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Committee on Herbal Medicinal Products (HMPC)

## Assessment report on *Sambucus nigra* L., flos

Final

Based on Article 16d(1), Article 16f and Article 16h of Directive 2001/83/EC (traditional use)

Herbal substance(s) (binomial scientific name of the plant, including plant part)	<i>Sambucus nigra</i> L., flos
Herbal preparation(s)	Comminuted herbal substance Liquid extract (DER 1:1), extraction solvent: ethanol 25% V/V Tincture (1:5) extraction solvent: ethanol 25% V/V
Pharmaceutical form(s)	Herbal substance or comminuted herbal substance as herbal tea for oral use Herbal preparations in liquid dosage forms for oral use
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# 1. Introduction

## 1.1. Description of the herbal substance(s), herbal preparation(s) or combinations thereof

- Herbal substance(s)

Elder flower (Sambuci flos) consists of the dried flowers of *Sambucus nigra* L. It contains not less than 0.80% of flavonoids, calculated as isoquercitroside (C<sub>21</sub>H<sub>20</sub>O<sub>12</sub>; Mr464.4) with reference to the dried drug (Ph. Eur., ref.: 1217).

- Herbal preparation(s)

Comminuted herbal substance

Liquid extract (DER 1:1), extraction solvent: ethanol 25% V/V

Tincture (1:5) extraction solvent: ethanol 25% V/V

- Combinations of herbal substance(s) and/or herbal preparation(s) including a description of vitamin(s) and/or mineral(s) as ingredients of traditional combination herbal medicinal products assessed, where applicable.

This assessment report includes data regarding monopreparations containing *Sambucus nigra* L., flos and herbal preparations from this herbal substance. Literature regarding combination products is not part of the assessment.

Constituents:

Flavonoids (up to 3%):	Chief components are quercetin, rutin, isoquercitrin, kaempferol, astragalinal (WHO 2002), nicotiflorin (Hänsel <i>et al.</i> 1994; Willer 1997) and hyperoside (Willer 1997; WHO 2002)
Triterpenes:	Approximately 1% $\alpha$ - and $\beta$ - amyrrin, occurring mainly as fatty acid esters; Triterpene acids: approximately 0.85% oleanolic and ursolic acids, 20 $\beta$ -hydroxyursolic acid (Bisset and Wichtl 2001)
Volatile oil:	Numerous constituent types have been identified, including ethers and oxides, ketones, aldehydes, alcohols, esters and acids like palmitic acid, linoleic, linolenic acid (Toulemonde and Richard 1983).
Caffeic acid derivatives (3%)	Chlorogenic acid (Fleming 2000)
Sterols:	About 0.11%, mainly $\beta$ -sitosterol, stigmasterol, campesterol (WHO 2002) and cholesterol (Hänsel <i>et al.</i> 1994; Willer 1997)
Minerals:	8-9% (Blumenthal <i>et al.</i> 2000), high in potassium (Steinegger and Hänsel 1988)
Other constituents:	Tannin, mucilage (Bradley 1992) , plastocynin (protein), pectin and sugar (Barnes <i>et al.</i> 2002)

## 1.2. Search and assessment methodology

This report is based on a scientific review of the scientific and traditional literature referring to *Sambucus fructus* L. The following electronic databases were searched 10th of August 2016 with these search terms:

Scientific databases: SciFinder

*Sambucus nigra*: 2778 references

Sambuci flos: 5 references

Medical databases: The Cochrane Library

Elder flower: 4

*Sambucus nigra* flos: 0

Other resources: European Scientific Cooperative on Phytotherapy. ESCOP Monographs. The Scientific Foundation for Herbal Medicinal Products. E/S/C/O/P Online Series, 2013: SAMBUCCI FLOS Elder flower: 28 articles

Toxicological databases: Toxline

*Sambucus nigra*: 182 references

*Sambucus nigra* flos: 3 references

Pharmacovigilance databases:

The World Health Organisation's Uppsala Monitoring Centre (WHO-UMC): 7 case reports

Search performed on 9.11.2016 for sambucus flower (synonym for *Sambucus nigra*)

Data from EU and non-EU regulatory authorities: Information about products on the market in the EU/EEA Member States (2.2.1)

