Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Suvalan 50 mg Film Coated Tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg of sumatriptan as the succinate salt.
Also includes 206.5 mg lactose as lactose monohydrate and lactose anhydrous.

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Film-coated tablet.
Pink, film-coated, capsule-shaped, biconvex tablets engraved ‘50’ on one face and plain on the other.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Suvalan tablets are indicated for the acute treatment of migraine attacks with or without aura, including the acute treatment of menstrually associated migraine.

4.2 Posology and method of administration

Suvalan is indicated for the acute intermittent treatment of migraine. Suvalan Tablets should not be used prophylactically.

Suvalan is recommended as monotherapy for the acute treatment of a migraine and should not be given concomitantly with other acute migraine therapies. If a patient fails to respond to a single dose of Suvalan there are no reasons, either on theoretical grounds or from limited clinical experience, to withhold products containing aspirin or non-steroidal anti-inflammatory drugs for further treatment of the attack.

It is advisable that Suvalan be given as early as possible after the onset of a migraine headache. It is equally effective at whatever stage of the attack it is administered.

Adults only:
The recommended adult dose of oral Suvalan is a single 50mg tablet. Some patients may require 100mg.

If a patient does not respond to the first dose of Suvalan, a second dose should not be taken for the same attack. Suvalan may be taken for subsequent attacks.

If the patient has responded to the first dose, but the symptoms recur, a second dose may be given in the next 24 hours, provided that not more than 300mg is taken in any 24 hour period. An interval of two hours should generally be allowed to elapse between doses.

The tablets should be swallowed whole with water.

Children (under 18 years of age):
The safety and effectiveness of Suvalan Tablets in children has not yet been established.

Elderly (over 65):
Experience of the use of Suvalan in patients aged over 65 years is limited. The pharmacokinetics do not differ significantly from a younger population but, until further clinical data are available, the use of Suvalan in patients aged over 65 years is not recommended.

Patients with Hepatic Impairment:
Impairment of hepatic function gives rise to an 80% increase in plasma sumatriptan levels after an oral dose of 100mg. The drug should therefore be used with extreme caution and at reduced dosage in these patients.

Patients with Renal Impairment:
There is no information on the effect of renal impairment.

4.3 Contraindications

Hypersensitivity to any component of the preparation.

(Suvalan) Sumatriptan should not be given to patients who have had a myocardial infarction or have ischaemic heart disease, coronary vasospasm (prinzmental's angina), peripheral vascular disease or patients who have symptoms or signs consistent with ischaemic heart disease.

Sumatriptan should not be administered to patients with a history of cerebrovascular accident (CVA) or transient ischaemic attack (TIA).

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

The use of sumatriptan in patients with uncontrolled hypertension is contra-indicated.

The concomitant administration of ergotamine, or derivatives of ergotamine (including methysergide) is contra-indicated (see *Interaction with other medicinal products and other forms of Interaction*).

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

Until further data are available the use of Suvalan is contra-indicated in patients receiving concurrent treatment with certain antidepressants e.g. selective 5-HT reuptake inhibitors (see section Interaction with other medicinal Products and other forms of Interaction) and lithium.

Suvalan Tablets should not be given to diabetic patients.

4.4 Special warnings and precautions for use

Suvalan Tablets should only be used where there is a clear diagnosis of migraine.

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

As with other acute migraine therapies, 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.

There have been a number of reports of CVA (stroke, paresis), where a temporal association with sumatriptan intake was seen. It should be noted that migraineurs may be at increased risk of certain cerebrovascular events (e.g. CVA, TIA).

Suvalan should not be used in patients with underlying cardiac disorders and in patients who, although asymptomatic, have significant risk factors predisposing to coronary artery disease. Therefore a careful history to exclude pre-existing cardiac disease should be taken before sumatriptan is prescribed.

Evaluations may not identify every patient who has cardiac diseases and, in very rare cases, serious cardiac events have occurred in patients without underlying cardiovascular disease and in the absence of known risk factors.

