PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

Echinaforce®
Sore Throat Spray

COMPLEMENTARY MEDICINE
Western Herbal Medicines
This unregistered medicine has not been evaluated by the South African Health Products Regulatory Authority for its quality, safety or intended use.

SCHEDULING STATUS:
S0

1 NAME OF THE MEDICINE
A.VOGEL ECHINAFORCE® SORE THROAT SPRAY

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each 1 ml contains:
Echinacea purpurea (L.) MOENCH (Purple cone-flower) ....863,3 mg
[Fresh aerial parts, 1:12 extract providing dry plant equivalent: 72 mg per ml drug product]
Echinacea purpurea (L.) MOENCH (Purple cone-flower) ....45,5 mg
[Fresh root, 1:11 extract providing dry plant equivalent: 4,1 mg per ml drug product]
Salvia officinalis (L.) (Sage) ....430 mg
[Fresh leaves, 1:17 extract providing dry plant equivalent: 25 mg per ml drug product]

1 spray ≈ 0,22 ml

Contains more than 40 % *v/v* alcohol.
Contains sugar: Sorbitol ....293,0 mg
Sucrose ....5,0 mg

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM
Clear, brown to yellow-green liquid with an aromatic odour of peppermint and a fresh, slightly bitter alcoholic taste.

4 CLINICAL PARTICULARS
4.1 Therapeutic indications
A.VOGEL ECHINAFORCE® SORE THROAT SPRAY is a herbal medicine used to treat pain, inflammation and infections of the mouth (stomatitis) and throat, such as pharyngitis, tonsillitis, sore throats and hoarseness associated with coughs, colds and flu.

4.2 Posology and method of administration
Posology
Adults and children over 12 years:
2 sprays 6 - 10 times daily

Special populations

Elderly population:
No dosage adjustment is required for this population.

Paediatric population:
Children 4 – 12 years:
1 Spray 6 – 10 times daily.
This product is not indicated in patients younger than 1 year.

Method of use:
For oropharyngeal mucosal and oral use only.
Shake before use.
Start therapy at first signs of symptoms.

Duration of use
Do not use A.VOGEL ECHINAFORCE® SORE THROAT SPRAY for more than 2 weeks continuously.
If the symptoms persist for more than 7 days, a doctor, pharmacist or other healthcare provider should be consulted.

4.3 Contraindications
- Do not use in cases of known hypersensitivity to the active substances, to plants of the *Asteraceae (Compositae)* family or to any of the excipients listed in section 6.1.
- Because of their immunostimulating activity, *Echinacea* extracts must not be used in cases of progressive systemic disorders, autoimmune diseases, immunodeficiencies, immunosuppression and diseases of the white blood cell system.
- Concomitant use with immunosuppressant medicines.
- Children under 1 year of age.

4.4 Special warnings and precautions for use
- If the symptoms worsen or high fever occurs during the use of A.VOGEL ECHINAFORCE® SORE THROAT SPRAY, a doctor, pharmacist or healthcare provider should be consulted.
- There is a possible risk of anaphylactic reactions in atopic patients. Atopic patients should consult their doctor before using products containing *Echinacea*. A.VOGEL ECHINAFORCE® SORE THROAT SPRAY contains alcohol and should be used with caution by individuals with a sensitivity or intolerance to alcohol.
- Due to Peppermint oil (*Mentha x piperita*) content - use with caution in patients with gastroesophageal reflux disease, and due to the menthol content, use with caution in epilepsy, asthma, persistent or chronic cough, or other chronic lung conditions.
- A.VOGEL ECHINAFORCE® SORE THROAT SPRAY contains sorbitol and sucrose:
  Sorbitol warning:
  Patients with the rare hereditary condition of sorbitol intolerance should not use A.VOGEL ECHINAFORCE® SORE THROAT SPRAY.
  Sucrose warning:
  Sucrose may have an effect on the glycaemic control of patients with diabetes mellitus.
  Patients with rare hereditary conditions such as fructose intolerance, glucose-galactose malabsorption or sucrase-isomaltase insufficiency should not use A.VOGEL ECHINAFORCE® SORE THROAT SPRAY.

4.5 Interaction with other medicines and other forms of interaction
Do not use with immunosuppressant medicines which cause immunosuppression (Refer to 4.3).
There is no evidence from limited interaction studies that Echinacea or Salvia extracts will interact with other medicinal products.

4.6 Fertility, pregnancy and lactation
Women of childbearing potential/Contraception in males and females
No information available.

Pregnancy
Data on a limited number (several hundreds) of exposed pregnancies indicate no adverse effects of *Echinacea* extracts on pregnancy or on the health of the foetus/new-born child. Data concerning the immune system of the new-born child is not available. To date, no other relevant epidemiological data are available.
Safety during pregnancy has not been established for *Salvia* extracts.
Non-clinical studies on reproductive toxicity have not been performed.
As a precautionary measure and in the absence of sufficient data, the use during pregnancy is not recommended unless advised by a doctor.

Breastfeeding
Safety during lactation has not been established for *Salvia* extracts.
As a precautionary measure and in the absence of sufficient data, the use during lactation is not recommended unless advised by a doctor.

Fertility
Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines
Based on its pharmacodynamic properties, A.VOGEL ECHINAFORCE® SORE THROAT SPRAY is likely to have no influence on the ability to drive or use machines. No studies on the effects on the ability to drive and use machines have been performed.
A.VOGEL ECHINAFORCE® SORE THROAT SPRAY, (due to its alcohol content) may have an effect on mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision in sensitive individuals.

4.8 Undesirable effects
Adverse reactions are grouped into the following frequency classifications: 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 assessed from the available data)

Tabulated list of adverse reactions

Body System	Undesirable effect	
	Common	Frequency not known
Immune system disorders:		Hypersensitivity reactions (rash, urticaria, Stevens-Johnson Syndrome, angioedema of the skin, Quincke oedema, bronchospasm with obstruction, asthma and anaphylactic shock) may occur. *Echinacea* can trigger allergic reactions in atopic patients.
Skin and subcutaneous tissue disorders:	Rash on the buccal mucosa and/or a burning sensation of the throat.	

a. Paediatric population
Frequency, type and severity of adverse reactions in children are expected to be the same as in adults.

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicine 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 Reaction Reporting Form**", found online under the SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
None known. Treatment of overdosage should be symptomatic and supportive. For *Salvia* leaves overdose has been reported with a sense of heat, tachycardia, vertigo and epileptic form convulsions (seizures) after intake corresponding to more than 15 g of *Salvia* leaves.

5 PHARMACOLOGICAL PROPERTIES
5.1 Pharmacodynamic properties
D33.6 Western Herbal Medicine
ATC code: Throat preparations: R02AX

In vitro
The antibacterial activity of A.VOGEL ECHINAFORCE® SORE THROAT SPRAY has been investigated by determining the inhibitory and bactericidal effects on various normal and (facultatively) pathogenic germs of the oral cavity including *Staphylococcus aureus*, *Streptococcus pyogenes*, *Streptococcus pneumoniae*, *Klebsiella pneumoniae*, *Moraxella catarrhalis*, and *Haemophilus influenzae*. Furthermore, A.VOGEL ECHINAFORCE® SORE THROAT SPRAY inhibited growth and was as bactericidal against *Streptococcus pneumoniae* as 0,1 % chlorhexidine which served as positive control. Furthermore, the experiments showed that A.VOGEL ECHINAFORCE® SORE THROAT SPRAY acted better than the single *Echinacea*- or *Salvia*-tinctures alone in this regard.

For ethanolic preparations made of *Echinacea purpurea* and *Salvia officinalis* anti-inflammatory, antibacterial and antiviral effects have been shown. A.VOGEL ECHINAFORCE® SORE THROAT SPRAY has demonstrated antiviral effects (inhibition of viral replication) against various strains of influenza virus (H3N2, H5N1, H7N7, H1N1) as well as *Herpes simplex* virus, with inhibitory concentrations (IC_{50}) of 1,6 ug/ml (H3N2) and 50 ug/ml (H5N1, H7N7, H1N1) and for *Herpes simplex* a MIC_{100} of 0,1 uL/ml was achieved i.e. significantly lower than local concentrations reached with oral treatment.

The *Echinacea* tincture mixture (Echinaforce®) contained in A.VOGEL ECHINAFORCE® SORE THROAT SPRAY, potently regulates the expression of cytokines like TNF-α and acts as an immune-modulator: Excessive production of inflammatory cytokines and chemokines are dampened. Alkylamides in Echinaforce® tincture mixture were shown to be key players in the process of immune modulation via acting on CB-2 receptors on immune cells. Interaction with CB-2 receptor was confirmed by computer modelling techniques.

Echinaforce® tincture mixture further induced phagocytotic capacity in human granulocytes by 56 % when compared to control.

Anti-oxidative effects were attributed to the Echinaforce® tincture mixture: Cyclooxygenase and Lipoxygenase enzymes were inhibited by 44,7 ± 15,3 % and 93 ± 7 %, respectively.

Direct and indirect antiviral activity by secretion of interferon was demonstrated for *Echinacea purpurea.*

Ex vivo
Leukocytes isolated from volunteers treated with Echinaforce® tincture mixture showed modulated activity. Expression of cytokines (IL-8 and TNF-α) was inhibited under ex vivo stimulation with LPS.

Clinical studies
A double blind, randomized, double-dummy clinical trial investigated the non-inferiority of A.VOGEL ECHINAFORCE® SORE THROAT SPRAY to a chlorhexidine/lidocaine spray in 154 patients with acute sore throats. After three days of the treatment, the number of respondents (patients with a decrease of their sore throat symptoms of at least 50 % compared to baseline) were the same in both groups, thus proving non-inferiority. Both treatments were equal regarding further secondary efficacy parameters and were both very well tolerated.

5.2 Pharmacokinetic properties
A randomized, open, single dose bioavailability and pharmacokinetic study has been performed with A.VOGEL ECHINAFORCE® SORE THROAT SPRAY in eight fasted volunteers. The participants received a daily dose of 4,4 ml (10 times a single dose of 0,44 ml) of the spray and blood samples were taken after 15, 30, 60 minutes, 1,5 and 3 hours. The mean C_{max} of dodeca-2E,4E,8Z,10E/Z-tetraenoic acid isobutylamides, a mixture of isomeric alkylamides from the Echinaforce® tincture mixture contained in A.VOGEL ECHINAFORCE® SORE THROAT SPRAY, appeared after 0,91 hours with a mean of 0,23 ng/ml plasma. The data show that pharmacologically active ingredients from A.VOGEL ECHINAFORCE® SORE THROAT SPRAY are bioavailable.

5.3 Preclinical safety data
Used in clinically relevant concentrations, A.VOGEL ECHINAFORCE® SORE THROAT SPRAY does not inhibit P450 enzymes or influence g-glycoproteins.

Echinacea purpurea showed no toxicity in single dose toxicity (rodents), repeated-dose toxicity (rodents) and genotoxicity/carcinogenicity studies.

Effects in non-clinical studies for *Salvia* were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.

Thujone is reported to be neurotoxic. The daily intake of α-thujone amounts to 1,5 mg (0,15 mg per single adult dose A.VOGEL ECHINAFORCE® SORE THROAT SPRAY). This intake is about 200 times lower than the NOEL derived from a 6 weeks' study in rats.

No mutagenic effects of Echinaforce® tincture mixture were detected in Ames' test (with or without metabolic activation).

Non-clinical studies on reproductive toxicity have not been performed.

6 PHARMACEUTICAL PARTICULARS
6.1 List of excipients
Ethanol
Peppermint oil
Sucrose (vegetable source)
Sorbitol
Soy lecithin (vegetable source)

Contains sugar: Sorbitol ....293,0 mg
Sucrose ....5,0 mg

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months unopened.
Use within 2 months of opening.

6.4 Special precautions for storage
No special storage conditions.
Store at or below 25 °C.
Store in the original package/container.

6.5 Nature and contents of container
Brown glass flasks of hydrolytic glass Type III with air pump (snap-on-cap with spray pump; polyethylene / polyoxymethylene / stainless steel) and adapter (spray nozzle and actuator; polyethylene / polypropylene).
Pack size: 30 ml (≈ 136 sprays)

6.6 Special precautions for disposal of a used medicine or waste materials derived from such medicine and other handling of the product
No special requirements.

7 THE HOLDER OF THE CERTIFICATE OF REGISTRATION
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Listing number: 519048

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

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