NARAMIG
Professional Information

SCHEDULING STATUS:

S4

1. NAME OF THE MEDICINE:

NARAMIG tablet (2,5 mg naratriptan)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION:

Each tablet contains 2,5 mg naratriptan as naratriptan hydrochloride.

Contains sugar (as anhydrous lactose 94,07 mg/tablet).

For a full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM:

Film-coated tablets.

NARAMIG tablets are green film-coated, D shaped, biconvex, with ‘GX CE5’ engraved on the one face.

4. CLINICAL PARTICULARS:

4.1 Therapeutic Indications:

NARAMIG tablets are indicated for the acute treatment of migraine attacks with or without aura.

4.2 Posology and method of administration:

NARAMIG should not be used prophylactically.

NARAMIG tablets should be taken as early as possible after the onset of a migraine headache but may be effective if taken at a later stage.

The tablets should be swallowed whole with water.

The recommended dose of NARAMIG Tablets is a single 2,5 mg tablet.

A minimum interval of four hours should be left between doses.

No more than two 2,5 mg tablets in any 24 hour period.

Maximum total daily dose in renal/hepatic impairment: one 2,5 mg tablet.

If a patient does not respond to the first dose of NARAMIG tablets it is unlikely that a second dose will be of benefit in the same attack.

4.3 Contraindications:

Hypersensitivity to naratriptan or to any component in NARAMIG, see section 6.1.

NARAMIG should not be used in patients who have had a myocardial infarction or have ischaemic heart disease, or Prinzmetal's angina/coronary vasospasm, peripheral vascular disease or patients who have symptoms or signs consistent with ischaemic heart disease.

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

The use of NARAMIG in patients with uncontrolled hypertension is contraindicated.

NARAMIG is contraindicated in patients with severely impaired renal or hepatic function.

The concomitant administration of ergotamine, derivatives of ergotamine (including methysergide) and other triptans/5-HT1 agonists with NARAMIG is not recommended (see section 4.5).

4.4 Special warnings and precautions for use:

NARAMIG should only be used where there is a 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. cerebrovascular accident (CVA) or transient ischaemic attack (TIA).

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

NARAMIG 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 and patients with risk factors for coronary artery disease. If symptoms consistent with ischaemic heart disease occur appropriate evaluation should be carried out.

The recommended dose of NARAMIG should not be exceeded.

Serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) has been reported following concomitant treatment with triptans, such as NARAMIG and selective serotonin reuptake inhibitors (SSRIs)/serotonin noradrenaline reuptake inhibitors (SNRIs). If concomitant treatment with NARAMIG and an SSRI/SNRI is clinically warranted, appropriate observation of the patient is advised (see section 4.5).

Overuse of acute migraine treatments has been associated with the exacerbation of headache (medication overuse headache, MOH) in susceptible patients. Withdrawal of the treatment may be necessary.

NARAMIG contains a sulphonamide component therefore there is a theoretical risk of a hypersensitivity reaction in patients with known hypersensitivity to sulphonamides.

The safety and effectiveness of NARAMIG in the elderly (over 65 years of age) have not been evaluated. There is a moderate decrease (26 %) in clearance with age.
NARAMIG is not recommended for use in children (under 12 years of age) or adolescents (12-17 years of age).

NARAMIG tablets contain lactose. Patients with rare hereditary conditions of galactose intolerance e.g. galactosaemia, the Lapp lactase deficiency or glucose-galactose malabsorption should not take NARAMIG.

4.5 Interactions with other medicines and other forms of interactions:

Serotonin syndrome (including altered mental status, autonomic instability and neuromuscular abnormalities) has been reported following concomitant treatment with triptans such as NARAMIG and SSRIs/SNRIs (see sections 4.3 and 4.4).
There is no evidence of a pharmacokinetic interaction between naratriptan and β-blockers, tricyclic antidepressants, selective serotonin reuptake inhibitors, alcohol or food.
There are limited data on interactions with ergotamine, ergotamine containing preparations, dihydroergotamine (DHE), or sumatriptan. The increased risk of coronary vasospasm is a theoretical possibility with co-administration of these and 5-HT1 receptor agonists (see section 4.3). At least 24 hours should elapse after the administration of NARAMIG before an ergotamine-containing preparation or any triptan/5-HT1 receptor agonist is given.
Conversely, at least 24 hours should elapse after the administration of an ergotamine-containing preparation before NARAMIG is given.
NARAMIG does not inhibit monoamine oxidase enzymes; therefore, interactions with monoamine oxidase inhibitors are not anticipated. In addition, the limited metabolism of

naratriptan and the wide range of cytochrome P450 isoenzymes involved suggest that significant interactions with NARAMIG are unlikely.

4.6 Fertility, pregnancy and lactation:

The safe use of NARAMIG in pregnant women has not been established

NARAMIG and/or related metabolites are secreted into the milk of lactating rats.

Caution should be exercised when considering administration of NARAMIG to breastfeeding women.

