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Committee on Herbal Medicinal Products (HMPC)

## Assessment report on *Species pectorales*

Draft

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>Althaea officinalis</i> L., radix <i>Cetraria islandica</i> (L.) Acharius s.l., thallus <i>Filipendula ulmaria</i> (L.) Maxim, flos <i>Foeniculum vulgare</i> Miller subsp. <i>vulgare</i> var. <i>vulgare</i> , fructus <i>Glycyrrhiza glabra</i> L.; <i>Glycyrrhiza inflata</i> Bat.; <i>Glycyrrhiza uralensis</i> Fisch., radix <i>Plantago lanceolata</i> L., folium <i>Pimpinella anisum</i> L., fructus <i>Polygonum aviculare</i> L., herba <i>Primula veris</i> L.; <i>Primula elatior</i> (L.) Hill, flos <i>Salix</i> [various species including <i>S. purpurea</i> L.; <i>S. daphnoides</i> Vill.; <i>S. fragilis</i> L.], cortex <i>Sambucus nigra</i> L., flos <i>Thymus vulgaris</i> L.; <i>Thymus zygis</i> L., herba <i>Tilia cordata</i> Miller; <i>Tilia platyphyllos</i> Scop.; <i>Tilia x vulgaris</i> Heyne, flos <i>Verbascum thapsus</i> L.; <i>V. densiflorum</i> Bertol. ( <i>V. thapsiforme</i> Schrad); <i>V. phlomoides</i> L., flos
Herbal preparation(s)	Combinations of the above-mentioned herbal substances
Pharmaceutical form(s)	Comminuted herbal substances as herbal tea for oral use
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Note: This draft assessment report is published to support the public consultation of the draft European Union herbal monograph on *Species pectorales*. It is a working document, not yet edited, and shall be further developed after the release for consultation of the monograph. Interested parties are welcome to submit comments to the HMPC secretariat, which will be taken into consideration but no 'overview of comments received during the public



consultation' will be prepared on comments that will be received on this assessment report. The publication of this draft assessment report has been agreed to facilitate the understanding by Interested Parties of the assessment that has been carried out so far and led to the preparation of the draft monograph.

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# 1. Introduction

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

- 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.

EU herbal monographs on herbal tea combinations are based on combinations which have been shown to fulfil the applicable criteria according to 2001/83/EC. In addition, the specific herbal preparations included have a documented traditional use on a specific indication already established in previous HMPC assessments for the single substance use. There are data showing their use in combinations in certain ranges that can be considered safe and plausible.

The legislation does not impose any limitation to the number/percentage of combination partners in herbal teas. However, the scientific opinion of the HMPC is:

Usually not more than 4 herbal substances should be used in a herbal tea as active substance and each substance should represent not less than 10% of the total weight. More combination partners at lower proportions imply technical obstacles in terms of quality testing and raise questions about the plausible contribution and the need/justification. These may be better considered excipients.

More than 4 substances or less than 10% of the total weight in a herbal tea would in principle not raise concerns from a public health viewpoint provided that the marketing authorisation holder/traditional use registration holder can control the quality of the product and that appropriate justification on the need and the plausibility as active substance as well as the safety for a specific indication, strength and posology is provided.

According to data from marketed products, pharmacopoeias, textbooks and literature, traditional herbal tea combinations in the EU member states contain mostly 3-4 main herbal substances with a well-documented single and combined use and plausibility in a specific indication. Accordingly, HMPC agreed and cover a large proportion of traditional combinations. Such limitation allows also a reasonable reference to previous single substance assessments and appropriate complexity of the monograph for use by applicants and assessors.

Tea combinations in EU herbal monographs can be considered plausible and safe in a certain indication and thus facilitate national registration procedures providing some flexibility for applicants. However, it is not supposed to be exhaustive or exclude other individual combinations. It is always possible to obtain registration/authorisation for a specific combination product provided that all requirements are met - even if not covered by the EU herbal combination monographs. Reference can be made to the established herbal tea monographs with an adequate justification of the deviation (e.g. inclusion of a preparation without an EU monograph or different number of combination partners).

It is further referred to Q&A EMA/HMPC/345132/2010 questions R1 and R8 as well as general HMPC guidance in this respect:

- Guideline on the clinical assessment of fixed combinations of herbal substances / herbal preparations (EMA/HMPC/166326/2005)
- Quality of combination herbal medicinal products/traditional herbal medicinal products (EMA/HMPC/CHMP/CVMP/214869/2006)

This assessment report refers to herbal tea combinations used in the therapeutic area 'cough and cold'. Herbal substances contained in such combinations for which an assessment by the HMPC has been performed for the use as single substance are: *Althaea officinalis* L., radix; *Cetraria islandica* (L.) Acharius s.l., thallus; *Filipendula ulmaria* (L.) Maxim, flos; *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, fructus; *Glycyrrhiza glabra* L.; *Glycyrrhiza inflata* Bat.; *Glycyrrhiza uralensis* Fisch., radix; *Plantago lanceolata* L., folium; *Pimpinella anisum* L., fructus; *Polygonum aviculare* L., herba; *Primula veris* L.; *Primula elatior* (L.) Hill, flos; *Salix* [various species including *S. purpurea* L.; *S. daphnoides* Vill.; *S. fragilis* L.], cortex; *Sambucus nigra* L., flos; *Thymus vulgaris* L.; *Thymus zygis* L., herba; *Tilia cordata* Miller; *Tilia platyphyllos* Scop.; *Tilia x vulgaris* Heyne, flos; *Verbascum thapsus* L.; *V. densiflorum* Bertol. (*V. thapsiforme* Schrad); *V. phlomoides* L., flos.

Other herbal substances that are linked to the therapeutic area but are not yet assessed by the HMPC leading to a EU herbal monograph for the single substance are not considered in this assessment report.

Additional herbal substances which may be combination partners but which are not linked to the therapeutic area are considered as excipients.

For the description of the herbal substances, their constituents, relevant pharmacopoeia monographs, non-clinical and clinical data please refer to the assessment reports of the single herbal substances.

## **1.2. Search and assessment methodology**

The information regarding herbal tea combinations in the therapeutic area 'cough and cold' was gathered from EU member states and the information provided by interested parties.

Also several scientific databases were searched for combinations: Pubmed, Embase, Medline, Healthlink, Scopus, in November 2023. Nevertheless, such review did not provide relevant results on the combinations.

Books, Book chapters, articles and letters in Journals, Medical press reviews, Acts of law and regulations Libraries: Standard handbooks of Phytotherapy and Pharmacognosy (Wichtl 1994, among others).

For the scientific data on safety and efficacy of the single herbal substances contained in the combinations please refer to the assessment reports of the single herbal substances.

## **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**

##### **Information on medicinal products marketed in the EU/EEA**

Not applicable.

##### **Information on relevant combination medicinal products marketed in the EU/EEA**

Herbal substances mentioned in brackets belong to different therapeutic area/indication.

Table 1: Overview of data obtained from marketed medicinal products

#	Active substance	Indication	Pharmaceutical form	Regulatory Status
1	Salviae officinalis folium 15 g Althaeae radix 15 g Polygوني avicularis herba 15 g Thymi herba 15 g Urticae herba 15 g Sambuci nigrae flos 5 g Plantaginis folium 5 g Foeniculi amari fructus 10 g Liquiritiae radix 5 g In 100 g of species	Traditional herbal medicine used as an adjuvant in acute and chronic diseases of the upper respiratory tract. It has an antiseptic and expectorant effect. The infusion can also be used for gargling or inhalation.	Species – herbal tea  1 tablespoon (5 g) is poured over a cup (¼ l) of boiling water and after 15 minutes of infusing in a covered container it is strained, the tea must not be boiled. It is drunk warm 3 times a day,  The preparation can be used by adults and adolescents from 12 years of age.	TU, 1971, CZ
2	Salviae officinalis folium 0.225 g Althaeae radix 0.225 g Polygوني avicularis herba 0.225 g Thymi herba 0.225 g Urticae herba 0.225 g Sambuci nigrae flos 0.075 g Plantaginis folium 0.075 g Foeniculi amari fructus 0.150 g Liquiritiae radix 0.075 g In one tea/infusion bag (1.5 g)	Traditional herbal medicine used as an adjuvant in acute and chronic diseases of the upper respiratory tract. It has an antiseptic and expectorant effect. The infusion can also be used for gargling or inhalation.	1 infusion bag is poured over a cup (¼ l) of boiling water and infused in a covered container for 5-10 minutes. Tea is drunk warm, 3 times a day,  The preparation can be used by adults and adolescents from 12 years of age.	TU, 1971, CZ
3	Plantaginis folium 375 mg Serpilli herba 225 mg Althaeae radix 300 mg Liquiritiae radix 225 mg Tiliae flos 75 mg Cynosbati fructus sine semine 300 mg In one tea/infusion bag (1.5 g)	Traditional herbal medicine used in acute diseases of the upper respiratory tract, accompanied by cough. Facilitates expectoration, dissolves and loosens phlegm. The preparation can be used by children from 4 years old,	Species - herbal tea 1 infusion bag is poured over 0.25 l of boiling water and left for 5 min. infuse in a covered container. It must not be cooked. Children from 4 to 12 years old drink tea 2 times a day, teenagers from 12 years old and adults drink tea 3 times a day.	TU, 1995, CZ

