PROFESSIONAL INFORMATION
LINCTAGON®-C PLUS
Effervescent tablets

- Complementary Medicine.
- D.33.7. Discipline-Specific Traditional Claims - Combination Product.
- 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
LINCTAGON®-C PLUS
(effervescent tablets)
2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each effervescent tablet contains:

Active ingredients	Per effervescent tablet	Per maximum daily dose (3 effervescent tablets)	%NRV# per max daily dose / %VVW# per maks daaglikse dosis
Pelargonium sidoides DC [DER 4-25:1 dry root extract, **equivalent to 78,4-490 mg of dried root]	28 mg**	84 mg	*
Methylsulfonylmethane (MSM)	500 mg	1500 mg	*
Vitamin C (ascorbic acid)	330 mg	990 mg	990 %
N-Acetyl-L-Cysteine provides: L-cysteine	200 mg 148,48 mg	600 mg 445,44 mg	*
Quercetin (quercetin dihydrate)	80 mg	240 mg	*
Zinc (zinc lactate hydrate)	5 mg	15 mg	136 %
Vitamin D3 (cholecalciferol)	290 IU (7,25 µg)	870 IU (21,75 µg)	145 %

#Nutrient reference values for adults and children older than 4 years.
*NRV not established.
Linctagon®-C PLUS is sugar and preservative free.
Linctagon®-C PLUS contains artificial sweeteners: sodium saccharin 20 mg / tablet, sodium cyclamate 30 mg / tablet, sorbitol 500 mg / tablet, isomalt 3,12 mg / tablet.
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Effervescent tablet.
Linctagon®-C PLUS are round, disk shaped, orange flavoured effervescent tablets.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
Linctagon®-C PLUS is a comprehensive effervescent tablet that contains N-Acetyl-L-Cysteine [as a source of L-cysteine] for its antioxidant properties and to enhance the effects of *Pelargonium sidoides*. Additional ingredients include vitamin D3, vitamin C, quercetin, and MSM, which work together for added health benefits that can assist with the relief of cough, mild congestion, body aches and sore throat.
Efficacy of support may vary between users.
4.2 Posology and method of administration
The recommended daily dosage is
Adults and children 12 years and older:
One (1) effervescent tablet three (3) times daily, dissolved in half a glass of water, after meals.
Advise patients not to use at the same time as other medication (see **4.5**)
4.3 Contraindications
- Must not be given to patients with known hypersensitivity to any of the ingredients of Linctagon®-C PLUS (see section 6.1 List of excipients). Patients should be advised to consult their medical practitioner if in doubt.
- Patients taking any chronic medication should not use this product without consulting their medical practitioner.

4.4 Special warnings and precautions for use
- Patients with bleeding disorders or taking anticoagulants/blood thinners or antiplatelet medication should use this product with caution (see **4.5**).
- Patients with a history of oxalate kidney stones should avoid high doses of vitamin C due to increased risk of kidney stone formation.
- Use with caution in patients with asthma as Linctagon®-C PLUS contains N-Acetyl-L-Cysteine.
- Use with caution in patients with autoimmune diseases as Linctagon®-C PLUS contains pelargonium (see **4.5**).
- Do not exceed the daily recommended dose.
- Do not use after the date of expiry.
- Products containing herbal ingredients may interact with some medication.

Porphyria
Safety has not been established.
4.5 Interaction with other medicinal products and other forms of interactions
No interaction studies have been performed on Linctagon®-C PLUS, see below interactions with individual ingredients.

Active ingredient	Medicine	Description
Pelargonium, N-Acetyl-L-Cysteine, quercetin	Blood thinners (anticoagulant or anti-platelet medication) e.g., warfarin	May have a blood thinning effect, increasing the risk of bleeding.
Zinc	Antibiotics	The absorption of antibiotics may be decreased. Oral antibiotics should be taken at least two (2) hours before, or four (4) hours after Linctagon®-C PLUS or similar supplements.
Pelargonium	Immunosuppressant medication	Concomitant use may cause immunostimulant effects.
N-Acetyl-L-Cysteine	Nitroglycerin	Concomitant use can cause hypotension and headaches.