## 2. Data on medicinal use

### 2.1. Information about products on the market

#### 2.1.1. Information about products on the market in the EU/EEA Member States

**Table 1:** Overview of data obtained from marketed medicinal products

Active substance	Indication	Pharmaceutical form Strength (where relevant) Posology Duration of use	Regulatory Status
Comminuted herbal substance	Relief of early symptoms of common cold	Herbal tea (infusion)  1 tea bag contains 2.0 g herbal substance  Adults, adolescents: 1 cup several times daily	01.2013  TU, AT

Active substance	Indication	Pharmaceutical form Strength (where relevant) Posology Duration of use	Regulatory Status
Sambuci flos	For the relief of early symptoms of common cold	Herbal tea 1 tea bag (= 1.5 g)/250 ml boiling water 3-5 times daily Not to be used for more than one week	Since 2000, switched to TU in 2011, CZ
Sambuci flos	Cough and cold Notes: If the symptoms persist longer than 3 days, when dyspnoea, fever or purulent sputum occurs, a doctor or a pharmacist should be consulted.	Herbal tea > 12 years: 3.0 g/150 ml boiling water 3-5 times daily	1986, MA, DE
Comminuted herbal substance	Traditional herbal medicinal product used to alleviate early common cold symptoms	Herbal tea Infusion of 2 g comminuted herbal substance (one sachet) in 200ml (one glass) of boiling water. Infuse 15 minutes, drink the infusion 3 times daily	09.1990, MA*, PL

This overview is not exhaustive. It is provided for information only and reflects the situation at the time when it was established.

*\*Authorisation according to national law in Poland.*

### 2.1.2. Information on products on the market outside the EU/EEA

Not applicable

### 2.2. Information on documented medicinal use and historical data from literature

The use of elder flower has been continuously documented in handbooks, pharmacopoeias and scientific literature. Elder is a highly valued plant with a history dating back to ancient Greece. Elder flower is used both in flavouring agent in foodstuff and as a medicinal herb. Elder flower is a commonly used ingredient in many combination products on the European market.

Traditional medicinal use of elder flower connected to the relief of the symptoms of the early phase of the common cold has been documented in handbooks. The following traditional uses and posologies have been recorded for elder flower (see table 2).

**Table 2:** Overview of historical data

Herbal preparation	Documented Use / Traditional Use	Pharmaceutical form Strength (where relevant) Posology Duration of use	Reference
Comminuted herbal substance	Traditional use: As a diaphoretic during treatment of common cold. It is used against catarrhal conditions such as laryngitis, bronchitis, cough, whooping cough, beginning pneumonia etc.	Oral dose: 5-15 g dried flowers as infusion	Lehrbuch der Biologischen Heilmittel (Madaus 1938)
Comminuted herbal substance	Traditional use: Common cold. As a diaphoretic during the treatment of the cold. Elder flower is also used in other feverish conditions as a tea, or as a gargle	Herbal tea: 3-4 g with approximately 150 ml hot water several times daily  Single dose: 1.5 g as infusion or decoction  Average daily dose: 10-15 g drug as infusion	Hagers Handbuch der Pharmazeutischen Praxis, Drogen P-Z (Hänsel <i>et al.</i> 1994) referring to Baz nr.50 1986 and Standardzulassung Nr. 1019.99.99 1986
Comminuted herbal substance	Traditional use: Common cold. As a diaphoretic during the treatment of the cold. Elder flower is also used in other feverish conditions as a tea, or as a gargle	Oral dose:  Daily dose: 5-15 g in 200 ml water as an infusion or 2 teaspoons in a cup for 10 min; drink 1-2 cups warm up to 5 cups daily. Average single dose 1.5 g  Single dose 1-2 g  Daily dose 3-6 g	Hagers Handbuch Der Pharmzeutischen Praxis: Sambucus (List <i>et al.</i> 1979) referring to several different references
Comminuted herbal substance	Traditional use: Diaphoretic. Treatment of feverish cold	Herbal tea  About 2 full teaspoons (3-4 g) elder flower with hot water (150 ml)  Especially in the second half of the day; 1-2 cups fresh prepared tea as hot as possible may be taken	Standardzulassungen für Fertigarzneimittel: Holunderblüten (Braun 1997)
Comminuted herbal substance	As a diaphoretic in feverish chills, etc. and also used in the preparation of gargles	Oral dose: 3 g Elder flower as a tea  Daily dose 10-15 g drug	Herbal Drugs and Phytopharmaceuticals (Bisset and Wichtl 2001)