#	Active substance	Indication	Pharmaceutical form	Regulatory Status
		adolescents and adults.		
4	Foeniculi dulcis fructus 225 mg Sambuci nigrae flos 375 mg Tiliae flos 375 mg Plantaginis folium 300 mg Liquiritiae radix 225 mg In one tea/infusion bag (1.5 g)	THMP used in colds, accompanied by increased temperature, in inflammations of the oral cavity and upper respiratory tract; promotes sweating.	1 infusion bag is poured over 0.25 l of boiling water and left to infuse for 5-10 minutes in a covered container. It must not be cooked. The tea is drunk warm 3 times a day  The preparation can be used by children from 3 years of age, adolescents and adults.	TU, 1997, CZ
5	Plantaginis folium 23 g Farfarae folium 22 g Althaeae radix 22 g Menthae piperitae herba 10 g Liquiritiae radix 1 g Verbasci flos 8 g Foeniculi amari fructus 5 g In 100 g of species	Traditional herbal medicine used as an adjuvant in acute and chronic diseases of the upper respiratory tract. It acts as an expectorant, mucilaginous and antiseptic.	Species 1 tablespoon (5 g) is poured over a cup (¼ l) of boiling water and after 15 minutes of infusing in a covered container it is strained, the tea must not be boiled. It is drunk warm 3 times a day.  The preparation can be used by adults and adolescents from 12 years of age.	TU, 1969, CZ From 2019 the product is not on the market because of the Farfarae folium (one of the components with PAs). However, the sunset is scheduled on 31.12.2025.
6	Salviae folium 0.225 g/ 15 g Althaeae radix 0.225 g/ 15 g Polygoni avic. herba 0.225 g/ 15 g Thymi herba 0.225 g/ 15 g Urticae herba 0.225 g/ 15 g Foeniculi fructus 0.150 g/ 10 g Sambuci flos 0.075 g/ 5 g Plantaginis folium 0.075 g/ 5 g	Adjuvant treatment of acute and chronic upper respiratory tract infections. It has expectorant and antiseptic properties. Infusion can be used as a gargle or for inhalation.	Herbal tea  Bags: Pour out a cup (1/4 L) of boiling water to 1 bag of herbal tea and macerate for 5-10 minutes. Drink 3-times daily. It can be sweetened. It should be prepared freshly before use.  Comminuted herbal substances: Pour out a cup (1/4 L) of boiling water to tablespoon (5 g) of herbal tea and macerate for 15 minutes. Do not cook. Drink 3-times daily. It can	TU, 1971, SK

#	Active substance	Indication	Pharmaceutical form	Regulatory Status
	Liquiritiae radix 0.075 g/ 5 g		be sweetened. It should be prepared freshly before use.	
7	Plantaginis folium 23 g Althaeae radix 22 g Farfarae folium 22 g Menthae pip.herba 10 g Liquiritiae radix 10 g Verbasci flos 8 g Foeniculi fructus 5 g	Adjuvant treatment of acute and chronic upper respiratory tract infections. It has expectorant, mucilaginous and antiseptic properties. Infusion can be used as a gargle.	Herbal tea  Posology: Pour out a cup (1/4 L) of boiling water to tablespoon (5 g) of herbal tea and macerate for 15 minutes. Do not cook. Drink 3-times daily. It can be sweetened. It should be prepared freshly before use.  <b>Duration of use:</b> Herbal tea contains Farfarae folium. Therefore, it should not be used for more than 4-6 weeks.	Species pectorales Planta, 1969, SK
8	1 tea bag (2.0 g) contains 0.7 g Tiliae flos, comminuted; 0.55 g Anisi fructus, comminuted; 0.55 g Thymi herba, comminuted	To improve the symptoms of common cold and dry irritating cough.	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 2 g DD: 6 g	WEU, At least since 1976, DE
9	1 tea bag (2.0 g) contains 1.2 g Salicis cortex, comminuted; 0.04 g Tiliae flos, comminuted	Common cold especially of febrile type and with headache.	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 2 g DD: 10 g	WEU, At least since 1976, DE
10	<b>Brusttee</b> 100 g herbal tea combination contain: 15 g Anisi fructus, 25 g Liquiritiae radix, 25 g Althaeae radix, 25 g Althaeae flos	Relief of mucosa irritation of the upper respiratory tract and associated dry cough.	Herbal tea SD: 3 g DD: 9-12 g  No longer than 4-6 weeks per year without medical advice.	Standard Marketing Authorisation 1993, DE
11	<b>Erkältungstee I</b> 100 g herbal tea combination contain: Active ingredients: 30 g Sambuci flos, 30 g Tiliae flos, 20 g Filipendulae flos; Other ingredients: 20 g Rosae pseudo-fructus	Febrile colds for which a sweating cure is desirable.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1987, DE
12	<b>Erkältungstee II*</b> 100 g herbal tea combination contain: Active ingredients:	Febrile colds for which a sweating cure is desirable.	Herbal tea 1 cup of a fresh infusion prepared from 1	Standard Marketing Authorisation,



#	Active substance	Indication	Pharmaceutical form	Regulatory Status
	20-40 g Sambuci flos, 20-40 g Tiliae flos, 20-35 g Salicis cortex		tablespoonful (4-5 g) herbal tea several times daily	1988, DE
13	<b>Erkältungstee III*</b> 100 g herbal tea combination contain: Active ingredients: 20-30 g Sambuci flos, 25-40 g Tiliae flos, 20-30 g Filipendulae flos	Febrile colds for which a sweating cure is desirable.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation  1988, DE
14	<b>Erkältungstee IV*</b> 100 g herbal tea combination contain: Active ingredients: 30-50 g Sambuci flos, 20-30 g Thymi herba, 20-35 g Salicis cortex	Febrile colds for which a sweating cure is desirable	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1988, DE
15	<b>Erkältungstee V*</b> 100 g herbal tea combination contain: Active ingredients: 20-40 g Sambuci flos, 20-40 g Tiliae flos, 20-30 g Thymi herba	Febrile colds for which a sweating cure is desirable	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1988, DE
16	<b>Hustentee</b> 100 g herbal tea combination contain: 25 g Althaeae radix, 10 g Foeniculi amari fructus, 10 g Cetrariae islandicae thallus, 15 g Plantaginis lanceolatae herba, 10 g Liquiritiae radix, 30 g Thymi herba	For signs of bronchitis as well as upper respiratory tract cold.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1987, DE
17	<b>Husten- und Bronchialtee I**</b> 100 g herbal tea combination contain: Active ingredients: 10-25 g Foeniculi amari fructus, 25-40 g Plantaginis lanceolatae herba, 25-35 g Liquiritiae radix, 10-40 g Thymi herba	Symptoms of bronchitis as well as irritation relief of upper respiratory tract cold with dry cough.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1988, DE
18	<b>Husten- und Bronchialtee II**</b> 100 g herbal tea combination contain: Active ingredients: 10-40 g Anisi fructus, 40-60 g Tiliae flos, 10-30 g Thymi herba	Symptoms of bronchitis as well as irritation relief of upper respiratory tract cold with dry cough.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4-5 g) herbal tea several times daily	Standard Marketing Authorisation, 1988, DE
19	1 tea bag (2 g) contains 0.6 g Sambuci flos, comminuted; 0.5 g Salicis cortex, comminuted; 0.5 g Tiliae	THMP to improve symptoms of febrile colds	Herbal tea <i>Adults:</i> SD: 2-4 g DD: 6-16 g	TUR, 2013, DE

#	Active substance	Indication	Pharmaceutical form	Regulatory Status
	flos, comminuted			
20	1 tea bag (1.6 g) contains 0.24 g <i>Foeniculi fructus</i> , comminuted; 0.21 g <i>Thymi herba</i> , comminuted; 0.19 g <i>Tiliae flos</i> , comminuted; 0.19 g <i>Polygoni avicularis herba</i> , comminuted; 0.18 g <i>Cetrariae islandicae thallus</i> , comminuted; 0.10 g <i>Primulae flos</i> , comminuted; 0.06 g <i>Lamii albi flos</i> , comminuted; 0.06 g <i>Verbasci flos</i> , comminuted	THMP to support expectoration in the respiratory tract. To facilitate coughing up during common colds	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 1.6 g DD: 6.4-9.6 g	TU, At least since 1976, DE TUR, 2013, DE
21	1 tea bag (1.5 g) contains 0.525 g <i>Plantaginis lanceolatae folium</i> , comminuted; 0.375 g <i>Thymi herba</i> , comminuted; 0.375 g <i>Althaeae radix</i> , comminuted; 0.225 g <i>Liquiritiae radix</i> , comminuted	THMP for expectoration and irritation relief in cough associated with colds.	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 3 g DD: 9-12 g <i>Children from 3 to 11 years of age:</i> SD: 1.5 g DD: 4.5-6 g	TUR, 2014, DE
22	1 tea bag (2.0 g) contains 0.7 g <i>Thymi herba</i> , comminuted; 0.5 g <i>Althaeae radix</i> , comminuted; 0.3 g <i>Plantaginis lanceolatae folium</i> , comminuted 0.3 g <i>Liquiritiae radix</i> , comminuted; 0.2 g <i>Cetrariae islandicae thallus</i> , comminuted	THMP for expectoration and irritation relief in cough associated with colds.	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 2-4 g DD: 6-16 g	TUR, 2013, DE
23	1 tea bag (1.5 g) contains 0.720 g <i>Plantaginis lanceolatae folium</i> , comminuted; 0.495 g <i>Thymi herba</i> , comminuted	THMP for expectoration in colds with cough and for relief of oropharyngeal irritations associated with dry cough.	Herbal tea <i>Adults and adolescents over 12 years of age:</i> SD: 1.5 g DD: 6 g	TUR, 2021, DE

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

#### Information on other products marketed in the EU/EEA (where relevant)

Not applicable.

