**IPAR**


**Public Assessment Report for a**
**Traditional Herbal Medicinal Product for Human Use**
**Digestisan Oral drops**
**Tinctures of artichoke leaves, dandelion root and herb, boldo leaves and peppermint herb**
**TR 2309/007/001**
**A. Vogel Ireland Limited**

Registration Date: 7th February 2014

**CONTENTS**

## 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 Digestisan oral drops, containing tinctures from artichoke leaves (*Cynara scolymus* L.), dandelion root and herb (*Taraxacum officinalis* Weber), boldo leaves (*Peumus boldus* Molina) and Peppermint herb (*Mentha x piperita* L.).

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 Digestisan Oral drops. The active ingredient of Digestisan is a combination of tinctures from artichoke leaves (*Cynara scolymus* L.), dandelion root and herb (*Taraxacum officinalis* Weber), boldo leaves (*Peumus boldus* Molina) and peppermint herb (*Mentha x piperita* L.).
One dose (20 drops) of oral liquid contains:
**218 mg** of tincture from fresh artichoke leaves (*Cynara scolymus* L., folium), (1:30-31). Extraction solvent ethanol 65 % v/v.
**218 mg** of tincture from fresh dandelion root and herb (*Taraxacum officinalis* Weber, radix cum herba), (1:17-18). Extraction solvent ethanol 51 % v/v.
**34 mg** of tincture from boldo leaves (*Peumus boldus* Molina, folium) (1:10-11). Extraction solvent ethanol 70 % v/v.
**15 mg** of tincture from fresh peppermint herb (*Mentha x piperita* L., herba) (1:18-19). Extraction solvent ethanol 65 % v/v.

### II.1 S.1 Herbal Substance

The herbal substance specifications are considered adequate to control the quality and meet appropriate requirements. Batch analytical data demonstrating compliance with the specifications have been provided.

### II.2 S.2 Herbal preparation

The herbal preparations are tinctures obtained from artichoke leaves (*Cynara scolymus* L.), dandelion root and herb (*Taraxacum officinalis* Weber), boldo leaves (*Peumus boldus* Molina) and peppermint herb (*Mentha x piperita* L.).

The herbal preparations are manufactured in accordance with the principles of Good Manufacturing Practice (GMP)

The herbal preparation specifications are considered adequate to control the quality and meet appropriate requirements. Batch analytical data demonstrating compliance with the specifications 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.

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.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*
All ingredients comply with Ph. Eur. or are adequately controlled by the manufacturer's specifications.

P.5 Control of the Finished Product
The Finished Product Specification is satisfactory 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 have been provided and demonstrate satisfactory compliance with the specification.

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 have been provided in accordance with current 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 Digestisan oral drops.

**III. NON-CLINICAL ASPECTS**

The product is a traditional herbal medicinal product as defined by Article 16a(1) of Directive 2001/83/EC. No new non-clinical studies have been submitted. An expert report on safety has been provided which includes an appropriate review of the available literature. No safety concern was identified. Overall, the information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable and 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 16a of Directive 2001/83/EC, as amended by Directive 2004/24/EC.
The proposed indication of this traditional herbal medicinal product is for the symptomatic relief of digestive disorders such as indigestion, feelings of fullness and flatulence, exclusively based on long-standing use.

**III.3.1 Clinical Efficacy**
No clinical efficacy data is required for registration of Traditional Herbal Medicinal Products (THMP). However, Article 16c1(c) 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. This traditional use data has been submitted with this application and is satisfactory and in accordance with Article 16c1(c).
The efficacy of this traditional herbal medicinal product is plausible on the basis of long-standing use and experience.
The indication proposed for Digestisan is in line with traditional indications recorded and hence, compatible with the requirements of the Traditional Herbal Medicinal Products Directive 2004/24/EC.

**III.3.2 Clinical Safety**
In accordance with Article 16c1(d) the applicant has provided a bibliographic review of the safety data together with an expert report.

Digestisan should not be used by patients who have an allergy or are hypersensitive to Artichoke, Dandelion, Boldo, Peppermint, plants of the daisy family or to menthol.

Digestisan is recommended for short-term oral use only. It is advised that patients do not take more than the recommended dose.

This product should not be given to children and adolescents under the age of 18 years.

It is recommended that if the condition being treated by Digestisan worsens or if symptoms do not improve after 1 week, a qualified healthcare professional e.g. a doctor or pharmacist should be consulted.

Digestisan should not be used by patients who have inflammation or blockage of a bile duct, gallstones, biliary disorders, liver disease, kidney failure, diabetes or heart failure.

Patients with gastro-oesophageal reflux (heartburn) should avoid taking Digestisan as heartburn may increase due to the peppermint leaf content.

Digestisan should not be used by women who are pregnant, may become pregnant or are breast-feeding.

It should be noted that Digestisan contains 60% alcohol (ethanol), i.e. up to 255 mg per 20 drop dose (187 mg per 15 drop dose), equivalent to 6.4 ml beer (4.6 ml per 15 drop dose) or 2.7 ml wine (1.9 ml per 15 drop dose) per dose. This may be harmful to those suffering from alcoholism. It should be taken into account in women who are pregnant, women who are breast-feeding, children and high-risk groups such as patients with liver disease or epilepsy. Digestisan should therefore also be avoided in patients taking other medicines known to interact with alcohol (e.g. Metronidazole).

Overdose of Digestisan could result in alcohol intoxication. This may affect the ability to drive or use machines.

The possible side effects that may occur when using this product include allergic reactions, stomach pain, digestive upset, excessive stomach acid and worsening of gastric reflux or heartburn.
In conclusion, this product proves not to be harmful in the specified conditions of use based on the bibliographic review of safety data, expert report and additional data provided.

**III.3.3 Pharmacovigilance**
It should be noted that in accordance with Article 16g of Directive 2001/83/EC, 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 Digestisan oral drops.

The HPRA, on the basis of the data submitted, considered that Digestisan 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 Digestisan Oral Drops is granted.

## VI. REVISION DATE

July 2018

## VII. UPDATES

| Scope | Procedure number | Product Information affected | Date of start of procedure | Date of end of procedure | Approval/non approval |
|---|---|---|---|---|---|
| To change the immediate packaging of the finished product to add a child-resistant closure (screw-cap/ring = HDPE/HDPE).<br>This change will be incorporated into section 6.5 of the SmPC. | CRN 2207081 | SPC section 6.5 | 03/07/2018 | 05/07/18 | Approved |