<b>Herbal preparation</b>	<b>Documented Use / Traditional Use</b>	<b>Pharmaceutical form Strength (where relevant) Posology Duration of use</b>	<b>Reference</b>
Herbal substance	Common cold	Oral, 2-4 g dried flowers by infusion three times daily	British Herbal Pharmacopoeia. (Keighley 1976, 1983)
Comminuted herbal substance	Common cold, feverish conditions	3-5 g dried flowers in infusion three times daily (preferably taken hot)	British Herbal Compendium (Bradley 1992)
Comminuted herbal substance	Mild diaphoreticum, diureticum and expectorans	Herbal tea: 1 tablespoon in a glass of water as a decoction, divided in 2 single doses daily	Receptariusz Zielarski (Gobiec 1967)
Liquid extract (1:1, 25% ethanol)	Common cold	Oral, 2-4 ml three times daily	British Herbal Pharmacopoeia. (Keighley 1976, 1983)
Liquid extract (1:1, 25% ethanol)	Common cold, feverish conditions	Oral, 3-5 ml ml three times daily	British Herbal Compendium (Bradley 1992)
Tincture (1:5) extraction solvent: ethanol 25% V/V	Common cold, feverish conditions	Oral, 10-25 ml three times daily	British Herbal Compendium (Bradley 1992)

### **2.3. Overall conclusions on medicinal use**

For each of the herbal preparations included in the monograph, the available sources that provide evidence of period of use are shown. The duration of use is restricted based on the type of indication that is intended and designed for use without the supervision of a medical practitioner.

Market and literature data supports the traditional use of Sambuci flos, with the following strength and posologies summarised in table 3:

**Table 3:** Overview of evidence on period of medicinal use

<b>Herbal preparation Pharmaceutical form</b>	<b>Indication</b>	<b>Posology, strength</b>	<b>Period of medicinal use</b>
Comminuted herbal substance	Cough and cold	Herbal tea  > 12 years: 3.0 g/150 ml boiling water	Since 1986, MA, DE

		3-5 times daily	
Herbal substance	Common cold	Oral, 2-4 g dried flowers by infusion three times daily	<i>British Herbal Medicine Association's</i> (Keighley 1976, 1983)
Comminuted herbal substance	Traditional use: Common cold. As a diaphoretic during the treatment of the cold. Elder flower is also used in other feverish conditions as a tea, or as a gargle	Oral use:  Daily dose: 5-15 g in 200 ml water as an infusion or 2 teaspoons in a cup for 10 min; drink 1-2 cups warm up to 5 cups daily. Average single dose 1.5 g  Single dose 1-2 g  Daily dose 3-6 g	Hagers Handbuch Der Pharmazeutischen Praxis: Sambucus (List <i>et al.</i> , 1979)
Comminuted herbal substance	Mild diaphoreticum, diureticum and expectorans	Oral use:  1 tablespoon in a glass of water as a decoction, divided in 2 single doses daily	Receptariusz Zielarski (Gobiec 1967)
Liquid extract (1:1, 25% ethanol)	Common cold	Oral, 2-4 ml three times daily	British Herbal Pharmacopoeia (Keighley 1976, 1983)
Liquid extract (1:1, 25% ethanol)	Common cold, feverish conditions	Oral, 3-5 ml three times daily	British Herbal Compendium (Bradley 1992).
Tincture (1:5) extraction solvent: ethanol 25% V/V	Common cold, feverish conditions	Oral, 10-25 ml three times daily	British Herbal Compendium (Bradley 1992).

Except from the comminuted herbal substance, the herbal substance defined as the dried flowers and the herbal preparations were included in the first version of the monograph, published in 2008. The herbal substance, preparation a (comminuted herbal substance) and preparation b (1:1, 25% ethanol) fulfil the criteria for traditional herbal medicinal use for at least 30 years (15 years within the European Union) according to Directive 2004/24/EC. However, for preparation b, the reference (BHP 1976) includes the posology 2-4 ml three times daily, while 5 ml three times daily is only supported by the reference BHC 1992. Since there are no known safety concerns, the higher posologies (5 g three times daily for preparation a; and 5 ml three times daily for preparation b) are retained in the revision of the monograph. Regarding preparation c (tincture 1:5, 25 % ethanol), the strength and posology are considered equivalent to the strength and posology of preparation b (1:1, 25% ethanol).