### **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***

Table 2: Overview of historical data

Herbal preparation	Documented use / Traditional use	Pharmaceutical form	Reference
Lichen islandicus 50 g Althaeae radix 200 g Liquiritiae radix 100 g Thymi herba 100 g Anisi vulgaris fructus 100 g Farfarae folium 100 g Verbasci flos 100 g Althaeae folium 250 g	Species pectorales  No further indication	No posology given	Czechoslovak Pharmacopoeia IV  Slovak Pharmaceutical Code, 2007
Lichen islandicus 50 g Althaeae radix 150 g Liquiritiae radix 150 g Thymi herba 50 g Anisi vulgaris fructus 50 g Malvae flos 50 g Verbasci flos 50 g Althaeae folium 550 g	Species pectorales  No further indication	No posology given	Czechoslovak Pharmacopoeia III
Current composition: Malvae flos 10 parts Verbasci flos 10 parts Althaeae folium 20 parts Thymi herba 10 parts Althaeae radix 20 parts Liquiritiae radix 25 parts Anisi fructus 5 parts  Original composition only 10 parts Althaeae folium, but additionally 10 parts Tussilaginis folium. Tussilago has been removed in the early 1990ies. (In the original composition Thymi folium was contained, as this herbal substance was contained in the national pharmacopoeia. Change to Thymi herba with the uptake of thyme into Ph. Eur.	Species pectorales	Single dose of 1.5 g	Since 1960 in the Austrian Ph

### 2.3. Overall conclusions on medicinal use

Table 3: Althaea radix in combinations

<b>Combination partner</b>	<b>Amount Althaea radix in combination</b>	<b>Single dose Althaea radix, Posology, Strength</b>	<b>Period of medicinal use (Reference # in table 1)</b>
Anisi fructus	15 g (15%)	0.75 g, 3 times daily	10
Foeniculi amari fructus	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150g, 3 times daily	6
	5 g (5%)	1.1 g, 3 times daily	7
	25 g (25%)	1-1.25 g, several times daily	16
Lichen islandicus	25 g (25%)	1-1.25 g /several times daily	16
Liquiritiae radix	15 g (15%)	0.75 g, 3 times daily	1,10
	0.225 g (15%)	0.225 g, 3 times daily	2,6
	10 g (10%)	1.1 g, 3 times daily	7
	25 g (25%)	1-1.25 g, several times daily	16
Plantaginis folium	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2,6
	23 g (23%)	1.1 g, 3 times daily	7
Polygoni avicularis herba	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2,6
Sambuci nigrae	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2,6
Thymi herba	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2,6
	25 g (25%)	1-1.25 g, several times daily	16
Verbasci flos	8 g (8%)	1.1 g, 3 times daily	7
<b>Summary</b>	<b>5-25%</b>	<p><i>Adolescents, adults and elderly</i></p> <p><b>Single dose: 0.75-1.25 g</b></p> <p><b>DD: 2.25-3.75 g</b></p> <p><b>Frequency: 3 times daily</b></p> <p>Monograph</p> <p><i>Children 3-5 years of age</i></p> <p>SD: 0.5-1.0 g, 3 times daily</p> <p>DD: 1.5-3.0 g</p> <p><i>Children 6-11 years of age</i></p> <p>SD: 0.5-1.5 g, 3 times daily</p> <p>DD: 1.5-4.5 g</p> <p><i>Adolescents, adults and elderly</i></p> <p>SD:0.5-3 g, several times daily</p> <p>Max DD: 15 g</p>	

Table 4: Anisi fructus in combinations

<b>Combination partner</b>	<b>Amount Anisi fructus in combination</b>	<b>Single dose Anisi fructus, Posology, Strength</b>	<b>Period of medicinal use (Reference # in table 1)</b>
Althaea radix	15 g (15%)	0.45 g, 3-4 times daily	10
Liquiritiae radix	15 g (15%)	0.45 g, 3-4 times daily	10
Thymi herba	0.55 g (27.5%)	0.55 g, 3 times daily	8,18
	10-40g (10-40%)	0.4-2 g, several times daily	

<b>Combination partner</b>	<b>Amount Anisi fructus in combination</b>	<b>Single dose Anisi fructus, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Tiliae flos	0.55 g (27.5%) 10-40g (10-40%)	0.55 g, 3 times daily 0.4-2 g, several times daily	8,18
<b>Summary</b>	<b>10-40%</b>	<i>Adolescents, adults and elderly</i> <b>Single dose: 0.4-2 g</b> <b>DD: 1.2-6 g</b> <b>Frequency: 3 times/several times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1- 3.5 g, 3 times daily	

Table 5: Filipendula ulmaria flos in combinations

<b>Combination partner</b>	<b>Amount Filipendula ulmaria flos in combination</b>	<b>Single dose Filipendula ulmaria flos, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Sambuci nigrae	20 g (20%) 20-30 g (20-30%)	0.8-1.0 g, several times daily 0.8-1.5 g, several times daily	11,13
Tiliae flos	20 g (20%) 20-30 g (20-30%)	0.8-1.0 g, several times daily 0.8-1.5 g, several times daily	11,13
<b>Summary</b>	<b>20-30%</b>	<b>Single dose: 0.8-1.5 g</b> <b>Frequency: several times daily</b>  Monograph <i>Adults, Elderly</i> DD: 2.5-6 g, divided in 1-3 single doses Max DD: 15 g	

Table 6: Foeniculi amari fructus in combinations

<b>Combination partner</b>	<b>Amount Foeniculi amari fructus in combination</b>	<b>Single dose Foeniculi amari fructus, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	10 g (10%)	0.5 g, 3 or several times daily	1,16
	0.150 g/ 10 g (10%)	0.15 g, 3 times daily	2
	5 g (5%)	0.15 g, 3 times daily	6
		0.25 g, 3 times daily	7
Lichen islandicus	10 g (10%)	0.5 g, 3 or several times daily	16
	0.24 g (15%)	0.24 g, 4-6 times daily	20

<b>Combination partner</b>	<b>Amount Foeniculi amari fructus in combination</b>	<b>Single dose Foeniculi amari fructus, Posology, Strength</b>	<b>Period of medicinal use (Reference # in table 1)</b>
Liquiritiae radix	10 g (10%) 0.150 g/ 10 g (10%) 5 g (5%) 10-25 g (10-25%)	0.5 g, 3 or several times daily 0.15 g, 3 times daily 0.150 g, 3 times daily 0.25 g, 3 times daily 0.4-1.25 g, several times daily	1,16 2 6 7 17
Polygoni avicularis herba	10 g (10%) 0.150 g/ 10 g (10%) 0.24 g (15%)	0.5 g, 3 times daily 0.15 g, 3 times daily 0.150 g, 3 times daily 0.24 g, 4-6 times daily	1 2 6 20
Plantaginis folium	10 g (10%) 0.150 g/ 10 g (10%) 5 g (5%) 10-25 g (10-25%)	0.5 g, 3 or several times daily 0.15 g, 3 times daily 0.150 g, 3 times daily 0.25 g, 3 times daily 0.4-1.25 g, several times daily	1,16 2 6 7 17
Primulae flos	0.24 g (15%)	0.24 g, 4-6 times daily	20
Sambuci nigrae	10 g (10%) 0.150 g/ 10 g (10%)	0.5 g, 3 times daily 0.15 g, 3 times daily 0.15 g, 3 times daily	1 2 6
Thymi herba	10 g (10%) 0.150 g/ 10 g (10%) 10-25 g (10-25%) 0.24 g (15%)	0.5 g, 3 or several times daily 0.15 g, 3 times daily 0.15 g, 3 times daily 0.4-1.25 g, several times daily 0.24 g, 4-6 times daily	1,16 2 6 17 20
Tiliae flos	0.24 g (15%)	0.24 g, 4-6 times daily	20
Verbasci flos	5 g (5%) 0.24 g (15%)	0.25 g, 3 times daily 0.24 g, 4-6 times daily	7 20
<b>Summary</b>	<b>5-25%</b>	<b>Single dose: 0.15-1.25 g</b> <b>Frequency: 3 to several times daily</b>  Monograph <i>Adults and adolescents</i> SD: 1.5 g, 3 times daily DD: 4.5 g  <i>Children between 4 and 12 years of age</i> SD: 1.0 g, 3 times daily DD: 3.0 g	

