

IPAR



**Public Assessment Report for a
Traditional Herbal Medicinal Product
for Human Use**

AvenaCalm *Avena sativa* Oral Drops

Expressed juice from *Avena sativa* L., herba (fresh oat herb) in ethanolic solution

TR2309/012/001

A. Vogel Ireland Limited

Registration Date: 1st July 2016

Scientific Discussion

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I. INTRODUCTION

Specific provisions were introduced for traditional herbal medicinal products (THMPs) in accordance with the Traditional Herbal Medicinal Products Directive (2004/24/EC). The national regulations, the Medicinal Products (Control of Placing on the Market) Regulations 2007 (S.I. No. 540 of 2007) which implement this Directive came into force on 23rd July 2007. Consequently the Health Products Regulatory Authority (HPRA) has established the Traditional Herbal Medicinal Products Registration Scheme.

The Public Assessment Report reflects the scientific conclusion reached by the HPRA at the end of the evaluation process and provides a summary of the grounds for approval of a Certificate of Traditional Use Registration for a specific traditional herbal medicinal product for human use. It is made available by the HPRA for information to the public, after deletion of commercially sensitive information. The legal basis for its creation and availability is contained in Article 21 of EC Directive 2001/83/EC, as amended by Directive 2004/27/EC and Directive 2004/24/EC. It is a concise document which highlights the main parts of the documentation submitted by the applicant and the scientific evaluation carried out by the HPRA leading to the approval of the traditional herbal medicinal product for marketing in Ireland.

Based on the review of the data on quality, safety and traditional use, the HPRA has granted A. Vogel Ireland Limited a Certificate of Traditional Use Registration for AvenaCalm *Avena Sativa* oral drops containing expressed juice from *Avena Sativa* L., herba (fresh oat herb), in ethanolic solution.

This application is for a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC, as amended, and was submitted as part of the Traditional Herbal Medicinal Product Registration Scheme.

The Summary of Product Characteristics (SmPC) for this traditional herbal medicinal product is available on the HPRA's website.

II. QUALITY ASPECTS

This application is for AvenaCalm *Avena sativa* oral drops. The active ingredient of AvenaCalm *Avena sativa* oral drops is an ethanolic solution of expressed juice obtained from *Avena sativa* L herba (fresh oat herb). 30 drops contains 381 mg of expressed juice from *Avena sativa* L., herba (fresh oat herb) in ethanolic solution. 1 ml is equivalent to 37 drops.

II.1 S.1 Herbal Substance

The herbal substance specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification have been provided.

II.2 S.2 Herbal preparation

The herbal preparation is an ethanolic solution of the expressed juice from the fresh aerial parts of *Avena sativa* L., harvested at flowering time, and is manufactured in accordance with the principles of good manufacturing practice (GMP).

The herbal preparation specification is considered adequate to control the quality and meets current pharmacopoeial requirements. Batch analytical data demonstrating compliance with this specification have been provided.

II.3 Medicinal product

P.1 Composition

The composition of the medicinal product is stated in sections 2 and 6.1 of the SmPC. A description of the product is included in section 3 of the SmPC.

P.2 Pharmaceutical Development

The product is an established pharmaceutical form and its development is adequately described in accordance with the relevant European guidelines.

P.3 Manufacture of the Product

The product is manufactured in accordance with the principles of GMP at suitably qualified manufacturing sites.

The manufacturing process is standard and has been validated according to relevant European guidelines and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients)

All ingredients comply with their respective Ph. Eur. specifications.

P.5 Control of the Finished Product

The Finished Product Specification is based on the pharmacopoeial monograph for liquid preparations for oral use, and the tests and control limits are considered appropriate for this type of product.

The analytical methods used are described in sufficient detail and are supported by validation data.

Batch analytical data for a number of batches from the proposed production site(s) have been provided, and demonstrate the ability of the manufacturer to produce batches of finished product of consistent quality.

P.6 Packaging material

The approved packaging for this product is described in section 6.5 of the SmPC.

Evidence has been provided that the packaging components comply with Ph. Eur. and EU food contact legislation requirements.

