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Committee on Herbal Medicinal Products (HMPC)

Assessment report on *Species sedativae*

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>Humulus lupulus</i> L., flos <i>Lavandula angustifolia</i> Mill., flos <i>Melissa officinalis</i> L., folium <i>Passiflora incarnata</i> L., herba <i>Valeriana officinalis</i> L., radix
Herbal preparation(s)	Combinations of the above mentioned herbal substances
Pharmaceutical form(s)	Comminuted herbal substances as herbal tea for oral use.
Rapporteur(s)	S.Flemisch
Peer-reviewer	R. Länger

Note: This draft assessment report is published to support the public consultation of the draft European Union herbal monograph on *Species sedativae*. 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) as ingredients of traditional combination herbal medicinal products assessed, where applicable.

This assessment report refers to herbal tea combinations used in the therapeutic area 'relief of mild symptoms of mental stress and to aid sleep'. Herbal substances traditionally and most frequently contained in such combinations for which an assessment by the HMPC has been already performed are *Humulus lupulus* L., flos; *Lavandula angustifolia* Mill., flos; *Melissa officinalis* L., folium; *Passiflora incarnata* L., herba; *Valeriana officinalis* L., radix.

After internal discussion at MLWP and based on Article 16a of Directive 2001/83/EC as amended (traditional use), where it is stated that the pharmacological effects or efficacy of the medicinal product are plausible on the basis of long-standing use and experience, herbal preparations which are not linked to the therapeutic area in the corresponding EU monograph 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, e.g. peppermint leaves.

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 'relief of mild symptoms of mental stress, e.g. to aid sleep' 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 preparations 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 excipients (no plausible contribution to the traditional indication).

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
1	1 tea bag (2 g) contains: Valerianae radix 0.7 g Melissae folium 0.4 g Passiflorae herba 0.3 g (Menthae piperitae folium 0.3 g Anisi fructus 0.1g Rosmarini folium 0.1g Liquiritiae radix 0.1g)	Traditional herbal medicinal product for relief of nervous restlessness and to aid sleep	1 tea bag 2-3 x daily and 1 additional tea bag before bedtime	Austria, TUR 2011
2	1 tea bag (2 g) contains: Valerianae radix 0.6 g Lavandulae flos 0.5 g Melissae folium 0.4 g (Menthae piperitae folium 0.3 g Foeniculi fructus 0.1 g Rosmarini folium 0.1 g)	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep	1-2 tea bags 2-3 x daily and 1-2 additional tea bags before bedtime	Austria, TUR 2012
3	1 tea bag (1.6 g) contains: Valerianae radix 0.64 g Melissae folium 0.40 g (Aurantii Amari flos 0.16 g Menthae piperitae folium 0.32 g Liquiritiae radix 0.08 g)	Traditional herbal medicinal product for relief of mild symptoms of mental stress / nervous restlessness and to aid sleep	1 tea bag up to 3 x daily	Austria, TUR 2011
4	1 tea bag (2 g) contains: Valerianae radix 1000 mg Melissae herba 600 mg Passiflorae herba 400 mg	restlessness, irritability, mild sleep disorders, mild digestive disorders associated with stress	Herbal tea, tea bags	Czech Republic, TUR 2010
5	1 tea bag (1.5 g) contains: Valerianae radix 450 mg Melissae herba 450 mg (Menthae piperitae herba 450 mg Foeniculi fructus 150 mg)	restlessness, irritability, mild sleep disorders, mild digestive disorders associated with stress	Herbal tea, tea bags	Czech Republic, in medicinal use since 1995, THMP since 2011
6	1 tea bag (1.5 g) contains: (Menthae piperitae herba 300 mg) Melissae herba 255 mg Lupuli flos 240 mg Valerianae radix 195 mg (Matricariae flos 240 mg Hyperici herba 270 mg)	For sedation after total prostration, for relief of irritability and nervous tension, in difficulties in falling asleep and mild sleep disorders, for relief of digestive disorders caused by nervous tension	Herbal tea, tea bags	Czech Republic, in medicinal use since 1995, THMP since 2011
7	100 g of the herbal tea contain: Lupuli flos 23 g Melissae folium 16 g (Hyperici herba 13 g Auranti amari flos 19 g) Lavandulae flos 7 g	Natural medicinal product for mild nervous tension and sleep disturbances	Herbal tea Posology: for nervous tension in adults 125 ml of herbal tea 2-3 times daily; for sleep disorders single dose of 125 ml of the herbal tea before bedtime	Denmark, marketing authorisation 1997-2006 (withdrawn by MAH)
8	1 tea bag (1.75 g) contains: Valerianae radix 0.525 g Passiflorae herba 0.480 g	States of agitation and difficulties to fall asleep due to nervousness	Herbal tea Adults and adolescents: 2 cups of tea (1 tea bag each) 2 times daily, for	Germany, WEU at least since 1976