Table 7: Lichen islandicus in combinations

<b>Combination partner</b>	<b>Amount Lichen islandicus in combination</b>	<b>Single dose Lichen islandicus, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	15 g (15%)	0.6-0.75 g, several times daily	16
Foeniculi amari fructus	15 g (15%) 0.18 g (11.25%)	0.6-0.75 g, several times daily 0.18 g, 4-6 times daily	16 20
Liquiritiae radix	15 g (15%)	0.6-0.75 g, several times daily	16
Polygoni avicularis herba	0.18 g (11.25%)	0.18 g, 4-6 times daily	20
Plantaginis folium	15 g (15%)	0.6-0.75 g, several times daily	16
Primulae flos	0.18 g (11.25%)	0.18 g, 4-6 times daily	20
Thymi herba	15 g (15%) 0.18 g (11.25%)	0.6-0.75 g, several times daily 0.18 g, 4-6 times daily	16 20
Tiliae flos	0.18 g (11.25%)	0.18 g, 4-6 times daily	20
Verbasci flos	0.18 g (11.25%)	0.18 g, 4-6 times daily	20
<b>Summary</b>	<b>11.25-15%</b>	<b>Single dose: 0.18-0.75 g</b> <b>Frequency: several times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1.5 g, 3 to 4 times daily DD: 4-6 g	

Table 8: Liquiritiae radix in combinations

<b>Combination partner</b>	<b>Amount Liquiritiae radix in combination</b>	<b>Single dose Liquiritiae radix, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
	10 g (10%)	0.5 g, 3 times daily	7
		0.4-0.5 g, several times daily	16
	25 g (25%)	0.75 g, 3-4 times daily	10
Anisi fructus	25 g (25%)	0.75 g, 3-4 times daily	10
Foeniculi amari fructus	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
	10 g (10%)	0.5 g, 3 times daily	7
		0.4-0.5 g, several times daily	16
	25-35 g (25-35%)	1-1.25 g, several times daily	17
Lichen islandicus	10 g (10%)	0.4-0.5 g, several times daily	16
Plantaginis folium	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
	10 g (10%)	0.5 g, 3 times daily	7
		0.4-0.5 g, several times daily	16
	25-35 g (25-35%)	1-1.25 g several times daily	17
Polygoni avicularis herba	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
Sambuci nigrae	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
Thymi herba	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
	10 g (10%)	0.4-0.5 g, several times daily	16



<b>Combination partner</b>	<b>Amount Liquiritiae radix in combination</b>	<b>Single dose Liquiritiae radix, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
	25-35 g (25-35%)	1-1.25 g several times daily	17
Verbasci flos	10 g (10%)	0.5 g, 3 times daily	7
<b>Summary</b>	<b>5-35%</b>	<b>Single dose: 0.075-1.25 g</b> <b>Frequency: 3 to several times daily</b>  Monograph <i>Adults and elderly</i> SD: 1.5 g, 2 times daily	

Table 9: Plantaginis lanceolatae folium in combinations

<b>Combination partner</b>	<b>Amount Plantaginis lanceolatae folium in combination</b>	<b>Single dose Plantaginis lanceolatae folium, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	5 g (5%) 0.075 g (5%) 23 g (23%) 15 g (15%)	0.25 g, 3 times daily 0.075 g, 3 times daily 1.15 g, 3 times daily 0.6-0.75 g, several times daily	1 2,6 7 16
Foeniculi amari fructus	5 g (5%) 0.075 g (5%) 23 g (23%) 15 g (15%) 25-40 g (25-40%)	0.25 g, 3 times daily 0.075 g, 3 times daily 1.15 g, 3 times daily 0.6-0.75 g, several times daily 1-1.6 g, several times daily	1 2,6 7 16 17
Lichen islandicus	15 g (15%)	0.6-0.75 g, several times daily	16
Liquiritiae radix	5 g (5%) 0.075 g (5%) 23 g (23%) 15 g (15%) 25-40 g (25-40%)	0.25 g, 3 times daily 0.075 g, 3 times daily 1.15 g, 3 times daily 0.6-0.75 g, several times daily 1-1.6 g, several times daily	1 2,6 7 16 17
Polygoni avicularis herba	5 g (5%) 0.075 g (5%)	0.25 g, 3 times daily 0.075 g, 3 times daily	1 2,6
Sambuci nigrae	5 g (5%) 0.075 g (5%)	0.25 g, 3 times daily 0.075 g, 3 times daily	1 2,6
Thymi herba	5 g (5%) 0.075 g (5%) 23 g (23%) 15 g (15%) 25-40 g (25-40%)	0.25 g, 3 times daily 0.075 g, 3 times daily 1.15 g, 3 times daily 0.6-0.75 g, several times daily 1-1.6 g, several times daily	1 2,6 7 16 17
Verbasci flos	23 g (23%)	1.15 g, 3 times daily	7
<b>Summary</b>	<b>5-40%</b>	<b>Single dose: 0.075-1.6 g</b>	

Combination partner	Amount Plantaginis lanceolatae folium in combination	Single dose Plantaginis lanceolatae folium, Posology, Strength	Period of medicinal use (Reference # in table 1)
		<b>Frequency: 3 to several times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 2 g, 2-3 times per day DD: 4-6 g	

Table 10: Polygoni avicularis herba in combinations

Combination partner	Amount Polygoni avicularis herba in combination	Single dose Polygoni avicularis herba, Posology, Strength	Period of medicinal use (Reference # in table 1)
Althaeae radix	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
Foeniculi amari fructus	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Lichen islandicus	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Liquiritiae radix	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
Plantaginis folium	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
Primulae flos	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Sambuci nigrae	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
Thymi herba	15 g (15%)	0.75 g, 3 times daily	1
	0.225 g (15%)	0.225 g, 3 times daily	2
	0.150 g (10%)	0.150 g, 3 times daily	6
	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Tiliae flos	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Verbasci flos	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
<b>Summary</b>	<b>10-15%</b>	<b>Single dose: 0.15-0.225 g</b> <b>Frequency: 3-6 times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1.5-2 g, 3-4 times daily DD: 4.5-8 g	

Table 11: Primulae flos in combinations

<b>Combination partner</b>	<b>Amount Primulae flos in combination</b>	<b>Single dose Primulae flos, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Foeniculi amari fructus	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
Lichen islandicus	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
Polygoni avicularis herba	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
Thymi herba	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
Tiliae flos	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
Verbasci flos	0.10 g (6.25%)	0.10 g, 4-6 times daily	20
<b>Summary</b>	<b>6.25%</b>	<b>Single dose: 0.10 g</b> <b>Frequency: 4-6 times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1 g, 3 times daily	

Table 12: Salicis cortex in combinations

<b>Combination partner</b>	<b>Amount Salicis cortex in combination</b>	<b>Single dose Salicis cortex, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Sambuci flos	20-35 g (20-35%)	0.8-1.5 g, several times daily	12,14
Tiliae flos	1.2 g (60%) 20-35 g (20-35%)	1.2 g, 5 times daily 0.8-1.5 g, several times daily	9 12,14
<b>Summary</b>	<b>20-60%</b>	<b>Single dose: 0.8-1.5 g</b> <b>Frequency: several times daily</b>  Monograph <i>Adults and elderly</i> SD: 1-3 g as an herbal infusion, 3 times daily <i>or</i> 4 g as a decoction, 3 times daily	

Table 13: Sambuci flos in combinations

<b>Combination partner</b>	<b>Amount Sambuci flos in combination</b>	<b>Single dose Sambuci flos, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
Filipendula flos	30 g (30%)	1.2-1.5 g, several times daily	11
	20-30 g (20-30%)	0.8-1.5 g, several times daily	13
Foeniculi amari fructus	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6
Liquiritiae radix	5 g (5%)	0.25 g, 3 times daily	1
	0.075 g (5%)	0.075 g, 3 times daily	2,6

<b>Combination partner</b>	<b>Amount Sambuci flos in combination</b>	<b>Single dose Sambuci flos, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Plantaginis folium	5 g (5%) 0.075 g (5%)	0.25 g, 3 times daily 0.075 g, 3 times daily	1 2,6
Polygoni avicularis herba	5 g (5%) 0.075 g (5%)	0.25 g, 3 times daily 0.075 g, 3 times daily	1 2,6
Salicis cortex	20-40 g (20-40%) 30-50 g (30-50%)	0.8-2 g, several times daily 1.2-2.5 g, several times daily	12,15 14
Thymi herba	5 g (5%) 0.075 g (5%) 30-50 g (30-50%)	0.25 g, 3 times daily 0.075 g, 3 times daily 1.2-2.5 g, several times daily	1 2,6
Tiliae flos	30 g (30%) 20-40 g (20-40%) 20-30 g (20-30%)	1.2-1.5 g, several times daily 0.8-2 g, several times daily 0.8-1.5 g, several times daily	11 12,15 13
<b>Summary</b>	<b>5-50%</b>	<b>Single dose: 0.075-2.5 g</b> <b>Frequency: several times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 2-5 g as a herbal infusion, 3 times daily  <i>or</i>  3-6 g as a decoction divided in 2 single doses	

