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Committee on Herbal Medicinal Products (HMPC)

Assessment report on *Species diureticae*

Draft

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

Herbal substance(s) (binomial scientific name of the plant, including plant part)	<i>Arctostaphylos uva-ursi</i> (L.) Spreng., folium <i>Agropyron repens</i> (L.) P. Beauv., rhizoma <i>Betula pendula</i> Roth and/or <i>Betula pubescens</i> Ehrh., folium <i>Equisetum arvense</i> L., herba <i>Ilex paraguariensis</i> St. Hilaire, folium <i>Juniperus communis</i> L., galbulus (synonym: <i>Juniperus communis</i> L., pseudo-fructus) <i>Levisticum officinale</i> Koch, radix <i>Ononis spinosa</i> L., radix <i>Orthosiphon stamineus</i> Benth., folium <i>Phaseolus vulgaris</i> L., fructus sine semine <i>Polygonum aviculare</i> L., herba <i>Solidago virgaurea</i> L., herba <i>Urtica dioica</i> L. and <i>Urtica urens</i> L., herba, folium
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 release for public consultation of the draft European Union herbal monograph on *Species diureticae*. It is a working document, not yet edited, and which 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

- Herbal substance(s)

Not applicable

- Herbal preparation(s)

Not applicable

- 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 refers to herbal tea combinations used in the therapeutic area 'urinary tract disorders'. Herbal substances contained in such combinations for which an assessment by the HMPC has been performed are *Betulae folium*, *Equiseti herba*, *Graminis rhizoma (Agropyri repentis rhizoma)*, *Juniperi galbulus (Juniperi pseudo-fructus)*, *Levistici radix*, *Mate folium*, *Ononidis radix*, *Orthosiphonis folium*, *Phaseoli fructus*, *Polygoni avicularis herba*, *Solidaginis virgaureae herba*, *Urticae folium*, *Urticae herba* and *Uvae ursi folium*.

Herbal substances linked to the therapeutic area but not yet assessed by the HMPC (e.g. *Herniariae herba*, *Solidaginis giganteae herba*) 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 'urinary tract disorders' was gathered from EU member states and the information provided by interested parties.

Standard handbooks of Phytotherapy were screened manually for relevant information.

Search in scientific databases for combinations did not provide any results.

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

Table 1: Overview of data obtained from marketed medicinal products

Herbal substances mentioned in brackets are considered as excipient (no plausible contribution to the traditional indication).

	Active substance	Indication	Pharmaceutical form	Regulatory Status
1	1 tea bag (2 g) contains: Betulae folium 0.6 g Orthosiphonis folium 0.6 g Solidaginis virg. herba 0.5 g	Traditional herbal medicinal product for flushing of the urinary tract as supportive treatment in mild urinary tract disorders	1 teabag, 3-4 x daily	AT, TUR 2011
2	1 tea bag (2 g) contains: Uvae ursi folium 0.7 g Betulae folium 0.4 g Orthosiphonis folium 0.3 g Solidaginis virg. herba 0.3 g	Traditional herbal medicinal product for flushing of the urinary tract as supportive treatment of recurrent infections after serious conditions have been excluded	1 teabag, 3-4 x daily	AT, TUR 2012
3	1 tea bag (1.3 g) contains: Equiseti herba 0.715 g Urticae folium 0.26 g Ononidis radix 0.195 g	Traditional herbal medicinal product for flushing of the urinary tract as supportive treatment in mild urinary tract disorders	1 teabag, 3-4 x daily	AT, TUR 2011
4	Betulae folium 25 parts Herniariae herba 25 parts Equiseti herba 37.5 parts Callunae herba 10 parts, impregnated with 2.5 parts sodium carbonate	Support of renal function, flushing of the urinary tract, supportive in inflammations of the urinary tract	1 table spoon (ca. 4 g) as infusion. 3 times daily	AT, WEU 1957
5	Betulae folium 413 mg Uvae ursi folium 337 mg Ononidis radix 150 mg Petroselini radix 150 mg Polygoni avicularis herba 165 mg Urticae herba 150 mg (Millefolii herba 105 mg) (Sambuci flos 30 mg)	An adjuvant for treatment of symptoms of mild lower urinary tract infections such as burning sensation during urination and frequent urination	1 tea bag (1.5 g) or 1 table spoon (5 g) /250 ml of boiling water as a herbal infusion 3-5 times daily	CZ In medicinal use since 1969 THMP since 2011

	Active substance	Indication	Pharmaceutical form	Regulatory Status
6	Uvae ursi folium 375 mg Equiseti herba 300 mg (Myrtilli herba 225 mg) (Matricariae flos 150 mg) (Sambuci flos 150 mg) Solidaginis herba 150 mg (Thymi herba 150 mg)	An adjuvant for treatment of symptoms of mild lower urinary tract infections such as burning sensation during urination and frequent urination	1 tea bag (1.5 g)/250 ml of boiling water as a herbal infusion 3-5 times daily	CZ In medicinal use since 1969 THMP since 2011
7	Betulae folium 450 mg Uvae ursi folium 450 mg (Menthae piperitae herba 225 mg) Ononidis radix 150 mg Petroselini radix 150 mg Herniariae herba 75 mg	An adjuvant for treatment of symptoms of mild lower urinary tract infections such as burning sensation during urination and frequent urination	1 tea bag (1.5 g)/250 ml of boiling water as a herbal infusion 3-5 times daily	CZ In medicinal use since 1995 THMP since 2011 (evidence of 30 years of medicinal use by references)
8	1 tea bag (1.75 g) contains: Betulae folium 0.875 g Equiseti herba 0.656 g	To achieve flushing of the urinary tract in bacterial and inflammatory diseases of the lower urinary tract and in renal gravel.	Herbal tea Adults and adolescents > 12 years: 2 cups of tea from 1 tea bag each 3 times daily Preparation: 1 tea bag + 150 ml boiling water, 15 min steeping time	DE, WEU, at least since 1976
9	1 tea bag (1.8 g) contains: Orthosiphonis folium 0.68 g Ononidis radix 0.68 g	To achieve flushing of the urinary tract in bacterial and inflammatory diseases of the lower urinary tract and in renal gravel.	Herbal tea Adults and adolescents > 12 years: 1 cup of tea from 1 tea bag 5 times daily Preparation: 1 tea bag + 150 ml boiling water, 15 min steeping time	DE, WEU, at least since 1976
10	1 tea bag (2 g) contains: Betulae folium 0.6 g Orthosiphonis folium 0.6 g Solidaginis virg. herba 0.5 g	Traditional herbal medicinal product to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints and to decrease sedimentation of renal gravel.	Herbal tea Adults: 1 cup of tea from 1-2 tea bags 3-4 times daily Adolescents > 12 years: 1 cup of tea from 1 tea bag 3-4 times daily No longer than 14 days in self-medication. Preparation: 1-2 tea bags + 150 ml boiling water, 15 min steeping time	DE, TUR 2012
11	1 tea bag (2 g) contains: Uvae ursi folium 0.7 g Betulae folium 0.4 g Orthosiphonis folium 0.3 g Solidaginis virg. herba 0.3 g	Traditional herbal medicinal product to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints and to decrease sedimentation of renal gravel.	Herbal tea Adults: 1-2 cups of tea from 1 tea bag each 3-4 times daily No longer than 7 days and max. 5 times per year without medical supervision. Preparation:	DE, TUR 2013

	Active substance	Indication	Pharmaceutical form	Regulatory Status
			1 tea bag + 150 ml boiling water, 5-10 min steeping time	
12	2 g (1 tablespoon) contain: Betulae folium 0.48 g Solidaginis virg. herba 0.26 g Equiseti herba 0.26 g Orthosiphonis folium 0.22 g Juniperi fructus 0.22 g	Traditional used to support renal excretion function.	Herbal tea Adults: 1 cup of tea from 2 g herbal tea 4-6 times daily Traditional duration of use is 2-4 weeks. Preparation: 1 tablespoon (ca. 2 g) herbal tea + 150 ml boiling water, 5-10 min steeping time	DE, TUR 2014
13	1 tea bag (2 g) contains: Betulae folium 0.6 g Orthosiphonis folium 0.6 g Solidaginis virg. herba 0.5 g	Traditional herbal medicinal product to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints and to decrease sedimentation of renal gravel.	Herbal tea Adults: 1 cup of tea from 1-2 tea bags 3-4 times daily Adolescents > 12 years: 1 cup of tea from 1 tea bag 3-4 times daily No longer than 14 days in self-medication. Preparation: 1-2 tea bags + 150 ml boiling water, 15 min steeping time	DE, TUR 2014
14	1 tea bag (1.2 g) contains: (Avenae herba 0.6 g) Urticae folium 0.12 g (Alchemillae alpinae herba 0.06 g)	Traditional used to support renal excretion function.	Herbal tea Adults: 1 cup of tea from 1-2 tea bags 3-6 times daily No longer than 2-4 weeks in self-medication. Preparation: 1-2 tea bags + 150 ml boiling water, 10 min steeping time	DE, TUR 2015

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

Belgium: list of tea combinations provided, but no clear diuretic tea among them.

