Thisilyn® Maximum Strength Milk Thistle capsules
Higher Nature Milk Thistle capsules

Thisilyn® Milk Thistle capsules

THR 23056/0010
THR 23056/0012

UKPAR

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LAY SUMMARY

The Medicines and Healthcare products Regulatory Agency (MHRA) granted Schwabe Pharma (UK) Ltd Traditional Herbal Registration Certificates for the traditional herbal medicinal products Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle capsules (Herbal Registration number: THR 23056/0010) and Thisilyn® Milk Thistle capsules (THR 23056/0012) on 1 October 2010.

Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle capsules are identical to each other, apart from the difference in product name. Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle contain a larger amount of the active ingredient than Thisilyn® Milk Thistle capsules.

All of these products are available without prescription and can be bought from pharmacies and other outlets.

These products contain milk thistle fruit extract as the active ingredient. These products are traditional herbal medicines used to relieve the symptoms associated with occasional over indulgence of food and drink, such as indigestion and upset stomach. These registrations are based exclusively upon the longstanding use of milk thistle fruit as a traditional herbal medicine and not upon data generated from clinical trials. There is no requirement under the Traditional Herbal Registration scheme to prove scientifically that a product works.

No new or unexpected safety concerns arose from these applications and it was, therefore, decided that Traditional Herbal Registration Certificates could be granted.
THISILYN® MAXIMUM STRENGTH MILK THISTLE CAPSULES
HIGHER NATURE MILK THISTLE CAPSULES

THISILYN® MILK THISTLE CAPSULES

THR 23056/0010 AND THR 23056/0012

SCIENTIFIC DISCUSSION

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INTRODUCTION

The MHRA granted Traditional Herbal Registration Certificates for the traditional herbal remedies Thisilyn® Maximum Strength Milk Thistle capsules, Higher Nature Milk Thistle capsules and Thisilyn® Milk Thistle capsules on 1 October 2010. These products are on the general sales list (GSL).

These applications were submitted according to Article 16.c of Directive 2001/83 EC, as amended, as part of the Traditional Herbal Medicines Registration Scheme.

Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle capsules contain 193 – 261 mg of milk thistle fruit extract and Thisilyn® Milk Thistle capsules contain 89 mg – 121 mg of milk thistle fruit extract.

The products are used to relieve the symptoms associated with occasional over indulgence of food and drink, such as indigestion and upset stomach, based on traditional use only.

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

HERBAL SUBSTANCE: MILK THISTLE FRUIT

Latin name: **Silybum marianum** (L.) Gaertner
Common name: Milk thistle
Family: Asteraceae
Parts of the plant used: Fruit

The plant is indigenous to Southern Europe, Russia, Asia Minor and North Africa.

**Manufacture**
The milk thistle plants are grown in the Czech Republic, Slovakia, Poland and Bulgaria.

The fruits are harvested by standard corn combine harvester between August and September. After harvesting, residual parts of plants are removed and the herbal substance is dried. After drying any remaining foreign matter is removed.

Production areas are fertilized in April using nitrogen fertilizers. No pesticides are used during the growing of the plant material.

Confirmation has been provided that the herbal substance is produced in line with the Guideline on Good Agricultural and Collection Practice (GACP) EMEA/HMPC/246816/2005 and that the herbal substance has not been fumigated or treated with ionizing radiation during growing or storage.

The manufacturing process is clearly defined and the controls necessary are carried out to verify correct manufacture of the herbal substance.

**Control of Herbal Substance**
An appropriate specification based on the Ph Eur monograph is applied and is acceptable. The specification is supported by the batch data provided.

**Container Closure System**
Satisfactory details of the container closure system are provided and confirmation has been given that all components of the container closure system comply with Directive 2002/72/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**
Confirmation is given that the herbal substance will be tested prior to being used to make the herbal preparation. A shelf-life for the herbal substance is not appropriate because it is only a precursor of the active substance, the herbal preparation. The actual guideline requires stability testing data for the herbal preparation and the herbal product in the application documents and not for the herbal substance.

HERBAL PREPARATION

General information

MHRA PAR; THISILYN® MAXIMUM STRENGTH MILK THISTLE CAPSULES AND HIGHER NATURE MILK THISTLE CAPSULES (THR 23056/0010) AND THISILYN® MILK THISTLE CAPSULES (THR 23056/0012)
The herbal preparation is a dry quantified extract of milk thistle.

**Manufacture**
Manufacture of the extract is a standard procedure. A satisfactory description of the manufacturing process of the herbal substance and flow diagram has been provided. There are no critical steps identified as the manufacture of the herbal preparation is considered a standard procedure.

Certificates of analysis for all materials used in the manufacture of the herbal preparation have been provided.

**Control of Herbal Preparation**
A satisfactory specification with appropriate tests and limits has been provided for the herbal preparation.

Satisfactory analytical procedures are used to control the quality of the herbal preparation. Analytical procedures have been validated as appropriate.

**Container Closure System**
The container closure system used to store the dry extract complies with Directive 2002/72/EC.

**Stability**
Batches were packed in the final container closure system and stored under ICH real time and accelerated conditions. The data support the storage conditions used.

**HERBAL PRODUCT**
**Description and Composition of the Herbal Product**
All products are hard gelatin capsules; Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle capsules are red and opaque and Thisilyn® Milk Thistle capsules are ivory and opaque. Thisilyn® Maximum Strength Milk Thistle capsules and Higher Nature Milk Thistle capsules contain 193 mg – 261 mg of extract from milk thistle fruit and Thisilyn® Milk Thistle capsules contain 89 mg – 121 mg of extract from milk thistle fruit.

Both products contain mannitol, cellulose microcrystalline, croscarmellose sodium, silica (colloidal anhydrous), magnesium stearate, gelatin, purified water, titanium dioxide (E171), sodium lauryl sulphate, and iron oxide hydrate E172 (yellow iron oxide). The higher strength capsules also contain Iron (III)-oxide E172 (red iron oxide).

**Manufacture**
A copy of the manufacturing licence for the finished product manufacturing site is provided. The site complies with GMP standards. A flow diagram summarising the manufacturing process and in-process controls has been provided.

A number of in-process control tests are performed during manufacture. All are considered adequate.

**Control of Excipients**
All excipients comply with the Ph Eur apart from the colouring agents (yellow iron oxide and red iron oxide) which comply with the USP. In the absence of an appropriate Ph Eur monograph this is acceptable.

Confirmation is provided that the magnesium stearate, sodium laurylsulfate and gelatine used in these products do not pose a risk of transmissible spongiform encephalopathies (TSE) transmission. The magnesium and sodium laurylsulfate that are used are of vegetable origin. Certificates of Analysis have been provided from all excipients.

**Control of Herbal Product**
The finished product specifications for release and end of shelf life are detailed and the tests and limits used were found to be satisfactory for a product of this nature.

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

Satisfactory batch data have been provided to support the specifications.

**Reference Standards or Materials**
Certificates of analysis have been provided for all reference standards used.

**Container Closure System**
The finished products are packed in PVC/ PVDC- aluminium blisters and inserted into a carton. The cartons contain either 21, 28, 30, 56, 60 or 90 hard capsules.

Specifications and certificates are provided from the manufacturers and the applicant has confirmed that all components of the final container closure system comply with Directive 2002/72/EC relating to plastic materials and articles intended to come into contact with foodstuffs.

**Stability**
Data is provided for production scale batches of both product strengths. Batches were packed in the final packaging and tested under ICH conditions of real, intermediate and accelerated time. Based on the data provided, a shelf life of 3 years has been set for the higher strength products and 2 years for the lower strength product. The storage precaution “Do not store above 25°C” is applied to these products.

**PRODUCT LITERATURE**
All product literature (SPCs, PILs and labels) is satisfactory. The package leaflets were submitted to the MHRA along with results of consultations with target patient groups ("user testing"), in accordance with Article 59 of Council Directive 2001/83/EC. The results indicate that the package leaflets are well-structured and organised, easy to understand and written in a comprehensive manner. The test shows that the patients/users are able to act upon the information that they contain.

**ADMINISTRATIVE**
The Quality Overall Summary has been written by a suitably qualified expert and is satisfactory.
ASSESSOR’S OVERALL CONCLUSIONS ON QUALITY
These products are satisfactory and Traditional Herbal Registrations can be granted.
NON-CLINICAL ASSESSMENT

Non-clinical aspects
The Expert Safety Report submitted by the applicant lists relevant references to published work studying the toxicology of milk thistle fruit.

Non-clinical overview
The applicant has submitted an adequate literature review with these applications. An Expert Safety Report was also provided, which included reviews of some non-clinical data.

The overview submitted in support of these applications is satisfactory.

Due to a shortage of published data on milk thistle fruit it is not possible to assess if the safety package for the phytochemical constituents of milk thistle fruit is acceptable to the standards of today’s 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.

Genotoxicity testing
The genotoxic potential of milk thistle fruit extract was investigated using a series of in vitro and in vivo genotoxicity studies. The test extract evaluated was representative of the marketed product and the results of testing did not give cause for mutagenic concern.

Summary of product characteristics
The Summaries of Product Characteristics for these products are satisfactory.

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

Conclusion
The information supplied demonstrating traditional use of milk thistle fruit is acceptable. An adequate literature review for milk thistle fruit has been carried out by the applicant and the results of the genotoxicity testing that were submitted for assessment with this application are acceptable. Granting of Traditional Herbal Registrations is acceptable.
CLINICAL ASSESSMENT

LEGAL STATUS
Milk thistle fruit is currently on the General Sales List for internal use.

PROPOSED INDICATION
The applicant has proposed the following indication for these products:
‘A traditional herbal medicinal product used to relieve the symptoms associated with occasional over indulge of food and drink such as indigestion and upset stomach based on traditional use only.’

This indication is appropriate.

POSOLOGY AND METHOD OF ADMINISTRATION
The applicant has submitted the following posology for these products:
‘For oral use only.
Adults and the elderly
Take 1 capsule up to twice daily. The capsules should be swallowed whole with some water or other liquid. The capsules should not be chewed.

Children and adolescents under 18 years of age
This medicine is not recommended for children and adolescents under 18 years of age (see Section 4.4 Special warnings and precautions for use).’

This is acceptable.

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

EVIDENCE OF TRADITIONAL USE
Article 16 c 1 (c) requires the Applicant to provide bibliographic or expert evidence showing 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 European Community.

The Applicant has provided a bibliographic review as evidence of the use of milk thistle fruit within the EU for a period exceeding 30 years.

The information provided is considered to satisfy the requirement to demonstrate use for at least 30 years, of which at least 15 years have been in an EU Member State. The requirements of the Directive are, therefore, addressed for this aspect.

SAFETY REVIEW
Article 16 c 1 (d) requires the Applicant to provide a bibliographic review of the safety data together with an Expert Safety Report.
A safety review has been provided as well as an Expert Safety Report written by a
suitably qualified professional who is a pharmacist with experience in herbal medicines.

The safety review and Expert Safety Report are satisfactory.

**SUMMARY OF PRODUCT CHARACTERISTICS**
The SPCs for these products are satisfactory.

**PATIENT INFORMATION LEAFLET**
The PILs for these products are satisfactory.

**LABELLING**
All labelling is satisfactory.

**DISCUSSION**
These are applications for registration under the Traditional Herbal Medicinal Products Directive. The data supplied by the Applicant are sufficient to demonstrate 30 years’ of traditional use within the European Community of corresponding products and satisfactory safety data have been provided, supporting the proposed products.

**RECOMMENDATIONS**
Traditional Herbal Registrations may be granted.
OVERALL CONCLUSION AND RISK ASSESSMENT

QUALITY
The quality data submitted with these applications are satisfactory.

NON-CLINICAL
The non-clinical data submitted with these applications are satisfactory.

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 milk thistle fruit within the EU for a period exceeding 30 years.

A satisfactory review of the safety data has been provided.

The SPCs, PILs and labelling are satisfactory.

RISK ASSESSMENT
The quality of the products is acceptable and no new preclinical or clinical safety concerns have been identified.
STEPS TAKEN FOR ASSESSMENT

1. The MHRA received the Traditional Herbal Registration applications on 16 January 2009.

2. Following standard checks and communication with the applicant, the MHRA considered the applications valid on 4 March 2009.

3. Following assessment of the applications, the MHRA requested further information relating to the clinical dossier on 23 October 2009 and the quality dossier on 25 November 2009.

4. The applicant responded to the MHRA’s requests, providing further information on the clinical and quality dossiers on 5 March 2010.

5. A THR was granted on 1 October 2010.
SUMMARY OF PRODUCT CHARACTERISTICS

1 NAME OF THE MEDICINAL PRODUCT
Thisilyn® Maximum Strength Milk Thistle capsules
Higher Nature Milk Thistle capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each hard capsule contains:

193 mg – 261 mg of extract (as dry extract) from Milk Thistle fruits (Silybum marianum (L.) Gaertner)(equivalent to 3.725 g – 10.818 g of Milk Thistle fruits) corresponding to 108 mg of silymarin, calculated as silibinin.

Extraction solvent: Acetone 95% v/v.  
For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Hard capsule.  
Red, opaque, hard gelatin capsule.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used to relieve the symptoms associated with occasional over indulgence of food and drink such as indigestion and upset stomach based on traditional use only.

4.2 Posology and method of administration
For oral use only.

Adults and the elderly
Take 1 capsule up to twice daily. The capsules should be swallowed whole with some water or other liquid. The capsules should not be chewed.

Children and adolescents under 18 years of age
This medicine is not recommended for children and adolescents under 18 years of age (see Section 4.4 Special warnings and precautions for use).

4.3 Contraindications
Hypersensitivity to Milk Thistle or to plants of the Asteraceae (Compositae) family or to any of the excipients.

4.4 Special warnings and precautions for use
Do not exceed the stated dose.
Patients suffering from active liver disease should consult their doctor before taking the product.

Milk Thistle may alter the way that certain drugs are broken down by the liver (see Section 4.5 Interaction with other medicinal products and other forms of interaction).

The use in children and adolescents under 18 years of age is not recommended as there is no relevant indication.

If symptoms worsen or persist a doctor or qualified healthcare practitioner should be consulted.

4.5 Interaction with other medicinal products and other forms of interaction

In vitro, Milk Thistle extract resulted in inhibition of CYP isoenzymes. However, the clinical relevance of these findings is not established.

4.6 Pregnancy and lactation

The safety of this product during pregnancy and lactation has not been established. In the absence of sufficient data the use during pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines

No studies of the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects

Gastrointestinal reactions (nausea, upset stomach, diarrhoea), headache, allergic reactions (urticaria, skin rash, pruritis, anaphylaxis). The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified healthcare practitioner should be consulted.

4.9 Overdose

No cases of overdose have been reported.

Supportive and symptomatic treatment should be provided as appropriate.

5 PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.2 Pharmacokinetic properties

Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.3 Preclinical safety data

Milk Thistle extract was not mutagenic in the mammalian murine micronucleus test.
Tests on reproductive toxicity and carcinogenicity have not been performed.

6 PHARMACEUTICAL PARTICULARS

6.1 List of excipients

Extract excipients
Mannitol

Capsule contents:
Capsule filling mass:
Mannitol
Cellulose microcrystalline
Croscarmellose sodium
Silica, colloidal anhydrous
Magnesium Stearate

Capsule shell:
Gelatin
Purified water
Titanium dioxide E171
Sodium lauryl sulphate
Iron (III)-oxide E172 (= red iron oxide)
Iron oxide hydrate E172 (= yellow iron oxide)

6.2 Incompatibilities
Not applicable.

6.3 Shelf life
3 years

6.4 Special precautions for storage
Do not store above 25°C.

6.5 Nature and contents of container
Thisilyn Maximum Strength Milk Thistle capsules are packed in PVC/ PVDC-
aluminium blisters and inserted into a carton.

Original packages contain 21, 28, 30, 56, 60 or 90 hard capsules.

Not all pack sizes may be marketed.

6.6 Special precautions for disposal
No special requirements
8 MARKETING AUTHORISATION NUMBER(S)
THR 23056/0010

9 DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION
01/10/2010

10 DATE OF REVISION OF THE TEXT
01/10/2010

1 NAME OF THE MEDICINAL PRODUCT
Thisilyn® Milk Thistle capsules

2 QUALITATIVE AND QUANTITATIVE COMPOSITION
Each hard capsule contains:

89 mg – 121 mg of extract (as dry extract) from Milk Thistle fruits (Silybum marianum (L.) Gaertner)(equivalent to 1.721 g – 5.000 g of Milk Thistle fruits) corresponding to 50 mg of silymarin, calculated as silibinin.

Extraction solvent: Acetone 95% v/v.

For full list of excipients, see section 6.1

3 PHARMACEUTICAL FORM
Hard capsule.
Ivory, opaque, hard gelatin capsule.

4 CLINICAL PARTICULARS

4.1 Therapeutic indications
A traditional herbal medicinal product used to relieve the symptoms associated with occasional over indulgence of food and drink such as indigestion and upset stomach based on traditional use only.

4.2 Posology and method of administration
For oral use only.
Adults and the elderly
Take 1 capsule up to twice daily. The capsules should be swallowed whole with some water or other liquid. The capsules should not be chewed.

Children and adolescents under 18 years of age
This medicine is not recommended for children and adolescents under 18 years of age (see Section 4.4 Special warnings and precautions for use).

4.3 Contraindications
Hypersensitivity to Milk Thistle or to plants of the Asteraceae (Compositae) family or to any of the excipients.

4.4 Special warnings and precautions for use
Do not exceed the stated dose.

Patients suffering from active liver disease should consult their doctor before taking the product.

Milk Thistle may alter the way that certain drugs are broken down by the liver (see Section 4.5 Interaction with other medicinal products and other forms of interaction).

The use in children and adolescents under 18 years of age is not recommended as there is no relevant indication.

If symptoms worsen or persist a doctor or qualified healthcare practitioner should be consulted.

4.5 Interaction with other medicinal products and other forms of interaction
In vitro, Milk Thistle extract resulted in inhibition of CYP isoenzymes. However, the clinical relevance of these findings is not established.

4.6 Pregnancy and lactation
The safety of this product during pregnancy and lactation has not been established. In the absence of sufficient data the use during pregnancy and lactation is not recommended.

4.7 Effects on ability to drive and use machines
No studies of the effect on the ability to drive and use machines have been performed.

4.8 Undesirable effects
Gastrointestinal reactions (nausea, upset stomach, diarrhoea), headache, allergic reactions (urticaria, skin rash, pruritis, anaphylaxis).
The frequency is not known.
If other adverse reactions not mentioned above occur, a doctor or a qualified healthcare practitioner should be consulted.
4.9 **Overdose**
No cases of overdose have been reported.

Supportive and symptomatic treatment should be provided as appropriate.

5 **PHARMACOLOGICAL PROPERTIES**

5.1 **Pharmacodynamic properties**
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.2 **Pharmacokinetic properties**
Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC as amended.

5.3 **Preclinical safety data**
Milk Thistle extract was not mutagenic in the mammalian murine micronucleus test.

Tests on reproductive toxicity and carcinogenicity have not been performed.

6 **PHARMACEUTICAL PARTICULARS**

6.1 **List of excipients**
**Extract excipients:**
Mannitol

**Capsule contents:**
Capsule filling mass:
Mannitol
Cellulose microcrystalline
Croskarmellose sodium
Silica, colloidal anhydrous
Magnesium Stearate

**Capsule shell:**
Gelatin
Purified water
Titanium dioxide E171
Sodium lauryl sulphate
Iron oxide hydrate E172 (= yellow iron oxide)

6.2 **Incompatibilities**
Not applicable.

6.3 **Shelf life**
2 years

6.4 **Special precautions for storage**
Do not store above 25°C.
6.5 **Nature and contents of container**
Thisilyn capsules are packed in PVC/ PVDC- aluminium blisters and inserted into a carton.

Original packages contain 21, 28, 30, 56, 60 or 90 hard capsules.

Not all pack sizes may be marketed.

6.6 **Special precautions for disposal**
No special requirements

7 **MARKETING AUTHORISATION HOLDER**
Schwabe Pharma (UK) Ltd
Alexander House
Mere Park
Dedmere Road
Marlow
Buckinghamshire
SL7 1PD

8 **MARKETING AUTHORISATION NUMBER(S)**
THR 23056/0012

9 **DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION**
01/10/2010

10 **DATE OF REVISION OF THE TEXT**
01/10/2010
6: Further information

Each hard capsule of this product contains 193 mg – 261 mg of standardised extract (as dry extract) from Milk Thistle fruits (Silybum marianum (L.) Gaertn.) (equivalent to 3.725 g – 10.818 g of Milk Thistle fruits).

This amount of standardised extract corresponds to 108 mg of silymarin, calculated as silibinin. Extraction solvent: Acetone 95% v/v.

This product also contains the following ingredients:

- **Extract excipients**: mannitol
- **Capsule contents**: mannitol, cellulose microcrystalline, croscarmellose sodium, silica colloidal anhydrous, magnesium stearate.
- **Capsule shell**: gelatin, purified water, titanium dioxide E171, sodium lauryl sulphate, iron (III)-oxide E172 (= red iron oxide), iron oxide hydrate E172 (= yellow iron oxide).

Each pack contains 21, 28, 30, 56, 60 or 90 hard capsules. Not all pack sizes may be marketed.

**Registration holder for this product**
Schwabe Pharma (UK) Ltd
Alexander House, Mere Park, Dedmere Road, Marlow, Bucks SL7 1PD

**Manufacturer of this product**
Wievellhove GmbH,
Dömebrink 19, 49479 Ibbenbüren, Germany

**Traditional herbal registration number:**
THR 23056/0010

If you would like further information about this product, please contact:
Schwabe Pharma (UK) Ltd
Alexander House, Mere Park, Dedmere Road, Marlow, Bucks, SL7 1PD
Telephone: 01628 401980
Email: info@schwabe-pharma.co.uk

This leaflet was prepared in August 2010

For large print, Braille or audio version of this leaflet, please call 01628 401980

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**Patient Information Leaflet**

**Thisilyn® Maximum Strength Milk Thistle capsules**

standardised fruit extract

Please read this leaflet carefully before you start taking these capsules. It contains some important information about Thisilyn® Maximum Strength Milk Thistle.

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

**What is in this leaflet**

1: What this product is and what it is used for ........................................... page 1
2: Before you take this product ................................................................. page 2
3: How to take this product ....................................................................... page 3
4: Possible side-effects ............................................................................... page 3
5: How to store this product ..................................................................... page 3
6: Further information ............................................................................... page 4

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

This product is a traditional herbal medicinal product containing Milk Thistle standardised fruit extract. Each capsule of this product contains 193 mg – 261 mg of standardised extract (as dry extract) from Milk Thistle fruits (Silybum marianum (L.) Gaertn.) (equivalent to 3.725 g – 10.818 g of Milk Thistle fruits). This amount of standardised extract corresponds to 108 mg of silymarin, calculated as silibinin. Extraction solvent: Acetone 95% v/v.

Thisilyn® Maximum Strength Milk Thistle is a traditional herbal medicinal product used to relieve the symptoms associated with occasional over indulgence of drink and food such as indigestion and upset stomach. This usage is based on traditional use only.
2: Before you take this product

DO NOT TAKE this product if you are:
- under 18 years of age
- pregnant or breast-feeding
- allergic to any of the ingredients or to plants of the Asteraceae/Compositae family such as daisies, marigolds or artichokes (see section 6)

Tell your doctor before taking this product if you are currently suffering from active liver disease.

3: How to take this product

Adults and the elderly
Take 1 capsule up to twice daily. Swallow the capsules whole with some water or other liquid. Do not chew the capsules.

Do not exceed the stated dose.
Do not give this product to children or adolescents under 18 years old.

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

4: Possible side-effects

Like all medicines, this product can have side-effects, although the frequency is not known. These are listed below.

<table>
<thead>
<tr>
<th>Side-effects</th>
<th>Advice</th>
</tr>
</thead>
<tbody>
<tr>
<td>nausea or feeling sick</td>
<td>If these persist for more than a few days, or become troublesome, stop taking this product. These side-effects are often only temporary. Stop taking this product immediately if you experience any allergic skin reaction.</td>
</tr>
<tr>
<td>diarrhoea</td>
<td></td>
</tr>
<tr>
<td>upset stomach</td>
<td></td>
</tr>
<tr>
<td>headache</td>
<td></td>
</tr>
<tr>
<td>mild allergic skin reactions</td>
<td></td>
</tr>
<tr>
<td>itching and/or skin rash, urticaria, hives, pruritus itching, anaphylaxis.</td>
<td></td>
</tr>
</tbody>
</table>

5: How to store this product

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 of sight of children.
Keep your capsules in the blister pack until it is time to take them.
PATIENT INFORMATION LEAFLET

Higher Nature Milk Thistle

Hard capsules

Standardised fruit extract

Please read this leaflet carefully before you start taking these capsules. It contains some important information about Higher Nature Milk Thistle.

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

What is in this leaflet

1. What this product is and what it is used for page 1
2. Before you take this product page 2
3. How to take this product page 2
4. Possible side-effects page 3
5. How to store this product page 3
6. Further information page 4

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

This product is a traditional herbal medicinal product containing Milk Thistle standardised fruit extract. Each capsule of this product contains 193mg – 261mg of standardised extract (as dry extract) from Milk Thistle fruits (Silybum marianum (L.) Gaertn.) (equivalent to 3.725g – 10.816g of Milk Thistle fruits). This amount of standardised extract corresponds to 108mg of silymarin, calculated as silibinin. Extraction solvent: acetone 95% v/v.

Higher Nature Milk Thistle is a traditional herbal medicinal product used to relieve the symptoms associated with occasional overindulgence of drink and food such as indigestion and upset stomach. This usage is based on traditional use only.

This leaflet was prepared in September 2010

MHRA PAR; THISILYN® MAXIMUM STRENGTH MILK THISTLE CAPSULES AND HIGHER NATURE MILK THISTLE CAPSULES (THR 23056/0010) AND THISILYN® MILK THISTLE CAPSULES (THR 23056/0012)
2. Before you take this product

DO NOT TAKE this product if you are:
- under 18 years of age
- pregnant or breastfeeding
- allergic to any of the ingredients or to plants of the Asteraceae/Compositae family such as daisies, marigolds or artichokes (see section 6)

Tell your doctor before taking this product if you are currently suffering from active liver disease.

3: How to take this product

- Adults and the elderly.
- Take 1 capsule up to twice daily.
- Swallow the capsule whole with some water or other liquid. Do not chew the capsules.
- Do not give this product to children or adolescents under 18 years old.

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

4: Possible side-effects

Like all medicines, this product can have side-effects, although the frequency is not known. These are listed below.

<table>
<thead>
<tr>
<th>Side-effects</th>
<th>Other side-effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>nausea or feeling sick</td>
<td>If these persist for more than a few days, or become troublesome, stop taking this product. These side-effects are often only temporary.</td>
</tr>
<tr>
<td>diarrhea</td>
<td>Stop taking this product immediately if you experience any allergic skin reaction.</td>
</tr>
<tr>
<td>upset stomach</td>
<td></td>
</tr>
<tr>
<td>headache</td>
<td></td>
</tr>
<tr>
<td>mild allergic skin reactions, itching and/or skin rash, urticaria, hives, pruritus itching, anaphylaxis.</td>
<td></td>
</tr>
</tbody>
</table>

5: How to store this product

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 your capsules out of the reach and sight of children.
- Keep your capsules in the blister pack until it is time to take them.
6: Further information

Each hard capsule of this product contains 89 mg – 121 mg of standardised extract (as dry extract) from Milk Thistle fruits (*Silybum marianum* (L.) Gaethn.) (equivalent to 1.721 g – 5.0 g of Milk Thistle fruits). This amount of standardised extract corresponds to 50 mg of silymarin, calculated as silybin. Extraction solvent: Acetone 95% v/v.

This product also contains the following ingredients:

**Extract excipients:** mannitol

**Capsule contents:** mannitol, cellulose microcrystalline, croscarmellose sodium, silica colloidal anhydrous, magnesium stearate.

**Capsule shell:** gelatin, purified water, titanium dioxide E171, sodium lauryl sulphate, iron oxide hydrate E172 (≤ yellow iron oxide).

Each pack contains 21, 28, 30, 56, 60 or 90 hard capsules. Not all pack sizes may be marketed.

Registration holder for this product
Schwabe Pharma (UK) Ltd
Alexander House, Mere Park, Dedmire Road, Marlow, Bucks SL7 1PD

Manufacturer of this product
Wiewelhove GmbH,
Dörnrebrink 19, 49479 Ibbenbüren, Germany

Traditional herbal registration number:
THR 23056/0012

If you would like further information about this product, please contact:
Schwabe Pharma (UK) Ltd
Alexander House, Mere Park, Dedmire Road, Marlow, Bucks, SL7 1PD
Telephone: 01628 401980
Email: info@schwabe-pharma.co.uk

This leaflet was prepared in August 2010

For large print, Braille or audio version of this leaflet, please call 01628 401980

**Patient Information Leaflet**

**Thisilyn® Milk Thistle capsules**

Milk Thistle standardised fruit extract

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

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

**What is in this leaflet**

1: What this product is and what it is used for ........................................ webpage 1
2: Before you take this product ..................................................................... page 2
3: How to take this product ............................................................................. page 2
4: Possible side-effects ...................................................................................... page 3
5: How to store this product ............................................................................ page 3
6: Further information ...................................................................................... page 4

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

This product is a traditional herbal medicinal product containing Milk Thistle standardised fruit extract. Each capsule of this product contains 89 mg – 121 mg of standardised extract (as dry extract) from Milk Thistle fruits (*Silybum marianum* (L.) Gaethn.) (equivalent to 1.721 g – 5.0 g of Milk Thistle fruits). This amount of standardised extract corresponds to 50 mg of silymarin, calculated as silybin. Extraction solvent: Acetone 95% v/v.

Thisilyn® Milk Thistle is a traditional herbal medicinal product used to relieve the symptoms associated with occasional over indulgence of drink and food such as indigestion and upset stomach. This usage is based on traditional use only.
2. Before you take this product

DO NOT TAKE this product if you are:
- under 18 years of age
- pregnant or breast-feeding
- allergic to any of the ingredients or to plants of the
  Asteraceae/Compositae family such as daisies, marigolds
  or artichokes (see section 6)

Tell your doctor before taking this product if you are currently suffering from active liver disease.

3. How to take this product

**Adults and the elderly**
Take 1 capsule up to twice daily. Swallow the capsules whole with some water or other liquid. Do not chew the capsules.

Do not exceed the stated dose.
Do not give this product to children or adolescents under 18 years old.

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

4. Possible side-effects

Like all medicines, this product can have side-effects, although the frequency is not known. These are listed below.

**Side-effects**

- **nausea** or feeling sick
- **diarrhoea**
- **upset stomach**
- **headache**
- **mild allergic skin reactions**
  - itching and/or skin rash,
  - urticaria, hives, pruritus itching,
  - anaphylaxis.

If these persist for more than a few days, or become troublesome, stop taking this product. These side-effects are often only temporary.

Stop taking this product immediately if you experience any allergic skin reaction.

5. How to store this product

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.
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.
LABELLING

THR 23056/0010:
Thisilyn® Maximum Strength
Milk Thistle
21 capsules

A traditional herbal medicinal product used to relieve the symptoms associated with occasional over-indulgence of drink and food, based on traditional use only.

Traditionally used for:
- Over-indulgence
- Indigestion
- Upset stomach

Do not exceed the stated dose. Do not take if you are:
- under 18 years of age
- pregnant or breast-feeding
- allergic to any of the ingredients

Do not use if you are allergic to Milk Thistle or other members of this family (Asteraceae/Compositae family).

Please read the enclosed information leaflet before taking these capsules. Keep out of sight and reach of children.

Do not store above 25°C. Expiry date on inner blister.

Manufactured in Germany
THI 23056/0001

Thisilyn® Maximum Strength
Milk Thistle
21 hard capsules
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