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
	Melissae folium 0.394 g (Menthae piperitae folium 0.070 g Millefolii herba 0.088 g Matricariae flos 0.088 g Liquiritiae radix 0.105 g)		sleep 2 cups of tea ½-1 h before going to bed. If necessary, 2 additional cups of tea earlier in the evening.	
9	Beruhigungstee I 100 g herbal tea contain: Valerianae radix 40 g Melissae folium 15 g Lupuli flos 20 g (Menthae piperitae folium 15 g Aurantii pericarpium 10 g)	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1987
10	Beruhigungstee II* Valerianae radix 30-40 % Lupuli flos 20-30 % Melissae folium 20-30 %	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
11	Beruhigungstee III* Valerianae radix 30-40 % Lavandulae flos 15-25 % Melissae folium 10-20 % (Menthae piperitae folium 10-30 %)	Nervous restlessness, difficulty in falling asleep.	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
12	Beruhigungstee IV* Lupuli flos 25-40 % Lavandulae flos 20-30 % Melissae folium 20-30 %	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (3 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
13	Beruhigungstee V* Valerianae radix 30-40 % Lupuli flos 15-30 % (Menthae piperitae folium 10-30 %) Melissae folium 10-20 %	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
14	Beruhigungstee VI* Valerianae radix 30-40 % Lupuli flos 15-25 % Passiflorae herba 10-20 % (Menthae piperitae folium 10-30 %)	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
15	Beruhigungstee VII* Valerianae radix 30-40 % Melissae folium 15-40 % Passiflorae herba 10-20 % (Menthae piperitae folium 10-30 %)	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1 tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, Standard Marketing Authorisation 1988
16	Beruhigungstee VIII* Valerianae radix 15-40% Lupuli flos 15-25%	Nervous restlessness, difficulty in falling asleep	Herbal tea 1 cup of a fresh infusion prepared from 1	Germany, Standard Marketing Authorisation 1988

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
	Lavandulae flos 15-25% Melissae folium 15-25%		tablespoonful (4 g) herbal tea (steeping time 10-15 min) 2-3 times daily and before bedtime	
17	1 tea bag (2 g) contains: Valerianae radix 0.6 g Lavandulae flos 0.5 g Melissae folium 0.4 g (Menthae piperitae folium 0.3 g)	Traditional herbal medicinal product for relief of mild symptoms of mental stress and exhaustion and to aid sleep	Herbal tea Adults and adolescents: 1 cup of fresh infusion prepared from 1 tea bag (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, TUR 2013
18	1 tea bag (2 g) contains: Valerianae radix 0.7 g Melissae folium 0.4 g Passiflorae herba 0.3 g (Menthae piperitae folium 0.3 g)	Traditional herbal medicinal product to aid sleep and for relief of mild symptoms of mental stress	Herbal tea Adults and adolescents: 1 cup of fresh infusion prepared from 1-2 tea bag (steeping time 10-15 min) 2-3 times daily and before bedtime	Germany, TUR 2014
19	3 g herbal tea contain: Melissae folium 0.75 g Valerianae radix 0.6 g (Crataegi folium cum flore 0.3 g) Lupuli flos 0.3 g Lavandulae flos 0.3 g and as aromaticum: (Menthae piperitae folium 0.45 g Anisi fructus 0.3 g)	For nervous tension, anxiety, irritability and sleeping difficulties/ disturbances, to mitigate stomach and heart complaints due to nervousness	Herbal tea Posology: Pour one cup (about 0.25 l) of hot water for 1 level tablespoon (about 3 g) of herbal tea mixture, cover it for half an hour and mix it sometimes. Than filter and drink it with a flavour to taste. Daily dose: 2-3 cups of tea. The last daily dose is recommended to drink half to one hour before going to sleep. The use in children under 12 years of age is not recommended. Maximum three months long administration is allowed as a cure. After three months of administration keep 2-3 weeks long break.	Hungary, healing product, registered since 1988
20	1 filter (1.5 g) contains: Melissae folium 300 mg (Hyperici herba 225 mg) Valerianae radix 150 mg Lavandulae flos 150 mg Lupuli flos 150 mg and as aromaticum: (Rosae pseudofructus 300mg, Liquiritiae radix 150 mg, Anisi fructus 75 mg)	Improvement or elimination of the symptoms of restlessness, nervousness, sleep disturbances, anxiety and depression due to various reasons, as first line or add-on therapy	Herbal tea in filter (1.5 g) Posology: Pour one cup (about 0.25 l) of boiling water for one filter of tea, cover it for 15 - 20 minutes. Drink it with flavour to taste. Daily dose: 1 cup of tea during the day and 1-2 cups of tea before going to sleep. The use in children under 12 years of age is not recommended. The use in adolescents between 12-18 years of age if recommended by a physician.	Hungary, healing product, registered since 1989