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

Calculation of the mass of the single dose / daily dose when 'spoon' is referred:

Based on information from pharmaceutical industry the bulk density of herbal teas depends on the individual components as well as on the particle size. Cut herbal teas have a lower bulk density (e.g.

less than 1 g for a traditional diuretic tea combination according to a German Standard Marketing Authorisation) compared to fine cut material for tea bags. However, the official information for the German Standard Marketing Authorisation mentions an equivalence of 1 teaspoon with 2-4 g of herbal tea combination. A similar calculation is cited in Fischer (1978). Therefore, as a mean 1 teaspoon is calculated as 2 grams.

Table 2: Overview of historical data

Herbal substances mentioned in brackets are considered as excipient (no plausible contribution to the traditional indication).

	Herbal preparation	Indication	Pharmaceutical form	Regulatory Status
15	Equal parts Ononidis radix (Liquiritiae radix) Levistici radix Juniperi galbulus	Species diureticae	Herbal tea Single dose 1.5 g as an infusion	Austrian Pharmacopoeia IX 1960
16	Uvae ursi folium 35 parts Herniariae herba 35 parts Betulae folium 30 parts	Species urologicae	Herbal tea Single dose 1.5 g as an infusion	Austrian Pharmacopoeia IX 1960
17	Equal parts Ononidis radix Petroselini radix (Liquiritiae radix) Juniperi galbulus	Species diureticae	-	Czechoslovak Pharmacopoeia 1970
18	Equal parts Ononidis radix Levistici radix Betulae folium (Liquiritiae radix) Juniperi galbulus	Species diureticae	-	Czechoslovak Pharmacopoeia 1987
19	Betulae folium 30 parts Uvae ursi folium 30 parts (Menthae pip. herba 15 parts) Ononidis radix 10 parts Petroselini radix 10 parts Herniariae herba 5 parts	Species urologicae	-	Czech Pharmaceutical Codex 1994
20	Scilla siccata 15 parts Sennae folium 15 parts Juniperi galbulus 15 parts Equiseti herba 15 parts Ononidis radix 20 parts Graminis rhizoma 20 parts	Species diureticae	Herbal tea Single dose 0.5-1 g as a decoction Daily dose 5 g as a decoction	VIIth Hungarian Pharmacopoeia 1970
21	Orthosiphonis folium 2 parts (Fragariae herba 6 parts) Vitis idaeae folium 2 parts		0.5 g per cup. 2-3 times daily	Muszynski 1954
22	Equal parts of Ononidis radix (Foeniculi fructus) (Liquiritiae radix) Juniperi fructus	Species diureticae	1 tea spoon (= 2 g) per cup. 2 times daily	Muszynski 1954 Roeske 1955
23	Equal parts of Graminis rhizome Polygoni avicularis herba		A handful per liter water, boil for half an hour. Drink during the day.	Muszynski 1954 Not assessed due to missing information on

	Herbal preparation	Indication	Pharmaceutical form	Regulatory Status
				dosing.
24	Equiseti herba 20 parts Betulae folium 35 parts Uvae ursi folium 20 parts (Cichorii radix 25 parts)	Species diureticae	Decoction of 3 spoons (= 6 g) in about 750ml of hot water (heat slowly under cover, boil 3-5 minutes, let stand for 5-10 min), drink 3-4 times daily for 2/3-1 glass (150-250ml) of the decoction, between meals.	Ozarowski et al. 1978
25	Equal parts Betulae folium Uvae ursi folium Herniariae herba Equiseti herba (Rosae pseudo-fructus)	Species urologicae	1 tea spoon (= 2 g) per cup. 3 times daily	Roeske 1955
26	Mate folium 10 parts Orthosiphonis folium 10 parts Uvae ursi folium 20 parts Phaseoli fructus 20 parts Equiseti herba 20 parts Betulae folium 20 parts	Species urologicae	10 ml of herbal tea as infusion with 150 ml boiling water. 3-5 x daily 10 ml tea mixture = 4 g	DE, NRF 9.1., since 1952
27	Equal parts Betulae folium Graminis rhizome Solidaginis gig. herba Ononidis radix (Liquiritiae radix)	To increase the amount of urine in inflammation (catarrh) of the lower urinary tract. To prevent formation of renal gravel and uroliths.	Herbal tea 2-3 tea spoons (= 4-6 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1987, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee I
28	Uvae ursi folium 35-50 parts Betulae folium 10-20 parts Phaseoli fructus 10-20 parts Equiseti herba 10-30 parts	As adjuvant treatment in mild inflammation (catarrh) of the bladder and the renal pelvis.	Herbal tea 1 tea spoon (2-4 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee II
29	Betulae folium 10-25 parts Solidaginis gig. herba 10-25 parts Ononidis radix 10-30 parts Equiseti herba 10-30 parts	To increase the amount of urine in inflammation (catarrh) of the lower urinary tract. To prevent formation of renal gravel and uroliths.	Herbal tea 2-3 tea spoons (= 4-6 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee III
30	Uvae ursi folium 35-50 parts Ononidis radix 10-25 parts Orthosiphonis folium 15-30 parts	As adjuvant treatment in mild inflammation (catarrh) of the bladder and the renal pelvis.	Herbal tea 1 tea spoon (2-4 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the

	Herbal preparation	Indication	Pharmaceutical form	Regulatory Status
	Graminis rhizoma 10-20 parts			German Medicinal Products Act Blasen- und Nierentee IV
31	Uvae ursi folium 35-50 parts Phaseoli fructus 10-20 parts Solidaginis gig. herba 10-25 parts Orthosiphonis folium 10-30 parts	As adjuvant treatment in mild inflammation (catarrh) of the bladder and the renal pelvis.	Herbal tea 1 tea spoon (2-4 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee V
32	Betulae folium 15-30 parts Solidaginis gig. herba 10-20 parts Ononidis radix 20-30 parts Orthosiphonis folium 20-30 parts	To increase the amount of urine in inflammation (catarrh) of the lower urinary tract. To prevent formation of renal gravel and uroliths.	Herbal tea 2-3 tea spoons (= 4-6 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee VI
33	Uvae ursi folium 35-50 parts Betulae folium 15-25 parts Graminis rhizoma 15-25 parts	As adjuvant treatment in mild inflammation (catarrh) of the bladder and the renal pelvis.	Herbal tea 1 tea spoon (2-4 g) of herbal tea + 150 ml boiling water, 15 min steeping time 3-4 times daily	1988, DE, Standard Marketing Authorisation according to section 36 of the German Medicinal Products Act Blasen- und Nierentee VII
34	Equiseti herba 20 g Levistici radix 10 g Betulae folium 10 g Vitis idaeae folium 10 g	Species diureticae	Herbal tea Single dose: 1 spoon (= 2 g) / 250 ml water(one cup) as an infusion Daily dose: 2 cups/day	Romania, Formulae magistralis, edition IV, 1986
35	Petroselini radix 20 g Levistici radix 10 g (Millefolii flos 5 g) (Liquiritiae radix 5 g) Juniperi fructus 5 g	Species diureticae	Herbal tea Single dose: 1 spoon (= 2 g) / 250 ml water(one cup) as an infusion Daily dose: 2 or 3 cups/day	Romania, Formulae magistralis, edition IV, 1986
36	Rubiae tinctori radix 10 g Solidaginis herba 10 g Trioni herba 10 g Cerasorum stipetes 10 g Maydis stigmata 5 g Juniperi fructus 5 g	To increase the amount of urine and helps the elimination of renal gravel and small uroliths	Herbal tea Single dose: 1 full spoon (= 2 g) is boiled with 250 ml water for 3 minutes, then rested until is just warm Should be used in the morning and with ½ h before meals. Daily dose: 3 cups	Romania, Formulae magistralis, edition IV, 1986
37	(Cyani flores sine receptaculis 0.5 parts) Betulae folium 2.5 parts	Species diureticae	Herbal tea Single dose: 5 g/ 250 ml water as an	Romania Produse Farmaceutice Romanesti, 1970