Patients in whom undiagnosed coronary artery disease is a possibility on the basis of age or the presence of other risk factors, such as family history of coronary artery disease, tobacco smoking, diabetes, hypercholesterolaemia, should receive the product only with great caution and if the benefit of treatment is judged to outweigh the possible risk. Use of sumatriptan should be carefully considered in patients who may be at risk of thrombotic episodes.

There have been rare reports of patients on hormone replacement therapy who have had cardiac ischaemic events.

Following administration, sumatriptan can be associated with transient symptoms including chest pain and tightness which may be intense and involve the throat and arms.

These symptoms may mimic angina pectoris but, in patients in whom cardiac investigations have been performed, they have only rarely been found to have been the result of coronary vasospasm. Although rare, the vasospasm may result in arrhythmia including ventricular fibrillation/ischaemia or myocardial infarction. If the patient experiences symptoms which are severe or persistent or are consistent with angina, further doses should not be taken until appropriate investigations have been carried out to check for the possibility of ischaemic changes.

There have been a number of fatalities from ventricular fibrillation and myocardial infarction.

Sumatriptan should be administered with caution to patients with controlled hypertension as transient increases in blood pressure and peripheral vascular resistance have been observed in a small proportion of patients.

Sumatriptan should be administered with caution to patients with conditions, which may affect significantly the absorption, metabolism or excretion of the drug, e.g. impaired hepatic or renal function.

Sumatriptan should be used with caution in patients with a history of seizures or other risk factors which lower the seizure threshold.

Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of sumatriptan. Reactions may range from cutaneous hypersensitivity to anaphylaxis.

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St. John’s wort (*Hypericum perefortum*).

The recommended dose of Suvalan should not be exceeded.

4.5 Interaction with other medicinal products and other forms of interaction

Studies in healthy subjects show that Sumatriptan does not interact with propranolol, flunarizine, pizotifen or alcohol.

There are limited data on an interaction with ergotamine containing preparations. The increased risk of coronary vasospasm is a theoretical possibility and concomitant administration is contra-indicated.
The period of time that should elapse between the use of sumatriptan and ergotamine containing preparations is not known. This will also depend on the doses and type of ergotamine containing products used. The effects may be additive. It is advised to wait at least 24 hours following the use of ergotamine containing preparations before administering sumatriptan. Conversely, it is advised to wait at least six hours following use of sumatriptan before administering an ergotamine containing product (see *Contra-indications).*

There is a risk of CNS toxicity when both MAOI’s ans SSRI’s are given with Imigran; hence concomitant use is contraindicated (see section 4.3).

4.6 Fertility, pregnancy and lactation

Pregnancy:
Caution should be exercised by considering the expected benefit to the mother against possible risk of the foetus.

Post-marketing data from multiple prospective pregnancy registries have documented the pregnancy outcomes in over 1,000 women exposed to sumatriptan. Although there is insufficient information to draw definitive conclusions, the findings have not detected an increase in the frequency of birth defects nor a consistent pattern of birth defects, amongst women exposed to sumatriptan compared with the general population.

Lacatation:
Sumatriptan is excreted in breast milk in animals. No data exist in humans therefore administration of Suvalan to a nursing woman is not recommended.

4.7 Effects on ability to drive and use machines

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

4.8 Undesirable effects

Adverse events are listed below by system organ class and frequency. Frequencies are defined as: very common (>1/10), common (>1/100, <1/10), uncommon (>1/1000, <1/100), rare (>1/10,000, <1/1000) and very rare (<1/10,000) including isolated reports. The data from clinical trials are estimates. It should be noted that the background rate in comparator groups was not taken into account. Post-marketing data refer to reporting rate rather than true frequency.

Clinical Trial Data

Nervous System Disorders
Common: Tingling, dizziness, drowsiness.

Vascular Disorders
Common: Transient increases in blood pressure arising soon after treatment. Flushing.

Gastrointestinal
Common: Nausea and vomiting occurred in some patients but the relationship to sumatriptan is not clear.

Musculoskeletal and Connective Tissue Disorders
The following symptom is usually transient and may be intense and can effect any part of the body including the chest and throat:
Common: Sensations of heaviness.