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
			Maximum three months long administration is allowed as a cure. After three months of administration keep 2-3 weeks long break.	
21	1 g herbal tea contains: (<i>Menthae piperitae folium</i> 0.333 g <i>Menyanthidis folium</i> 0.333 g) <i>Valerianae radix</i> 0.167 g <i>Lupuli flos</i> 0.167 g	Traditional herbal medicinal product for use in the specified indication exclusively based upon long-standing use indicated for nervous tension and improvement of sleep	Herbal tea Posology: Adults and adolescents 12 years and over Preparation for use: 1 tablespoon of herbal tea (around 3 g) pour with 150 ml hot water, cover, leave for 10-15 min. and filter. Drink 3 times per day. Duration of use no longer than 7 days.	Lithuania, THMP, in medicinal use since 1994
22	<i>Valerianae radix</i> 40 parts <i>Melissae folium</i> 15 parts (<i>Menthae piperitae folium</i> 15 parts <i>Millefolii herba</i> 20 parts <i>Matricariae flos</i> 10 parts)	Indications described in 1956: nervous system disorders, neuroses, nervous exhaustion, anxiety, insomnia, also related to the puberty and menopause. Indications in 1978: states of nervous agitation; nervous tension of different origin (antinervinum, psychosedativum). Supplementary in disturbances of puberty and menopause	Herbal tea Posology 1956, 1967: Bring to boil 1 spoon (6.8 g) of the herbal mixture in a glass (200-250 ml) of water (decoction). Since 1978 infuse in the same amount of boiling water. Keep under cover 20 min., strain. The infusion was prepared for drinking twice daily (in the morning and in the evening before bedtime); average single dose: 3.4g	Poland, on list of permitted pharmaceutical means before 1963, medicinal properties and indications described in 1956, 1967 and 1978.
23	<i>Lupuli flos</i> 20% <i>Melissae folium</i> 20% (<i>Leonuri cardiaceae herba</i> 20%) <i>Lavandulae flos</i> 10% (<i>Angelicae radix</i> 10% <i>Rosae pseudofructus</i> 20%)	In excessive nervous excitability	Herbal tea, infusion bags 2g 1 infusion bag pour with 200ml of boiling water, leave under cover 10 min. Adults and elderly: drink the infusion 4 times daily	Poland, first agreement R/0218 prolonged 1991 with MH&SW permission 3133 for pharmaceutical mean. TUR since 2007-2008
24	<i>Melissae folium</i> 60% <i>Lupuli flos</i> 25% <i>Lavandulae flos</i> 15%	Supplementary in nervous agitations, neuroses, sleeping difficulties, feeling of anxiety	Herbal tea, sachets 1 g Posology: Infusion of two 1 g sachets used 3 times a day	Poland, pharmaceutical mean, permission of MH&SW 3524, 03.06.1992
25	<i>Valerianae radix</i> 30 parts (<i>Crataegi folium cum flore</i> 20 parts) <i>Melissae folium</i> 15 parts <i>Lupuli flos</i> 15 parts (<i>Menthae piperitae folium</i> 10 parts <i>Matricariae flos</i> 10 parts)	Supplementary in mild periodic nervous states. Nervous tension and periodic difficulties falling asleep on the nervous base (a mild sleeping aid)	Herbal tea, sachets 1.5 g Posology: Adults and adolescents 2 sachets (3 g) pour with 1 glass (250 ml) of boiling water and infuse under cover for 10-15 min. In mild nervous tension 1 to 4 glasses of infusion a day. In difficulties falling asleep 1-2 glasses of infusion 30-60 min before sleep.	Poland, herbal medicinal product, TUR 2004

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
26	3 g herbal tea contain: Valeriane radix 900 mg (Crataegi folium cum flore 600 mg) Melissae folium 450 mg Lupuli flos 450 mg (Menthae piperitae folium 300 mg Matricariae flos 300 mg)	Traditionally in mild temporary states of nervous tension and periodic difficulties falling asleep	Herbal tea, sachets 3 g Posology: 1 sachet (3 g) pour with a glass of boiling water and infuse under cover 10-15 min. Adults and adolescents (from 12 years): one glass of freshly prepared infusion 1- 4 times daily in nervous tension states. In difficulties falling asleep 1- 2 infusion glasses before sleep.	Poland, herbal medicinal product, TUR 2005
27	2 g herbal tea contain: Valeriane radix 600 mg (Crataegi folium cum flore 400 mg) Melissae folium 300 mg Lupuli flos 300 mg (Menthae piperitae folium 200 mg Matricariae flos 200 mg)	Supplementary in states of increased nervous tension	Herbal tea, sachets 2 g Posology: 2 sachets (4 g) pour with a glass (200 ml) of boiling water. Infuse under cover 10-15 minutes. Drink prepared infusion 1 – 4 times a day	Poland, TUR 2005
28	1 sachet (2 g) contains: Valerianae radix 0.8g (40%) Melissae folium 0.3g (15%) (Menthae piperitae folium 0.3g (15%) Millefolii herba 0.4g (20%) Matricariae flos 0.2g (10%))	Traditional herbal medicinal product used for mild states of nervous tension and difficulties falling asleep. Contraindications: Hypersensitivity to any component of combination	Herbal tea, sachets 2 g Posology: Adolescents, adults and elderly: 2 sachets (4 g) pour with a glass (200-250ml) of boiling water and infuse about 15 min. under cover. Drink freshly prepared infusion 3 times a day.	Poland, pharmaceutical mean, permission of MH 4412 in 1999, THMP since 2014
29	1.5 g herbal tea contain: (Menthae piperitae folium 300 mg Hyperici herba 270 mg) Melissae folium 255 mg Lupuli flos 240 mg (Matricariae flos 240 mg) Valerianae radix 195 mg	For sedation after total prostration, for relief of irritability and nervous tension, in difficulties falling asleep and mild sleep disorders, for relief of digestive disorders caused by nervous tension	Posology: Pour 1/4 L of boiling water over 1-2 tea bags and allow steeping for 10 minutes. The tea must always be prepared freshly and just before consumption. It is best consumed at night, 30-60 minutes before sleep. If needed, the beverage can also be used during the evening and then before retiring to sleep. For children 3 – 12 years of age, adjust the volume of beverage to be consumed in accordance with weight of the child. For children up to 40 kg, prepare 1 cup using 1 infusion bag; for children up to 25 kg, they should only consume ½ cup prepared in the same way.	Slovakia, in medicinal use since 1996, THMP since 2008
30	1 tea bag (1.5 g) contains: Valerianae radix 450 mg	Used in restlessness, irritability, light forms of sleep disorders, light	Posology: Pour 1/4 L of boiling water over 1 infusion bag and allow	Slovakia, in medicinal use since 1998

	Active substance	Indication	Pharmaceutical form, posology	Country, regulatory status
	Melissae herba 450 mg (Menthae piperitae herba 450 mg Foeniculi fructus 150 mg)	digestive disorders associated with stress	steeping for 5 minutes with the vessel covered. Do not allow the tea to boil. