MIGRAHERB HARD CAPSULES

THR 23056/0004

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MIGRAHERB HARD CAPSULES

THR 23056/0004

LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted M H Pharma (UK) Ltd a Traditional Herbal Registration Certificate for the traditional herbal medicinal product MigraHerb Hard capsules (Traditional Herbal Registration number: THR 23056/0004). This product is available without prescription and can be bought from pharmacies and other outlets.

The active ingredient of MigraHerb Hard capsules comes from the aerial parts of the plant *Tanacetum parthenium*, also known as Feverfew. MigraHerb Hard capsules is a traditional herbal medicinal product used for the prevention of migraine headaches. This registration is based exclusively upon evidence of traditional use of Feverfew as a herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that the product works.

No new or unexpected safety concerns arose from this application and it was, therefore, decided that a Traditional Herbal Registration Certificate could be granted.

MIGRAHERB HARD CAPSULES

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SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted a Traditional Herbal Registration Certificate for the traditional herbal remedy MigraHerb Hard capsules to M H Pharma (UK) Ltd on 3 April 2007. This product has been granted a general sales licence (GSL).

This application was submitted as a complex application according to Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme.

The data supplied by the Applicant demonstrate 30 years of traditional use of Feverfew in the European Community. A satisfactory review of the available safety data on Feverfew has also been provided, together with an Expert Safety Report supporting the proposed product.

PHARMACEUTICAL ASSESSMENT REPORT

I REQUESTS FOR INSPECTION ACTION PRIOR TO AUTHORISATION

None. A translated copy of the Current GMP certificate from the authorities that inspected the manufacturing site has been provided.

II INTRODUCTION

This is a national application submitted by MH Pharma (UK) Ltd, trading as Medic Herb, under the Traditional Herbal Medicines Registration Scheme. The proposed product, MigraHerb Hard capsules, consists of hard capsules containing 100 mg Feverfew herb (*Tanacetum parthenium* L. Schultz Bip) indicated as '*a traditional herbal medicinal product used for the prevention of migraine headaches based on traditional use only*'.

Feverfew products are currently widely available in the UK as herbal remedies exempt from licensing, under Section 12(2) of the Medicines Act 1968. There are no other Feverfew products with current marketing authorisations.

This product is on the General Sales List and can be bought, without prescription, from pharmacies and other outlets.

A satisfactory manufacturing licence has been provided by the batch release and manufacturing site of the finished herbal product.

The manufacturer of the herbal active ingredient, powdered Feverfew herb, is suitably qualified. A declaration has been provided from the Qualified Person confirming that the active ingredient supplier operates in compliance with the detailed guidelines on GMP for starting materials.

III.A HERBAL SUBSTANCE

III.A.1 General information

HERBAL SUBSTANCE: FEVERFEW HERB

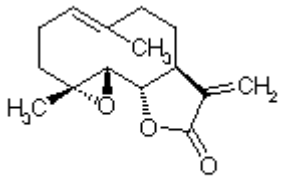
Scientific name of the plant:	*Tanacetum parthenium* L. Schultz Bip
Family:	Asteraceae (Compositae)
Synonyms of the herbal substance:	Feverfew (English); Mutterkraut (German)
Parts of the plant used:	Dried, whole or fragmented aerial parts
Name of the herbal substance:	Feverfew Herb

Constituents:

Terpenoids: Sesquiterpene lactones:
Germacranolides: eg. **parthenolide* (major component)**, 3-β-hydroxy-parthenolide, costunolide, 3-β-hydroxycostunolide, artemorin, 8-α-hydroxyestafiatin, chrysanthemonin.
Guaianolides: eg. artecanin, chrysanthemin A & B, chrysanthemolide, partolide, two chlorine-containing sesquiterpene lactones.
Eudesmanolides: eg. magnolialide, reynosin, santamarine, 1-β-hydroxyarbusculin, 5-β-

hydroxyreynosin.

Parthenolide



Essential oil: camphor, trans-chrysanthenyl acetate, borneol, α-pinene derivatives, germacrene, farnesene and their esters.
Other constituents: pyrethrin, flavonoids, tannins, melatonin.