	Herbal preparation	Indication	Pharmaceutical form	Regulatory Status
	Vitis idaeae folium 1 part Equiseti herba 1.5 parts Ononidis radix 1 part Graminis rhizoma 1.5 part (Cynosbati semen 1 part) Maydis stigmata 1 part		infusion Daily dose: 2 or 3 cups/day	
38	Levistici radix 30 parts Liquiritiae radix 25 parts Ononidis radix 25 parts Juniperi galbulus 25 parts			Hungary, Formulae Normales VII for pharmacists, 2003 (Not considered for assessment, no 30 years of medicinal use)

2.3. Overall conclusions on medicinal use

Table 3: Betulae folium in combinations

Combination partner	Amount Betulae folium in combination (excl. excipients)	Single dose Betulae folium/ daily dose Frequency	Reference (# in tables 1 and 2)
Callunae herba	25%	1 g / 3 g, 3 x daily	4
Equiseti herba	25%	1 g / 3 g, 3 x daily	4
	57%	1.75 g / 5.25 g, 3 x daily	8
	33%	0.48 g / 1.9 – 2.9 g, 4-6 x daily	12
	47%	0.7 - 0.9 g / 2.8 g, 3-4 x daily	24
	25%	0.25 g / 0.75 g, 3 x daily	25
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
	10-25%	0.4 – 1.5 g / 1.2 – 6 g, 3-4 x daily	29
	20%	0.4 g / 0.8 g, 2 x daily	34
	31%	1.5 g / 3 – 4.5 g, 2-3 x daily	37
Graminis rhizoma	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
	15-25%	0.3 – 1 g / 0.9 – 4 g, 3-4 x daily	33
	31%	1.5 g / 3 – 4.5 g, 2-3 x daily	37
Herniariae herba	25%	1 g / 3 g, 3 x daily	4
	30%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	30%	0.5 g, -	16
	35%	-	19
	25%	0.25 g / 0.75 g, 3 x daily	25
Juniperi galbulus	33%	0.48 g / 1.9 – 2.9 g, 4-6 x daily	12
	25%	-	18
Levistici radix	25%	-	18
	20%	0.4 g / 0.8 g, 2 x daily	34
Mate folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
Maydis stigmata	20%	1.5 g / 3 – 4.5 g, 2-3 x daily	37
Ononidis radix	27%	0.413 g / 1.24 – 2.1 g, 3-5 x daily	5
	30%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	25%	-	18
	35%	-	19
	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
	10-25%	0.4 – 1.5 g / 1.2 – 6 g, 3-4 x daily	29
	15-30%	0.6 – 1.8 g / 1.8 – 7.2 g, 3-4 x daily	32
	31%	1.5 g / 3 – 4.5 g, 2-3 x daily	37
Orthosiphonis folium	35%	0.6 g / 2.8-2.4 g, 3-4 x daily	1, 13
	24%	0.4 g / 1.2-1.6 g, 3-4 x daily	2
	35%	0.6 – 1.2 g / 1.8 – 4.8 g, 3-4 x daily	10

Combination partner	Amount <i>Betulae folium</i> in combination (excl. excipients)	Single dose <i>Betulae folium</i> / daily dose Frequency	Reference (# in tables 1 and 2)
	23%	0.4 – 0.8 g/ 1.2 – 3.2 g, 3-4 x daily	11
	33%	0.48 g / 1.9 – 2.9 g, 4-6 x daily	12
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	15-30%	0.6 – 1.8 g / 1.8 – 7.2 g, 3-4 x daily	32
<i>Petroselinum radix</i>	27%	0.413 g / 1.24 – 2.1 g, 3-5 x daily	5
	30%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	35%	-	19
<i>Phaseolus fructus</i>	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
<i>Polygonum aviculare herba</i>	27%	0.413 g / 1.24 – 2.1 g, 3-5 x daily	5
<i>Solidaginis gigantea herba</i>	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
	10-25%	0.4 – 1.5 g / 1.2 – 6 g, 3-4 x daily	29
	15-30%	0.6 – 1.8 g / 1.8 – 7.2 g, 3-4 x daily	32
<i>Solidaginis virginica herba</i>	35%	0.6 g / 2.8-2.4 g, 3-4 x daily	1, 13
	24%	0.4 g / 1.2-1.6 g, 3-4 x daily	2
	35%	0.6 – 1.2 g / 1.8 – 4.8 g, 3-4 x daily	10
	23%	0.4 – 0.8 g/ 1.2 – 3.2 g, 3-4 x daily	11
	33%	0.48 g / 1.9 – 2.9 g, 4-6 x daily	12
<i>Urticae herba/folium</i>	27%	0.413 g / 1.24 – 2.1 g, 3-5 x daily	5
<i>Uvae ursi folium</i>	24%	0.4 g / 1.2-1.6 g, 3-4 x daily	2
	27%	0.413 g / 1.24 – 2.1 g, 3-5 x daily	5
	30%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	23%	0.4 – 0.8 g/ 1.2 – 3.2 g, 3-4 x daily	11
	30%	0.5 g, -	16
	35%	-	19
	47%	0.7 - 0.9 g / 2.8 g, 3-4 x daily	24
	25%	0.25 g / 0.75 g, 3 x daily	25
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
	15-25%	0.3 – 1 g / 0.9 – 4 g, 3-4 x daily	33
<i>Vitis idaea folium</i>	20%	0.4 g / 0.8 g, 2 x daily	34
	31%	1.5 g / 3 – 4.5 g, 2-3 x daily	37
Summary	10-57%	Single dose 0.2 – 1.8 g Daily dose 1.8 – 7.2 g Frequency: 3-6 x daily Monograph: Single dose 2-3 g Daily dose: up to 12 g Frequency: up to 4 x daily	

grey: no European Union herbal monograph developed so far

Table 4: *Equisetum herba* in combinations

Combination partner	Amount <i>Equisetum herba</i> in combination (excl. excipients)	Single dose <i>Equisetum herba</i> / daily dose Frequency	Reference (# in tables 1 and 2)
<i>Betulae folium</i>	37.5 %	1.5 g / 4.5 g, 3 x daily	4
	43%	0.6 – 1.2 g/ 1.8 – 3.6 g, 3 x daily	8
	18%	0.26 g / 1 – 1.6 g, 4-6 x daily	12
	27%	0.4 – 0.55 g / 1.6 g, 3-4 x daily	24
	25%	0.25 g / 0.75 g, 3 x daily	25
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-30%	0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	28
	10-30%	0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily	29
	40%	0.8 g / 1.6 g, 2 x daily	34
	19%	1 g / 2 – 3 g, 2-3 x daily	37

