EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

20 September 2016
EMA/HMPC/294187/2013
Committee on Herbal Medicinal Products (HMPC)

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

Draft

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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

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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 as amended *Silybum marianum* (L.) Gaertn., dried fruit (milk thistle) i) Herbal substance Not applicable ii) Herbal preparations a) Comminuted herbal substance 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) Liquid extract (DER 10-17:1), extraction solvent ethanol 60% (V/V)

[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).

3. Pharmaceutical form

Well-established use	Traditional use
	Comminuted herbal substance as herbal tea for oral use. Herbal preparations in liquid or solid 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 relief of dyspepsia and digestive complaints of hepatic origin, 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 tea preparation Single dose: 3-5 g in 100 ml of boiling water Daily dose: 2 or 3 times daily, before meals b) Powdered herbal substance Single dose: 300 mg–600 mg Daily dose: 2-3 times daily, up to 1800 mg daily, before meals c) Dry extract (DER 20-70:1), extraction solvent acetone Single dose: 82-239 mg dry extract Daily dose: 2-3 times daily, up to 478 mg, before

[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
	meals d) Dry extract (DER 30-40:1), extraction solvent ethanol 96% (V/V) Single dose: 200 mg dry extract Daily dose: 200 mg dry extract e) Dry extract (DER 20-35:1), extraction solvent ethyl acetate Single dose: 162.5-250 mg dry extract Daily dose: 3-4 times daily f) Dry extract (DER 26-45:1), extraction solvent ethyl acetate Single dose: 123-208.3 mg dry extract Daily dose: 3-4 times daily g) Dry extract (DER 36-44:1), extraction solvent ethyl acetate Single dose: 173.0-186.7 mg extract Daily dose: 3 times daily h) Dry extract (DER 20-34:1), extraction solvent methanol 90% (V/V) Single dose: 70 mg dry extract Daily dose: 3 times daily i) Liquid extract Single dose: 15 ml equivalent to 392 mg soft extract Daily dose: 30 ml (2 times 15 ml) equivalent to 784 mg soft extract 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

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. 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 as amended.

5.2. Pharmacokinetic properties

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

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

20 September 2016