III.A.2 Manufacture

The plants are mechanically harvested in summer. The whole or fragmented herbal drug is dried and subsequently stored protected from light, heat and moisture. The herbal drug is stated to comply with the Ph Eur monograph, which refers to Feverfew herb which may be collected after flowering. The herbal drug is tested according to a specification according to the monograph "Feverfew" of European Pharmacopoeia to prevent possible contamination with related species.

The herbal active ingredient manufacturer has provided information confirming that herbicides and fertiliser are used during cultivation but the plant material is not subjected to insecticides, fumigation or irradiation. The manufacturer carries out a test for pesticide residues that is capable of detecting and limiting the specific herbicide treatments used. Assurance has been provided that the herbal substance is produced in accordance with the principles in Good Agricultural and Collection Practice (GACP).

III.A.3 Characterisation

Please see section III.A.4, Specification for further information.

III.A.4 Control of Herbal Substance

Specification
The specification of the herbal substance is provided. The starting material complies with the Ph Eur monograph for Feverfew herb and the additional tests carried out are detailed.

Analytical Procedures/ Validation of Analytical Procedures
Satisfactory details have been provided on all analytical procedures these analytical procedures have been satisfactorily validated.

Batch Analyses
Satisfactory batch data have been provided to support the specifications.

III.A.5 Reference Standards or Materials

Please refer to section IV.6.

III.A.6 Container Closure System

The herbal substance is not stored but used to produce the herbal preparation (powdered

Feverfew).

III.A.7 Stability

As the herbal substance is powdered and directly filled into the capsules during manufacture stability testing of the herbal substance is not applicable.

III.B HERBAL PREPARATION

III.B.1 General information

The herbal preparation consists simply of the powdered herbal drug.

III.B.2 Manufacture

Preparation of the powdered Feverfew is a standard process and is uncomplicated. A satisfactory description of this process has been provided.

Controls of Critical Steps and Intermediates

There are no critical steps identified as the manufacturing of the herbal preparation is considered as a standard procedure.

Process Validation and/or Evaluation

The applicant has referred to batch analyses as evidence of a valid process.

III.B.3 Characterisation

Please see section III.B.4, Specification for further information.

III.B.4 Control of Herbal Preparation (powdered Feverfew)

Specification

The herbal preparation is controlled by a specification that is appropriate for a product of this nature.

Analytical Procedures/ Validation of Analytical Procedures

Satisfactory details have been provided on all analytical procedures these analytical procedures are valid.

Batch analyses

Satisfactory batch data have been provided to support the specifications.

III.B.5 Reference Standards or Materials

Please refer to section IV.6.

III.B.6 Container Closure System

The herbal preparation is stored in suitable primary packaging that complies with Directive 2002/72/EC.

III.B.7 Stability

As the herbal preparation is directly filled into the capsules during manufacture stability testing of the herbal substance is not applicable.

IV HERBAL PRODUCT

IV.1 Description and Qualitative Composition of the Herbal Product

Component	Ref std	Function
Drug substance		
Powdered Feverfew		Active ingredient
Other constituents		
Capsule filling mass:		
Dextrin, white	Ph Eur	Binding agent
Silica, colloidal anhydrous	Ph Eur	To aid flowability, antiadhesive
Magnesium stearate	PhEur	Lubricant
Talcum	Ph Eur	Lubricant
Capsule shell:		
Hypromellose	Ph Eur	Excipient of capsule shell
Titanium dioxide E 171	Ph Eur	Colouring agent
Purified water	Ph Eur	Solvent for capsule manufacture

Type of container
The cellulose hard capsules are sealed into binary blisters made of PVC/PVDC-aluminium.

IV.2 Pharmaceutical Development

The formulation combines the active ingredient with well known pharmaceutical excipients. The choice of excipients is based on experience with similar herbal powders. The compatibility of the chosen excipients with the drug substance is confirmed by stability testing of the drug product. The dosage form (hard cellulose capsule, size 1, white-opaque) is commonly used and is easy to handle.

The manufacture of the herbal product by the filling and packaging of the hard capsules into commonly used containers is a standard and uncomplicated method. Interaction of the herbal product with the container is not expected based on the results of stability testing.

IV.3 Manufacture

Manufacture
The herbal product is manufactured at a suitable site where the capsules are filled with the filling mass. The capsule shells are manufactured and supplied by a suitably qualified manufacturer.

