IPAR

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

Natures Aid Jointeeze Devil's Claw
Devil's claw root

TR0126/318/001
TR Holder Clonmel Healthcare Ltd

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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 Clonmel Healthcare Limited a Certificate of Traditional Use Registration for Natures Aid Jointeeze Devil's Claw tablets, containing devil's claw root extract.

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.

Name of the product	Natures Aid Jointeeze Devil's Claw Tablets
Name of the active substance	Devil's claw root extract
Pharmacotherapeutic classification (ATC code)	V03AX-Other therapeutic products
Pharmaceutical form	Tablet
Traditional-use Registration Number in Ireland (TR)	TR0126/318/001
Traditional-use Registration Holder	Clonmel Healthcare Ltd
MRP/DCP No.	Not applicable.

II. QUALITY ASPECTS

This application is for Natures Aid Jointeeze Devil's Claw Tablets. The active ingredient of Natures Aid Jointeeze Devil's Claw Tablets is obtained from devil's claw root (*Harpagophytum procumbens* D.C. and/or *Harpagophytum zeyheri* L. Decne).

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 devil's claw dry extract, described in the European Pharmacopoeia, 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 involves standard operations only and the process is considered to be sufficiently validated.

P.4 Control of Other Substances (Excipients/*Ancillary Substances)*

All ingredients comply with Ph. Eur. monographs, where these exist, or are adequately controlled by the manufacturer's specification. No ingredients of animal origin are used.

P.5 Control of the Finished Product

The Finished Product Specification reflects the requirements of the pharmacopoeial monograph for tablets and the European guideline on specifications for herbal medicinal products (EMEA/CVMP/815/00). 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 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.

The glass bottles meet the requirements of the European Pharmacopoeia for Type III glass and are suitable for the packaging of solid dosage forms for oral administration.

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 Natures Aid Jointeeze Devil's Claw tablets.

III. NON-CLINICAL ASPECTS

Due to the nature of the application it is not possible to assess if the safety standards for the phytochemical constituents of Natures Aid Jointeeze Devil's Claw Tablets are acceptable by the standards of today's GLP and safety testing requirements.

The product is a traditional herbal medicinal product as defined by Article 16a(1). 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. Information presented demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package is acceptable in compliance with guideline EMEA/HMPC/32116/05.

Genotoxicity testing did not reveal any safety concerns. Carcinogenicity and reproductive toxicity testing has not been conducted. Due to the lack of data, the use of the product during pregnancy and lactation should be avoided unless under the guidance of a medical practitioner.

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

IV. CLINICAL ASPECTS

Natures Aid Jointeeze Devil's Claw tablets are a traditional herbal medicinal product for the relief of minor joint pain in adults over 18 years of age, 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 long standing use of Natures Aid Jointeeze Devil's Claw tablets 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 Natures Aid Jointeeze Devils Claw 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 contraindicated in those with hypersensitivity to devil's claw or any of the excipients listed in section 6.1 of the SmPC.
It is also contraindicated in patients with active gastric or duodenal ulcer, and in patients under 18 years of age.

Articular pain accompanied by swelling of joint, redness or fever should be examined by a doctor.

Patients with gallstones should consult a doctor prior to use of devil's claw.

If the symptoms worsen during the use of the medicinal product or if symptoms persist for more than 4 weeks, a qualified professional e.g. a doctor or a pharmacist should be consulted.
Patients with rare glucose-galactose malabsorption should not take this medicine.

The stated dose should not be exceeded.

Some animal studies done with high concentrations of devil's claw have indicated that it may have calcium antagonistic effects similar to the calcium channel blocker verapamil. Therefore, caution should be taken when devil's claw is administered to patients with cardiac disorders.

There is no evidence from limited interaction studies that devil's claw root extracts will interact with other medicinal products.

There are no or a limited amount of data from the use of Devil's claw in pregnant women (see section 5.3). Jointeeze Devil's Claw Tablets is not recommended during pregnancy and in women of childbearing potential not using contraception.
There is insufficient information on the excretion of devil's claw/metabolites in human milk. A risk to newborns/infants cannot be excluded. Jointeeze Devil's Claw Tablets should not be used during breastfeeding.

No studies on the effect on the ability to drive and use machines have been performed. In rare cases some patients have experienced dizziness and somnolence while taking Devil's claw. If affected, patients should not drive or use machinery.

Gastrointestinal symptoms (diarrhoea, nausea, vomiting, abdominal pain) have been reported.
Central nervous system effects (headache, vertigo) have been reported.
Hypersensitivity reactions (e.g. rash, hives, facial oedema) have been reported.
The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or qualified healthcare professional should be consulted.

There are no data on human overdose with devil's claw. Symptomatic and supportive measures should be taken as appropriate.

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 Natures Aid Jointeeze Devil's Claw tablets.

The HPRA, on the basis of the data submitted, considered that Jointeeze Devil's Claw tablets demonstrated adequate evidence of traditional use for the approved indication and no new non-clinical or clinical safety concerns have been identified.

A Certificate of Traditional Use Registration for Natures Aid Jointeeze Devil's Claw tablets is granted.

VI. REVISION DATE

VII. UPDATES