COUNSELLING *CORNER*

SUVEXX®: ONE pill that takes on migraine attacks with BOTH a triptan and an NSAID[1]

SUVEXX (sumatriptan succinate and naproxen sodium) is indicated for the acute treatment of migraine attacks with or without aura in adults.[1]

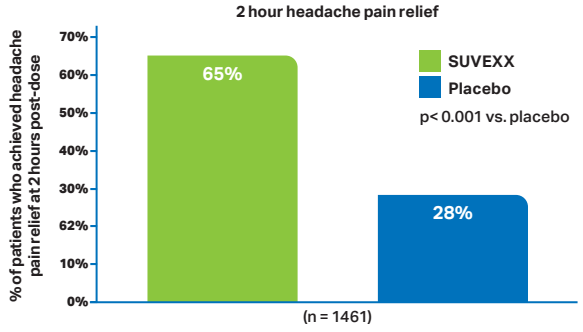
2-in-1 SUVEXX

Formulated with a triptan and an NSAID fixed-dose combination:[1]

- **Triptan** – sumatriptan 85 mg
- **NSAID** – naproxen sodium 500 mg

Demonstrated efficacy in migraine pain relief

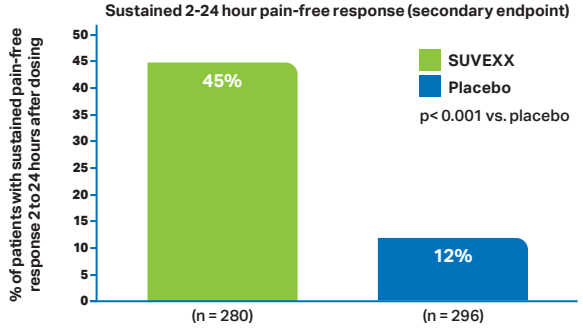
SUVEXX demonstrated pain relief at 2 hours post-dose in a single-dose study.[1,2*†]



Adapted from Product Monograph.

- Significantly more SUVEXX patients achieved 2-hour headache pain relief vs. placebo (p<0.001).[1,2]
- SUVEXX significantly decreased migraine associated symptoms of photophobia and phonophobia at 2 hours post-dose vs. placebo:[2]
  - Photophobia: SUVEXX 58% vs. placebo 36%, p < 0.001
  - Phonophobia: SUVEXX 61% vs. placebo 38%, p < 0.001

SUVEXX delivered sustained pain-free (2-24 hour) response (secondary endpoint)[1,3‡§]



Adapted from Product Monograph.

- 45% of patients who were pain free at 2 hours post-dose, remained pain-free at 24 hours without the use of additional rescue medication.

Pharmacokinetics—Median T_{max}[¶]

- Median T_{max} for sumatriptan when given as a component of SUVEXX was 1 hour (range 0.3 to 4 hours) versus a median T_{max} of 1.5 hours for sumatriptan succinate 100 mg alone.[1]
- Median T_{max} of the naproxen when given as SUVEXX was 6 hours (range 0.3 to 12 hours), approximately 5 hours later than from naproxen sodium tablets (550 mg).[1]

T_{max} =time to maximum plasma concentration

Dosing

Recommended dose: 1 tablet[1£]

COUNSELLING TIPS

- It is advisable that SUVEXX be taken as early as possible during the migraine attack. SUVEXX is effective when administered at any stage of the attack.
- Maximum recommended dosage in a 24-hour period is 2 tablets, taken at least 2 hours apart.
- Tablets should not be split, crushed or chewed.
- SUVEXX can be taken with or without food.

See Product Monograph for complete dosing and administration information.

Clinical use:

SUVEXX is not intended for the prophylactic therapy of migraine or for use in the management of hemiplegic, basilar, or ophthalmoplegic migraine. Safety and efficacy of SUVEXX has not been established for cluster headache, which is present in an older, predominantly male population.

SUVEXX should only be used if a clear diagnosis of migraine headache has been established.