Batch Formula
The batch formula for the usual production batch has been provided.
Description of Manufacturing Process and Process Controls
A satisfactory flow diagram outlining the various stages of the manufacturing process and the in-process controls has been provided.
Control of Critical Steps and Intermediates
There are no major critical steps in the process. Details of the in-process controls carried out are provided.

Process Validation and/or Evaluation
The manufacturing method is a standard procedure for encapsulating and blistering.

Data on in-process controls have been provided, together with their batch analyses.

IV.4 Control of Excipients

All the excipients and analytical procedures are as specified by the pharmacopoeia monographs. Purified water is not present in the finished product. The colouring agent, titanium dioxide E171, is stated to comply with Directive 95/45/EC. The Applicant has confirmed that all the relevant excipients comply with the monographs in the current Ph Eur. Certificates of analysis (CoA) of the excipients have been provided by the suppliers. Water used in the manufacture of the finished product is purified water corresponding to the standards of the Ph Eur.

Excipients of Human or Animal Origin

The applicant has confirmed that the magnesium stearate is of vegetable origin.

IV.5 Control of Herbal Product

Specification

The release specification lists appropriate tests and sets suitable limits.

Analytical Procedures

Satisfactory details have been provided of all analytical procedures.

Validation of Analytical Procedures

Satisfactory validation of analytical procedures has been carried out.

Batch Analyses

Satisfactory batch data have been provided to support the specifications.

IV.6 Reference Standards or Materials

The reference substance, parthenolide, serves as an external standard within the HPLC assay. The identity and purity of the parthenolide has been established.

IV.7 Container Closure System

The cellulose capsules are sealed into binary blisters of PVC/PVDC-aluminium. Suitable specifications for the packaging have been provided by the suppliers. The primary packaging materials comply with Directive 2002/72/EC.

The finished product manufacturer carries out a suitable testing protocol upon receipt of the packaging materials.

IV.8 Stability

Stability Summary and Conclusion

Stability studies have been carried out on production scale batches. Samples have been stored in ICH long term and accelerated conditions in the containers proposed for marketing. The batches have been tested according to the proposed shelf-life specification using the test methods described.

Stability results

Results are presented up to 24 months for batches stored in long-term and intermediate conditions and for 6 months in accelerated conditions. Based on the results, a shelf life of 36 months with the storage condition 'Do not store above 25°C' is justified.

A discussion of the stability of parthenolide in Feverfew preparations is presented in the Expert

Report.

Post-approval Stability Protocol and Stability Commitment
The Applicant has provided a commitment to include a further production scale batch in the stability programme post-approval.

V. ASSESSOR'S COMMENTS ON THE SUMMARY OF PRODUCT CHARACTERISTICS, LABEL AND PATIENT INFORMATION LEAFLET

Summary of Product Characteristics (SPC)
The SPC for this product is satisfactory.

Patient Information Leaflet (PIL)
The PIL for this product is satisfactory.

Labelling
All product labelling is satisfactory.

VI. ADMINISTRATIVE

MAA Form
The application for submitted for this product is satisfactory**.**

VII. ASSESSOR'S OVERALL CONCLUSIONS ON QUALITY

The grant of a Traditional Herbal Registration is acceptable.

PRECLINICAL ASSESSMENT

I. Introduction

This is a national application submitted by M H Pharma UK (Ltd) trading as Medic Herb under Article 16.c of Directive 2001/83 EC, as amended (Traditional Herbal Medicines Registration Scheme). The product is a capsule for oral use containing 100mg Feverfew (*Tanacetum parthenium*) dry leaf. The product is a proposed traditional herbal medicinal product indicated for the prevention of migraine headaches based exclusively on traditional use.

II. Nonclinical aspects

Preclinical Safety Data

The Safety Expert Report submitted by the applicant lists relevant references to published work studying the toxicology of Feverfew.

III. Nonclincial overview

The applicant has submitted an adequate literature review with this application. An Expert Safety Report was also provided, which included reviews of some nonclinical data. The Expert Safety Report was written by a pharmacist with expertise in herbal medicines and is dated 3 February 2006.

The overview contains a short review of non-clinical data on Feverfew. Some of the studies in the literature review were conducted and published before GLP was a regulatory requirement. Moreover, it is not possible to ascertain if the data assessed in the review would comply with today's regulatory safety testing requirements with regards to design, conduct and analysis.