In addition, comminuted herbal substance as a decoction, cited in Receptariusz Zielarski (Gobiec 1967), has been included in the revised version of the monograph. The posology in the Receptariusz

Zielarski has been concluded to correspond to 3-6 g comminuted herbal substance in 200 ml water the available information listed in handbooks.

The mentioning of the phytotherapeutic traditional use of elder flower as a diaphoretic and a diuretic are interpreted as pharmacological effects to alleviate symptoms in the early phase of common cold. Hence, these effects are not appropriate as separate therapeutic indications.

Based on literature and the information available, the following traditional indication is included in the monograph:

“Traditional herbal medicinal product used for the relief of early symptoms of common cold.

The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.”

This indication can be approved for the following herbal substance and herbal preparations:

- a) Herbal substance or comminuted herbal substance
- b) Liquid extract (DER 1:1), extraction solvent: ethanol 25% V/V
- c) Tincture (1:5) extraction solvent: ethanol 25% V/V

The following posologies are included in the monograph:

*Adolescents, adults and elderly*

- a) Single dose: Herbal tea: 2-5 g of the herbal substance or comminuted herbal substance in 150 ml boiling water as a herbal infusion three times daily.

Daily dose: 6-15 g

Single dose: Herbal tea: 3-6 g of the comminuted herbal substance in 200 ml water divided in 2 single doses daily as a decoction.

- b) Single dose: 2-5 ml three times daily

Daily dose: 6-15 ml

- c) Single dose: 10-25 ml three times daily

Daily dose: 30-75 ml

### **Duration of use**

If the symptoms persist longer than 1 week during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

### **Method of administration**

Oral use

## 3. Non-Clinical Data

### 3.1. Overview of available pharmacological data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof

#### 3.1.1. Primary pharmacodynamics

##### Data on antibacterial activity

Izzo *et al.* (1995) investigated 68 plant extracts from 65 species (including elder flower ethanol extract) for antibacterial activity against eight gram-positive and eight gram-negative bacteria. Elder flower showed activity against *Bacillus subtilis*, *Staphylococcus aureus*, *Salmonella typhi*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*. According to Izzo *et al.* (1995), a search of the literature showed that antibacterial properties of elder flower could be attributed to chlorogenic and caffeic acids.

##### Immunological activity

The ability of aqueous extracts from elder flower to inhibit the proinflammatory activity of major virulence factors from the periodontal pathogens *Porphyromonas gingivalis* and *Actinobacillus actinomycetemcomitans* has been investigated. The study indicated that elder flower extract inhibits macrophage release of pro-inflammatory cytokines induced by *P. gingivalis*, *A. actinomycetemcomitans*, and selected components of these pathogens. Moreover, the elder flower extract suppressed the activation of neutrophils, which have also been implicated as effectors of periodontal tissue destruction. These effects could be attributed to inhibition of activation of NF- $\kappa$ B and phosphatidylinositol 3-kinase (PI3K), according to the authors (Harokopakis *et al.* 2006).

Barsett *et al.* (2012) studied the immunomodulatory effects in order to clarify the pharmacology of compounds isolated from crude extracts of *Sambucus nigra* L. flos. The authors wanted to investigate if the immunomodulating activity of compounds present in berries and flowers of *Sambucus nigra* were of the same order, or different, and also if the most active components were of high or low molecular weight nature. Defatted material of berries and flowers of *Sambucus nigra* were extracted with 50% ethanol and with water of 50°C and 100°C. High molecular weight fractions were obtained after gel filtration on BioGelP6DG. The different fractions were investigated for their monosaccharide contents and carbohydrate structures. The immunomodulating effects were investigated using a complement fixing assay as well as a system for measuring the production of NO after stimulation of macrophages with the different fractions. All fractions contained substantial amounts of carbohydrates. Removal of low molecular weight material revealed polysaccharide fractions containing monosaccharides typical for pectins and showed enhanced bioactivity. High molecular weight fractions from elderflowers showed higher bioactivity than the equally extracted fractions from elderberries.

