PROFESSIONAL INFORMATION FOR MEDICINES FOR HUMAN USE

CRATAEGUS OXY

COMPLEMENTARY MEDICINE

Western Herbal Medicine

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 CRATAEGUS OXY (oral drops)
Western Herbal Medicine

2 QUALITIVE AND QUANTITIVE COMPOSITION

Each 1 ml contains:

Crataegus species (Hawthorn) ..... 970 mg

[From: *Crataegus oxyacantha* L. and *Crataegus monogyna* Jacq., fresh fruits, 1:3,2 extract providing dry plant equivalent: 301 mg per ml]

Contains approximately 50 % *v/v* alcohol.
Sugar free.

For full list of excipients, see section 6.1.

3 PHARMACEUTICAL FORM

Clear to slightly turbid, brown to reddish-brown liquid with an aromatic odour and an aromatic, slightly bitter taste.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A.VOGEL CRATAEGUS OXY is a herbal medicine which assists in promoting the function of the heart.

As a cardiac tonic it assists with impaired heart performance specifically due to congestive and ischemic heart disease.

With broad acting cardiac supportive action (in heart failure, cardiac oppression, mild angina, arrhythmia, and geriatric heart weakness), it assists to improve exercise tolerance, quality of life, and breathlessness and fatigue in cardiac patients.

4.2 Posology and method of administration

Posology

Adults and children over 12 years:
Take 30 drops 3 times daily.

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

Paediatric population
This product is not indicated in patients younger than 12 years.

Method of administration
For oral use only.
Take preferably 30 minutes before meals.
Take drops diluted in a small volume of water.

4.3 Contraindications

- A.VOGEL CRATAEGUS OXY should not be used in patients who have a hypersensitivity to the active substances, Crataegus species (Hawthorn), or to any of the excipients listed in section 6.1.

4.4 Special warnings and precautions for use

- A.VOGEL CRATAEGUS OXY contains alcohol and should be used with caution by individuals with a sensitivity or intolerance to alcohol.
- If the condition worsens or does not improve after 6 weeks, consult a healthcare practitioner.
- If symptoms include: pain occurring in the region of the heart and spreading out to the arms, upper abdomen or neck; shortness of breath at rest or during usual daily exercise; the accumulation of fluid in the legs, medical advice must be sought immediately.
- Patients taking medication for diseases of the cardiovascular system should consult their doctor before using A.VOGEL CRATAEGUS OXY.

Paediatric population

- A.VOGEL CRATAEGUS OXY is not recommended for use in children under 12 years of age due to a lack of data on safety.

4.5 Interaction with other medicines and other forms of interaction

None confirmed.

4.6 Fertility, pregnancy and lactation

Women of childbearing potential/Contraception in males and females
No information available.

Pregnancy
The safety of this product during pregnancy has not been established. In the absence of sufficient data, the use of A.VOGEL CRATAEGUS OXY during pregnancy is not recommended, unless advised by and under the supervision of a healthcare provider.
Caution should be exercised when prescribing to pregnant women:

- For Hawthorn berry extracts, no clinical data on exposed pregnancies are available. Animal studies do not indicate direct or indirect harmful effects with respect to pregnancy, embryonal/foetal development, parturition or postnatal development.
- According to Bone & Mills (2013), Hawthorn has a Category B1 pregnancy safety rating i.e. no increase in frequency of malformation or other harmful effects on the foetus from limited use in women & no evidence of increased foetal damage in animal studies.

Breastfeeding
A.VOGEL CRATAEGUS OXY during breastfeeding is not recommended, unless advised by and under the supervision of a healthcare provider.
Caution should be exercised when prescribing to breastfeeding women:

- According to Bone & Mills (2013), Hawthorn is considered compatible with breastfeeding.

Fertility
Fertility studies have not been performed.

4.7 Effects on ability to drive and use machines

Based on its pharmacodynamic properties A.VOGEL CRATAEGUS OXY is not likely to negatively influence the ability to drive and use machines. No studies on the effects on the ability to drive and use machines have been performed.

It is not always possible to predict to what extend A.VOGEL CRATAEGUS OXY 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 A.VOGEL CRATAEGUS OXY affects them.

A.VOGEL CREATEGUS OXY contains alcohol.

4.8 Undesirable effects

Nausea and gastrointestinal discomfort may occur less frequently.