General Disorders and Administration Site Conditions
The following symptoms are usually transient and may be intense and can affect any part of the body including the chest and throat.
Common: Pain, sensations of heat, pressure or tightness.

The following symptoms are mostly mild to moderate in intensity and transient:
Common: Feelings of weakness, fatigue

Investigations
Very Rare: Minor disturbances in liver function Tests have occasionally been observed.

Injection:
The most common side effects associated with treatment with sumatriptan administered subcutaneously are:

General Disorders and Administration Site Conditions
Very common: Transient injection site pain
Injection site stinging/burning, swelling, erythema, bruising and bleeding have also been reported.

Although direct comparisons are not available, flushing and sensations of tingling, heat, pressure, and heaviness may be more common after sumatriptan injection.

Conversely, nausea, vomiting and fatigue appear to be less frequent with subcutaneous administration of sumatriptan injection than with tablets.

Nasal Spray

Respiratory, Thoracic and Mediastinal Disorders
Common: Following administration of sumatriptan nasal spray mild, transient irritation or burning sensation in the nose or the throat or epistaxis have been reported.

Post Marketing Data
Immune System Disorders
Very rare: Hypersensitivity reactions ranging from cutaneous hypersensitivity to rare cases of anaphylaxis.

Nervous System Disorders
Very rare: Seizures, although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures thee are also reports in patients where no such predisposing factors are apparent. Tremor, dystonia, nystagmus, scotoma.

Eye disorders
Very rare: Flickering, diplopia, reduced vision. Loss of vision (usually transient). However, visual disorders may also occur during a migraine attack itself.

Visual disorders may also occur during a migraine attack itself. Patients treated with Suvalan rarely exhibit visual disorders like flickering and diplopia. Additionally cases of nystagmus, scotoma, reduced vision and retinal vascular occlusions have been observed. Very rarely loss of vision has occurred, which although usually transient, has included isolated irreversible cases.

Cardiac Disorders
Very rare: Bradycardia, tachycardia, palpitations,
Cardiac arrythmias, transient ischaemic ECG changes, coronary artery vasospasm,, myocardial infarction (see Contraindication, Warnings and Precautions).

Vascular disorders
Very rare: Hypotension, Raynaud's phenomenon.

Gastrointestinal
Vary rare: Ischaemic colitis.

4.9 Overdose

There have been some reports of overdosage with Sumatriptan.
Patients have received single injections of up to 12mg subcutaneously without significant adverse effects. Doses up to 16mg subcutaneously and up to 400mg orally were not associated with side effects other than those mentioned. There is no experience of doses greater than these.

If overdosage with Suvalan occurs, the patient should be monitored for at least ten hours and standard supportive treatment applied as required.

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

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective $5HT_1$ receptor agonist.
ATC code: N02CC01.

Sumatriptan has been demonstrated to be a selective vascular 5-hydroxytryptamine-1-($5HT_{1d}$) receptor agonist with no effect at other 5HT receptor ($5HT_2$-$5HT_7$) subtypes. The vascular $5HT_{1d}$ receptor is found predominantly in cranial blood vessels and mediates vasoconstriction. In animals sumatriptan selectively constricts the carotid arterial circulation, the carotid arterial circulation supplies blood to the extracranial and intracranial tissues such as the meninges and dilatation and/or oedema formation in these vessels is thought to be the underlying mechanism of migraine in man. In addition, evidence from animal studies suggests that sumatriptan inhibits trigeminal nerve activity. Both these actions (cranial vasoconstriction and inhibition of trigeminal nerve activity) may contribute to the anti-migraine action of sumatriptan in humans.

Clinical response begins 30 minutes following a 100mg oral dose.

Although the recommended dose of oral Suvalan is 50mg, migraine attacks vary in severity both within and between patients. Doses of 25-100mg have shown greater efficacy than placebo in clinical trials, but 25mg is statistically significantly less effective than 50 and 100mg.

5.2 Pharmacokinetic properties

Absorption:

Rapid. However bioavailability is low (approximately 14% of a dose), primarily because of presystemic hepatic metabolism and, to a lesser extent, because of incomplete absorption. The rate and extent of absorption are not affected to a clinically significant extent by administration with food or by the gastric stasis that may accompany migraine headaches.

Bioavailability is increased by 80% in patients with hepatic impairment.

Distribution:

Sumatriptan is rapidly and extensively distributed to tissues, but passage across the blood-brain barrier is limited.

Protein binding:

In plasma - low (14 to 21%).

Biotransformation:

Hepatic and extensive; approximately 80% of a dose is metabolised.
The major metabolite is an inactive indole acetic acid derivative.

Half-life:

Elimination: Approximately 2 hours. One study reported a terminal half-life of approximately 7 hours that became apparent about 12 hours after administration of multiple oral doses, but did not contribute substantially to the overall disposition of the medication.

Onset of action:

Within 30 minutes.

Time to peak concentration:

In serum (single 100mg dose): Approximately 1.5 hours (range, 0.5 to 5 hours). The wide interindividual variability found in pharmacokinetic studies may be related to the appearance of multiple peaks in the concentration over time. Approximately 80% of the maximum value is achieved within 45 minutes.

Peak concentration:

In serum (single 100mg dose): Approximately 54 nanograms per ml; (0.13 micromoles/L) (range 26.7 to 137 nanograms per ml; 0.06 to 0.33 micromoles/L).

Time to peak effect:

Relief of headache (i.e. moderate or severe pain being reduced to mild or no pain)-

Single 100mg dose: Within 2 hours in 50 to 75%, and within 4 hours in an additional 15 to 25% of patients.

Relief of associated symptoms (nausea, vomiting, photophobia, phonophobia)-

Single 100mg dose: Within 2 hours.

Duration of action:

Return of migraine headache occurs within 24 to 48 hours in approximately
40% of patients who initially obtain a beneficial response to sumatriptan, i.e. after moderate or severe headache pain has been reduced to mild or no pain. Whether this represents development of a new migraine or breakthrough of a prolonged migraine after the effects of sumatriptan have worn off has not been established.

Elimination:

Renal, via active renal tubular secretion, following hepatic metabolism. Approximately 80% of a dose is eliminated as metabolites. After oral administration, approximately 57% of a dose is eliminated in the urine (3% of the dose as unchanged sumatriptan, 35% as the indole acetic acid metabolite) and another 38% of the dose is eliminated in the faeces (9% as unchanged sumatriptan and 11% as the indole acetic acid metabolite).

The effects of renal function impairment on clearance of sumatriptan have not been studied. Hepatic impairment produces an increase of 80% in plasma levels after oral dosing.

5.3 Preclinical safety data

Reproduction Toxicity:
In a rat fertility study a reduction in success of insemination was seen at exposure sufficiently in excess of the maximum human exposure. In rabbits embryolethality, without marked Teratogenic defects, was seen. Although no teratogenic effects have been seen in rats or rabbits, reproduction studies in rabbits, using high and maternally toxic doses, associated with blood levels more than fifty times those seen in humans after therapy, have shown an increased incidence of minor variation in the position of certain foetal blood vessels.

Reproduction studies preformed in rats have revealed no evidence of impaired fertility or postnatal development due to sumatriptan. The relevance for humans of these findings is unknown.

Mutagenicity and Carcinogenicity
Sumatriptan was devoid of genotoxic and carcinogenic activity in *in-vitro* system and animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Lactose anhydrous
Lactose monohydrate
Microcrystalline cellulose
Croscarmellose sodium
Magnesium stearate
Opadry YS-1-1441-G containing:
Hypromellose
Titanium dioxide
Triacetin
Iron oxide red (E172)

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

Double foil blister packs within a cardboard carton.
Pack sizes: 2,6 or 12 tablets.
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

GlaxoSmithKline Consumer Healthcare (Ireland) Limited
12 Riverwalk
Citywest Business Campus
Dublin 24
Ireland

8 MARKETING AUTHORISATION NUMBER

PA 0678/108/001

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

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10 DATE OF REVISION OF THE TEXT

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