The safety and efficacy of SUVEXX in pediatric patients (<18 years) and the elderly population (>65 years of age) have not been established. SUVEXX is not indicated for use in pediatric patients.

Contraindications:

- Ischemic coronary artery disease (CAD) (angina pectoris, history of myocardial infarction, or documented silent ischemia) or coronary artery vasospasm, including Prinzmetal's angina.
- In the setting of coronary artery bypass graft surgery.
- Wolff-Parkinson-White syndrome or arrhythmias associated with other cardiac accessory conduction pathway disorders.
- History of stroke or transient ischemic attack or history of hemiplegic, basilar, or ophthalmoplegic migraine because these patients are at a higher risk of stroke.
- Peripheral vascular disease.
- Ischemic bowel disease.
- Uncontrolled hypertension.
- Recent use (i.e., within 24 hours) of ergotamine-containing medication, ergot-type medication (such as dihydroergotamine or methysergide), or another 5-hydroxytryptamine1 agonist.
- Concurrent administration of a monoamine oxidase (MAO)-A inhibitor or recent (within 2 weeks) use of an MAO-A inhibitor.
- History of asthma, urticaria, or allergic-type reactions after taking acetylsalicylic acid (ASA) or other nonsteroidal anti-inflammatory (NSAID). Severe, sometimes fatal, anaphylactic reactions to NSAIDs have been reported in such patients. The potential for cross-reactivity between different NSAIDs must be kept in mind.
- Third trimester of pregnancy because of risk of premature closure of the ductus arteriosus and prolonged parturition.
- Breastfeeding women.
- Moderate or severe hepatic impairment or active liver disease.
- Severe uncontrolled heart failure.
- Active gastric/duodenal/peptic ulcer, active GI bleeding.
- Cerebrovascular bleeding or other bleeding disorders.
- Inflammatory bowel disease.

* Randomized, phase 3, double-blind, parallel-group, single-dose study of 1,461 patients with acute migraine with or without aura utilizing placebo and each individual active component of SUVEXX as comparisons (SUVEXX, n=370; placebo, n=365; sumatriptan succinate 85 mg, n=365; naproxen sodium 500 mg, n=361). Co-primary endpoints were superiority of SUVEXX over placebo at 2h post-dose for the following endpoints: pain relief (no or mild pain); incidence of photophobia, phonophobia and nausea; and superiority of SUVEXX vs. the individual components for sustained pain-free at 24 hours.

† Headache relief was defined as a reduction in headache severity from moderate to severe pain to mild or no pain.

‡ In a randomized, double-blind, parallel group, placebo controlled, single attack study of patients with a migraine attack with or without aura (n=576). SUVEXX or placebo was taken within 1 hour of onset of migraine head pain and while pain was mild. Rescue medication was allowed at any point 2 hours after study drug ingestion. The primary endpoint was the percentage of patients who became pain-free (grade 0 on pain scale with no rescue) 2 hours after treatment. Secondary endpoints included the percentage of patients who were pain-free at 0.5, 1, and 4 hours post-dose.

§ Defined as pain-free at 2 hours with no return of pain or use of rescue medication through 24 hours.

¶ Comparative clinical significance has not been established.

£ The safety of treating an average of more than 5 migraine headaches in a 30-day period has not been established. See the Product Monograph for complete dosing and administration instructions.

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- Severe renal impairment (creatinine clearance <30 mL/ min or 0.5 mL/ sec) or deteriorating renal disease (individuals with lesser degrees of renal impairment are at risk of deterioration of their renal function when prescribed NSAIDs and must be monitored).
- Known hyperkalemia.

Most serious warnings and precautions:

Risk of cardiovascular adverse events: Sumatriptan, a component of SUVEXX, can cause coronary artery vasospasm. SUVEXX is contraindicated in patients with uncontrolled hypertension, ischemic CAD, cardiac arrhythmias, and those with history of myocardial infarction. SUVEXX is not recommended in patients with family history or risk factors predictive of CAD.

Naproxen sodium, a component of SUVEXX, is an NSAID. Use of some NSAIDs is associated with an increased incidence of cardiovascular adverse events (such as myocardial infarction, stroke or thrombotic events) which can be fatal. The risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.

Caution should be exercised in prescribing NSAIDs such as naproxen sodium, which is a component of SUVEXX, to any patient with ischemic heart disease (including but NOT limited to acute myocardial infarction, history of myocardial infarction and/or angina), cerebrovascular disease (including but NOT limited to stroke, cerebrovascular accident, transient ischemic attacks and/or amaurosis fugax) and/or congestive heart failure (NYHA II-IV).

Use of NSAIDs, such as naproxen sodium, which is a component of SUVEXX, can promote sodium retention in a dose-dependent manner, through a renal mechanism, which can result in increased blood pressure and/or exacerbation of congestive heart failure.

Risk of gastrointestinal (GI) adverse events: Use of NSAIDs, such as naproxen sodium, which is a component of SUVEXX, is associated with an increased incidence of gastrointestinal (GI) adverse events (such as peptic/ duodenal ulceration, perforation and obstruction of the upper and lower gastrointestinal tract, and gastrointestinal bleeding). These events can occur at any time during use and without warning symptoms. Elderly patients and those with history of peptic ulcer disease and/ or GI bleeding are at greater risk for serious GI events.

Risk in pregnancy: Caution should be exercised in prescribing SUVEXX during the first and second trimesters of pregnancy. Use of NSAIDs at approximately 20 weeks of gestation or later may cause fetal renal dysfunction leading to oligohydramnios and neonatal renal impairment or failure. SUVEXX is contraindicated for use during the third trimester because of risk of premature closure of the ductus arteriosus and uterine inertia.

Other relevant warnings and precautions:

- Use only when a clear migraine diagnosis has been established.
- Use in cluster headache.
- Psychomotor impairment.
- Use in medication overuse headache.
- Not recommended for use with other NSAIDs, except low-dose ASA for cardiovascular prophylaxis.
- Serious cardiac events and fatalities associated with 5-HT1 agonists.
- Cerebrovascular events and fatalities with 5-HT1 agonists.
- Other vasospasm-related events.
- Increased blood pressure; use with caution in patients with controlled hypertension.
- Congestive heart failure and edema.
- Interference of platelet function.
- Use with anticoagulants.
- Anti-platelet effects.
- Blood dyscrasias.
- Increased liver enzymes; evaluate patients with signs of liver dysfunction.
- Hypersensitivity and anaphylactoid reactions.
- Do not use in ASA-intolerance.
- Cross-sensitivity to other NSAIDs.
- Masking of inflammation and fever.
- Excluding other neurologic conditions.
- History of seizures.
- Serotonin syndrome; monitor patients on other serotonergic treatments.
- Blurred and/or diminished vision.
- Renal impairment; use with caution in patients with severe dehydration or pre-existing kidney disease.
- Sodium retention and hyperkalemia.
- ASA-induced asthma.
- May impair fertility; not recommended in women trying to conceive.
- Serious skin reactions (e.g., drug reaction with eosinophilia and systemic symptoms (DRESS), Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis and erythema multiforme).
- Use with caution during first and second trimesters; evaluate risk-benefit.
- Not recommended during labour and delivery.
- Use in breastfeeding women.

For more information:

Please consult the Product Monograph at: https://www.miravohealthcare.com/wp-content/uploads/2022/01/Suvexx-PM-ENG-Dec2021.pdf for adverse reactions, interactions, dosing and conditions of clinical use. The Product Monograph is also available by calling Miravo Medical Information at 1-866-391-4503.

References:

1. SUVEXX® Product Monograph. Aralez Pharmaceuticals Canada Inc., December 2021.
2. Brandes J et al. Sumatriptan-naproxen for acute treatment of migraine: a randomized trial. *JAMA* 2007 Apr 4;297(13):1443-54. **3.** Silberstein S et al. Multimechanistic (sumatriptan-naproxen) early intervention for the acute treatment of migraine. *Neurology* 2008;71:114-121.

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