Due to a shortage of published data on Feverfew it is not possible to assess if the safety package for the phytochemical constituents of Feverfew meet current standards of GLP and safety testing requirements. However, the information supplied demonstrating traditional use is acceptable and thus the lack of provision of a complete standard safety package may be acceptable and in compliance with guideline EMEA/HMPC/32116/05.

In view of the absence of results of genotoxicity testing the applicant has provided assurance that results will be provided before the renewal of the registration.

IV. Summary of product characteristics

The Summary of Product Characteristics for this product is satisfactory.

V. Environmental risk assessment

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

VI. Conclusion

The information supplied demonstrating traditional use of Feverfew is acceptable. An adequate literature review for Feverfew has been carried out by the applicant and no new nonclinical data were submitted for assessment with this application. Granting of a THR is acceptable.

CLINICAL ASSESSMENT

INTRODUCTION

This is a national application submitted by MH Pharma (UK) Ltd under Article 16.c of Directive 2001/83 EC, as amended (Traditional Herbal Medicines Registration Scheme). The proposed product, MigraHerb, consists of hard capsules containing 100 mg Feverfew herb (*Tanacetum parthenium* L. Schultz Bip).

Feverfew products are currently widely available in the UK as herbal remedies exempt from licensing, under Section 12(2) of the Medicines Act 1968. There are no Feverfew products with current marketing authorisations.

EVIDENCE OF TRADITIONAL USE

Article 16 c 1 (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.

The Applicant has provided a bibliographic review which shows evidence for the use of Feverfew within the EU for a period exceeding 30 years.

PROPOSED INDICATION

The indication:

'A traditional herbal medicinal product used for the prevention of migraine headaches based on traditional use only.'

is appropriate for a product of this nature.

SAFETY REVIEW

Article 16 c 1 (D) requires the Applicant to provide a bibliographic review of safety data together with an expert report.

A safety review has been provided and an Expert Report written by a suitably qualified expert who is a pharmacist with expertise in herbal medicines. His CV has also been provided.

The applicant has provided the following summary of the safety review in support of their application:

Summary
Feverfew appears to be a safe medicine with no serious ADRs reported from its use.
In fact, the incidence of side-effects associated with its use appears to be similar to that of placebo. Mouth ulcers have been reported as a common side-effect, but this appeared to be associated with the ingestion of fresh leaves. Whilst some constituents of Feverfew are known to

be contact allergens, it has been stated that such problems can be avoided by the use of more carefully prepared formulations of Feverfew (Pittler and Ernst, 2004). In fact one study, which used capsules of dried Feverfew leaves, reported a greater incidence of mouth ulcers following placebo than Feverfew (Murphy et al., 1988).

SUMMARY OF PRODUCT CHARACTERISTICS (SPC)

The SPC for this product is satisfactory.

PATIENT INFORMATION LEAFLET (PIL)

The PIL for this product is satisfactory.

LABELLING

All labelling is satisfactory.

ASSESSMENT OF SUITABILITY FOR GSL STATUS

Section 51 of the Medicines Act 1968 states that "GSL may be appropriate for medicines which can, with reasonable safety, be sold or supplied otherwise than by or under the supervision of a pharmacist". The term "reasonable safety" may usefully be defined as: "Where the hazard to health and the risk of misuse and the need for special precautions in handling are small, and where wider sale would be a convenience to the purchaser".

Suitability of indication for GSL:

1. Hazard to health

There are mainly two hazards to be considered, the risk of suffering side effects and the risk of missing a more adequate treatment. The data presented by the applicant, and those held internally by the MHRA suggest an acceptable safety profile. All those AEs reported in clinical trails were mild and transient. The spontaneously reported drug-induced side effects that are known to the MHRA indicate no specific concerns. More importantly, no fatalities have been recorded so far that may be related to the use of Feverfew. Special mention should be made of the risk of withdrawal syndrome. This may affect only a fraction of Feverfew users (those who take it for a long term to control their migraines) and is similar in description to withdrawal of other substances such as caffeine. Both the practitioner and patients should be advised to this effect, i.e. through adequate information in the SPC and PIL.

Missing out on a more adequate treatment is also considered a hazard to health. Headaches and migraines may be the manifestations of more serious neurological diseases. Feverfew users that suffer from migraines should be first diagnosed by a doctor, and any changes in the pattern of the migraines should be properly evaluated by a specialist. All headache sufferers who take this medicine to alleviate the pain should also be instructed to change their medication if this does not work. As long as these warnings are made clear to the prescriber and patient the risk of missing

on more adequate treatments is then felt to be low.

Additionally, current experience with other licensed products marketed as GSL and approved for similar indications suggest the hazard to health is low.

2. Risk of misuse

In the case of Feverfew, the indications are clear and easily understandable to the patient. Doses are also clearly stated. Moreover, other GSL products, such as paracetamol and aspirin, have a more general indication such as "headaches" (with no specification of the type).

Although there is some suggestion that chronic users who suddenly stop taking feverfew may develop a withdrawal syndrome, this is not sufficient grounds to assume dependency. Moreover, this syndrome has not been described in those who do not take it chronically. The withdrawal syndrome can be managed relatively easily by tapering down the dose over a period of time. In essence, the risk of misuse of this product is felt to be low.

3. Need to take special precautions in handling

There are no special precautions in handling this product other than keeping it out of the reach and sight of children (as with any other GSL medicine).

4. Wider sales are convenient to the purchaser

Tension type headaches and migraines are relatively common in the general population and rapid symptom relief is desirable. Easy accessibility to GSL medicines to treat these two conditions is beneficial to the sufferer and may alleviate the overburdened local surgeries. There are a number of licensed medicines (i.e paracetamol and NSAIDs, including aspirin) available on the GSL to treat headaches which support this approach.

In summary, it is considered that the four above mentioned criteria have been met and this product should be suitable for GSL status.

RECOMMENDATIONS

A Traditional Registration may be granted.

OVERALL CONCLUSION AND RISK BENEFIT ASSESSMENT

QUALITY

The quality data submitted with this application are satisfactory.

PRECLINICAL

No new preclinical data were submitted and none are required for an application of this type.

EFFICACY AND SAFETY

No clinical efficacy data are required for registration of Traditional Herbal Medicinal Products (THMP).

The Applicant has provided a bibliographic review which shows ample evidence for the use of Feverfew within the EU for a period exceeding 30 years.

A satisfactory review of the safety data has been provided.

The SPC, PIL and labelling are satisfactory.

RISK ASSESSMENT

The quality of the product is acceptable and no new preclinical or clinical safety concerns have been identified.

MIGRAHERB HARD CAPSULES

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STEPS TAKEN FOR ASSESSMENT

1	The MHRA received the Traditional Herbal Registration on 27 February 2006
2	Following standard checks and communication with the applicant the MHRA considered the applications valid on 27 March 2006
3	Following assessment of the application the MHRA requested information relating to the quality dossier on 26 July and 3 August 2006
4	The applicant responded to the MHRA's requests, providing further information on 21 November 2006
5	Following assessment of the response and consultation with the Herbal Medicines Advisory Committee the MHRA requested further information relating to the quality, non-clinical and clinical dossiers on 24 November 2006
6	The applicant responded to the MHRA's requests, providing further information on the quality, non-clinical and clinical dossiers in 2 January 2007
7	Following assessment of the response the MHRA requested further information relating to the dossier on 13 February 2007
8	The applicant responded to the MHRA's requests, providing further information on the dossier on 19 February 2007
9	Following assessment of the response the MHRA requested further information relating to the dossier on 19th March
10	The applicant responded to the MHRA's requests, providing further information on the dossier on 19 March 2007
11	Following assessment of the response the MHRA requested further information relating to the dossier on 20th March
12	The applicant responded to the MHRA's requests, providing further information on the dossier on 21st March 2007
13	Following assessment of the response the MHRA requested further information relating to the dossier on 28th March
14	The applicant responded to the MHRA's requests, providing further information on the dossier on 29th March 2007
15	The application was determined on 3 April 2007

SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT

MigraHerb® Hard capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION

1 hard capsule contains
100mg Feverfew herb (*Tanacetum parthenium*)

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM

Hard white capsule

4 CLINICAL PARTICULARS

4.1 Therapeutic indications

A traditional herbal medicinal product used for the prevention of migraine headaches based on traditional use only.

4.2 Posology and method of administration

For oral short term use only. The patient should consult a doctor if symptoms worsen or do not improve after 12 weeks.

