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 SAHPRA for its quality, safety or intended use.

SCHEDULING STATUS:
S0

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

2 QUALITIVE AND QUANTITIVE COMPOSITION
Each 1 ml contains:
Echinaforce®:
863,3 mg of extract (as tincture) from fresh *Echinacea purpure*a (L.) MOENCH herba (Purple coneflower herb) (1: 12-13)
Dry plant equivalent (dpe): 72 mg per ml drug product
Fresh plant equivalent (fpe): 245 – 440 mg per ml drug product

45,5 mg of extract (as tincture) from fresh *Echinacea purpurea* (L.) MOENCH radix (Purple coneflower root) (1: 11-12)
Dry plant equivalent (dpe): 4,1 mg per ml drug product
Fresh plant equivalent (fpe): 12 – 23 mg per ml drug product

430.0 mg of extract (as tincture) from fresh *Salvia officinalis* (L.) folium (Sage leaves) (1: 17-18)
Dry plant equivalent (dpe): 25 mg per ml drug product
Fresh plant equivalent (fpe): 100 – 175 mg per ml drug product

1 spray = 0,22 ml

Contains Alcohol: 40 - 47 % v/v
Contains sugar: Sorbitol 293 mg
Sucrose 5,0 mg

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
A 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 to 12 years: 1 spray 6 – 10 times daily
The use in children below 1 year of age is contraindicated (see section 4.3 Contraindications).

Method of administration
For oropharyngeal mucosal and oral use only.
Shake well before use.

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 substance, to plants of the Asteraceae (Compositae) family, to Salvia or to any of the excipients listed in section 6.1.
- Because of their immunomodulating activity, Echinacea extracts must not be used in cases of progressive systemic disorders, autoimmune diseases, therapeutic 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.
- *Sorbitol warning:*
  A.VOGEL ECHINAFORCE SORE THROAT SPRAY contains sorbitol. Patients with a rare hereditary condition of sorbitol intolerance should not use A.VOGEL ECHINAFORCE SORE THROAT SPRAY.
- *Sucrose warning:*
  A.VOGEL ECHINAFORCE SORE THROAT SPRAY contains sucrose which 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.

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 and lactation 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 and lactation is not recommended unless advised by a doctor.

Breastfeeding
Safety during pregnancy and lactation has not been established for Salvia extracts. As a precautionary measure and in the absence of sufficient data, the use during pregnancy and 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
A.VOGEL ECHINAFORCE SORE THROAT SPRAY has no or negligible influence on the effect of mental and/or physical abilities to perform or execute tasks or activities requiring mental alertness, judgment and/or sound coordination and vision.

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 have been reported in a clinical trial and are common (1/80).	

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 professionals are asked to report any suspected adverse reactions to the SAHPRA via the "6.04 Adverse Drug Reaction Reporting Form", found online under SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose
No case of overdose has been reported.
In case of overdose, symptoms according to the ingested amount of ethanol can be expected.
For Salvia leaves overdose, the following has been reported: 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
Pharmacotherapeutic group and ATC code:
Throat preparations /R02AX
Pharmacodynamic effects:

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. The spray inhibited growth and was as bactericidal as 0,1 % chlorhexidine which served as positive control. Furthermore, the experiments showed that the A.VOGEL ECHINAFORCE SORE THROAT SPRAY acted better than the single Echinacea- or Salvia-tinctures alone.
For ethanolic preparations made of *Echinacea purpurea* and *Salvia officinalis* anti-inflammatory, antibacterial and antiviral effects have been shown. For the A.VOGEL ECHINAFORCE SORE THROAT SPRAY antiviral and antibacterial activity have been demonstrated.
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 comparing 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 randomised, open, single dose bioavailability and pharmacokinetic study has been performed with the 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.
These 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)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
36 months.
After opening, use within 2 months

6.4 Special precautions for storage
Store at or below 25 °C in a cool, dry place.
Store in the original package.

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 sizes: 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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8 REGISTRATION NUMBER(S)
Listing number: 029794

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

10 DATE OF REVISION OF TEXT
August 2019

41576/PI.08/2019