Summary of Product Characteristics

1 NAME OF THE MEDICINAL PRODUCT

Sumatriptan Pfizer 50mg tablets

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

Each tablet contains 50 mg sumatriptan (as sumatriptan succinate).

For a full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Tablet.

White to off – white, capsule shaped, biconvex, uncoated tablets, debossed with ‘C’ on one side and ‘33’ on the other side. The size is 11 X 5 mm.

4 CLINICAL PARTICULARS

4.1 Therapeutic Indications

Sumatriptan Pfizer is indicated for the acute treatment of migraine attacks with or without aura.

4.2 Posology and method of administration

General recommendations with regard to use and administration:

Sumatriptan should not be used prophylactically.

Sumatriptan is recommended as monotherapy for the acute treatment of a migraine attack and should not be given concomitantly with ergotamine or derivatives of ergotamine (including methysergide) (see section 4.3).

It is advisable that sumatriptan 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
The recommended dose sumatriptan is a single 50 mg tablet. Some patients may require 100 mg.

If the patient does not respond to the first dose of sumatriptan, a second dose should not be taken for the same attack. Sumatriptan tablets 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 there is a minimum interval of 2 hours between the doses and that not more than 300 mg is taken in any 24 hour period.

The tablets should be swallowed whole with water.

Children (under 12 years of age)
Sumatriptan tablets are not recommended for use in children below 12 as sumatriptan tablets have not been studied in children.

Adolescents (12 to 17 years of age)
The efficacy of sumatriptan tablets in adolescents could not be demonstrated in the clinical studies performed in this age group. Therefore the use in adolescents is not recommended (see section 5.1).

- **Elderly (over 65 years of age)**

Experience of the use of sumatriptan tablets 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 sumatriptan in patients aged over 65 years is not recommended.

Hepatic impairment:
Patients with mild to moderate hepatic impairment: low doses of 25-50 mg should be considered for these patients.

Renal impairment:
Sumatriptan Pfizer should be used with caution in patients with renal impairment.

4.3 Contraindications

- Hypersensitivity to sumatriptan or to any of the excipients.
- Sumatriptan should not be given to patients who have had myocardial infarction or have ischaemic heart disease, coronary vasospasm (Prinzmetal's angina), peripheral vascular disease or symptoms or sings 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 moderate and severe hypertension and mild uncontrolled hypertension is contraindicated.
- The concomitant administration of ergotamine, or ergotamine derivatives (including methysergide) or any triptan-5-hydroxytryptaminel (5-HT1) receptor agonist is contraindicated (see section 4.5).
- Concurrent administration of reversible (e.g. moclobemide) or irreversible (e.g. selegiline) monoamine oxidase inhibitors (MAOIs) and sumatriptan is contraindicated.
- Sumatriptan must not be used within 2 weeks of discontinuation of therapy with monoamine oxidase inhibitors.

4.4 Special warnings and precautions for use

Sumatriptan Pfizer should only be used where there is a clear diagnosis of migraine.

Sumatriptan is not indicated for use in 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.

It should be noted that migraineurs may be at increased risk of certain cerebrovascular events (e.g. cerebrovascular accident, transient ischaemic attack).

Following administration, sumatriptan can be associated with transient symptoms including chest pain and tightness, which may be intense and involve the throat (see section 4.8). Where such symptoms are thought to indicate ischaemic heart disease, no further doses of sumatriptan should be given, and an appropriate evaluation should be carried out.

There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan. Serotonin syndrome has been reported following concomitant treatment with triptans and serotonin noradrenaline reuptake inhibitors (SNRIs).

If concomitant treatment with sumatriptan and an SSRI/SNRI is clinically warranted, appropriate observation of the patient is advised (see section 4.5)

Sumatriptan should be administered with caution to patients with conditions that 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, as seizures have been reported in association with sumatriptan (see section 4.8).

Patients with known hypersensitivity to sulphonamides may exhibit an allergic reaction following administration of sumatriptan. Reactions may range from cutaneous hypersensitivity to anaphylaxis. Evidence of cross sensitivity is limited, however, caution should be exercised before using sumatriptan in these patients.

Undesirable effects may be more common during concomitant use of triptans and herbal preparations containing St John's Wort (*Hypericum perforatum*).

Prolonged use of any painkiller for headaches can make them worse. If this situation is experienced or suspected, medical advice should be obtained and treatment should be discontinued. The diagnosis of medication overuse headache (MOH) should be suspected in patients who have frequently or daily headaches despite (or because of) the regular use of headache medications.

The recommended dose of sumatriptan should not be exceeded.