For adults and the elderly, take one capsule daily. Capsules should be swallowed whole with water or a little liquid. The capsules should not be chewed.

This product should be taken continuously for three months in order to achieve maximum benefit.

This product is not indicated for use in patients less than 18 years old.

4.3 Contraindications

Hypersensitivity to any of the ingredients or to Feverfew, chrysanthemums, daisies, marigolds, or other members of the Asteraceae (Compositae) family, including ragweed.

Due to lack of data this product is contraindicated in children and adolescents under 18 years.

4.4 Special warnings and precautions for use

Do not exceed the stated dose.

Patients who take Feverfew for migraine should have been previously diagnosed by a doctor of this condition. If the patient experiences changes in the migraines (i.e. increase in attacks, worsening of pain, new symptoms) they should be instructed to consult their doctor.

Long-term Feverfew users who stop treatment suddenly may experience withdrawal symptoms, including rebound headaches, anxiety, difficulty sleeping, muscle stiffness, and joint pain. Patients who are on long term therapy with Feverfew should be instructed to seek professional advice before stopping treatment.

Although it has not been clearly shown in humans, laboratory tests suggest that Feverfew may affect blood platelets. There is a theoretical risk of increased risk of bleeding. A careful risk benefit assessment should be made in patients with bleeding disorders or taking drugs that may increase the risk of bleeding before Feverfew is given. Dosing adjustments may be necessary.

Feverfew is amongst a group of herbals that, in theory, may increase the risk of bleeding. This is based on laboratory research, and has not been reported clearly in humans.

Patients should be instructed to warn their doctors or dentists prior to some surgical or dental procedures, due to a theoretical increase in bleeding risk.

Photosensitivity (to sunlight or sunlamps) has been reported with other herbs in the Asteraceae (Compositae) plant family, and may be possible with Feverfew.

Feverfew may also alter the way that certain drugs are broken down by the liver.

4.5 Interaction with other medicinal products and other forms of interaction

Drugs that affect coagulation and bleeding:
Feverfew theoretically may increase the risk of bleeding when taken with drugs that affect coagulation and bleeding. Some examples include aspirin, anticoagulants such as warfarin or heparin, anti-platelet drugs such as clopidogrel, and non-steroidal anti-inflammatory drugs such as aspirin, ibuprofen and naproxen.

Doxycycline and Isotretinoin:
Sun sensitivity caused by certain drugs like doxycycline or isotretinoin may be increased by Feverfew.

Iron:
Feverfew may decrease the oral absorption of certain iron formulations since the herb contains tannin and tannin-iron insoluble complexes may be formed if administered together.

Rizatriptan and zolmitriptan:
The concomitant administration of rizatriptan and zolmitriptan with Feverfew may lead to an increase in blood pressure and heart rate to dangerous levels.

4.6 Pregnancy and lactation

There are no adequate data of the use of Feverfew in pregnancy and lactation. However, traditional experience suggests that Feverfew may stimulate menstrual flow and induce abortion. As a general precaution, use is not recommended in pregnancy.

It is not known whether Feverfew is excreted in the milk or not. As a general precaution use is not recommended during lactation.

4.7 Effects on ability to drive and use machines

No data on the effects on the ability to drive and use machines are available.

4.8 Undesirable effects

The review of the adverse drug reactions reported in clinical trials indicate that most side-effects are mild and reversible.

Mouth inflammation or ulcers, including swelling of the lips, tongue irritation, bleeding of the gums, and loss of taste have been reported, usually after direct contact of the mouth with the leaves, although some people report burning after swallowing a capsule containing dried leaf.

Photosensitivity (sensitivity to sunlight or sunlamps) has been reported with other herbs in the Asteraceae (Compositae) plant family (see Section 4.4).

Indigestion, nausea, flatulence, constipation, diarrhoea, abdominal bloating, and heartburn have been reported rarely.

Feverfew can also cause allergic rashes.

Increased heart rate in some patients has been reported in one small study.

Other side effects that have been reported spontaneously are eosinophilia, abnormal liver function tests, arthritis, renal failure, Raynaud's phenomenon and hypertension. These were spontaneously generated adverse drug reactions during post-marketing surveillance and the causal relation to Feverfew cannot be established.