Table 14: Thymi herba in combinations

<b>Combination partner</b>	<b>Amount Thymi herba in combination</b>	<b>Single dose Thymi herba, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Althaeae radix	15 g (15%) 0.225 g (15%) 30 g (30%)	0.75 g, 3 times daily 0.225 g, 3 times daily 1.2-1.5 g, several times daily	1 2,6 16
Anisi fructus	0.55 g (27.5%) 10-30 g (10-30%)	0.55 g, 3 times daily 0.4-1.5 g, several times daily	8 18
Foeniculi amari fructus	15 g (15%) 0.225 g (15%) 30 g (30%) 40 g (40%) 0.21 g (13.125%)	0.75 g, 3 times daily 0.225 g, 3 times daily 1.2-1.5 g, several times daily 1.6-2 g, several times daily 0.21 g, 4-6 times daily	1 2,6 16 17 20
Lichen islandicus	30 g (30%) 0.21 g (13.125%)	1.2-1.5 g, several times daily 0.21 g, 4-6 times daily	16 20
Liquiritiae radix	15 g (15%) 0.225 g (15%) 30 g (30%) 40 g (40%)	0.75 g, 3 times daily 0.225 g, 3 times daily 1.2-1.5 g, several times daily 1.6-2 g, several times daily	1 2,6 16 17
Plantaginis folium	15 g (15%) 0.225 g (15%) 30 g (30%) 40 g (40%)	0.75 g, 3 times daily 0.225 g, 3 times daily 1.2-1.5 g, several times daily 1.6-2 g, several times daily	1 2,6 16 17

<b>Combination partner</b>	<b>Amount Thymi herba in combination</b>	<b>Single dose Thymi herba, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Polygoni avicularis herba	15 g (15%) 0.225 g (15%) 0.21 g (13.125%)	0.75 g, 3 times daily 0.225 g, 3 times daily 0.21 g, 4-6 times daily	1 2,6 20
Primulae flos	0.21 g (13.125%)	0.21 g, 4-6 times daily	20
Salicis cortex	20-30 g (20-30%)	0.8-1.2 g, several times daily	14
Sambuci flos	15 g (15%) 0.225 g (15%) 20-30 g (20-30%)	0.75 g, 3 times daily 0.225 g, 3 times daily 0.8-1.2 g, several times daily	1 2,6 14,15
Tiliae flos	0.55 g (27.5%) 20-30 g (20-30%) 10-30 g (10-30%) 0.21 g (13.125%)	0.55 g, 3 times daily 0.8-1.2 g, several times daily 0.4-1.5 g, several times daily 0.21 g, 4-6 times daily	8 15 18 20
Verbasci flos	0.21 g (13.125%)	0.21 g, 4-6 times daily	20
<b>Summary</b>	<b>10-40%</b>	<b>Single dose: 0.21-2 g</b> <b>Frequency: several times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1-2 g, 3-4 times daily	

Table 15: Tiliae flos in combinations

<b>Combination partner</b>	<b>Amount Tiliae flos in combination</b>	<b>Single dose Tiliae flos, Posology, Strength</b>	<b>Period of medicinal use</b> (Reference # in table 1)
Anisi fructus	0.7 g (35%) 40-60 g (40-60%)	0.7 g, 3 times daily 1.6-3 g, several times daily	8 18
Filipendula flos	30 g (30%) 25-40 g (25-40%)	1.2-1.5 g, several times daily 1-2 g, several times daily	11 13
Foeniculi fructus	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Lichen islandicus	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Polygoni avicularis herba	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Primulae flos	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
Salicis cortex	0.04 g (2%) 20-40 g (20-40%)	0.04 g, 5 times daily 0.8-2 g, several times daily	9 12
Sambuci flos	30 g (30%) 20-40 g (20-40%) 25-40 g (25-40%)	1.2-1.5 g, several times daily 0.8-2 g, several times daily 1-2 g, several times daily	11 12,15 13
Thymi herba	0.7 g (35%) 20-40 g (20-40%) 40-60 g (40-60%) 0.19 g (11.875%)	0.7 g, 3 times daily 0.8-2 g, several times daily 1.6-3 g, several times daily 0.19 g, 4-6 times daily	8 15 18 20
Verbasci flos	0.19 g (11.875%)	0.19 g, 4-6 times daily	20
<b>Summary</b>	<b>2-60%</b>	<b>Single dose: 0.19-2 g</b> <b>Frequency: several times daily</b>  Monograph	

<b>Combination partner</b>	<b>Amount Tiliae flos in combination</b>	<b>Single dose Tiliae flos, Posology, Strength</b>	<b>Period of medicinal use (Reference # in table 1)</b>
		<i>Adolescents, adults and elderly</i> SD: 1.5 g, 2-4 times daily DD: 3-6 g	

Table 16: Verbasci flos in combinations

<b>Combination partner</b>	<b>Amount Verbasci flos in combination</b>	<b>Single dose Verbasci flos, Posology, Strength</b>	<b>Period of medicinal use (Reference # in table 1)</b>
Althaea radix	8 g (8%)	0.4 g, 3 times daily	7
Foeniculi fructus	8 g (8%) 0.06 g (3.75%)	0.4 g, 3 times daily 0.06 g, 4-6 times daily	7 20
Lichen islandicus	0.06 g (3.75%)	0.06 g, 4-6 times daily	20
Liquiritiae radix	8 g (8%)	0.4 g, 3 times daily	7
Plantaginis folium	8 g (8%)	0.4 g, 3 times daily	7
Polygoni avicularis herba	0.06 g (3.75%)	0.06 g, 4-6 times daily	20
Primulae flos	0.06 g (3.75%)	0.06 g, 4-6 times daily	20
Thymi herba	0.06 g (3.75%)	0.06 g, 4-6 times daily	20
Tilia flos	0.06 g (3.75%)	0.06 g, 4-6 times daily	20
<b>Summary</b>	<b>3.75-8%</b>	<b>Single dose: 0.046-0.4 g</b> <b>Frequency: 3-6 times daily</b>  Monograph <i>Adolescents, adults and elderly</i> SD: 1.5-2 g, 3-4 times daily DD: 4.5-8 g	

Table 17: Combination of a herbal substance (left row) with other herbal substances (excipients excluded) based on documented traditional medicinal use. Numbers indicate the percentage of the herbal substance. (Instructions and an example how to apply the table are given on the following page.)

	<b>Althaea radix</b>	<b>Anisi fructus</b>	<b>Filipendula ulmaria flos</b>	<b>Foeniculi amari fructus</b>	<b>Lichen islandicus</b>	<b>Liquiritiae radix</b>	<b>Plantaginis folium</b>	<b>Polygoni avicularis herba</b>	<b>Primulae flos</b>	<b>Salicis cortex</b>	<b>Sambuci flos</b>	<b>Thymi herba</b>	<b>Tiliae flos</b>	<b>Verbasci flos</b>	<b>RANGE</b>
<b>Althaea radix</b>		15%		5-25%	25%	10-25%	15-23%	15%			15%	15-25%		8%	5-25%
<b>Anisi fructus</b>	15%					15%						10-40%	10-40%		10-40%
<b>Filipendula ulmaria flos</b>											20-30%		20-30%		20-30%
<b>Foeniculi amari fructus</b>	5-10%				10-15%	5-25%	5-25%	10-15%	15%		10%	10-25%	15%	5-15%	5-25%
<b>Lichen islandicus</b>	15%			11.25-15%		15%	15%	11.25%	11.25%			11.25-15%	11.25%	11.25%	11.25-15%
<b>Liquiritiae radix</b>	15-25%	25%		5-35%	10%		5-35%	5%			5%	5-35%		10%	5-35%
<b>Plantaginis folium</b>	5-23%			5-40%	15%	5-40%		5%			5%	5-40%		23%	5-40%
<b>Polygoni avicularis herba</b>	10-15%			10-15%	11.87%	10-15%	10-15%		11.87%		10-15%	10-15%	11.87%	11.87%	10-15%
<b>Primulae flos</b>				6.25%	6.25%			6.25%				6.25%	6.25%	6.25%	6.25%
<b>Salicis cortex</b>											20-35%		20-60%		20-60%
<b>Sambuci flos</b>	5%		20-30%	5%		5%	5%	5%		20-50%		5-50%	20-40%		5-50%
<b>Thymi herba</b>	15-30%	10-30%		13.12-40%	13.12-30%	15-40%	15-40%	13.12-15%	13.12%	20-30%	15-30%		10-30%	13.12%	10-40%
<b>Tiliae flos</b>		35-60%	25-40%	11.87%	11.87%			11.87%	11.87%	2-40%	20-40%	11.87-60%		11.87%	2-60%
<b>Verbasci flos</b>	8%			3.75-8%	3.75%	8%	8%	3.75%	3.75%			3.75%	3.75%		3.75-8%

### How to use the information on traditional medicinal use of these combinations?

Evidence for combination: the filled fields in table 17 indicate combinations with evidence of traditional medicinal use. Example: Filipendula ulmaria flos has evidence of combination with Sambuci flos and Tilia flos. Out of these documented combinations the combination partners for an application for a traditional herbal medicinal product may be chosen.

Number of combination partners: The number of active substances in a herbal tea combination should be limited to a maximum of 4 based on the corresponding products and the references used for assessment. Further herbal substances may be added as excipients, their number, amount and function should be justified.

Amount of each herbal substance in the combination: The very right column indicates the traditional percentages of the herbal substance in the combinations. The calculation is based on those combination partners only, which are mentioned in the table. The amount in a traditional herbal medicinal product should be within this range. The sum of active ingredients should end up with 100%. Excipients are not considered in this range.

Example: Combination of Foeniculi amari fructus + Lichen islandicus + Liquiritiae radix + Sambuci flos. The combination should contain 5-25% Foeniculi amari fructus, 11.25-15% Lichen islandicus, 5-25% Liquiritiae radix, 5-50% Sambuci flos. Therefore a combination of 20% Foeniculi amari fructus, 15% Lichen islandicus, 25% Liquiritiae radix and 40% Sambuci flos is covered by this assessment and by the European Union monograph.

### Information from published European Union herbal monographs

#### Therapeutic indication

Table 18: Therapeutic indication for each active substance according to the HMPC monographs

	<b>Indication</b>
Althaea radix	THMP used as a demulcent preparation for the symptomatic treatment of oral or pharyngeal irritation and associated dry cough
Anisi fructus	THMP used as an expectorant in cough associated with cold
Filipendula ulmaria flos	THMP for the supportive treatment of common cold
Foeniculi amari fructus	THMP used as an expectorant in cough associated with cold
Lichen islandicus	THMP used as a demulcent for the symptomatic treatment of oral or pharyngeal irritation and associated dry cough
Liquiritiae radix	THMP used as an expectorant in cough associated with cold
Plantaginis folium	THMP as a demulcent for the symptomatic treatment of oral or pharyngeal irritations and associated dry cough
Polygoni avicularis herba	THMP used for the relief of symptoms of common cold
Primulae flos	THMP used as an expectorant in cough associated with cold
Salicis cortex	THMP used for the relief of fever associated with common cold
Sambuci flos	THMP used for the relief of early symptoms of common cold
Thymi herba	THMP used in productive cough associated with cold
Tiliae flos	THMP used for the relief of symptoms of common cold
Verbasci flos	THM used to relieve symptoms of sore throat associated with dry cough and cold

*Assessment for combinations: According to the indications of medicinal products on the market and the terminology of the monographs already approved, the indication "Traditional herbal medicinal product*



THMP used to relieve cough and symptoms associated with common cold" appears suitable to all combinations.

### Posology

Based on the information from marketed products the single dose of herbal tea combinations is in the range between 1.5 and 5g. The single and daily dosages of most herbal substances are below the dosages states in the monographs for the single herbal substances. Thus, the single dose for the combinations should be set to about 1.5–5 g (active herbal substances, excluding excipients).

When the herbal substance percentage is below 10 in the combination it can be considered as excipient and thus, it is not taken in account for the daily frequency, which should be conditioned by a certain product. Only the daily dose is included.

The mean dosage frequency is 3 times daily. Nonetheless, many references do report a "several times daily" frequency which is reflected in the corresponding European Union herbal monographs for the single herbal substances.

Combinations containing *Althaeae radix*, *Anisi fructus*, *Foeniculi amari fructus*, *Lichen islandicus*, *Plantaginis folium*, *Polygoni avicularis herba*, *Primula flos*, *Sambuci nigrae flos*, *Thymi herba*, *Tiliae flos* and *Verbasci flos* can be given to Adolescents, adults and elderly.

The possible daily dosages of the herbal substances in combination products is below the maximum posology as given in the HMPC monographs for the single active substances

Table 19 shows the posology for each one of the herbal substances when used alone or in combination products.

Table 19: Comparison of the daily dose in the combinations with the upper limit according to the HMPC monographs

	<b>Range in combinations</b>	<b>Single dose/ Frequency</b>	<b>Posology and maximum daily dose HMPC monograph</b>
<i>Althaea radix</i>	5-25%	<i>Adolescents, adults and elderly</i> Single dose: 0.75-1.25 g DD: 2.25-3.75 g Frequency: 3 times daily	<i>Children 3-5 years of age</i> SD: 0.5–1.0 g, 3 times daily DD: 1.5–3.0 g <i>Children 6-11 years of age</i> SD: 0.5–1.5 g, 3 times daily DD: 1.5–4.5 g <i>Adolescents, adults and elderly</i> SD:0.5-3 g, several times daily Max DD: 15 g
<i>Anisi fructus</i>	10-40%	<i>Adolescents, adults and elderly</i> SD: 0.4-2 g DD: 1.2-6 g Frequency: 3 times/several times daily	<i>Adolescents, adults and elderly</i> SD: 1- 3.5 g, 3 times daily
<i>Filipendula ulmaria flos</i>	20-30%	SD: 0.8-1.5 g	<i>Adults, Elderly</i>

		Frequency: several times daily	DD: 2.5-6 g, divided in 1-3 single doses Max DD: 15 g
Foeniculi amari fructus	5-25%	SD: 0.15-1.25 g Frequency: 3 to several times daily	<i>Adults and adolescents</i> SD: 1.5 g, 3 times daily DD: 4.5 g  <i>Children between 4 and 12 years of age</i> SD: 1.0 g, 3 times daily DD: 3.0 g
Lichen islandicus	11.25-15%	SD: 0.18-0.75 g Frequency: several times daily	<i>Adolescents, adults and elderly</i> SD: 1.5 g, 3 to 4 times daily DD: 4-6 g
Liquiritiae radix	5-35%	SD: 0.075-1.25 g Frequency: 3 to several times daily	<i>Adults and elderly</i> SD: 1.5 g, 2 times daily
Plantaginis folium	5-40%	SD: 0.075-1.6 g Frequency: 3 to several times daily	<i>Adolescents, adults and elderly</i> SD: 2 g, 2-3 times per day DD: 4-6 g
Polygoni avicularis herba	10-15%	SD: 0.15-0.225 g Frequency: 3-6 times daily	<i>Adolescents, adults and elderly</i> SD: 1.5-2 g, 3-4 times daily DD: 4.5-8 g
Primulae flos	6.25%	SD: 0.10 g Frequency: 4-6 times daily	<i>Adolescents, adults and elderly</i> SD: 1 g, 3 times daily
Salicis cortex	20-60%	SD: 0.8-1.5 g Frequency: several times daily	<i>Adults and elderly</i> SD: 1-3 g as an herbal infusion, 3 times daily <i>or</i> 4 g as a decoction, 3 times daily
Sambuci flos	5-50%	SD: 0.075-2.5 g Frequency: several times daily	<i>Adolescents, adults and elderly</i> SD: 2-5 g as a herbal infusion, 3 times daily <i>or</i> 3-6 g as a decoction divided in 2 single doses
Thymi herba	10-40%	SD: 0.21-2 g Frequency: several times daily	<i>Adolescents, adults and elderly</i> SD: 1-2 g, 3-4 times daily
Tiliae flos	2-60%	SD: 0.19-2 g Frequency: several times daily	<i>Adolescents, adults and elderly</i> SD: 1.5 g, 2-4 times daily DD: 3-6 g
Verbasci flos	3.75-8%	SD: 0.046-0.4 g Frequency: 3-6 times daily	<i>Adolescents, adults and elderly</i> SD: 1.5-2 g, 3-4 times daily DD: 4.5-8 g

### Age limits and Duration of use

Table 20: Age limits and Duration of use for each active substance according to the HMPC monographs

	Age limits	Duration of use
Althaea radix	Adolescents, adults and elderly	1 week
Anisi fructus		2 weeks
Foeniculi amari fructus		2 weeks
Lichen islandicus		1 week
Plantaginis folium		1 week
Polygoni avicularis herba		1 week
Primulae flos		1 week
Sambuci flos		1 week
Thymi herba		1 week
Tiliae flos		1 week
Verbasci flos		1 week
Filipendula ulmaria flos		Adults and elderly
Liquiritiae radix	1 week	
Salicis cortex	3 days	
Althaea radix	<i>Children 3-5 years of age</i> SD: 0.5–1.0 g, 3 times daily DD: 1.5–3.0 g <i>Children 6-11 years of age</i> SD: 0.5–1.5 g, 3 times daily DD: 1.5–4.5 g	1 week
Foeniculi dulcis fructus	<i>Children between 4 and 12 years of age</i> SD: 1.0 g, 3 times daily DD: 3.0 g	1 week

✓ **Paediatric Population**

There is very limited information for the paediatric use of herbal tea combinations in the therapeutic area cough and cold. Only some combinations including Althaea radix and Foeniculi dulcis fructus have been reported for the use in children below 12 years of age. This limit is also included in the corresponding EU monograph. Thus, children between 3-12 years are included in the monograph for Species pectorales combinations only when Althaea radix and Foeniculi dulcis fructus are the only active components.

✓ **Duration of Use**

Duration of 1 week for every combination is justified taking in account the symptoms to be treated, the duration of use of the marketed combinations and the one included in the corresponding EU monographs.

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.

**Contraindications, Special warnings and precautions for use and Interactions**

Table 21: Contraindications, Special warnings and precautions for use and Interactions for each active substance according to the HMPC monographs

	Contraindications	Special warnings	Interactions
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Althaea radix	Hypersensitivity to the active substance	<p>If dyspnoea, fever or purulent sputum occurs during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.</p> <p>The use in children under 3 years of age is not recommended because of concerns requiring medical advice.</p>	None reported
Anisi fructus	Hypersensitivity to the active substance or to Apiaceae (Umbelliferae) (caraway, celery, coriander, dill and fennel) or to anethole.	-	
Filipendula ulmaria flos	Hypersensitivity to the active substance. Hypersensitivity to salicylates.	<p>Concomitant use with salicylates and other NSAIDs is not recommended without medical advice.</p> <p>If fever exceeds 39°C, persists or is associated with severe headache, or if symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted</p>	
Foeniculi amari fructus	Hypersensitivity to the active substance or to Apiaceae (Umbelliferae) family (aniseed, caraway, celery, coriander and dill) or to anethole. Hypersensitivity to mugwort pollen, due to cross-reactivity with fennel.	The use in children between 4 and 12 years of age is not recommended if the daily intake of estragole exceeds the guidance value of 1.0 µg/kg bw, unless justified by a risk assessment based on adequate safety data	
Lichen islandicus	Hypersensitivity to the active substance(s)	If dyspnoea, fever or purulent sputum occurs during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.	

		Absorption of concomitantly administered medicines may be delayed. As a precautionary measure, the product should not be taken ½ to 1 hour before or after intake of other medicinal products.	
Liquiritiae radix	Hypersensitivity to the active substance(s)	<p>Patients taking liquorice medication should not take other liquorice containing products as serious adverse events may occur such as water retention, hypokalemia, hypertension, cardiac rhythm disorders.</p> <p>Liquorice medication is not recommended to be used in patients affected by hypertension, kidney diseases, liver or cardiovascular disorders or hypokalemia, as they are more sensitive to the adverse effects of liquorice.</p> <p>If dyspnoea, fever or purulent sputum occurs, a doctor or a qualified health care practitioner should be consulted.</p>	<p>Liquorice root may counteract antihypertensive action of prescribed medications.</p> <p>Not to be used concomitantly with diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance</p>
Plantaginis folium	Hypersensitivity to the active substance	If dyspnoea, fever or purulent sputum occurs during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.	None reported
Polygoni avicularis herba	Hypersensitivity to the active substance	-	
Primulae flos	Hypersensitivity to the active substance or to other Primula species.	<p>Caution is recommended in patients with gastritis or gastric ulcer.</p> <p>If dyspnoea, fever or purulent sputum occurs, a doctor or a qualified health care</p>	

		practitioner should be consulted	
Salicis cortex	<p>Hypersensitivity to the active substance.</p> <p>Hypersensitivity to salicylates or to other NSAIDs (e.g. history of angioedema, bronchial spasm, or chronic urticaria in response to salicylates or to other NSAIDs).</p> <p>Asthma due to sensitivity to salicylates.</p> <p>Active peptic ulcer disease.</p> <p>Third trimester of pregnancy.</p> <p>Glucose-6-phosphate dehydrogenase deficiency.</p> <p>Children and adolescents under 18 years of age due to the risk of Reye's syndrome.</p> <p>Severe liver or renal dysfunction.</p> <p>Coagulation disorders.</p>	<p>If fever exceeds 39°C, persists or is associated with severe headache or if symptoms worsen during the use of the medicinal product, a doctor should be consulted.</p> <p>Concomitant use with salicylates and other NSAIDs is not recommended without medical advice.</p>	Willow bark may increase the effects of anticoagulants such as coumarin derivatives.
Sambuci flos	Hypersensitivity to the active substance(s)	If dyspnoea, fever or purulent sputum occurs, a doctor or a qualified health care practitioner should be consulted.	None reported
Thymi herba	Hypersensitivity to the active substance or to other plants of the Lamiaceae (Labiatae) family.	If dyspnoea, fever or purulent sputum occurs, a doctor or a qualified health care practitioner should be consulted.	
Tiliae flos	Hypersensitivity to the active substance(s)	-	
Verbasci flos	Hypersensitivity to the active substance(s)	If dyspnoea, fever or purulent sputum occurs, a doctor or a qualified health care	

		practitioner should be consulted.	
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All combinations have to include the **Contraindication**

Hypersensitivity to the active substance(s).

- Combinations containing *Anisi fructus* or *Foeniculi amari fructus*:

Additionally: Hypersensitivity to Apiaceae (Umbelliferae) (caraway, celery, coriander, dill and fennel) or to anethole.

- Combinations containing *Foeniculi amari fructus*:

Additionally: Hypersensitivity to mugwort pollen, due to cross-reactivity with fennel.

- Combinations containing *Filipendula ulmaria flos*:

Hypersensitivity to salicylates.

- Combinations containing *Primulae flos*:

Additionally: Hypersensitivity to other *Primula* species.

- Combinations containing *Salicis cortex*:

Additionally: Hypersensitivity to salicylates or to other NSAIDs (e.g. history of angioedema, bronchial spasm, or chronic urticaria in response to salicylates or to other NSAIDs). Asthma due to sensitivity to salicylates. Active peptic ulcer disease. Third trimester of pregnancy. Glucose-6-phosphate dehydrogenase deficiency. Children and adolescents under 18 years of age due to the risk of Reye's syndrome. Severe liver or renal dysfunction. Coagulation disorders.

- Combinations containing *Thymi herba*:

Additionally: Hypersensitivity to other plants of the Lamiaceae (Labiatae) family

Under the **Special warnings section**,

All combinations include:

If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Depending on the herbal substances included:

The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

Or

The use in children under 12 years of age has not been established due to lack of adequate data.

Or

The use in children under 3 years of age is not recommended because of concerns requiring medical advice.

- Combinations containing *Salicis cortex*

Children and adolescents under 18 years of age due to the risk of Reye's syndrome.

- Combinations containing *Althaea radix*, *Lichen islandicus*, *Liquiritiae radix*, *Plantaginis folium*, *Primula flos*, *Sanbuci flos*, *Thymi herba* or *Verbasci flos*

If dyspnoea, fever or purulent sputum occurs during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

- Combinations containing *Filipendula ulmaria flos*:

Concomitant use with salicylates and other NSAIDs is not recommended without medical advice. If fever exceeds 39°C, persists or is associated with severe headache, or if symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

- Combinations containing *Foeniculi amari fructus*:

The use in children between 4 and 12 years of age is not recommended if the daily intake of estragole exceeds the guidance value of 1.0 µg/kg bw, unless justified by a risk assessment based on adequate safety data

- Combinations containing *Liquiritiae radix*:

Patients taking liquorice medication should not take other liquorice containing products as serious adverse events may occur such as water retention, hypokalemia, hypertension, cardiac rhythm disorders. Liquorice medication is not recommended to be used in patients affected by hypertension, kidney diseases, liver or cardiovascular disorders or hypokalemia, as they are more sensitive to the adverse effects of liquorice.

- Combinations containing *Primula flos*:

Caution is recommended in patients with gastritis or gastric ulcer.

- Combinations containing *Salicis cortex*:

If fever exceeds 39°C, persists or is associated with severe headache or if symptoms worsen during the use of the medicinal product, a doctor should be consulted. Concomitant use with salicylates and other NSAIDs is not recommended without medical advice.

Under the **Interactions** section

- All combinations except for those containing *Liquiritiae radix* and/or *Salicis cortex* have to include the sentence:

None reported.

- Combinations containing *Liquiritiae radix*:

Liquorice root may counteract antihypertensive action of prescribed medications. Not to be used concomitantly with diuretics, cardiac glycosides, corticosteroids, stimulant laxatives or other medications which may aggravate electrolyte imbalance

- Combinations containing *Salicis cortex*:

Willow bark may increase the effects of anticoagulants such as coumarin derivatives.

Table 22: Fertility, pregnancy and lactation; effects on ability to drive and use machines



	<b>Fertility, pregnancy and lactation</b>	<b>Effects on ability to drive and use machines</b>
Althaea radix	<p>Safety during pregnancy and lactation has not been established. In the absence of sufficient data, the use during pregnancy and lactation is not recommended.</p> <p>No fertility data available.</p>	<p>No studies on the effect on the ability to drive and use machines have been performed</p>
Anisi fructus		
Filipendula ulmaria flos		
Lichen islandicus		
Plantaginis folium		
Polygoni avicularis herba		
Primulae flos		
Sambuci flos		
Thymi herba		
Tiliae flos		
Verbasci flos		
Foeniculi amari fructus	<p>Safety during pregnancy and lactation has not been established (see sections 5.3 'Preclinical safety data' and 6 'Pharmaceutical particulars' regarding preclinical safety data related to the content of estragole).</p> <p>In the absence of sufficient data, the use during pregnancy and lactation is not recommended.</p> <p>There is evidence that trans-anethole is excreted in human breast milk.</p> <p>No fertility data available.</p>	
Liquiritiae radix	<p>Studies in animals have shown reproductive toxicity.</p> <p>Not recommended (safety during pregnancy and lactation has not been established)</p> <p>No fertility data available.</p>	
Salicis cortex	<p>The use during the first and second trimester of pregnancy and during lactation is not recommended.</p> <p>Salicylates cross the placenta and appear in breast milk.</p> <p>Contraindicated in the third trimester of pregnancy.</p> <p>No fertility data available.</p>	

- All combinations except for those containing *Foeniculi amari*, *Liquiritiae radix* and/or *Salicis cortex*:

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.

- Combinations containing *Foeniculi amari* fructus:

Safety during pregnancy and lactation has not been established (see sections 5.3 'Preclinical safety data' and 6 'Pharmaceutical particulars' regarding preclinical safety data related to the content of estragole).

In the absence of sufficient data, the use during pregnancy and lactation is not recommended.

There is evidence that trans-anethole is excreted in human breast milk.

No fertility data available.

- Combinations containing *Liquiritiae radix*:

Studies in animals have shown reproductive toxicity.

Not recommended (safety during pregnancy and lactation has not been established)

No fertility data available.

- Combinations containing *Salicis cortex*:

The use during the first and second trimester of pregnancy and during lactation is not recommended. Salicylates cross the placenta and appear in breast milk.

Contraindicated in the third trimester of pregnancy.

No fertility data available.

Under the Effects on ability to drive and use machines:

- All combinations:

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

Table 23: Undesirable effects and Overdose

	<b>Undesirable effects</b>	<b>Overdose</b>
Althaea radix	None known	No case of overdose has been reported
Filipendula ulmaria flos		
Lichen islandicus		
Plantaginis folium		
Polygoni avicularis herba		
Sambuci flos		
Tiliae flos		
Verbasci flos		
Anisi fructus	Allergic reactions to aniseed affecting the skin or the respiratory system may occur. The frequency is not known.	
Foeniculi amari fructus	Allergic reactions to fennel, affecting the skin or the respiratory system may occur. The frequency is not known.	
Liquiritiae radix	None known	Cases of overdose have been reported with prolonged use (more than 4 weeks) and/or intake of high amount of liquorice, with symptoms such as water retention, hypokalaemia, hypertension,

		cardiac rhythm disorders, hypertensive encephalopathy.
Primula flos	Allergic reactions may occur. The frequency is not known.	Overdose may lead to stomach upset, vomiting or diarrhoea.
Salicis cortex	Allergic reactions such as rash, pruritis, urticaria, asthma, exanthema and gastrointestinal symptoms such as, nausea, vomiting, abdominal pain, diarrhea, dyspepsia, heartburn, may occur. The frequency is not known.	No case of overdose has been reported
Thymi herba	Gastric disorders may occur. The frequency is not known	

#### For **Undesirable effects**

- *Combinations containing Althaea radix, Filipendula ulmaria flos, Lichen islandicus, Liquiritiae radix, Plantaginis folium, Polygoni avicularis herba, Sambuci flos, Tiliae flos, Verbasci flos:*

None known.

If adverse reactions occur, a doctor or a qualified health care practitioner should be consulted.

- *Combinations containing Anisi fructus:*

Allergic reactions to aniseed affecting the skin or the respiratory system have been reported. The frequency is not known. If other adverse reactions not mentioned above occur, a doctor or a qualified health care practitioner should be consulted.

- *Combinations containing Foeniculi amari fructus:*

Allergic reactions to fennel, affecting the skin or the respiratory system 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.

- *Combinations containing Primula flos:*

Allergic reactions 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.

- *Combinations containing Salicis cortex:*

Allergic reactions such as rash, pruritis, urticaria, asthma, exanthema and gastrointestinal symptoms such as, nausea, vomiting, abdominal pain, diarrhea, dyspepsia, heartburn, 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.

- *Combinations containing Thymi herba:*

Gastric disorders 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.

#### Under the **Overdose** section

- *All combinations except for those containing Liquiritiae radix and/or Primula flos:*

No case of overdose has been reported.

- Combinations containing *Liquiritiae radix*:

Cases of overdose have been reported with prolonged use (more than 4 weeks) and/or intake of high amount of liquorice, with symptoms such as water retention, hypokalaemia, hypertension, cardiac rhythm disorders, hypertensive encephalopathy.

- Combinations containing *Primula flos*:

Overdose may lead to stomach upset, vomiting or diarrhoea.

## Preclinical safety data

### Fertility, pregnancy and lactation

- Combinations containing *Filipendula flos*, *Lichen islandicus*, *Polygoni avicularis herba*, *Primula flos*, *Salici cortex*, *Sambuci flos*:

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

- Combinations containing *Althaea radix*, *Plantaginis folium*, *Tilia flos*:

Adequate tests on genotoxicity have not been performed.

Tests on reproductive toxicity and carcinogenicity have not been performed.

- Combinations containing *Thymi herba*, *Verbasci flos*:

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

- Combinations containing *Anisii fructus*

An aniseed extract prepared with water was tested in an Ames test on *Salmonella typhimurium* strains TA98, TA100, TA102 and turned out as negative.

Results from non-clinical studies showed a weak mutagenic potential of anethole. Anethole and its metabolites are unlikely to be genotoxic in vivo.

The genotoxic risk related to estragole is not considered to be relevant in the specified conditions of use (short term use in adolescents, adults and elderly) due to the small amount present in herbal infusions prepared from aniseed.

- Combinations containing *Foeniculi fructus*

A fennel aqueous extract was tested in an Ames test on *Salmonella typhimurium* strains TA98, TA100 and turned out as negative. Results from studies carried out in laboratory animals showed a weak mutagenic activity of anethole.

Several studies have shown the carcinogenic effects of estragole and some of its metabolites in mice (liver tumours) and displayed suggestive but indirect evidence of carcinogenicity in rats. Estragole is considered a genotoxic carcinogen in rodents (see section 6 'Pharmaceutical particulars' for further details).

An aqueous extract of fennel seeds given daily to 24 female BALB/c mice from day 6 to day 15 of pregnancy showed a dose-dependent teratogenic effect. The embryotoxic effect resulted in morphological changes, skeletal disorders, and cellular alterations.

Adequate tests on reproductive toxicity have not been performed.

- Combinations containing *Liquiritiae radix*

The risks related to *Liquiritiae radix* as described in the single monograph are not considered in the present monograph because they are not considered to be relevant in the specified conditions of use due to the small amount present in herbal infusions prepared with such herbal substance.

#### Pharmaceutical particulars

- Combinations containing *Foeniculi amari fructus*:

In the general population exposure to estragole should be kept as low as practically achievable. In pregnant and breast-feeding women, the daily intake of estragole has to be below 0.05 mg/person per day. In children below 12 years of age, the daily intake of estragole has to be below 1.0 µg/kg bw.

For further details see "Public statement on the use of herbal medicinal products containing estragole" (EMA/HMPC/137212/2005 Rev 1).

### 3. Non-Clinical Data

Please refer to the assessment reports of the individual herbal substances.

For further information on products containing estragole (i.e. combinations including *Foeniculi amari fructus*), "Public statement on the use of herbal medicinal products containing estragole" (EMA/HMPC/137212/2005 Rev 1).

### 4. Clinical Data

Please refer to the assessment reports of the individual herbal substances.

### 5. Clinical Safety/Pharmacovigilance

Please refer to the assessment reports of the individual herbal substances.

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

The following herbal substances, for which a EU herbal monograph has been established, are traditionally used in herbal tea combinations with the a therapeutic indication related to the relief of symptoms related to cold or common cold such as cough: *Althaea officinalis* L., *radix*; *Cetraria islandica* (L.) Acharius *s.l.*, *thallus*; *Filipendula ulmaria* (L.) Maxim, *flos*; *Foeniculum vulgare* Miller subsp. *vulgare* var. *vulgare*, *fructus*; *Glycyrrhiza glabra* L.; *Glycyrrhiza inflata* Bat.; *Glycyrrhiza uralensis* Fisch., *radix*; *Plantago lanceolata* L., *folium*; *Pimpinella anisum* L., *fructus*; *Polygonum aviculare* L., *herba*; *Primula veris* L.; *Primula elatior* (L.) Hill, *flos*; *Salix* [various species including *S. purpurea* L.; *S. daphnoides* Vill.; *S. fragilis* L.], *cortex*; *Sambucus nigra* L., *flos*; *Thymus vulgaris* L.; *Thymus zygis* L., *herba*; *Tilia cordata* Miller; *Tilia platyphyllos* Scop.; *Tilia x vulgaris* Heyne, *flos*; *Verbascum thapsus* L.; *V. densiflorum* Bertol. (*V. thapsiforme* Schrad); *V. phlomoides* L., *flos*.

The evidence on traditional medicinal use of the single herbal substances is discussed and justified in the corresponding assessment reports. The evidence on traditional medicinal use of the combinations is based on marketed products in the member states, on monographs in national pharmacopoeias, on standard marketing authorisations and on publications.

Based on the composition of traditionally used combinations, a matrix is developed indicating what herbal substances are traditionally combined and in what percentage they are traditionally combined. This matrix can be used as basis for evidence of traditional medicinal use for individual applications for registration as traditional herbal medicinal product.

The traditional medicinal use is plausible due to the longstanding medicinal use in the proposed indication: "*Traditional herbal medicinal product THMP used to relieve cough and symptoms associated with common cold*".

The safety of the individual herbal substances has been assessed in the assessment reports published together with the respective European Union monographs. Potential risks and undesirable effects are properly addressed in the proposed European Union monograph for the combinations. Based on the longstanding medicinal use no potentiation of undesirable effects due to the combination is to be expected.

Depending on the safety data of the individual herbal substances the medicinal use of the combinations is for adults and elderly or for adolescents and adults.

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

## **Annex**

### ***List of references***