P.7 Stability of the Finished Product

Stability data on the finished product in the proposed packaging have been provided in accordance with EU guidelines and support the shelf-life and storage conditions listed in sections 6.3 and 6.4 of the SmPC.

II.4 Conclusion on quality

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of AvenaCalm *Avena sativa* oral drops.

III. NON-CLINICAL ASPECTS

AvenaCalm *Avena Sativa* oral drops is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC as amended.

No new non-clinical studies have been submitted. Given the type of application and limited data available, it is not possible to assess if the safety package for the phytochemical constituents of AvenaCalm *Avena Sativa* oral drops are acceptable to the standards of today's GLP and safety testing requirements.

An expert report on safety has been provided which includes an appropriate review of the available literature.

Overall the information presented demonstrating traditional use is considered to be acceptable and the lack of provision of a complete standard safety package is in line with the EMA 'Guideline on Non-clinical Documentation for Herbal Medicinal Products in Applications for Marketing Authorisation (bibliographical and mixed applications) and in Applications for Simplified Registration' (EMEA/HMPC/32116/05).

An environmental risk assessment is not required for herbal medicinal products according to guidance CPMP/SWP/4447/00.

IV. CLINICAL ASPECTS

This is a national application submitted by A. Vogel Ireland Limited under Article 16c of Directive 2001/83/EC, as amended.

AvenaCalm *Avena Sativa* oral drops is a traditional herbal medicinal product used for the temporary relief of symptoms of mild mental stress and to aid sleep, exclusively based on long standing use.

IV.1 Clinical Efficacy

There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product is efficacious, the registration is based exclusively upon the longstanding use of AvenaCalm *Avena sativa* oral drops as a traditional herbal medicine and not upon data generated from clinical trials.

Article 16c1(c) of Directive 2001/83/EC requires the applicant to provide bibliographic or expert evidence to show that the medicinal product in question, or a corresponding product, has been in medicinal use throughout a period of at least 30 years, including at least 15 years within the Community. With regard to this traditional use data, the requirements of Article 16c1(c) have been met.

The efficacy of this traditional herbal medicinal product is plausible on the basis of long standing use and experience.

The indication proposed for AvenaCalm *Avena sativa* oral drops is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

IV.2 Clinical Safety

In accordance with Article 16c1(d) the applicant has provided a bibliographic review of the safety data together with an expert report.

This Traditional Herbal Medicinal product is not indicated for use in those under 18y of age or in pregnant or breastfeeding women.

If symptoms persist, worsen or do not improve or if new symptoms develop a qualified healthcare professional should be consulted.

This THMP should not be used by those with a known hypersensitivity to oats or oat preparations.

Those with coeliac disease should see a doctor before taking this product as the protein content is unknown.

This product contains 51% vol ethanol (alcohol) and therefore could be harmful for those suffering from alcoholism. The alcohol content should be taken into account in high risk group such as those with liver disease or epilepsy.

AvenaCalm *Avena sativa* oral drops should be avoided by those taking other medicines known to interact with alcohol. (e.g metronidazole).

No known undesirable/adverse effects listed but if adverse reactions occur a qualified health care professional should be consulted.

Please see the Summary of Product Characteristics (SmPC) for AvenaCalm *Avena sativa* oral drops for full prescribing and safety information.

In conclusion, this product proves not to be harmful in the specified conditions of use based on the review of safety data, expert report and additional data provided.

IV.3 Pharmacovigilance

It should be noted that in accordance with Article 16g of Directive 2001/83/EC, as amended, the pharmacovigilance requirements described in Articles 101- 108 of Directive 2001/83/EC, as amended, also apply in respect of traditional herbal medicinal products.

V. OVERALL CONCLUSIONS

The important quality characteristics of the product are well-defined and controlled. Satisfactory pharmaceutical documentation has been provided, assuring consistent quality of AvenaCalm *Avena sativa* oral drops.

The HPRA, on the basis of the data submitted, considered that AvenaCalm *Avena sativa* oral drops demonstrated adequate evidence of traditional use for the approved indications and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for AvenaCalm *Avena sativa* oral drops is granted.