4.7 Effects on ability to drive and use machines:

Drowsiness may occur as a result of migraine or its treatment with naratriptan. Caution is recommended when skilled tasks are to be performed 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 (≥ 1/1 000, < 1/100), rare (≥ 1/10 000, < 1/1 000) and very rare (< 1/10 000). Common and uncommon frequencies were determined from clinical trial data.

Clinical trial data:

At therapeutic doses of naratriptan, the incidence of side effects reported in clinical trials was similar to placebo.

Nervous system disorders:

Common: tingling

This is usually of short duration, may be severe and may affect any part of the body including the chest or throat

Gastrointestinal disorders:

Common: nausea and vomiting

Musculoskelatal and connective disorders:

Common: sensations of heaviness

This is usually of short duration, may be severe and may affect any part of the body including the chest or throat

General disorders and administration site conditions:

The following symptoms are usually of short duration, may be severe and may affect any part of the body including the chest or throat:

Common: pain, sensations of heat

Uncommon: sensations of pressure or tightness.

Post-marketing data:

Immune system disorders: hypersensitivity reactions ranging from cutaneous hypersensitivity to anaphylaxis

Nervous system disorders: somnolence

Cardiovascular disorders*:* coronary artery vasospasm transient ischaemic ECG changes, angina and myocardial infarction (see sections 4.3 and 4.4)

Vascular disorders: peripheral vascular ischaemia

Gastrointestinal disorders: ischaemic colitis.

Reporting of suspected adverse events:

Reporting suspected adverse reactions after authorisation of the medicine is important. It allows continued monitoring of the benefit/risk balance of the medicine. Health care providers are asked to report any suspected adverse reactions to SAHPRA via the "6.04 Adverse Drug Reactions Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose:

Administration of a high dose of 25 mg naratriptan in one healthy male subject increased blood pressure by up to 71 mmHg and resulted in adverse events including light-headedness, tension in the neck, tiredness and a loss of co-ordination. Blood pressure returned to baseline by 8 hours after dosing without other pharmacological intervention.

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

Treatment: If overdosage with naratriptan occurs, the patient should be monitored for at least 24 hours and standard supportive treatment applied as required.

5. PHARMACOLOGICAL PROPERTIES:

A 7.3 Vascular medicines, migraine preparations

5.1 Pharmacodynamic properties:

Naratriptan is a selective agonist for the vascular 5-hydroxytryptamine$_1$ (5-HT$_1$) receptor. This receptor is found predominantly in intracranial (cerebral and dural) blood vessels. Naratriptan has high affinity for human cloned 5-HT$_{1B}$ and 5-HT$_{1D}$ receptors; the human 5-HT$_{1B}$ receptor is

thought to correspond to the vascular 5-HT_1 receptor mediating contraction of intracranial blood vessels. Naratriptan has little effect at other 5-HT receptor (5-HT_2, 5-HT_3, 5-HT_4 and 5-HT_7) subtypes. In animals, naratriptan selectively constricts the carotid arterial circulation which supplies blood to the extracranial and intracranial tissues such as the meninges. In addition, experimental evidence suggests that naratriptan inhibits trigeminal nerve activity. Both these actions may contribute to the anti-migraine action of naratriptan in humans.

5.2 Pharmacokinetic properties:

Following oral administration, naratriptan is absorbed with maximum plasma concentrations observed at 2-3 hours. After administration of a 2,5 mg naratriptan tablet, C_{max} is approximately 8,3 ng/ml in women and 5,4 ng/ml in men. The mean elimination half-life is 6 hours.

Naratriptan is predominantly excreted in the urine with 50 % of an oral dose recovered as unchanged naratriptan and 30 % recovered as inactive metabolites. *In vitro*, naratriptan is metabolised by a wide range of cytochrome P450 isoenzymes and does not interact with monoamine oxidase.

6. PHARMACEUTICAL PARTICULARS:

6.1 List of Excipients:

Tablet core: Microcrystalline cellulose, anhydrous lactose, croscarmellose sodium, magnesium stearate.

Film coat: Methylhydroxypropylcellulose, titanium dioxide (E171), triacetin, Iron oxide yellow (E172), indigo carmine aluminium lake (E132).

6.2 Incompatibilities:

Not applicable.

6.3 Shelf-life:

36 months

6.4 Special precautions for storage:

Store at or below 30 °C.

Protect from light.

Keep out of reach of children.

6.5 Nature of contents and container:

NARAMIG tablets are packed in double foil blister packs or child-resistant foil packs of 2, 4, 6 and 12 tablets.

6.6 Special precautions for disposal:

No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION:

GlaxoSmithKline South Africa (Pty) Ltd

39 Hawkins Avenue

Epping Industria 1, 7460

8. REGISTRATION NUMBER:

32/7.3/0463

9. DATE OF FIRST AUTHORISATION / RENEWAL OF THE AUTHORISATION:

25 February 1999

10. DATE OF REVISION OF TEXT:

28 February 2021

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