4.6 Fertility, pregnancy and lactation
Pregnancy
Safety of some of the ingredients for use during pregnancy has not been established, therefore this product should not be used in patients who are pregnant.
Breastfeeding
Safety of some of the ingredients for use during lactation (breastfeeding) has not been established, therefore this product should not be used if patients are lactating (breastfeeding).
Fertility
There are no known effects of Linctagon®-C PLUS on fertility.
4.7 Effects on the ability to drive and use machines.
Based on the side effect profile, Linctagon®-C PLUS should not affect your ability to drive or operate machinery.
It is not always possible to predict to what extent Linctagon®-C PLUS may interfere with the daily activities of a patient. Patients should ensure that they do not engage in the above activities until they are aware of the measure to which Linctagon®-C PLUS affects them.
4.8 Undesirable effects
Linctagon®-C PLUS effervescent tablets are generally well tolerated with the occurrence of adverse events unknown.
Patients experiencing any side effects or sensitivity to any of the ingredients, should discontinue use.
Adverse reactions reported in the literature 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)

System Organ Class	Frequency	Adverse Event
Immune system disorders	Not known	Hypersensitivity reactions or anaphylaxis, symptoms include: difficulty breathing or swallowing, angioedema, itchy throat, urticaria and itching.
Nervous system disorders	Not known	Headache.
Gastrointestinal disorders	Not known	Abdominal discomfort, - pain, - cramps and - fullness, diarrhoea, dyspepsia, heartburn, bloating, nausea, vomiting and dry mouth.
Skin and subcutaneous tissue disorders	Not known	Hypersensitivity reaction (skin rash and itching).

If symptoms persist, or if any adverse reactions occur, advise the patient to consult a healthcare provider.
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.
Health care providers are requested to report any suspected adverse drug reactions to SAHPRA via the Med Safety APP (Medsafety X SAHPRA) and eReporting platform (who-umc.org) found on SAHPRA website.
4.9 Overdose
Symptoms
See **4.8 Undesirable effects**
In overdose, side effects can be precipitated and/or be increased. There is no evidence that this product can lead to an overdose when used as recommended. Excessive dosage of N-Acetyl-L-Cysteine has been associated with hypotension and kidney failure. Vitamin D intoxication can occur when vitamin D supplements are taken orally in excessive doses.
Treatment
If an accidental overdose occurs, treatment is symptomatic and supportive.
5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Category and class: D.33.7 Complementary Medicines: Discipline-Specific Traditional Claims - Combination Product.
Pharmacotherapeutic classification: Herbal medicinal product for acute bronchitis.
ATC code: R05CP05
Pharmacotherapeutic classification: Other cough and cold preparations.
ATC code: R05X
Pelargonium sidoides root extract
A study reported the *in vitro* antiviral activity of *Pelargonium sidoides* extract against influenza viruses. During this study, the abundance of the catechin polymer, prodelphinidin, in the extract resulted in the inhibition of influenza, and the impairment of viral haemagglutination and neuraminidase activity. Poly phenols in *Pelargonium sidoides* (including catechin, gallocatechin, and gallic acid) are theorised to stimulate the release of tumour necrosis factor and interleukins, stimulate interferon activity, and increase the activity of natural killer cells. *Pelargonium* root extracts have also been shown to promote phagocytosis and decrease adhesion of bacteria to tissues. The study conducted by Terlizzi *et al.*, 2023 demonstrated increased antibacterial effects and heightened antioxidant activity arising from the synergistic combination of *Pelargonium sidoides* and N-Acetyl-L-Cysteine.
Methylsulfonylmethane:
Research has suggested that MSM may have anti-inflammatory activity, however, MSM does not decrease inflammatory markers C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). MSM appears to reduce homocysteine levels. Human studies have shown that MSM appears to reduce malondialdehyde (MDA) levels and improve antioxidant status. This suggests that MSM might reduce lipid peroxidation. *In vitro* studies have shown that MSM possesses anti-inflammatory activity by inhibiting the oxidative function of activated neutrophils and reducing levels of nuclear factor-kappaB (NF-kappaB), interleukin-1, -6 and -8 (IL-1, IL-6, IL-8) and tumor necrosis factor-alpha (TNF-alpha). A clinical trial has shown the benefit of MSM in relieving upper respiratory symptoms in conditions of allergic rhinitis.
Quercetin
Quercetin may influence immune function. The effect of quercetin on nuclear factor-kappaB may reduce the production of interleukin-1beta, tumour necrosis factor alpha, monocyte chemoattractant protein, and macrophage inflammatory protein. The anti-inflammatory activity of quercetin may be attributed to the inhibition of leukotriene and prostaglandin production and activity, as well as the inhibition of histamine release from basophils and mast cells.
N-Acetyl-L-Cysteine
N-Acetyl-L-Cysteine is a precursor of glutathione, which is a potent antioxidant. While glutathione cannot cross cell membranes, N-Acetyl-L-Cysteine can and is then converted to cysteine and subsequently glutathione. N-Acetyl-L-Cysteine appears to reduce the cellular production of the pro-inflammatory mediators, TNF-alpha and interleukin-1. *In vitro* research has suggested that N-Acetyl-L-Cysteine inhibits markers of inflammation like phospholipid metabolism, pro-inflammatory cytokine release and protease activity.
Vitamins and minerals
A sufficient intake of vitamins and minerals is necessary to maintain normal energy metabolism, and physiological function. Unbalanced diet and insufficient dietary intake of vitamins and minerals can result in subnormal health.
5.2 Pharmacokinetic properties
Pelargonium sidoides root extract
Absorption: There is currently no information available on the biodistribution of *Pelargonium* extracts or their phytochemical constituents. However, the pharmacokinetics of the coumarin constituent has been investigated in a number of species, including humans, as a standalone pharmacophore.
Studies performed on humans have shown that coumarin is completely absorbed from the gastrointestinal tract following oral administration. After absorption, coumarins undergo extensive first-pass metabolism in the liver with only 2 to 6 % reaching systemic circulation unchanged.
Metabolism: Studies have shown, in humans, that coumarin is metabolised, mainly by hepatic enzyme CYP2A6, to 7-hydroxycoumarin.
Excretion: After administration of coumarin, 68 - 92 % of the dose was recovered in the urine as 7-hydroxycoumarin glucuronide and sulfate conjugates. The rapid excretion into the urine suggests that in humans there is very little or no biliary excretion of coumarin metabolites.
Methylsulfonylmethane
Absorption: Pharmacokinetic studies have demonstrated that MSM is absorbed rapidly (within about an hour) from the intestinal tract into the bloodstream with results suggesting near complete bioavailability.
Distribution: Earlier animal studies suggest that MSM is well distributed and completely excreted. MSM can cross the blood-brain barrier and is found in human cerebrospinal fluid in concentrations ranging from 0-25 micromol/L.
Metabolism: MSM is metabolised systemically (forms part of the body's endogenous methanethiol metabolism) and provides sulphur for amino acids cysteine and methionine.
Excretion: Pharmacokinetic studies have suggested that MSM is terminally eliminated from the bloodstream with an approximate half-life of 8 hours.
Quercetin
Absorption: Quercetin is poorly absorbed from the gastrointestinal tract. Time to maximum plasma concentration is dose dependent; with 8, 20 and 50 mg resulting in Tmax values of 1,9, 2,7, and 4,9 hours respectively. Quercetin absorption appears to be promoted by concomitant intake of dietary fat.
Distribution: Quercetin is extensively plasma protein-bound, this may affect the activity of quercetin. Quercetin is found in the plasma as glucuronides, sulfates, and O-methylated derivatives with only small fractions of the aglycone form present.
Metabolism: After conjugation, quercetin is metabolised in the liver, by method of methylation, to isorhamnetin and tamarixetin. Some research suggests that 23 to 80 % of quercetin is metabolised to carbon dioxide and is eliminated through expired air.
Excretion: Quercetin is excreted in the urine as glucuronide and sulfate conjugates as well as methylated metabolites with half-lives ranging from 6-28 hours.
Vitamins and minerals
The combination of vitamins and minerals is typical of a normal diet. Therefore, the pharmacological metabolism and fate of Linctagon®-C PLUS is anticipated to be similar.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Citric acid anhydrous
Hydrated magnesium silicate
Flavouring (orange and naartjie)
Polyethylene glycol 6000
Sodium bicarbonate
Sodium carbonate anhydrous
Colourant (sunset yellow)
Colloidal silicon dioxide
Polyvinylpyrrolidone
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.
- Do not use after the expiry date printed on the carton.

6.5 Nature and contents of container
Linctagon®-C PLUS are round, disk-shaped effervescent tablets with an orange-naartjie flavour.
Linctagon®-C PLUS is available in a white plastic tube container with a spiral cap, that contains a desiccant. It contains 12 effervescent tablets, packaged 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 2024

PPIL328/02