PROFESSIONAL INFORMATION
CRAMPEASE® FIZZY

- Complementary Medicine
- Discipline: D34.12 Complementary Medicines: Health Supplements – Multiple substance formulation.
- Health Supplements are intended only to complement health or supplement the diet.
- This unregistered medicine has not been evaluated by the SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS
S0

1. NAME OF THE MEDICINE
CRAMPEASE® FIZZY

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each tablet contains:

Active ingredients	Per effervescent tablet	% NRV# per effervescent tablet
Calcium (calcium carbonate)	200 mg	15,38 %
Magnesium (magnesium sulphate)	100 mg	23,81 %
Phosphate Provided by:	48,84 mg	1,27 %
Sodium phosphate	51 mg	*
Potassium phosphate	27 mg	*
L-Carnitine tartrate	200 mg	*
L-Aspartic acid	40 mg	*
L-Glutamate	50 mg	*
Vitamin B6 (pyridoxine hydrochloride)	12 mg	705,88 %
Vitamin D3 (cholecalciferol)	200 IU (5 µg)	33,33 %

Nutrient reference values for adults and children older than 4 years.
* NRV not established
CrampEase® Fizzy contains sugar: sucrose 660 mg/ effervescent tablet.
CrampEase® Fizzy contains the artificial sweeteners: sodium saccharin 15 mg/ effervescent tablet and sodium cyclamate 25 mg/ effervescent tablet.
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Effervescent tablets.
CrampEase® Fizzy Original are white, round, lemon-lime flavoured effervescent tablets.
CrampEase® Fizzy Strawberry are white pink speckled, round, strawberry flavoured effervescent tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
CrampEase® Fizzy helps in the preventative treatment of muscular cramps and assists in the management of muscular cramps and associated discomfort.
4.2 Posology and method of administration
The recommended daily dosage is
Adults 18 years and older:
Non-specific day time cramps: one (1) effervescent tablet in the morning after breakfast. Advise patient that the tablet must be dissolved in 250 ml water and drank once the effervescing has stopped.
Non-specific night time cramps: one (1) effervescent tablet in the evening after dinner. Advise patient that the tablet must be dissolved in 250 ml water and drank once the effervescing has stopped.
4.3 Contraindications
- Hypersensitivity to the active substances or any of the other ingredients in CrampEase® Fizzy (see 6.1 List of excipients).
- CrampEase® Fizzy is contraindicated in patients with renal impairment.
- CrampEase® Fizzy is contraindicated in patients with acute dehydration.
- CrampEase® Fizzy is contraindicated in patients with gastric lesion or gastric disorders.

4.4 Special warnings and precautions for use
- Not suitable for children under the age of 18 years.
- Contains sucrose which may have an effect on the glycaemic control of patients with Diabetes mellitus.
- Contains sucrose. Must not be given to patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency.

Porphyria
Safety has not been established.
4.5 Interaction with other medicinal products and other forms of interactions

Active ingredient	Medicine	Description
Calcium carbonate	Bisphosphonates	Calcium supplementation can decrease the absorption of bisphosphonates, advise patients to take bisphosphonates 30 minutes before taking CrampEase® Fizzy.
Potassium phosphate	Potassium-sparing diuretics (amiloride, spironolactone).	Concomitant use of potassium containing supplements and potassium-sparing diuretics may increase the risk of hyperkalaemia.
Magnesium sulphate	Levodopa/carbidopa	Magnesium may decrease the bioavailability of levodopa/carbidopa by creating an alkaline environment in the gastrointestinal tract and promoting the degradation of levodopa/ carbidopa.
L-Carnitine	Warfarin and acenocoumarol	L-carnitine may enhance the anticoagulant effect of acenocoumarol and possibly warfarin. Concomitant use may increase the risk of bleeding.
L-Carnitine	Thyroid hormone replacement therapy	L-carnitine may act as a thyroid hormone antagonist, concomitant use may decrease the effectiveness of thyroid hormone replacement therapy.

4.6 Fertility, pregnancy and lactation
Pregnancy
CrampEase® Fizzy may be used during pregnancy. However, it is still advisable to consult a healthcare practitioner before use.
Breastfeeding
CrampEase® Fizzy may be used during breastfeeding. However, it is still advisable to consult a healthcare practitioner before use.
Fertility
There are no known effects of CrampEase® Fizzy is safe on fertility.
4.7 Effects on the ability to drive and use machines
Based on the side effect profile, CrampEase® Fizzy is not expected to affect the ability to drive or operate machinery.
4.8 Undesirable effects
Patients experiencing any side effects or sensitivity to any of the ingredients should discontinue use.

System organ class	Frequency	Adverse Event
Eye disorders	Very rare	Nystagmus, visual impairment
Gastrointestinal Disorders	Common Uncommon	Bloating, constipation, gastrointestinal irritation, heartburn, stomach upset Abdominal cramps and pain, colitis diarrhoea, flatulence, gastritis, indigestion, loss of appetite, nausea, and vomiting.
Neurological disorders	Uncommon	Headaches, malaise.
Skin and subcutaneous tissue disorders	Uncommon	Body odour

Advise patient to consult a healthcare provider if symptoms persist, or if any adverse reactions occur.
Reporting of suspected adverse reactions
Reporting of suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicine. Healthcare 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
Symptoms
In overdose, side effects can be precipitated and/or be of increased severity.
No case of oral overdosage has been reported.
Advise patients not to exceed the recommended daily dosage.
See 4.8 **Undesirable effects**
There is no evidence that this product can lead to an overdose when used as recommended.
Treatment
If an accidental overdose occurs, treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Category and class: D34.12 Complementary Medicines: Health Supplements – Multiple substance formulation.
Pharmacotherapeutic classification:
Multivitamins, other combinations. **ATC code**: A11AB.
Calcium: Calcium is essential for nerve transmission, muscle contraction, and renal function. It also plays a role in the uptake, storage, and binding of amino acids.
Magnesium: Extracellular magnesium is essential to maintaining nerve and muscle electrical potentials. Oral magnesium has been reported to reduce pregnancy-related leg cramps brought on by low serum levels of magnesium.
Phosphate: Phosphate is the most common form of phosphorus; it is the most abundant intracellular anion in the body. Phosphate plays an integral role in the buffering of bodily fluid systems and is critical to membrane structure, transport and energy storage.
L-Carnitine: L-carnitine plays a key role in cellular energy production. It is essential for beta-oxidation of long-chain fatty acids in the mitochondria. Carnitine has been shown to increase the oxidative capacity of the liver and muscle during exercise and to promote the recovery of muscle fibre thickness. Benefits of L-carnitine supplementation also include diminished intermittent hypoxia-induced oxidative stress, resulting in delayed muscle fatigue and increased time to exhaustion.
L-Aspartic acid: L-Aspartic acid is a nonessential amino acid and a building block in proteins. It functions in the nervous and reproductive system.
L-Glutamine: Glutamine acts as an inter-organ nitrogen and carbon transporter. Glutamine is essential for maintaining intestinal function, immune response, and amino acid homeostasis during times of severe stress. Glutamine may increase the amount of glycogen stored in muscles following exercise.
Pyridoxine(Vitamin B6): Pyridoxine is essential for amino acid metabolism and to a lesser extent carbohydrate and fat metabolism.
Cholecalciferol (Vitamin D3): Cholecalciferol is biologically inert and requires hydroxylation in the body to its active metabolite, calcitriol. Vitamin D is a fat-soluble vitamin and appears to have immunological activity. It is also an essential vitamin for the proper regulation of calcium and phosphate absorption and homeostasis as well as bone mineralisation.
5.2 Pharmacokinetic properties
Calcium:
Absorption: Calcium absorption is variable and is affected by age, diet, and race. Calcium exhibits threshold absorption, meaning that, above a certain dose, an increase in the amount of calcium ingested will not affect the absorption thereof.
Distribution: More than 99 % of the total body calcium is contained within the bones and teeth, calcium is also present in the blood, muscle tissue, and extracellular fluids. Approximately 50 % of serum calcium is plasma protein bound.
Excretion: Calcium is eliminated through the urine and faeces with varying extents influenced by age and protein intake.
Magnesium:
Absorption: The absorption of magnesium is dependent on both vitamin D and parathyroid hormone, it is absorbed throughout the gastrointestinal tract with an approximate dietary bioavailability of 30 %. Plasma levels of magnesium generally peak 4 hours after oral administration.
Distribution: The body stores an approximate amount of 25 grams of magnesium, which is equally divided between the skeleton and soft tissues. Approximately 30 % of skeletal magnesium is stored at the surface of bone structures and acts as a reserve for the replenishing of extracellular magnesium levels. In plasma, magnesium is 55 % ionised or free, 30 % plasma protein bound, and 15 % complexed to anions.
Excretion: Magnesium is primarily excreted via the kidneys and urine. Excretion can range from 10 to 5000 mg over a 24-hour period.
Phosphate:
Absorption: Generally, 60 to 70 % of dietary phosphate is absorbed via the small intestine. Phosphate absorption from the gastrointestinal tract is partially regulated by cholecalciferol.
Distribution: 85 % of phosphorus in the human body is located in bone, with normal plasma levels ranging from 2,5 to 5 mg/dL. It is also present in various soft tissues and enzymes involved in energy transfer.
Excretion: Phosphates are excreted via the urinary system. Renal tubular reabsorption of phosphate is regulated by cholecalciferol and its metabolites.
L-Carnitine:
Absorption: Dietary L-carnitine appears to be absorbed by active and passive transfer across enterocyte membranes.
Distribution: Carnitine appears to be distributed into extracellular water at first, subsequent tissue entry is slow with complex kinetics.
Metabolism: Following a single dose of L-carnitine, acetyl-L-carnitine and propionyl-L-carnitine are formed, with maximum plasma levels lower than that of carnitine.
Excretion: Orally administered L-Carnitine has a half-life of approximately 15 hours. Carnitine is eliminated in the urine, and is normally reabsorbed in the proximal tubules of the kidneys.
L-Aspartic acid:
Absorption: Amino acids, such as aspartic acid, are transported through intestinal mucosa cells to portal blood by a carrier system. Aspartic acid is released into systemic blood if not utilised by the liver.
Metabolism: L-Aspartic acid is used by the body in the synthesis of other amino acids such as lysine, threonine, and methionine.
L-Glutamine:
Absorption: Glutamine is absorbed from the jejunum.
Distribution: Glutamine is produced primarily by skeletal muscle and then released into systemic circulation. Tissues that require glutamine such as the immune system, gastrointestinal tract, kidneys, and liver obtain glutamine as necessary from the blood.
Metabolism: Glutamine is primarily oxidised. A small fraction (7 to 10 %) is used for gluconeogenesis.
Excretion: The alanyl-glutamine dipeptide is rapidly hydrolised, resulting in elimination half-life of less than four minutes in humans.
Pyridoxine (Vitamin B6):
Absorption: Pyridoxine is absorbed via passive diffusion from the upper gastrointestinal tract.
Metabolism: Pyridoxine is metabolised to coenzyme pyridoxal phosphate in the liver.
Excretion: The metabolites of pyridoxine are excreted via the urinary system.
Vitamin D3:
Absorption: Cholecalciferol is well absorbed from the gastrointestinal tract. The bioavailability of vitamin D in fortified foods appears to be comparable to that of vitamin D in supplements.
Distribution: Dietary vitamin D is transported by chylomicrons to peripheral tissues or the liver, where it is converted to calcitriol.
Metabolism: Cholecalciferol is biologically inert and requires hydroxylation to calcitriol, this process appears to occur first in the liver and then in the kidneys.
Excretion: Vitamin D may be rapidly eliminated from the body in disease cases such as diabetes, HIV, and certain cancers.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Citric acid
Polyethylene glycol 6000
Raspberry red colourant (Fizzy Stawberry)
Sodium bicarbonate
Sodium cyclamate
Sodium saccharin
Strawberry flavour (Fizzy Strawberry)
Sucrose.
6.2 Incompatibilities
None known
6.3 Shelf life
24 months
6.4 Special precautions for storage
- Store in a dry place at or below 25 °C.
- Protect from light and moisture.
- Keep in original packaging until required for use.

6.5 Nature and contents of container
CrampEase® Fizzy Original are white, round, lemon-lime flavoured effervescent tablets, packed in white plastic tube containers with a cap, containing 10 effervescent tablets. One tube or 3 tubes are packed in a printed unit carton that includes a patient information leaflet. CrampEase® Fizzy Strawberry are white pink speckled, round, strawberry flavoured effervescent tablets, packed in white plastic tube containers with a cap, containing 10 effervescent tablets. One tube or 3 tubes are packed in a printed unit carton that includes a patient information leaflet.
6.6 Special precautions for disposal and other handling
No special requirements.

7. HOLDER OF CERTIFICATE OF REGISTRATION
Nativa (Pty) Ltd
260 Cradock Avenue, Lyttelton, Centurion, 0157, Gauteng, South Africa
Tel: +27 (0) 12 664 7110
Customer care line: 0860 628 482
Email: health@nativa.co.za

8. REGISTRATION NUMBER(S)
To be allocated

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
To be allocated

10. DATE OF REVISION OF THE TEXT
June 2022