Callunae herba	37.5 %	1.5 g / 4.5 g, 3 x daily	4
Graminis rhizoma	15% 19%	0.075 – 0.15 g / 0.75 g, 5 x daily 1 g / 2 – 3 g, 2-3 x daily	20 37
Herniariae herba	37.5 % 25%	1.5 g / 4.5 g, 3 x daily 0.25 g / 0.75 g, 3 x daily	4 25
Juniperi galbulus	18% 15%	0.26 g / 1 – 1.6 g, 4-6 x daily 0.075 – 0.15 g / 0.75 g, 5 x daily	12 20
Levistici radix	40%	0.8 g / 1.6 g, 2 x daily	34
Mate folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
Maydis stigmata	19%	1 g / 2 – 3 g, 2-3 x daily	37
Ononidis radix	61% 15% 10-30% 19%	0.715 g / 2.1 – 2.9 g, 3-4 x daily 0.075 – 0.15 g / 0.75 g, 5 x daily 0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily 1 g / 2 – 3 g, 2-3 x daily	3 20 29 37
Orthosiphonis folium	18% 20%	0.26 g / 1 – 1.6 g, 4-6 x daily 0.8 g / 2.4 – 4 g, 3-5 x daily	12 26
Phaseoli fructus	20% 10-30%	0.8 g / 2.4 – 4 g, 3-5 x daily 0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	26 28
Solidaginis gig. herba	10-30%	0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily	29
Solidaginis virg. herba	36% 18%	0.3 g / 0.9 – 1.5 g, 3-5 x daily 0.26 g / 1 – 1.6 g, 4-6 x daily	6 12
Urticae herba/folium	61%	0.715 g / 2.1 – 2.9 g, 3-4 x daily	3
Uvae ursi folium	36% 27% 25% 20% 10-30%	0.3 g / 0.9 – 1.5 g, 3-5 x daily 0.4 – 0.55 g / 1.6 g, 3-4 x daily 0.25 g / 0.75 g, 3 x daily 0.8 g / 2.4 – 4 g, 3-5 x daily 0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	6 24 25 26 28
Vitis idaeae folium	40% 19%	0.8 g / 1.6 g, 2 x daily 1 g / 2 – 3 g, 2-3 x daily	34 37
Summary	10-61%	Single dose 0.075 – 1.8 g Daily dose 0.6 – 7.2 g Frequency: 3-6 x daily Monograph: Single dose 1-4 g Daily dose: up to 16 g Frequency: 3-4 x daily	

grey: no European Union herbal monograph developed so far

Table 5: Graminis rhizoma in combinations

Combination partner	Amount Graminis rhizoma in combination (excl. excipients)	Single dose Graminis rhizoma / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	25% 15-25% 19%	1-1.5 g / 3 – 6 g, 3-4 x daily 0.3 - 1 g / 0.9 – 4 g, 3-4 x daily 1 g / 2 – 3 g, 2-3 x daily	27 33 37
Equiseti herba	20% 19%	0.1 – 0.2 g / 1 g, 5 x daily 1 g / 2 – 3 g, 2-3 x daily	20 37
Juniperi galbulus	20%	0.1 – 0.2 g / 1 g, 5 x daily	20
Maydis stigmata	19%	1 g / 2 – 3 g, 2-3 x daily	37
Ononidis radix	20% 25% 10-20% 19%	0.1 – 0.2 g / 1 g, 5 x daily 1-1.5 g / 3 – 6 g, 3-4 x daily 0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily 1 g / 2 – 3 g, 2-3 x daily	20 27 30 37
Orthosiphonis folium	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	30
Polygoni avic. herba	50%	-	23
Solidaginis gig. herba	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
Uvae ursi folium	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily 0.3 - 1	30

	15-25%	g / 0.9 – 4 g, 3-4 x daily	33
Vitis idaeae folium	19%	1 g / 2 – 3 g, 2-3 x daily	37
Summary	10-50%	Single dose 0.1-1.5 g Daily dose 0.6 – 6 g Frequency: 3-5 x daily Monograph: Single dose 3-6 g Daily dose: up to 20 g Frequency: several times daily	

grey: no European Union herbal monograph developed so far

Combination Graminis rhizoma – Polygoni avicularis herba: Data regarding the single and daily dose of the combination are not clearly reported in the literature. Therefore this combination is not taken up into the monograph.

Table 6: Juniperi galbulus in combinations

Combination partner	Amount Juniperi galbulus in combination (excl. excipients)	Single dose Juniperi galbulus / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	15% 25%	0.22 g / 0.9 – 1.3 g -	12 18
Equiseti herba	15% 15%	0.22 g / 0.9 – 1.3 g 0.075 – 0.15 g / 0.75 g, 5 x daily	12 20
Graminis rhizoma	15%	0.075 – 0.15 g / 0.75 g, 5 x daily	20
Levistici radix	33% 25% 14%	0.5 g/ - - 0.3 g / 0.6 – 0.9 g, 2-3 x daily	15 18 35
Maydis stigmata	10%	0.2 g / 0.6 g, 3 x daily	36
Ononidis radix	33% 33% 25% 15% 50%	0.5 g/ - - - 0.075 – 0.15 g / 0.75 g, 5 x daily 1 g / 2 g, 2 x daily	15 17 18 20 22
Orthosiphonis folium	15%	0.22 g / 0.9 – 1.3 g	12
Petroselini radix	33% 14%	- 0.3 g / 0.6 – 0.9 g, 2-3 x daily	17 35
Solidaginis virg. herba	15% 10%	0.22 g / 0.9 – 1.3 g 0.2 g / 0.6 g, 3 x daily	12 36
Summary	10-50%	Single dose 0.075 – 1 g Daily dose 0.6 – 2 g Frequency: 3-5 x daily Monograph: Single dose 2 g Daily dose: up to 6 g Frequency: 2-3 x daily	

grey: no European Union herbal monograph developed so far

Table 7: Levistici radix in combinations

Combination partner	Amount Levistici radix in combination (excl. excipients)	Single dose Levistici radix / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	25% 20%	- 0.4 g / 0.8 g, 2 x daily	18 34
Equiseti herba	20%	0.4 g / 0.8 g, 2 x daily	34
Juniperi galbulus	33% 25%	0.5 g/ - -	15 18

	29%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	35
Ononidis radix	33%	0.5 g/ -	15
	25%	-	18
Petroselini radix	29%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	35
Vitis idaeae folium	20%	0.4 g / 0.8 g, 2 x daily	34
Summary	20-33%	Single dose 0.4 – 0.6 g Daily dose: 0.8 – 1.8 g Frequency: 2-3 x daily Monograph: Single dose 2-3 g Daily dose: up to 6 g Frequency: up to 2 x daily	

Dosage frequency: although the monograph on Levistici radix as single active ingredient states a dosage frequency of up to 2 times daily the proposed frequency of 3-4 times daily is acceptable due to the considerable lower posology in combinations.

Table 8: Mate folium in combinations

Combination partner	Amount Mate folium in combination (excl. excipients)	Single dose Mate folium / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Equiseti herba	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Orthosiphonis folium	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Phaseoli fructus	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Uvae ursi folium	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Summary	10%	Single dose 0.4 g Daily dose: 1.2 – 2 g Frequency: 3-5 x daily Monograph: Single dose 2.5 g Daily dose: up to 5 g Frequency: 1-2 x daily	

Table 9: Ononidis radix in combinations

Combination partner	Amount Ononidis radix in combination (excl. excipients)	Single dose Ononidis radix / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	11%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	5
	12%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	7
	25%	-	18
	12%	-	19
	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
	10-30%	0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily	29
20-30%		0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32
	12%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	37
Equiseti herba	17%	0.195 g / 0.58 – 0.78 g, 3-4 x daily	3
	20%	0.1 – 0.2 g / 1 g, 5 x daily	20
	10-30%	0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily	29
12%		0.6 g / 1.2 – 1.8 g, 2-3 x daily	37
	20%	0.1 – 0.2 g / 1 g, 5 x daily	20
		25%	1-1.5 g / 3 – 6 g, 3-4 x daily
10-25%		0.2 – 1 g / 0.6 – 4 g, 3-4 x daily	30
	12%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	37
Herniariae herba	12%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	7
	12%	-	19
Juniperi galbulus	33%	0.5 g/ -	15
	33%	-	17

	25%	-	18
	20%	0.1 – 0.2 g / 1 g, 5 x daily	20
	50%	1 g / 2 g, 2 x daily	22
Levistici radix	33%	0.5 g/ -	15
	25%	-	18
Maydis stigmata	12%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	37
Orthosiphonis folium	50%	0.68 g / 3.4 g, 5 x daily	9
	10-25%	0.2 – 1 g / 0.6 – 4 g, 3-4 x daily	30
	20-30%	0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32
Petroselini radix	11%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	5
	12%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	7
	33%	-	17
	12%	-	19
Polygoni avic. herba	11%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	5
Solidaginis gig. herba	25%	1-1.5 g / 3 – 6 g, 3-4 x daily	27
	10-30%	0.4 – 1.8 g / 1.2 – 7.2 g, 3-4 x daily	29
	20-30%	0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32
Urticae herba/folium	17%	0.195 g / 0.58 – 0.78 g, 3-4 x daily	3
	11%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	5
Uvae ursi folium	11%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	5
	12%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	7
	12%	-	19
	10-25%	0.2 – 1 g / 0.6 – 4 g, 3-4 x daily	30
Vitis idaeae folium	12%	0.6 g / 1.2 – 1.8 g, 2-3 x daily	37
Summary	10-50%	Single dose 0.1 – 1.8 g Daily dose 0.45 – 7.2 g Frequency: 2-5 x daily Monograph: Single dose 2-3 g Daily dose: up to 12 g Frequency: 3-4 x daily	

grey: no European Union herbal monograph developed so far

Table 10: Orthosiphonis folium in combinations

Combination partner	Amount Orthosiphonis folium in combination (excl. excipients)	Single dose Orthosiphonis folium / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	35%	0.6 g / 1.8 – 2.4 g, 3-4 x daily	1
	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	35%	0.6 - 1.2 g/ 1.8 – 4.8 g, 3-4 x daily	10
	18%	0.3 – 0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
	15%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Equiseti herba	20-30%	0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32
	15%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Graminis rhizoma	15-30%	0.3 – 1.2 g / 0.9 – 4.8 g, 3-4 x daily	30
Juniperi galbulus	15%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
Mate folium	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
Ononidis radix	50%	0.68 g / 3.4 g, 5 x daily	9
	15-30%	0.3 – 1.2 g / 0.9 – 4.8 g, 3-4 x daily	30
	20-30%	0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32
Phaseoli fructus	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
	10-30%	0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	31
Solidaginis gig. herba	10-30%	0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	31
	20-30%	0.8 – 1.8 g / 2.4 – 7.2 g, 3-4 x daily	32

Solidaginis virg. herba	35%	0.6 g / 1.8 – 2.4 g, 3-4 x daily	1
	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	35%	0.6 - 1.2 g/ 1.8 – 4.8 g, 3-4 x daily	10
	18%	0.3 – 0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
	15%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
Uvae ursi folium	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	18%	0.3 – 0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
	10%	0.4 g / 1.2 – 2 g, 3-5 x daily	26
	15-30%	0.3 – 1.2 g / 0.9 – 4.8 g, 3-4 x daily	30
	10-30%	0.2 – 1.2 g / 0.6 – 4.8 g, 3-4 x daily	31
Vitis idaeae folium	50%	0.25 g/0.5 – 0.75 g, 2-3 x daily	21
Summary	10-50%	Single dose 0.2 – 1.8 g Daily dose 0.6 – 7.2 g Frequency: 3-6 x daily Monograph: Daily dose 6-12 g in divided doses	

grey: no European Union herbal monograph developed so far

Table 11: Phaseoli fructus in combinations

Combination partner	Amount Phaseoli fructus in combination (excl. excipients)	Single dose Phaseoli fructus / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
Equiseti herba	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
Mate folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
Orthosiphonis folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	31
Solidaginis gig. herba	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	31
Uvae ursi folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	28
	10-20%	0.2 – 0.8 g / 0.6 – 3.2 g, 3-4 x daily	31
Summary	10-20%	Single dose 0.2 – 0.8 g Daily dose 0.6 – 4 g Frequency: 3-4 x daily Monograph: Single dose 2.5 g Daily dose up to 15 g Frequency: 2 - 6 x daily	

grey: no European Union herbal monograph developed so far

Table 12: Polygoni avicularis herba in combinations

Combination partner	Amount Polygoni herba in combination (excl. excipients)	Single dose Polygoni herba / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	12%	0.165 g / 0.49 – 0.85 g, 3-5 x daily	5
Graminis rhizoma	50%	-	23
Ononidis radix	12%	0.165 g / 0.49 – 0.85 g, 3-5 x daily	5
Petroselinii radix	12%	0.165 g / 0.49 – 0.85 g, 3-5 x daily	5
Urticae herba/folium	12%	0.165 g / 0.49 – 0.85 g, 3-5 x daily	5
Uvae ursi folium	12%	0.165 g / 0.49 – 0.85 g, 3-5 x daily	5
Summary	12-50%	Single dose 0.165 g Daily dose 0.49 – 0.85 g Frequency: 3-5 x daily	

		Monograph: Single dose 3 g Daily dose 6 g Frequency: 2 x daily	
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grey: no European Union herbal monograph developed so far

Combination Polygoni avicularis herba - Graminis rhizoma: Data regarding the single and daily dose of the combination are not clearly reported in the literature. Therefore this combination is not taken up into the monograph.

Table 13: Solidaginis virgaureae herba in combinations

Combination partner	Amount Solidaginis virg. herba in combination (excl. excipients)	Single dose Solidaginis virg. herba / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	29%	0.5 g / 1.5 – 2 g, 3-4 x daily	1
	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	29%	0.5 – 1 g / 1.5 – 4 g, 3-4 x daily	10
	18%	0.3-0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
	18%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
Equiseti herba	18%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	6
	18%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
Juniperi galbulus	18%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
	20%	0.4 g / 1.2 g, 3 x daily	36
Maydis stigmata	20%	0.4 g / 1.2 g, 3 x daily	36
Orthosiphonis folium	29%	0.5 g / 1.5 – 2 g, 3-4 x daily	1
	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	29%	0.5 – 1 g / 1.5 – 4 g, 3-4 x daily	10
	18%	0.3-0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
	18%	0.22 g / 0.88 – 1.32 g, 4-6 x daily	12
Uvae ursi folium	18%	0.3 g / 0.9 – 1.2 g, 3-4 x daily	2
	18%	0.15 g / 0.45 – 0.75 g, 3-5 x daily	6
	18%	0.3-0.6 g / 0.9 – 2.4 g, 3-4 x daily	11
Summary	18-29%	Single dose 0.15 - 1 g Daily dose 0.45 – 4 g Frequency: 3-6 x daily Monograph: Single dose 3-5 g Daily dose up to 20 g Frequency: 2-4 x daily	

Table 14: Urticae herba / folium in combinations

Combination partner	Amount Urticae herba / folium in combination (excl. excipients)	Single dose Urticae herba / folium / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	11%	0.41 g / 1.2 – 2.1 g, 3-5 x daily	5
Equiseti herba	22%	0.26 g / 0.78 – 1.05 g, 3-4 x daily	3
Ononidis radix	22%	0.26 g / 0.78 – 1.05 g, 3-4 x daily	3
	11%	0.41 g / 1.2 – 2.1 g, 3-5 x daily	5
Petroselini radix	11%	0.41 g / 1.2 – 2.1 g, 3-5 x daily	5
Polygoni avic. herba	11%	0.41 g / 1.2 – 2.1 g, 3-5 x daily	
Uvae ursi folium	11%	0.41 g / 1.2 – 2.1 g, 3-5 x daily	5
Summary	11-22 %	Single dose 0.26 – 0.41 g Daily dose 0.78 – 2.1 g Frequency: 3-5 x daily	

		Monograph: Single dose 2-4 g Daily dose up to 24 g (Urticae folium), 12 g (Urticae herba) Frequency: 3-6 x daily (Urticae folium), up to 3 x daily (Urticae herba)	
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grey: no European Union herbal monograph developed so far

Table 15: Uvae ursi folium in combinations

Combination partner	Amount Uvae ursi folium in combination (excl. excipients)	Single dose Uvae ursi folium / daily dose Frequency	Reference (# in tables 1 and 2)
Betulae folium	41%	0.7 g / 2.1 – 2.8 g, 3-4 x daily	2
	25%	0.34 g / 1 – 1.7 g, 3-5 x daily	5
	35%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	41%	0.7 – 1.4 g / 2.1 – 5.6 g, 3-4 x daily	11
	35%	0.5 g / -, -	16
	35%	-	19
	27%	0.4 – 0.55 g / 1.6 g, 3-4 x daily	24
	25%	0.25 g / 0.75 g, 3 x daily	25
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	28
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	33
Equiseti herba	45%	0.375 g / 1.12 – 1.9 g, 3-5 x daily	6
	27%	0.4 – 0.55 g / 1.6 g, 3-4 x daily	24
	25%	0.25 g / 0.75 g, 3 x daily	25
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
Graminis rhizoma	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	30
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	33
Herniariae herba	35%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	35%	0.5 g / -, -	16
	35%	-	19
	25%	0.25 g / 0.75 g, 3 x daily	25
Mate folium	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
Ononidis radix	25%	0.34 g / 1 – 1.7 g, 3-5 x daily	5
	35%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	35%	-	19
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	30
Orthosiphonis folium	41%	0.7 g / 2.1 – 2.8 g, 3-4 x daily	2
	41%	0.7 – 1.4 g / 2.1 – 5.6 g, 3-4 x daily	11
	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	30
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	31
Petroselini radix	25%	0.34 g / 1 – 1.7 g, 3-5 x daily	5
	35%	0.45 g / 1.35 – 2.25 g, 3-5 x daily	7
	35%	-	19
Phaseoli fructus	20%	0.8 g / 2.4 – 4 g, 3-5 x daily	26
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	28
	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	31
Polygoni avic. herba	25%	0.34 g / 1 – 1.7 g, 3-5 x daily	5
Solidaginis gig. herba	35-50%	0.7 – 2 g / 2.1 – 8 g, 3-4 x daily	31
Solidaginis virg. herba	41%	0.7 g / 2.1 – 2.8 g, 3-4 x daily	2
	45%	0.375 g / 1.12 – 1.9 g, 3-5 x daily	6
	41%	0.7 – 1.4 g / 2.1 – 5.6 g, 3-4 x daily	11
Urticae herba/folium	25%	0.34 g / 1 – 1.7 g, 3-5 x daily	5
Summary	20-50%	Single dose 0.25 - 2 g	

Combination partner	Amount <i>Uvae ursi folium</i> in combination (excl. excipients)	Single dose <i>Uvae ursi folium</i> / daily dose Frequency	Reference (# in tables 1 and 2)
		Daily dose 0.75 – 8 g Frequency: 3 – 5 x daily Monograph: Single dose 1.5 - 4 g Maximum daily dose 8 g Frequency: 2 - 4 x daily	

grey: no European Union herbal monograph developed so far

Table 16:

Numbers indicate the percentage of a herbal substance (left row) in a combination with other herbal substances (excipients excluded) based on documented traditional medicinal use.

Example: When *Betulae folium* is combined with *Ononidis radix* then 10-35% of *Betulae folium* is traditionally used in combinations. This combination contains 10-30% *Ononidis radix*.

	<i>Betulae folium</i>	<i>Equiseti herba</i>	<i>Graminis rhizoma</i>	<i>Juniperi galbulus</i>	<i>Levistici radix</i>	<i>Mate folium</i>	<i>Ononidis radix</i>	<i>Orthosiphonis folium</i>	<i>Phaseoli fructus</i>	<i>Polygoni avicul. herba</i>	<i>Solidaginis virg. herba</i>	<i>Urticae herba / folium</i>	<i>Uvae ursi folium</i>	Range
<i>Betulae folium</i>	-	10-57%	15-31%	25-33%	20-25%	20%	10-35%	15-35%	10-20%	27%	23-35%	27%	10-47%	10-57%
<i>Equiseti herba</i>	10-43%	-	15-19%	15-18%	-40%	20%	10-61%	18-20%	10-30%	-	18-36%	61%	10-36%	10-61%
<i>Graminis rhizoma</i>	15-25%	19-20%	-	20%	-	-	10-25%	10-20%	-	-	-	-	10-25%	10-50%
<i>Juniperi galbulus</i>	15-25%	15%	15%	-	14-33%	-	15-50%	15%	-	-	10-15%	-	-	10-50%
<i>Levistici radix</i>	20-25%	20%	-	25-33%	-	-	25-33%	-	-	-	-	-	-	20-33%
<i>Mate folium</i>	10%	10%	-	-	-	-	-	10%	10%	-	-	-	10%	10%
<i>Ononidis radix</i>	10-30%	10-30%	10-25%	20-50%	25%	-	-	10-50%	-	11%	-	11-17%	10-25%	10-50%
<i>Orthosiphonis folium</i>	10-35%	10-15%	15-30%	15%	-	10%	15-50%	-	10-30%	-	15-35%	-	10-30%	10-50%
<i>Phaseoli fructus</i>	10-20%	10-20%	-	-	-	20%	-	10-20%	-	-	-	-	10-20%	10-20%
<i>Polygoni avic. herba</i>	12%	-	-	-	-	-	12%	-	-	-	-	12%	12%	12-50%
<i>Solidaginis virg. herba</i>	18-29%	18%	-	18-20%	-	-	-	18-29%	-	-	-	-	18%	18-29%
<i>Urticae herba/folium</i>	11%	22%	-	-	-	-	11-22%	-	-	11%	-	-	11%	11-22%
<i>Uvae ursi folium</i>	20-50%	20-50%	35-50%	-	-	20%	25-50%	20-50%	20-50%	25%	41-45%	25%	-	20-50%

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

Evidence for combination: the grey shaded fields in the table above indicate combinations with evidence of traditional medicinal use. Example: *Solidaginis virgaureae herba* has evidence of combination with *Betulae folium*, *Equiseti herba*, *Juniperi galbulus*, *Orthosiphonis folium* and *Uvae ursi folium*. 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 row 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. Usually the sum of all excipients should not exceed 10% in the final combination.

Example:

Combination of *Solidaginis virgaureae herba* + *Betulae folium* + *Orthosiphonis folium*. The combination should contain 18-29% *Solidaginis virgaureae herba*, 10-57% *Betulae folium* and 10-50% *Orthosiphonis folium*. Therefore a combination of 25% *Solidaginis virgaureae herba*, 40% *Betulae folium* and 35% *Orthosiphonis folium* is covered by this assessment and by the European Union monograph. Excipients: e.g. *Menthae piperitae folium* may be added for flavouring purposes.

Information from published European Union herbal monographs

Indication:

Betulae folium Equiseti herba Graminis rhizoma Juniperi galbulus Levistici radix Mate folium Ononidis radix Orthosiphonis folium Phaseoli fructus Polygoni avicularis herba Solidaginis virgaureae herba Urticae folium Urticae herba	Traditional herbal medicinal product to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints.
Uvae ursi folium	Traditional herbal medicinal product used for treatment of symptoms of mild recurrent lower urinary tract infections such as burning sensation during urination and/or frequent urination in women, after serious conditions have been excluded by a medical doctor.

Assessment for combinations: According to the indications of medicinal products on the market and according to the terminology of the herbal tea combinations in pharmacopoeias and text books the first indication appears suitable to all combinations.

Posology:

Assessment for combinations:

Based on the information from marketed products the single dose of herbal tea combinations is in the range between 1.3 and 2 g, in some combinations up to 4 g. With the exception of *Uvae ursi folium*, where the maximum daily dosage reported from marketed products is equal to the one stated in the European Union herbal monograph, the single and daily dosages of all other herbal substances are clearly below the dosages states in the monographs for the single herbal substances. The single dose for new combinations should be set to about 1.5 – 2 g (active herbal substances, excluding excipients).

The mean dosage frequency is 3-5 x daily. Only one combination product is recommended up to 6 times daily. Many references do not report a concrete dosage frequency. It can be assumed that the traditional use of herbal teas in general is linked to a '3 x daily' dosage frequency. Particularly in the case of 'Species diureticae' a higher frequency can be assumed as in literature the sufficient uptake of fluid was related with the traditional efficacy. Considering the European Union herbal monographs for the single herbal substances the dosage frequency is set to 3-4 x daily for all combinations.

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

Table 17: Comparison of the daily dose in the combinations with the upper limit according to the HMPC monographs

	Range in a combination (excl. excipients)	Daily dose (2 g combination, 4 x daily)	Maximum daily dose HMPC monograph
Betulae folium	10-57%	0.8 – 4.56 g	Up to 12 g
Equiseti herba	10-61%	0.8 – 4.88 g	Up to 16 g
Graminis rhizoma	10-50%	0.8 – 4 g	Up to 20 g
Juniperi galbulus	10-50%	0.8 – 4 g	Up to 6 g
Levistici radix	20-33%	1.6 – 2.64 g	Up to 6 g
Mate folium	10%	0.8 g	Up to 5 g
Ononidis radix	10-50%	0.8 – 4 g	Up to 12 g
Orthosiphonis folium	10-50%	0.8 – 4 g	Up to 12 g
Phaseoli fructus	10-20%	0.8 – 1.6 g	Up to 15 g
Polygoni avic. herba	12-50%	0.96 g – 4 g	Up to 6 g
Solidaginis virg. herba	18-29%	1.44 – 2.32 g	Up to 20 g
Urticae herba/folium	11-22%	0.88 – 1.76 g	Up to 24 g (Urticae folum) Up to 12 g (Urticae herba)
Uvae ursi folium	20-50%	1.6 – 4 g	Up to 8 g

Age limits:

Betulae folium Equiseti herba Graminis rhizoma Ononidis radix Polygoni avicularis herba Solidaginis viragureae herba Urticae folium Urticae herba	Adolescents, adults and elderly
Juniperi galbulus Levistici radix Mate folium Orthosiphonis folium Phaseoli fructus	Adults and elderly
Uvae ursi folium	Female adults and elderly

Assessment for combinations:

Tea combinations containing Juniperi galbulus, Levistici radix, Mate folium, Orthosiphonis folium, Phaseoli fructus or Uvae ursi folium are restricted to the use in adults and elderly. Other combinations may be used in adolescents.

The restriction of combinations containing Uvae ursi folium to female adults is not applicable due to the indication.

Duration of use:

Betulae folium Equiseti herba Graminis rhizoma Solidaginis viragureae herba	2-4 weeks
Juniperi galbulus Mate folium Phaseoli fructus Polygoni avicularis herba	2 weeks
Ononidis radix	1 week
Orthosiphonis folium	No restriction
Levistici radix Urticae folium	Not to be used for more than 2-4 weeks
Urticae herba	Up to 4 weeks
Uvae ursi folium	Not to be used for more than 1 week

Assessment for combinations:

The restriction to 1 week in case of Uvae ursi folium in the European Union herbal monograph is justified by the indication. As the indication for the combinations is different no such restriction applies.

As a suitable compromise duration of use of 2 weeks is justified.

Contraindications:

Betulae folium	Hypersensitivity to the active substance or to birch pollen. Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease).
Equiseti herba Graminis rhizoma Ononidis radix Polygoni avicularis herba Solidaginis viragureae herba Urticae folium Urticae herba	Hypersensitivity to the active substance. Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease).
Juniperi galbulus	Hypersensitivity to the active substance. Severe renal disease including infectious interstitial nephritis,

	pyelitis and pyelonephritis. Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease).
Levistici radix	Hypersensitivity to the active substance and to other plants of the Apiaceae (Umbelliferae) family or to anethole.
Mate folium	Hypersensitivity to the active substance. Gastric and duodenal ulcers, cardiovascular disorders such as hypertension and arrhythmia, hyperthyroidism. Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease).
Orthosiphonis folium Phaseoli fructus	Hypersensitivity to the active substance
Uvae ursi folium	Hypersensitivity to the active substance. Kidney disorders.

Assessment for combinations:

All combinations have to include the contraindications:

- Hypersensitivity to the active substance.
- Conditions where a reduced fluid intake is recommended (e.g. severe cardiac or renal disease).

Combinations including Betulae folium:

Additionally: Hypersensitivity to birch pollen.

Combinations including Juniperi galbulus:

According to the data obtained Juniperi galbulus is included in herbal tea combinations with a single dose of up to 0.22 g and a daily dose of up to 1.3 g. This considerably reduced posology compared to the traditional use as single active ingredient justifies that the special contraindications are not taken into account for herbal tea combinations.

Combinations containing Levistici radix:

Additionally: Hypersensitivity to other plants of the Apiaceae family or to anethole.

Combinations containing Mate folium:

According to the data obtained Mate folium is contained in an amount of 10% in traditional herbal tea combinations. A mean single dose of 2 g herbal tea combination would result in a single dose of 0.2 g Mate folium which is 5-10% of the recommended dose of Mate folium as only active ingredient. This considerably reduced posology compared to the traditional use as single active ingredient justifies that the special contraindications are not taken into account for herbal tea combinations.

Combinations containing Uvae ursi folium:

The general contraindication 'kidney disorders' is summarised in the contraindication related to conditions where a reduced fluid intake is recommended.

Special warnings and precautions for use:

Betulae folium Equiseti herba	The use in children under 12 years of age has not been established due to lack of adequate data. If complaints or symptoms such as fever, dysuria, spasms or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
Graminis rhizoma Juniperi galbulus Levistici radix	The use in children and adolescents under 18 years of age has not been established due to lack of adequate data. If complaints or symptoms such as fever, dysuria, spasms or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Mate folium	The use in children and adolescents under 18 years of age has not been established due to lack of adequate data. If complaints or symptoms such as fever, dysuria, spasms or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted. Not recommended before bedtime as it may cause sleep disturbances.
Ononidis radix Polygoni avicularis herba	The use in children under 12 years of age has not been established due to lack of adequate data. To ensure an increase of the amount of urine, adequate fluid intake is required during the treatment. If urinary tract complaints worsen and symptoms such as fever, dysuria, spasm, or blood in the urine occur during the use of medicinal product, a doctor or a qualified health care practitioner should be consulted.
Orthosiphonis folium	The use in children and adolescents under 18 years of age has not been established due to lack of adequate data. Appropriate fluid intake is recommended. If complaints of symptoms such as fever, dysuria, spasms or blood in the urine occur during the use of the medicinal product, a doctor or a qualified health care professional should be consulted. The use of this product is not recommended in case of oedema due to limited heart and kidney function.
Phaseoli fructus	The use in children and adolescents under 18 years of age has not been established due to lack of data.
Solidaginis viragureae herba	The use in children under 12 years of age has not been established due to lack of available experience. If complaints of symptoms such as fever, dysuria, spasms or blood in the urine occur during the use of the medicinal product, a doctor or a qualified health care professional should be consulted. Concomitant treatment with synthetic diuretics is not recommended.
Urticae folium	The use in children under 12 years of age has not been established due to lack of adequate data. If minor urinary tract complaints worsen and symptoms such as fever, dysuria, spasm, or blood in the urine occur during the use of medicinal product, a doctor or a qualified health care professional should be consulted.
Urticae herba	The use in children under 12 years of age has not been established due to lack of available experience. If urinary tract complaints worsen and symptoms such as fever, dysuria, spasm, or blood in the urine occur during the use of medicinal product, a doctor or a qualified health care practitioner should be consulted.
Uvae ursi folium	The use in children and adolescents under 18 years of age is not recommended because of concerns requiring medical advice. The use in men is not recommended because of concerns requiring medical supervision. If complaints or symptoms such as fever, dysuria, spasms, or blood in urine occur during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Assessment for combinations:

All combinations have to include the warning statements:

If urinary tract complaints worsen or symptoms such as fever, dysuria, spasm, or blood in the urine occur during the use of medicinal product, a doctor or a qualified health care practitioner should be consulted.

Depending on the age limit specified above the respective warning has to be given:

The use in children under 12 years of age has not been established due to lack of adequate data or The use in children and adolescents under 18 years of age has not been established due to lack of adequate data.

Combinations containing Uvae ursi folium:

The warning related to the use in men is not relevant due to the different indication.

Interactions:

Betulae folium Equiseti herba Graminis rhizoma Juniperi galbulus Levistici radix Ononidis radix Orthosiphonis folium Phaseoli fructus Polygoni avicularis herba Solidaginis viragureae herba Urticae folium Urticae herba Uvae ursi folium	None reported
Mate folium	Persons taking MAO-inhibitor drugs should use mate with caution. Caffeine containing preparations reduce sedatives action and increase side effects caused by sympathomimetic drugs.

Assessment for combinations:

All combinations have to include the statement: None reported

Combinations containing Mate folium:

According to the data obtained Mate folium is contained in an amount of 10% in traditional herbal tea combinations. A mean single dose of 2 g herbal tea combination would result in a single dose of 0.2 g Mate folium which is 5-10% of the recommended dose of Mate folium as only active ingredient. This considerably reduced posology compared to the traditional use as single active ingredient justifies that the special interactions are not taken into account for herbal tea combinations.

Fertility, pregnancy and lactation:

Betulae folium Equiseti herba Graminis rhizoma Juniperi galbulus Levistici radix Ononidis radix Orthosiphonis folium Phaseoli fructus Polygoni avicularis herba Urticae folium Urticae herba	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.
Mate folium	There are no or limited data from use during pregnancy and lactation. Use should be avoided during pregnancy and lactation.
Solidaginis viragureae herba	In the absence of sufficient data the use during pregnancy and lactation is not recommended.
Uvae ursi folium	Safety during pregnancy and lactation has not been established. The use should be avoided during pregnancy. In the absence of sufficient data the use during lactation is not recommended. No fertility data available.

Assessment for combinations:

All combinations not containing Uvae ursi folium have to include the statement:

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 Uvae ursi folium:

As Uvae ursi folium may be contained in herbal tea combinations up to 50% the wording of the European Union herbal monograph on Uvae ursi folium should be used:

Safety during pregnancy and lactation has not been established. The use should be avoided during pregnancy. In the absence of sufficient data the use during lactation is not recommended. No fertility data available.

Effects on ability to drive and use machines

Betulae folium Equiseti herba Graminis rhizoma Juniperi galbulus Levistici radix Mate folium Ononidis radix Orthosiphonis folium Polygoni avicularis herba Solidaginis viragureae herba Urticae folium Urticae herba Uvae ursi folium	No studies on the effect on the ability to drive and use machines have been performed.
Phaseoli fructus	Not relevant

Assessment for combinations:

All combinations have to include the statement:

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

Undesirable effects:

Betulae folium	Gastrointestinal complaints (nausea, vomiting, diarrhoea) and allergic reactions (itching, rash, urticaria, allergic rhinitis) have been reported. The frequency is not known.
Equiseti herba	Mild gastrointestinal complaints and allergic reactions (e.g. rash, swelling of the face) have been reported. The frequency is not known.
Juniperi galbulus	Allergic skin reactions have been reported. The frequency is not known.
Graminis rhizoma Levistici radix Ononidis radix Orthosiphonis folium Phaseoli fructus Polygoni avicularis herba	None known
Solidaginis viragureae herba	Hypersensitivity reactions or gastrointestinal disorders may occur. The frequency is not known.
Urticae folium Urticae herba	Mild gastrointestinal complaints (e.g. nausea, vomiting, diarrhoea) and skin reactions (e.g. itching, exanthema, hives) may occur. The frequency is not known.
Uvae ursi folium	Nausea, vomiting, stomach-ache have been reported. The frequency is not known.

Assessment for combinations:

The section 'Undesirable effects' should contain the combined information taken from the European Union herbal monographs for the single ingredients.

For all combinations: The frequency is not known.

Overdose:

Betulae folium Equiseti herba Graminis rhizoma Levistici radix Mate folium Ononidis radix Orthosiphonis folium Phaseoli fructus Solidaginis viragureae herba Urticae folium Urticae herba Uvae ursi folium	No case of overdose has been reported.
Juniperi galbulus	In case of prolonged use and overdose, urine will smell of violets. There may be renal irritation and pain in and near the kidney, strong diuresis, albuminuria, haematuria, purplish urine, gastrointestinal upsets, accelerated heartbeat and blood pressure. Rarely symptoms of central stimulation like convulsions occur as well as metrorrhagia and abortion.

Assessment for combinations:

All combinations should include the statement:

No case of overdose has been reported.

Combinations containing Juniperi galbulus:

According to the data obtained Juniperi galbulus is included in herbal tea combinations with a single dose of up to 0.22 g and a daily dose of up to 1.3 g. This considerably reduced posology compared to the traditional use as single active ingredient justifies that the special wording related to prolonged use and overdose is not taken into account for herbal tea combinations.

Preclinical safety data:

Betulae folium Equiseti herba Ononidis radix Urticae herba	Adequate tests on genotoxicity have not been performed. Tests on reproductive toxicity and carcinogenicity have not been performed.
Graminis rhizoma Juniperi galbulus Levistici radix Mate folium	Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.
Orthosiphonis folium Phaseoli fructus Polygoni avicularis herba Solidaginis viragureae herba Urticae folium	Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.
Uvae ursi folium	Available tests on genotoxicity of water and ethanolic extracts of Uvae ursi folium are inadequate. Reproductive toxicity has not been studied. Available carcinogenicity studies have been negative. Arbutin, the principal component of Uvae ursi folium, displayed some maternal and fetal toxicity in rats after subcutaneous administration of 400 mg/kg/day. No effect on reproduction has been observed at doses of 100 mg/kg/day. Toxicity tests with hydroquinone, a hydrolysis product of arbutin, have demonstrated some evidence of genotoxicity and carcinogenicity. Risks posed by the exposure of hydroquinone during the short-term treatment with Uvae ursi folium preparations are considered minimal.

Assessment for combinations:

All combinations not containing *Uvae ursi folium* have to include the statement:

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

Combinations containing Uvae ursi folium:

As *Uvae ursi folium* may be contained in herbal tea combinations up to 50% the wording of the European Union herbal monograph on *Uvae ursi folium* should be used:

Available tests on genotoxicity of water and ethanolic extracts of *Uvae ursi folium* are inadequate. Reproductive toxicity has not been studied. Available carcinogenicity studies have been negative. Arbutin, the principal component of *Uvae ursi folium*, displayed some maternal and fetal toxicity in rats after subcutaneous administration of 400 mg/kg/day. No effect on reproduction has been observed at doses of 100 mg/kg/day. Toxicity tests with hydroquinone, a hydrolysis product of arbutin, have demonstrated some evidence of genotoxicity and carcinogenicity. Risks posed by the exposure of hydroquinone during the short-term treatment with *Uvae ursi folium* preparations are considered minimal.

3. Non-Clinical Data

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

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 herbal substances *Betulae folium*, *Equiseti herba*, *Graminis rhizoma* (*Agropyri repentis rhizoma*), *Juniperi galbulus* (*Juniperi pseudo-fructus*), *Levistici radix*, *Mate folium*, *Ononidis radix*, *Orthosiphonis folium*, *Phaseoli fructus*, *Polygoni avicularis herba*, *Solidaginis virgaureae herba*, *Urticae folium*, *Urticae herba* and *Uvae ursi folium*, for which a EU herbal monograph has been established, are traditionally used in herbal tea combinations with the indication 'Traditional herbal medicinal product to increase the amount of urine to achieve flushing of the urinary tract as an adjuvant in minor urinary complaints'.

The evidence on traditional medicinal use of the single herbal substances is discussed and justified in the 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.

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 restricted to adults or adolescents and adults.

As the data on genotoxicity are limited no European Union list entry can be proposed.

Annex

List of references