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 SAHPRA's publications: https://www.sahpra.org.za/Publications/Index/8

4.9 Overdose

No toxic effects are expected.
In overdose, side effects can be precipitated and/or be of increased severity (see section 4.8).
Treatment of overdosage should be symptomatic and supportive.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Western Herbal Medicine D33.6

Pharmacotherapeutic group and ATC code:
Other cardiac preparations, crataegus glycosides / C01EB04

Clinical studies
Extensive research has provided good evidence of the efficacy of adjunctive Hawthorn extract in congestive heart disease (NYHA Class I and II) due to ischemia, hypertension or other causes. (Bone and Mills 2013) Both a meta-analysis (Pittler, Guo *et al.* 2008) and a Cochrane systematic review concluded that adjunctive Hawthorn therapy offers significant benefit in the treatment of chronic heart failure, Hawthorn specifically improving:

- Maximal workload (Pittler, Guo *et al.* 2008)
- Exercise tolerance
- Pressure-heart rate product (index of cardiac oxygen consumption) (Pittler, Guo *et al.* 2008)
- Shortness of breath (Pittler, Guo *et al.* 2008)
- Fatigue (Pittler, Guo *et al.* 2008)

A.VOGEL CRATAEGUS OXY demonstrated broad-acting cardiac supportive effect in an open, multicentre phase IV trial. 44 cardiac patients (CCF NYHA I & II, cardiac oppression, elderly with impaired heart performance, NYHA Class 1 angina or mild bradyarrhythmia) were treated with A.VOGEL CRATAEGUS OXY (Crataegisan N) 30 drops three times daily and efficacy determined by symptomatic regression or disappearance of symptoms by the respective clinician. Treatment (average of 27 days) resulted in improvements in 96% (38/44) of participants good tolerability and no adverse events. (Degenring 1996)

Condition	Effect of A.VOGEL CRATAEGUS OXY – after two weeks			
	Good	Moderate	Improved	None
Cardiac failure (NYHA Class I or II) (n=16)	2 (12%)	11 (69%)	13 (81%)	3 (19%)
Cardiac oppression (constriction around heart) (n=27)	15 (56%)	9 (33%)	24 (89%)	3 (11%)
Elderly with impaired heart performance (n=8)	7 (88%)	1 (12%)	8 (100%)	0 (0%)
Mild arrhythmia (n=9)	5 (56%)	3 (33%)	8 (89%)	1 (11%)

A randomised, double blind placebo-controlled trial on 143 patients with congestive heart failure (NYHA Class II) applied A.VOGEL CRATAEGUS OXY or placebo 30 drops three times daily for 8 weeks. Significant improvements (superior to placebo) in exercise tolerance (maximum wattage sustained in a 2 min bicycle test) were achieved. (Degenring, Suter *et al.* 2003)

A randomised, double blind placebo-controlled study applied fresh Crataegus berry extract in 88 patients with CCF (NYHA Class II) at a dosage of 25 drops three times daily for 3 months. Exercise time improved significantly (superior to placebo), quality of life (Minnesota Questionnaire) improved by 31% (placebo by 18%) and the Dyspnoea-Fatigue Index improved by 12% and dyspnoea improved by 11% in response to Crataegus. (Rietbrock, Hamel *et al.* 2001)

Clinical safety data
A systematic review specifically of adverse events from 24 trials (Daniele, Mazzanti *et al.* 2006) including data from 5 577 patients reported that Hawthorn is well tolerated with adverse events being mild to moderate. Further, both a meta-analysis of 8 trials (632 patients) and a Cochrane systematic review of 10 trials (855 patients) report infrequent adverse events of mild and transient nature (Pittler, Guo *et al.* 2008). Thus, there is no evidence to refute that Crataegus may, at most, cause infrequent, mild adverse effects. (Tassell, Kingston *et al.* 2010)

5.2 Pharmacokinetic properties

No pharmacokinetic data available.

5.3 Preclinical safety data

Toxicology studies on rats administered 600 mg/kg/day over 30 days showed unremarkable adverse effects (Fehri, Aiache *et al.* 1991). In another study the acute oral toxicity in undefined animals was reported as 6 g/kg and no target organ toxicity was determined at 100 times the human dose (2,7 mg/kg), mutagenic and clastogenic tests were also negative (Schlegelmilch and Heywood 1994). Another study in mice determined a LD50 of 13,5 g/kg for an aqueous extract of *C. laevigata* (Oxyacantha). (Jouad, Lemhadri *et al.* 2003)

Oral doses of 2,8 g/kg (ethanolic extract of Hawthorn – alcohol below teratogenic threshold) were administered to rats on days 1-15 of gestation without negative reproductive outcomes. Foetal weight was slightly increased when administered on gestational days 8-15, however there were no differences in placenta weight, number of resorptions or litter size or any visible malformations. (Yao, Brown-Woodman *et al.* 2001, Bone and Mills 2013) In a reproductive screening of Hawthorn on rats, 56 times the human oral dose did not lead to any adverse effects.(Yao, Ritchie *et al.* 2008)

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Contains approximately 50 % *v/v* alcohol.
Purified water.

6.2 Incompatibilities

Not applicable.

6.3 Shelf life

36 months unopened.
Use within 6 months of opening.

6.4 Special precautions for storage

No special storage conditions.
Store at or below 25 °C in a cool, dry place.
Store in the original package/container.

6.5 Nature and contents of container

Packed in an amber type III glass bottle, with plastic dropper (LDPE) and screw cap (HDPE) with tamper evident seal.

Pack size: 50 ml & 100ml
Not all pack sizes may be marketed.

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)/REFERENCE NUMBER

Listing number: D490323

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

To be allocated.

10 DATE OF REVISION OF TEXT

December 2020