Förster-Waldl *et al.* (2003) examined the possible allergens in extracts from elderberry pollen, flowers and berries by testing *in vitro* in sera from patients. Flowers, berries and pollen were ground in liquid nitrogen before extraction. Proteins were extracted 10% (w/v) in 10 mmol/L potassium phosphate buffer (pH 7.0). N-terminal sequence analysis of purified elderberry allergen indicated that the elderberry allergen is a ribosomal inactivating protein (RIP) called Sam n 1.

#### 3.1.2. Secondary pharmacodynamics

##### Effect on blood glucose

In a two-armed study, aqueous extract of elder flower significantly increased glucose uptake, glucose oxidation, and gluconeogenesis in rat abdominal muscle. Elder flower extract incubated with rat pancreatic cells also had a dose-dependent stimulatory effect on insulin secretion. The authors concluded that

elder flower contains water-soluble components capable of stimulating insulin secretion and enhancing muscle glucose uptake and metabolism. However, the chemical nature of potential antihyperglycemic components of elder flower remains to be established (Gray *et al.* 2000).

### **Anti-inflammatory activity**

The active ingredients responsible for the anti-inflammatory action of elder flower aqueous extract are unknown. The ability of aqueous extract (SNAE) to inhibit P13K has been suggested to be mediated at least partially through quercetin. The presence in *Sambucus nigra* of anthocyanins with antioxidant action may be responsible for the ability of SNAE to inhibit oxidative burst of neutrophils, and partially, the inhibitory effect of SNAE on NF- $\kappa$ B activation, as suggested by Harokopakis *et al.* 2006. A study by Yeşilada *et al.* (1997) showed that the methanolic extract of elder flower and its lipophilic fractions possess a medium to low inhibitory effect on the biosynthesis of interleukin-1 $\alpha$ , interleukin-1 $\beta$  and tumor necrosis factor  $\alpha$ .

### **Diuretic activity**

According to Rebuelta *et al.* (1983), intragastric administration of an elder flower infusion (20 ml/kg body weight), or of a potassium-and flavonoid-rich extract of the elder flower extract, had a diuretic effect in rats. The diuretic effect was greater than that observed with theophylline (5 mg/kg body weight). In another study done by Beaux *et al.* (1999) the authors reported that elder flower caused diuresis from 2-24 hours compared with the control in rats given 50 mg/kg aqueous extracts via the i.p route.

### **3.1.3. Safety pharmacology**

No data available.

### **3.1.4. Pharmacodynamic interactions**

Elder flower extract (2 ml/kg), administered orally to rats, caused a decrease of the sleep induction time of pentobarbitone and increased sleeping time when compared with rats administered pentobarbitone only. Elder flower had no effect on the analgesic activity of morphine at this dosage (Jakovljevic *et al.* 2001).

### **3.1.5. Conclusions**

Results from relevant experimental studies on elder flower are limited. None of the reported pharmacological studies constitute any cause for safety concern.

## **3.2. Overview of available pharmacokinetic data regarding the herbal substance(s), herbal preparation(s) and relevant constituents thereof**

No data are available on pharmacokinetics of *Sambucus nigra* L. flos.

The flavonoids rutin and quercetin, which are found in elder flower, have been reported to inhibit xanthine oxidase (Nagao *et al.* 1999), and may theoretically affect caffeine and theophylline plasmatic levels.

### **3.3. Overview of available toxicological data regarding the herbal substance(s)/herbal preparation(s) and constituents thereof**

#### **3.3.1. Single dose toxicity**

No data found.

#### **3.3.2. Repeat dose toxicity**

No data found.

#### **3.3.3. Genotoxicity**

No data found.

#### **3.3.4. Carcinogenicity**

No data found.

#### **3.3.5. Reproductive and developmental toxicity**

No data found.

#### **3.3.6. Local tolerance**

No data found.

#### **3.3.7. Other special studies**

No data found.

#### **3.3.8. Conclusions**

Non-clinical information on the safety of elder flower is scarce.

No studies on reproductive toxicity, genotoxicity or carcinogenicity are available for *Sambucus nigra* L., flos.

### **3.4. Overall conclusions on non-clinical data**

Results from relevant experimental studies on elder flower to support the proposed indication are very limited. None of the reported pharmacological studies constitute any cause for safety concern.

Specific data on pharmacokinetics and interactions are not available.

Non-clinical information on the safety of elder flower is scarce.

Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

As there is no information on reproductive and developmental toxicity, the use during pregnancy and lactation cannot be recommended.

Oral administration of elder flower can be regarded as safe at traditionally used doses.

A European Union list entry is not supported due to lack of adequate data on genotoxicity.

## 4. Clinical Data

### 4.1. Clinical pharmacology

No data found.

#### 4.1.1. Overview of pharmacodynamic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No data found.

#### 4.1.2. Overview of pharmacokinetic data regarding the herbal substance(s)/preparation(s) including data on relevant constituents

No data found.

### 4.2. Clinical efficacy

#### 4.2.1. Dose response studies

No data found.

#### 4.2.2. Clinical studies (case studies and clinical trials)

No data found.

### 4.3. Clinical studies in special populations (e.g. elderly and children)

No data found.

### 4.4. Overall conclusions on clinical pharmacology and efficacy

No data found.

## 5. Clinical Safety/Pharmacovigilance

### 5.1. Overview of toxicological/safety data from clinical trials in humans

No data available.

### 5.2. Patient exposure

Products containing elderflower is widely available. The products have various regulatory statuses. A considerable patient/consumer exposure must be anticipated as elder flower is widely used as a natural source of food flavouring (Barnes *et al.*, 2007). There are also traditional herbal medicinal products on the market in the European Member States.

Aside from market presence and data from studies, there are no concrete data concerning patient exposure.

No special risks have been identified.

### **5.3. Adverse events, serious adverse events and deaths**

In the VigiLyze search database of the World Health Organization's Uppsala Monitoring Centre for the period up to November 2017, there were 2 spontaneous reports of suspected adverse drug reactions associated with the single-ingredient *Sambucus nigra* L., flower. The reactions were spread over several organ classes.

Assessor's comment: There are not sufficient safety data to include any undesirable effects in section 4.8 in the monograph.

### **5.4. Laboratory findings**

No data found.

### **5.5. Safety in special populations and situations**

#### **5.5.1. Use in children and adolescents**

No data found.

The oral use of elder flower is not recommended in children due to the lack of adequate data. There are no studies in adolescents between 12 and 18 years available. The recommended dosage for oral use in adults and adolescents over 12 years is supported by use in member states.

#### **5.5.2. Contraindications**

No data found. However, for safety reasons the use is contraindicated in persons with hypersensitivity to the active substance.

#### **5.5.3. Special Warnings and precautions for use**

Patients using the product should consult a doctor or a qualified health care practitioner if dyspnoea, fever or purulent sputum occurs.

#### **5.5.4. Drug interactions and other forms of interaction**

No data found.

#### **5.5.5. Fertility, pregnancy and lactation**

Safety during fertility, pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

#### **5.5.6. Overdose**

No cases of overdose from elder flower have been reported.

#### **5.5.7. Effects on ability to drive or operate machinery or impairment of mental ability**

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

### **5.5.8. Safety in other special situations**

Not applicable

### **5.6. Overall conclusions on clinical safety**

Sambuci flos can be recognised as safe when used in recommended dosages under specified conditions.

For Sambuci flos there are no clinical safety data available and use in children or adolescents is not described.

For safety reasons the use is contraindicated in persons with hypersensitivity to the active substance.

## **6. Overall conclusions (benefit-risk assessment)**

There are sufficient data available to support a European Union monograph on the traditional use of elder flower. Traditional use has shown that elder flower can be recognised as safe when used in recommended dosages under the conditions specified in the monograph.

There are no clinical data available. The criteria for “well-established medicinal use” require clinical data according to directive 2001/83/EC.

Traditional medicinal use of elder flower has been found to fulfil the requirement of medicinal use for at least 30 years (15 years within the European Union) according to Directive 2004/24/EC for the following indication:

“Traditional herbal medicinal product used for the relief of early symptoms of common cold.

The product is a traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use.”

Due to the lack of sufficient safety data the use of elder flower cannot be recommended during pregnancy and lactation.

As no safety data from the use in children are available, the use of elder flower is not recommended in children under 12 years of age. However, based on the long-standing medicinal use, as well as the absence of reports of serious adverse events, a sufficient degree of safety as necessary for traditional herbal medicinal products can be assumed in adults and adolescents (over 12 years of age).

A European Union list entry is not supported due to lack of adequate data on genotoxicity.

## **Annex**

### **List of references**