PROFESSIONAL INFORMATION
LINCTAGON®-C JUNIOR EFFERVESCENT TABLETS

- Complementary Medicine
- Discipline: D 5.8 Preparations for the common cold including nasal decongestants.
- 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 JUNIOR (effervescent tablets)

2. QUALITATIVE AND QUANTITATIVE COMPOSITION
Each effervescent tablet contains:

Active ingredients	Per effervescent tablet	Per 2 effervescent tablets (max. daily dosage)	% NRV# per 2 effervescent tablets (max. daily dosage)
Pelargonium sidoides DC Dry root extract (DER 4-25:1), extraction solvent ethanol 11 % m/m. **Equivalent to 28 – 175 mg of dried root.	**10 mg	20 mg	*
Vitamin A (vitamin A retinyl palmitate)	500 IU (151 µg)	1000 IU (303 µg)	34 %
Vitamin C (ascorbic acid)	325 mg	650 mg	650 %
MSM (methylsulfonylmethane)	200 mg	400 mg	*
Zinc (zinc lactate hydrate)	2,5 mg	5 mg	45 %

Nutrient reference values for adults and children older than 4 years.
*NRV not established
Linctagon®-C Junior effervescent tablets berry flavour is sugar free. Contains artificial sweeteners: sorbitol 850 mg/ tablet, sodium saccharin 20 mg/ tablet, sodium cyclamate 30 mg/ tablet.
Linctagon®-C Junior effervescent tablets orange flavour is sugar free. Contains artificial sweeteners sorbitol 950 mg/ tablet, sodium saccharin 20 mg/ tablet and sodium cyclamate 30 mg/ tablet.
For full list of excipients, see section 6.1.

3. PHARMACEUTICAL FORM
Effervescent tablets.
Linctagon®-C Junior effervescent tablets are available in different flavour variants.
Orange flavour: Round, disk shaped, orange coloured and orange flavoured effervescent tablet.
Berry flavour: Round, disk shaped, pink colour and berry flavoured effervescent tablet.

4. CLINICAL PARTICULARS
4.1 Therapeutic indications
A combination effervescent tablet for the relief of symptoms associated with the common cold and flu such as congestion, sneezing, allergies, coughs and muscle aches. Offers immune support. High in vitamin C. Non-drowsy.
4.2 Posology and method of administration
The recommended daily dosage is
Children 2 – 6 years:
One (1) effervescent tablet dissolved in half a glass of water once per day, after meals.
Children 6 – 12 years:
One (1) effervescent tablet dissolved in half a glass of water twice per day, after meals.
Advise patients not to exceed the daily dose.
The recommended duration of use is at least 5 – 7 days.
Advise the patient to consult a healthcare provider if the symptoms do not improve within 5 days of the use of this medicinal product.
4.3 Contraindications
- Hypersensitivity to the any of the active substances or any other ingredients in Linctagon®-C Junior effervescent tablets (see 6.1 List of excipients).

4.4 Special warnings and precautions for use
- Must not be given to patients with known hypersensitivity or allergy towards any of the ingredients. Patients should be advised to consult their medical practitioner if in doubt.
- Hepatotoxicity and hepatitis cases have been reported in association with the administration of products similar to Linctagon®-C Junior effervescent tablets. Advise patients to discontinue use in the event of signs of hepatotoxicity, and to consult a healthcare provider.
- Use with caution in patients presenting with or prone to iron overload, hemochromatosis, thalassemia and sideroblastic anaemia as Linctagon®-C Junior effervescent tablets contains vitamin C which can increase iron absorption and may worsen these conditions.
- Use with caution in patients with a history of oxalate kidney stones as Linctagon®-C Junior effervescent tablets contains vitamin C that can increase the risk of stone formation.
- Must not be given to patients with the rare hereditary condition of sorbitol/malitol/lactitol intolerance.
- Discontinue use two weeks prior to surgery.

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

Active ingredient	Medicine	Description
Pelargonium sidoides DC., Vitamin C	Blood thinners (anticoagulant- or antiplatelet medication) e.g. Warfarin	May have a blood thinning effect increasing the risk of bleeding.
Vitamin A	Retinoid drugs	Could have additive toxic effects when taken with vitamin A supplements. Advise patients taking retinoids to avoid vitamin A supplements.
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 Junior effervescent tablets or similar supplements.

4.6 Fertility, pregnancy and lactation
Pregnancy
Use during pregnancy is not recommended as safety during pregnancy has not been established.
Breastfeeding
Use is not recommended as safety during lactation has not been established.
Fertility
There are no known effects of Linctagon®-C Junior effervescent tablets on fertility.
4.7 Effects on the ability to drive and use machines.
Based on the side effect profile, Linctagon®-C Junior effervescent tablets is not expected to affect the ability to drive or operate machinery.
4.8 Undesirable effects
Linctagon®-C Junior 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
Gastrointestinal disorders	Not known	Abdominal discomfort and pain, diarrhoea, dry mouth, dyspepsia, heartburn, indigestion, mouth irritation, nausea and vomiting.
Immune system disorders	Not known	Hypersensitivity reactions or anaphylaxis, symptoms include: difficulty breathing or swallowing, angioedema, itchy throat, urticarial and itching.
Skin and subcutaneous tissue disorders	Not known	Hypersensitivity reaction (skin rash).