Sumatriptan should not be given to patients with risk factors for ischaemic heart disease, including patients with diabetes and patients who are heavy smokers or users of nicotine substitution therapies, without prior cardiovascular evaluation (see section 4.3). Special consideration should be give to postmenopausal women and males over 40 with these risk factors. These evaluations however, may not identify every patient who has cardiac disease and, in very rare cases, serious cardiac events have occurred in patients without underlying cardiovascular disease.

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.

In rare cases, asthenia, hyperreflexia and incoordination have been described in post-marketing reports following use of a selective serotonin reuptake inhibitor (SSRI) and sumatriptan.

4.5 Interaction with other medicinal products and other forms of interaction

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

There are limited data on an interaction with preparations containing ergotamine or another triptan/5-HT_1 receptor agonist. The increased risk of coronary vasospasms is a theoretical possibility and concomitant administration is contraindicated (see section 4.3).

The period of time that should elapse between the use of sumatriptan and ergotamine-containing preparations or another triptan/5-HT_1 receptor agonist is not known. This will also depends on the doses and types of products used. The effects may be additive. It is advised to wait at least 24 hours following the use of ergotamine-containing preparations or another triptan/5-HT_1 receptor agonist before administering sumatriptan. Conversely, it is advised to wait at least 6 hours following the use of sumatriptan before administering an ergotamine-containing product and at least 24 hours before administering another triptan/5-HT_1 receptor agonist (see section 4.3).

An interaction may occur between sumatriptan and MAOIs and concomitant administration is contraindicated (see section 4.3).

There have been rare post-marketing reports describing patients with serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) following the use of SSRIs and sumatriptan. Serotonin syndrome has also been reported following concomitant treatment with triptans and SNRIs (see section 4.4).

There may be a risk of serotonergic syndrome also if sumatriptan is used concomitantly with lithium.

4.6 Fertility, pregnancy and lactation

Pregnancy
Post-marketing data on the use of sumatriptan during the first trimester of pregnancy in over 1,000 women are available. Although these data contain insufficient information to draw definitive conclusions, they do not point to an increased risk of congential defects. Experience with the use of sumatriptan in the second and third trimester is limited.

Evaluation of experimental animal studies does not indicate direct teratogenic effects or harmful effects on peri-and postnatal development. However, embryo-foetal viability might be affected in the rabbit (see section 5.3). Administration of sumatriptan should only be considered if the expected benefits to the mother is greater than any possible risk to the foetus.

Lactation
It has been demonstrated that following subcutaneous administration sumatriptan is secreted into breast milk. Infant exposure can be minimised by avoiding breast-feeding for 12 hours after treatment, during which time any breast milk expressed should be discarded.

4.7 Effects on ability to drive and use machines

No studies on the effects on the ability to drive and use machines have been performed. Drowsiness may occur as a result of maigraine, or its treatment with sumatriptan. This may influence the ability to drive and operate 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 to <1/10),

Uncommon (≥1/1,000 to <1/100),

Rare (≥1/10,000 to <1/1,000),

Very rare (<1/10,000), not known (cannot be estimated from the available data).
Some of the symptoms reported as undesirable effects may be associated symptoms of migraine.

Immune system disorders
Not known: Hypersensitivity reactions ranging from cutaneous hypersensitivity (such as urticaria) to anaphylaxis.

Nervous system disorders
Common: Dizziness, drowsiness, sensory disturbance including paraesthesia and hypoaesthesia.
Not known: Seizures, although some have occurred in patients with either a history of seizures or concurrent conditions predisposing to seizures.
There are also reports in patients where no such predisposing factors are apparent; Tremor, dystonia, nystagmus, scotoma.

Eye disorders
Not known: Flickering, diplopia, reduced vision. Loss of vision including reports of permanent defects. However, visual disorders may also occur during a migraine attack itself.

Cardiac disorders
Not known: Bradycardia, tachycardia, palpitations, cardiac arrhythmias, transient ischaemic ECG changes, coronary artery vasospasm, angina, myocardial infarction (see section 4.3 and 4.4).

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

Not known: Hypotension, Raynaud's phenomenon.

Respiratory, thoracic and mediastinal disorders
Common: Dyspnoea.

Gastrointestinal disorders
Common: Nausea and vomiting occurred in some patients but it is unclear if this is related to sumatriptan or the underlying condition.
Not known: Ischaemic colitis, Diarrhoea.

Musculoskeletal and connective tissue disorders
Common: Sensations of heaviness (usually transient and may be intense and can affect any part of the body including the chest and throat). Myalgia.
Not known: Neck stiffness, Arthralgia.

General disorders and administration site conditions
Common: Pain, sensations of heat or cold, pressure or tightness (these events are usually transient and may be intense and can affect any part of the body including the chest and throat); feelings of weakness, fatigue (both events are mostly mild to moderate in intensity and transient).
Uncommon: Somnolence (mostly mild to moderate in intensity and transient)

Investigations
Very rare: Minor disturbances in liver function tests have occasionally been observed.