4.9 Overdose

There are well documented cases of overdose with Feverfew. In cases of overdose the treatment should be supportive. Since there is a theoretical increased risk of bleeding, patients should be closely monitored for signs of bleeding.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: Other anti-migraine preparations, ATC: N02CX.

Preclinical studies suggest that Feverfew may inhibit the secretion of serotonin from blood platelets, and may have anti-inflammatory and vascular effects (inhibition of vasoconstriction). Clinical studies have not demonstrated any effect in vivo on the secretion of serotonin but indicate that Feverfew may relieve the pain associated with migraines and other types of headaches.

5.2 Pharmacokinetic properties

There is no pharmacokinetic data available.

5.3 Preclinical safety data

The preclinical toxicology data available are limited. There are no repeat-dose toxicity data available. Appropriate tests on genotoxicity and carcinogenicity have not been performed.

In two small teratogenicity studies, pregnant rats were administered very high doses of Feverfew (0.86 g/kg/day) as an ethanolic extract; this dose represents the highest possible for which ethanol remained below the the teratogenic threshold. Results showed that extracts of Feverfew induced both maternal and embryotoxic effects of reduced foetal weights with Feverfew administered from day 8 to 15 of gestation, and enlarged placentae on administration of Feverfew from day 1 to 8, or day 8 to 15. However, the percentages of implantation loss and litter size were not significantly different from controls.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Dextrin, white
Silica, colloidal anhydrous
Talc
Magnesium stearate
Titanium dioxide E 171
Hypromellose

6.2 Incompatibilities

Not applicable

6.3 Shelf life

The shelf life is 3 years

6.4 Special precautions for storage

Do not store above 25°C.

6.5 Nature and contents of container

Original packages containing 30, 60 or 90 hard capsules

MigraHerb capsules are packed in PVC/ PVDC- aluminium blisters and inserted into a carton.

6.6 Special precautions for disposal

No special requirements

7. REGISTRATION HOLDER

M H Pharma (UK) Ltd
t/a Medic Herb
PO Box 2835
Brewery Courtyard
Draymans Lane
Marlow
Buckinghamshire
SL7 2XG

8. REGISTRATION NUMBER

THR 23056/0004

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

03/04/2007

10 DATE OF REVISION OF THE TEXT

03/04/2007

PATIENT INFORMATION LEAFLET

Patient Information Leaflet

MigraHerb® Hard capsules

MedicHerb

Feverfew herb 100mg

Please read this leaflet carefully before you start taking these capsules.
It contains some important information about MigraHerb®.

Keep this leaflet with the capsules.
You may want to read it again or show it to your doctor, pharmacist or healthcare practitioner.

What is in this leaflet

1: What this product is and what it is used for

This product is a traditional herbal medicinal product containing Feverfew herb. Each hard capsule of this product contains 100mg of dry Feverfew herb (*Tanacetum parthenium*)

MigraHerb is a traditional herbal medicinal product used for the prevention of migraine headaches. This usage is based on traditional use only.

1

2: Before you take this product

Patients who take this product for migraine should have been previously diagnosed by a doctor of this condition. If you experience changes in your symptoms (increase in attacks, worsening of pain, new symptoms), you should consult your doctor.

DO NOT TAKE this product if you:

- are **pregnant** or **breastfeeding**
- are **allergic to any of the ingredients** or to plants from the Asteraceae (Compositae) family such as daisies, marigolds or artichokes (see section 6)
- are **under 18 years of age**
- are **taking the following medicines from your doctor:** doxycycline, isotretinoin, rizatriptan, zolmitriptan.

If you are already taking warfarin, clopidogrel, aspirin, ibuprofen or other non-steroidal anti-inflammatory drugs, there is a theoretical risk that taking this product may increase the risk of bleeding.

3: How to take this product

Adults and the elderly
Take 1 capsule daily – try to take the capsule at the same time each day. Swallow the capsules whole with some water or other liquid. Do not chew the capsules. You can take the capsules with or without food. The maximum beneficial effect of this product may take several months to develop for some people.
Do not exceed the stated dose.

If you take too much of this product (overdose)
If you take more than the recommended dose, speak to a doctor, pharmacist or healthcare practitioner and take this leaflet with you.

If you forget to take this product
Continue to take your usual dose at the usual time. It does not matter if you have missed a dose.