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://sahpra.org.za/wp-content/uploads/2020/01/6.04_ARF1_v5.1_27Jan2020.pdf
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 vitamin A may lead to hypervitaminosis. Due allowance should always be made for intake of these vitamins from other sources.
Treatment
If an accidental overdose occurs, treatment is symptomatic and supportive.

5. PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
Category and class: D 5.8 Preparations for the common cold including nasal decongestants.
Pharmacotherapeutic classification: Herbal medicinal product for treatment of symptoms associated with colds and flu.
ATC- code: R05CP05
other cough and cold preparations
ATC - code: R05X
Pelargonium sidoides DC. [root extract]
A study reported the *in vitro* antiviral activity of *Pelargonium sidoides* DC. 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.
Polyphenols in *Pelargonium sidoides* DC. (including catechin, gallocatechin, and gallic acid) are theorized to stimulate the release of tumor 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.
Vitamin A
Retinol is important for immune function. Retinoic acid is required in maintaining adequate levels of natural killer cells. Preliminary evidence suggests that retinoic acid might increase the production of cytokines, such as interleukin 1 (IL-1). Additionally, B lymphocyte growth, differentiation, and activation are dependent on vitamin A.
Vitamin C
T-lymphocyte activity, phagocyte function, leukocyte mobility, and antibody and interferon production appear to be increased by vitamin C. There is also interest in using ascorbic acid for allergies, such as allergic rhinitis; evidence suggests that a low levels of ascorbic acid are associated with higher plasma histamine levels.
Methylsulfonylmethane
Researchers have 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 improves 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). Animal studies have shown that administration of MSM modifies and mitigates abnormal immune reactions that trigger inflammation. A clinical trial has shown the benefit of MSM in relieving upper respiratory symptoms in conditions of allergic rhinitis.
Zinc
Zinc is an essential trace element and plays a role in normal immune functioning. The mechanism by which zinc affects common colds is unclear.
5.2 Pharmacokinetic properties
Pelargonium sidoides DC. [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
Distribution: There is currently no information available on the biodistribution of *Pelargonium* extracts or their phytochemical constituents.
Metabolism: Studies have shown that, in humans, 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
Vitamin A
Absorption: 70 – 90 % of preformed vitamin A is absorbed from the intestinal tract. Retinyl esters are metabolised (hydrolysed) by pancreatic and intestinal enzymes where after the unesterified retinol is absorbed directly into intestinal cells by both diffusion and active transport.
Distribution: The liver, through storage and release, narrowly maintains vitamin A concentrations. Vitamin A is bound to retinol-binding protein in the plasma. Vitamin A is stored as retinol, mainly in the liver and to a lesser extent in the retina, kidneys, lungs, adrenal glands and intraperitoneal fat.
Metabolism: Systemically, vitamin A is metabolised to 11-cis-retinoids and acidic retinoids.
Excretion: Vitamin A is primarily excreted through the urine, with a lesser fraction excreted through the faeces and expiration. Biliary excretion increases in conditions of vitamin A excess.
Vitamin C
Absorption: Orally administered vitamin C is well absorbed however, absorption decreases as the dose increases. This is due to the saturable sodium-dependent vitamin C transporter responsible for transporting vitamin C from the intestines into the bloodstream.
Excretion: Ascorbic acid, as it is highly hydrophilic, is mainly excreted through the kidneys into the urine.
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 µmol/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.
Zinc
Absorption: 15 to 40 % of dietary zinc is absorbed from the gastrointestinal tract. Zinc is absorbed primarily in the small intestine.
Distribution: Plasma zinc levels are narrowly regulated at 10 to 15 µmol/L with more than 85 % of the total zinc content in the body being stored in skeletal muscle and bone.
Metabolism: After administration, zinc is rapidly transported to the liver. After oral administration, zinc levels decreased from a maximum of 1.2 % of the administered dose to 0.7 % of the administered dose after 24 hours.
Excretion: Zinc is primarily excreted through the faeces with a small fraction excreted through the urine.

6. PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Citric acid (anhydrous)
Hydrated magnesium silicate
Polyethylene glycol 6000
Polysorbate 60
Colloidal silicon dioxide
Sodium bicarbonate
Sodium carbonate (anhydrous)
Sodium cyclamate
Sorbitol (spray dried)
Sunset yellow colourant (orange flavour effervescent)
Tangerine flavouring (orange flavour effervescent)
Orange juice flavour (orange flavour effervescent)
Strawberry flavour (berry flavour effervescent)
Red raspberry colourant (berry flavour effervescent)
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
Linctagon®-C Junior effervescent tablets are available in different flavour variants.
Orange flavour: Round, disk shaped, orange colour and orange flavoured effervescent tablet.
Berry flavour: Round, disk shaped, pink colour and berry flavoured effervescent tablet.
Linctagon®-C Junior effervescent tablets are packed in a white plastic tube container with a cap, containing 12 or 20 effervescent tablets, in a unit carton and 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
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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
July 2022

PPIL309/02