Psychiatric disorders
Not known: Anxiety.

Skin and subcutaneous tissue disorders
Not known: Hyperhidrosis.

4.9 Overdose

Symptoms and signs
Doses in excess of 400 mg orally and 16 mg subcutaneously were not associated with side effects other than those mentioned. Patients have received single injections of up to 12 mg subcutaneously without significant adverse effects.

Treatment
If overdose occurs, the patient should be monitored for at least 10 hours and standard supportive treatment applied. It is unknown what effect haemodialysis or peritoneal dialysis has on the plasma concentrations of sumatriptan.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Selective serotonin ($5HT_1$) agonists
ATC code: N02CC01

Sumatriptan is a specific and selective 5-hydroxytryptamine-1d receptor agonist, and has not demonstrated activity on the other 5HT ($5HT_2$-$5HT_7$) receptors.

The vascular $5HT_{1d}$ receptor is found predominantly in the cranial blood vessels and has a vasoconstrictor effect. In experimental animals, it has been shown that sumatriptan causes vasoconstriction of the arterioles and the arteriovenous anastomata of the carotid vascular bed. This vascular bed provides the blood supply to the extracranial and intracranial tissues, such as the meninges.

It has been proposed that dilatation of these arterial vessels, and the formation of oedema here, is the underlying cause of a migraine attack in humans. There is also evidence from animal experiments to suggest that sumatriptan inhibits the activity of the trigeminal nerve. Both effects (cranial vasoconstriction and inhibition of the activity of the trigeminal nerve) might contribute to the anti-migraine effect of sumatriptan in humans.

A clinical response occurs approximately 30 minutes after oral administration of a dose of 100 mg.

Sumatriptan is effective for the acute treatment of migraine attacks that occur during menstruation in women, i.e. in the period from 3 days before to 5 days after the beginning of menstruation.

A number of placebo-controlled clinical studies assessed the safety and efficacy of oral sumatriptan in 600 adolescent migraineurs aged 12-17 years. These studies failed to demonstrate relevant differences in headache relief at 2 hours between placebo and any sumatriptan dose. The undesirable effects profile of oral sumatriptan in adolescents aged 12-17 years was similar to that reported from studies in the adult population.

5.2 Pharmacokinetic properties

Following oral administration sumatriptan is rapidly absorbed, the maximum concentration being reached after 2 (0.5-5) hours. Absolute bioavailability after oral administration is on average 14%. This is partly due to presystemic metabolism and partly to incomplete absorption. In patients with hepatic impairment, presystemic clearance after oral administration is reduced, resulting in an increase in the plasma levels of sumatriptan.

Protein binding is low (14-21%) and the mean volume of distribution is 170 litres. The elimination half-life is approximately 2 hours. Mean total clearance is 1160 ml/minute and mean renal clearance is approximately 260 ml/minute. Non-renal clearance is approximately 80% of total clearance, suggesting that sumatriptan is primarily cleared through oxidative metabolism mediated by monoamine oxidase A. The major metabolite, the indole acetic acid analogue of sumatriptan, is excreted in the urine as the acid or as the glucuronide conjugate. This metabolite has no known 5HT1 or 5HT2 activity. Minor metabolites have not been identified. The pharmacokinetics of the oral administration of sumatriptan does not appear to be influenced by a migraine attack.

Pharmacokinetics in special groups:
Elderly:
The kinetics in elderly subjects has not been sufficiently studied to permit a statement on possible differences in the kinetics between elderly and young volunteers.

5.3 Preclinical safety data

In a fertility study in the rat, a reduction in the success of insemination was seen on exposure to concentrations higher than the maximum exposure in humans. In rabbits embryolethality was observed, without marked teratogenic effects. Sumatriptan was devoid of genotoxic and carcinogenic activity in *in-vitro* systems and animal studies.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Croscarmellose sodium
Polysorbate 80
Calcium hydrogen phosphate anhydrous
Cellulose microcrystalline
Sodium hydrogen carbonate
Magnesium stearate

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

4 years

6.4 Special precautions for storage

This medicinal product does not require any special storage condition.

6.5 Nature and contents of container

Sumatriptan Pfizer tablets are available in Polyamide/PVC/Aluminium blister packs.
Pack sizes:
2, 3, 4, 6, 8, 12, 18, 20, 30, 50 and 100 tablets.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal

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

7 MARKETING AUTHORISATION HOLDER

Pfizer Healthcare Ireland
9 Riverwalk
National Digital Park
Citywest Business Campus
Dublin 24

8 MARKETING AUTHORISATION NUMBER

PA 822/48/1

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

Date of first authorisation: 3 June 2011

10 DATE OF REVISION OF THE TEXT