If you have any questions, or are unsure about anything, please ask your doctor, pharmacist or healthcare practitioner.

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4: Side-effects

Like all medicines, this product can have side-effects. These are listed below.

Common side-effects (affecting up to 1 in 20 people)	
• **abdominal bloating** • **indigestion** • **heartburn** • **digestive upsets** such as wind, bloating, nausea, constipation or diarrhoea	If these side-effects persist for more than a few days, or become troublesome, stop taking this product. These common side-effects are often only temporary.
Uncommon side-effects (affecting fewer than 1 in 300 people)	
• **mouth inflammation or mouth ulcers** • **mild allergic skin reactions** itching and/or rash of the skin	Stop taking this product immediately if you experience any of these side-effects.
• **photosensitivity** ***(sensitivity to sunlight or sunlamps) has been reported with other herbs related to Feverfew from the Asteraceae (Compositae) plant family.***	
Other side-effects	
These include increased heart rate, raised blood pressure, eosinophilia, abnormal liver function tests, arthritis, renal failure and Raynaud's phenomenon. Tell your doctor or pharmacist, if you notice any other side-effect.	

5: After taking this product

You must speak to a healthcare practitioner if your symptoms worsen, if they do not improve after 12 weeks, or if side-effects not mentioned in this leaflet occur.

Long-term Feverfew users who stop treatment suddenly may experience withdrawal symptoms, including rebound headaches, anxiety, insomnia, muscle stiffness and joint pain. Patients who are on long-term therapy with this product should seek advice from their doctor, pharmacist or healthcare professional before stopping treatment.

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Do not use your capsules after the expiry date. Return any out-of-date capsules to your pharmacist who will dispose of them for you. The expiry date is printed on the box and the blister pack.

Store the capsules in a cool dry place below 25°C.

Keep the capsules out of the reach and sight of children.

Keep your capsules in the blister pack until it is time to take them.

6: Product description

Each hard capsule contains 100 mg of dry Feverfew herb (*Tanacetum parthenium*).

This product also contains the following ingredients:
Dextrin white, silica colloidal anhydrous, talc, magnesium stearate, hypromellose, titanium dioxide E171.

Each pack contains 30, 60 or 90 hard capsules.

Registration holder for this product
M H Pharma (UK) Ltd, t/a MedicHerb, PO Box 2835,
Brewery Courtyard, Draymans Lane,
Marlow, Bucks, SL7 2XG

Manufacturer of this product
Wiewelhove GmbH, Gildestrasse 39, 49477 Ibbenbüren, Germany

Traditional herbal registration number: THR 23056/0004

If you would like further information about this product, please contact:
M H Pharma (UK) Ltd, PO Box 2835, Marlow, Bucks SL7 2XG

Telephone: 01628 488487
Email: info@medicherb.co.uk

This leaflet was prepared in January 2007

For a large print, Braille or audio version of this leaflet, call 01628 488487

❹

LABELLING

Blister:

Carton:


MedicHerb
MigraHerb® 30 capsules
NEW
MedicHerb
MigraHerb®
hard capsules
Feverfew herb 100mg
A traditional herbal medicinal product used for the prevention of migraine headaches based on traditional use only
30 capsules
30 capsules
MigraHerb®
MedicHerb
NEW
MedicHerb
MigraHerb®
A traditional herbal medicinal product used for the prevention of migraine headaches, based on traditional use only.
Active Ingredients: Each MigraHerb® capsule contains 100mg of Feverfew dry herb (Tanacetum parthenium)
Dosage: For oral use only. Adults and the elderly. For prevention of migraine headaches, take one capsule daily. The capsules should be swallowed whole with some water or other liquid.
Warning: Do not exceed the stated dose
Do not use if you: are under 18
are pregnant or breastfeeding
are allergic to any of the ingredients
Please read the enclosed information leaflet before taking these capsules. Keep out of sight and reach of children.
Do not store above 25°C
THR 23056/0004
Store in original packaging
Expiry date: see base
Manufactured in Germany
THR holder: M H Pharma (UK) Ltd (trading as MedicHerb)
PO Box 2835, Marlow, Bucks SL7 2XG
Telephone: 01628 488487 Email: info@medicherb.co.uk
30 capsules
MigraHerb®
MedicHerb
Batch No:
Expiry date:
5 060067 790110

Carton with Braille: