5 June 2018
EMA/HMPC/294187/2013
Committee on Herbal Medicinal Products (HMPC)

European Union herbal monograph on *Silybum marianum* (L.) Gaertn., fructus

Final

Discussion in Working Party on European Union monographs and list (MLWP)	May 2013 July 2013 November 2013 January 2014 May 2014 July 2014 November 2014 January 2015 May 2015
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Keywords	Herbal medicinal products; HMPC; European Union herbal monographs; well-established medicinal use; traditional use; *Silybum marianum* L. Gaertn., fructus; Silybi mariani fructus; milk thistle fruit

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

BG (bulgarski): Бял трън, плод CS (čeština): plod ostropestřece mariánského DA (dansk): Marietidselfrugt DE (Deutsch): Mariendistelfrüchte EL (elliniká): Σιλύβου μαριανού καρπός EN (English): Milkthistle Fruit ES (español): Cardo mariano, fruto de ET (eesti keel): maarjaohakavili FI (suomi): maarianohdake, hedelmä FR (français): Chardon-marie (fruit de) HU (magyar): Máriatövis termés HR (hrvatski): paskvičine peteljke IT (italiano): Cardo mariano frutto	LT (lietuvių kalba): Margainių vaisiai LV (latviešu valoda): Īstā mārdadža augļi MT (Malti): Għerq tax-Xewk tal-Madonna NL (Nederlands): Mariadistel PL (polski): Owoc ostropestu plamistego PT (português): Cardo-mariano RO (română): fruct de armurariu SK (slovenčina): Plod pestreca SL (slovenščina): plod pegastega badlja SV (svenska): Mariatistelfrukt IS (íslenska): NO (norsk): Marietistelfrukt

European Union herbal monograph on *Silybum marianum* (L.) Gaertn., fructus

1. Name of the medicinal product

To be specified for the individual finished product.

2. Qualitative and quantitative composition[1, 2]

Well-established use	Traditional use
	With regard to the registration application of Article 16d(1) of Directive 2001/83/EC *Silybum marianum* (L.) Gaertn., dried fruit (milk thistle) i) Herbal substance Not applicable. ii) Herbal preparations a) Comminuted herbal substance for herbal tea b) Powdered herbal substance c) Dry extract (DER 20-70:1), extraction solvent acetone d) Dry extract (DER 30-40:1), extraction solvent ethanol 96% (V/V) e) Dry extract (DER 20-35:1), extraction solvent ethyl acetate f) Dry extract (DER 26-45:1), extraction solvent ethyl acetate g) Dry extract (DER 36-44:1), extraction solvent ethyl acetate h) Dry extract (DER 20-34:1), extraction solvent methanol 90% (V/V) i) Soft extract (DER 10-17:1), extraction solvent ethanol 60% (V/V)

3. Pharmaceutical form

Well-established use	Traditional use

[1] The declaration of the active substance(s) for an individual finished product should be in accordance with relevant herbal quality guidance.

[2] The material complies with the Ph. Eur. monograph (ref.: 1860).

Well-established use	Traditional use
	Comminuted herbal substance as herbal tea for oral use. Herbal preparations in solid or liquid dosage forms for oral use. The pharmaceutical form should be described by the European Pharmacopoeia full standard term.

4. Clinical particulars

4.1. Therapeutic indications

Well-established use	Traditional use
	Traditional herbal medicinal product for the symptomatic relief of digestive disorders, sensation of fullness and indigestion and to support the liver function, after serious conditions have been excluded by a medical doctor. The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.

4.2. Posology and method of administration[3]

Well-established use	Traditional use
	Posology *Adults and elderly* a) Comminuted herbal substance for herbal tea Single dose: 3-5 g in 100 ml of boiling water, 2-3 times daily, before meals b) Powdered herbal substance Single dose: 300 mg–600 mg, 2-3 times daily Daily dose: up to 1800 mg, before meals c) Dry extract (DER 20-70:1), extraction solvent acetone Single dose: 82-239 mg, 2-3 times daily Daily dose: up to 478 mg, before meals d) Dry extract (DER 30-40:1), extraction solvent ethanol 96% (V/V) Single dose: 200 mg Daily dose: 200 mg

[3] For guidance on herbal substance/herbal preparation administered as herbal tea or as infusion/decoction/macerate preparation, please refer to the HMPC 'Glossary on herbal teas' (EMA/HMPC/5829/2010 Rev.1).

Well-established use	Traditional use
	e) Dry extract (DER 20-35:1), extraction solvent ethyl acetate Single dose: 162.5-250 mg, 3-4 times daily f) Dry extract (DER 26-45:1), extraction solvent ethyl acetate Single dose: 123-208.3 mg, 3-4 times daily g) Dry extract (DER 36-44:1), extraction solvent ethyl acetate Single dose: 173.0-186.7 mg, 3 times daily h) Dry extract (DER 20-34:1), extraction solvent methanol 90% (V/V) Single dose: 70 mg, 3 times daily i) Soft extract Single dose: 392 mg 2 times daily The use in children and adolescents under 18 years of age is not recommended (see section 4.4 'Special warnings and precautions for use') **Duration of use** If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. **Method of administration** Oral use

4.3. Contraindications

Well-established use	Traditional use
	Hypersensitivity to the active substance and to plants of the Asteraceae (Compositae) family.

4.4. Special warnings and precautions for use

Well-established use	Traditional use
	The use in children and adolescents under 18 years of age has not been established due to lack of adequate data. If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. If icterus or a change in colour of urine or stool appears,

Well-established use	Traditional use
	the medical doctor should be consulted immediately. For tinctures and extracts containing ethanol, the appropriate labelling for ethanol, taken from the 'Guideline on excipients in the label and package leaflet of medicinal products for human use', must be included.

4.5. Interactions with other medicinal products and other forms of interaction

Well-established use	Traditional use
	None reported

4.6. Fertility, pregnancy and lactation

Well-established use	Traditional use
	Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended. No fertility data available.

4.7. Effects on ability to drive and use machines

Well-established use	Traditional use
	No studies on the effect on the ability to drive and use machines have been performed.

4.8. Undesirable effects

Well-established use	Traditional use
	Mild gastrointestinal symptoms such as dry mouth, nausea, upset stomach, gastric irritation and diarrhoea may occur; headache; allergic reactions (dermatitis, urticaria, skin rash, pruritus, anaphylaxis, asthma) may occur. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted.

4.9. Overdose

Well-established use	Traditional use
	No case of overdose has been reported.

5. Pharmacological properties

5.1. Pharmacodynamic properties

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.2. Pharmacokinetic properties

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC.

5.3. Preclinical safety data

Well-established use	Traditional use
	Not required as per Article 16c(1)(a)(iii) of Directive 2001/83/EC, unless necessary for the safe use of the product. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

6. Pharmaceutical particulars

Well-established use	Traditional use
	Not applicable

7. Date of compilation / last revision

5 June 2018