contains Sumatriptan Succinate equivalent to Sumatriptan Anhydrous 100 mg.

PHARMACOLOGICAL CLASSIFICATION:

A 7.3 Vascular medicines, Migraine preparations.

PHARMACOLOGICAL ACTION:

Sumatriptan is a selective 5-hydroxytryptamine, ($5HT_1$) receptor agonist. This receptor is found mainly in cranial blood vessels and in animals sumatriptan selectively constricts the carotid arterial circulation, which supplies blood to the extracranial and intracranial tissues such as the meninges.

Pharmacokinetics:

Absorption is variable and maximum concentration occurs at 0,5 to 4 hours after oral administration. Mean absolute oral bioavailability is 11-22 % partly due to pre-systemic metabolism and partly due to incomplete absorption.

Plasma protein binding is low (14-21 %), mean volume of distribution is 170 litres. 80 % of the total clearance is eliminated primarily by oxidative metabolism. Indole acetic acid analogue, the major metabolite which is an active of sumatriptan, is mainly excreted in the urine where it is present as a free acid and the glucuronide conjugate.

The pharmacokinetics of oral sumatriptan do not appear to be significantly affected by migraine attacks.

INDICATIONS:

SUROGRAN is indicated for the acute relief of migraine attacks with or without aura.

CONTRA-INDICATIONS:

SUROGRAN is contra-indicated in patients with hypersensitivity to any component of the preparation.

Following administration of **SUROGRAN** patients with known hypersensitivity to sulphonamides can experience an allergic reaction. Hypersensitivity reactions may range from cutaneous hypersensitivity to anaphylaxis.

SUROGRAN should not be used in patients who have had a myocardial infarction, ischaemic heart disease, Prinzmetal's angina/coronary vasospasm or ischaemic cerebro-vascular disease.

SUROGRAN is not recommended in patients with uncontrolled hypertension. The concomitant use of **SUROGRAN** and ergotamine containing preparations is contra-indicated.

Concurrent administration of monoamine oxidase inhibitors or use within two weeks of discontinuation of MAOI therapy is contra-indicated.

SUROGRAN should not be administered to patients with severe hepatic impairment.

SUROGRAN is not indicated for use in the management of hemiplegic, basilar or ophthalmoplegic migraine.

Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of **SUROGRAN .** Reactions may range from cutaneous hypersensitivity to anaphylaxis. Caution should be exercised before using **SUROGRAN** in these patients.

WARNINGS:

Following administration of **SUROGRAN** patients with known hypersensitivity to sulphonamides can experience an allergic reaction. Hypersensitivity reactions may range from cutaneous hypersensitivity to anaphylaxis.

The use of **SUROGRAN** can be associated with transient symptoms, including chest pain and chest tightness, which may be intense and involve the throat. Although these symptoms can mimic angina pectoris, they are only in exceptional circumstances the result of myocardial ischaemia/coronary vasospasm. Vasospasm may present as an arrhythmia.

The recommended dose of **SUROGRAN** should not be exceeded.

Drowsiness may occur as a result of migraine or its treatment with **SUROGRAN** . Caution is advised in patients performing skilled tasks, e.g. operating machinery or driving.

SUROGRAN should only be used where there is clear diagnosis of migraine.

Before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms, care should be taken to exclude other potentially serious neurological conditions. It should be noted that migraineurs may be at risk of certain cerebrovascular events (e.g. CVA, TIA).

SUROGRAN should not be given to patients in whom unrecognised cardiac disease is likely without a prior evaluation for underlying cardiovascular disease. Such patients include postmenopausal women, males over 40 years of age and patients with risk factors for coronary artery disease. However, these evaluations may not identify every patient who has cardiac disease. Serious cardiac events have occurred in patients without underlying cardiovascular disease.

SUROGRAN should be administered with caution to patients with controlled hypertension as increases in blood pressure and peripheral vascular resistance have been observed.

If concomitant treatment with **SUROGRAN** and a selective serotonin reuptake inhibitor (SSRI) is clinically warranted, appropriate observation of the patient is advised as there is a risk of serotonin syndrome (see **"Interactions"**).

SUROGRAN should be used with caution in patients with a history of epilepsy or structural brain lesions, which lower their convulsion threshold.

Children (under 18 years of age) and patients aged more than 65 years:

The safety and effectiveness of **SUROGRAN** in children (under 18 years of age) and patients over 65 years has not yet been established.

INTERACTIONS:

Prolonged vasospastic reactions have been reported with ergotamine. Since these effects may be additive, 24 hours should pass before **SUROGRAN** can be administered following an ergotamine preparation. Conversely, ergotamine containing preparations should not be taken until 6 hours having passed following **SUROGRAN** administration.

There is no evidence of interactions with flunarizine, propranolol, dihydroergotamine, pizotifen or alcohol.

An interaction may occur between **SUROGRAN** and MAOI's and concomitant administration is contraindicated. Rarely an interaction may occur between **SUROGRAN** and SSRIs.

PREGNANCY AND LACTATION:

Safety in pregnancy and lactation has not been established.

DOSAGE AND DIRECTIONS FOR USE:

SUROGRAN is indicated for the acute intermittent treatment of migraine.

SUROGRAN SHOULD NOT BE USED PROPHYLACTICALLY

Tablets:

The recommended dose for initial therapy is 50 mg, depending on response this may be increased to 100 mg.

If symptoms recur, a further dose may be given at any time in the next 24 hours provided not more than 3 x 100 mg tablets or 6 x 50 mg tablets are taken in any 24 hour period and that each dose is separated by at least two hours. A second dose has not proven to provide relief if the first dose did not have a beneficial effect on the migraine.

The tablet should be swallowed whole with water.

The dose of **SUROGRAN** should be reduced in patients with impaired liver function. It is recommended that **SUROGRAN** be administered as early as possible after the onset of migraine however it is equally effective at whatever stage of the attack it is given.

SIDE-EFFECTS AND SPECIAL PRECAUTIONS:

SUROGRAN should only be used if there is clear diagnosis of migraine.

Care should be taken to exclude other potentially serious neurological conditions before treating headaches in patients not previously diagnosed as migraineurs, and in migraineurs who present with atypical symptoms.

There have been less frequent reports where patients received **SUROGRAN** for severe headaches which subsequently were shown to have been secondary to an evolving neurological lesion (cerebrovascular accident, subarachnoid haemorrhage). In this regard, it should be noted that migraineurs may be at a risk of certain cerebrovascular events e.g. (cerebrovascular accident, transient

ischaemic attack). If a patient does not respond to the first dose, the opportunity should be taken to review the diagnosis before a second dose is administered.

Side-effects which have been reported include the following:

Cardiac Disorders

Less frequent: chest-pain, sensations of tingling, heaviness, heat, pressure or tightness. These symptoms are usually transient and may be intense and can affect any part of the body including the throat and chest. In extremely rare cases serious coronary events have been reported which have included cardiac arrhythmias, transient ischaemic ECG changes or myocardial infarction. Thus **SUROGRAN** should not be given to patients in whom unrecognised cardiac disease is likely without a prior evaluation for underlying cardiovascular disease. These patients include males over 40 years of age, postmenopausal women and patients with risk factors for coronary disease.

If any symptoms that are consistent with ischaemic heart disease occur, appropriate evaluation must be performed.

The following side effects have been reported and frequencies are unknown: Transient increases in blood pressure, peripheral vascular resistance, bradycardia, hypotension, palpitations and tachycardia.

Gastrointestinal Disorders:

Frequent: Nausea and vomiting occurred in some patients but the relationship to **SUROGRAN** is not clear.

The following side effects have been reported and frequencies are unknown: Disturbances in liver function tests have been observed.

SUROGRAN should also be administered with caution to patients with diseases which may alter the absorption, metabolism or excretion of drugs, such as impaired hepatic function.

Lower doses should be considered in patients with hepatic impairment.

Nervous System Disorders:

Less frequent: Seizures

SUROGRAN should be used with caution in patients with a history of epilepsy or structural brain lesions which lower their convulsion threshold.

Vascular Disorders:

Less frequent: Flushing

General Disorders:

Less frequent: Dizziness, feelings of weakness, fatigue and drowsiness

KNOWN SYMPTOMS OF OVERDOSAGE AND PARTICULARS OF ITS TREATMENT:

The patient should be monitored for at least ten hours and supportive treatment applied as required in the case of overdosage.

It is unknown what effect haemodialysis or peritoneal dialysis has on the plasma concentrations of **SUROGRAN** .

IDENTIFICATION:

SUROGRAN 50 mg:

White to off white, capsule shaped, biconvex uncoated tablets, debossed with 'C' on one side and '33' on other side.

SUROGRAN 100 mg:

White to off white, capsule shaped, biconvex uncoated tablets, debossed with 'C' on one side and '34' on other side.

PRESENTATION:

SUROGRAN 50 mg:

1. Cold form Alu - Alu Blister Pack:

   Tablets are packed in 25 micron Polyamide/45 micron Aluminium foil / 60 micron PVC and 25 microns Printed Aluminium foil with 6-8 gsm Heat seal Lacquer. Each blister contains 2 tablets.

   Pack size: 2's **-** Each carton contains 1 blister of 2 tablets.

2. Cold form Alu - Alu Blister Pack:

   Tablets are packed in 25 micron OPA/45 micron Aluminium foil / 60 micron PVC and 25 microns Printed Aluminium foil with 6-8 gsm Heat seal Lacquer. Each blister contains 6 tablets.

   Pack size: 6's **-** Each carton contains 1 blister of 6 tablets.

SUROGRAN 100 mg:

Cold form Alu - Alu Blister Pack:

Tablets are packed in 25 micron Polyamide/45 micron Aluminium foil / 60 micron PVC and 25 microns Printed Aluminium foil with 6-8 gsm Heat seal Lacquer. Each blister contains 4 tablets.

Pack size: 4's – Each carton contains 1 blister of 4 tablets.

STORAGE CONDITIONS:

Store at or below 30°C.

KEEP OUT OF REACH OF CHILDREN.

REGISTRATION NUMBERS:

SUROGRAN 50 mg: 42/7.3/0267.

SUROGRAN 100 mg: 42/7.3/0268.

NAME AND BUSINESS ADDRESS OF THE HOLDER OF THE CERTIFICATE OF REGISTRATION:

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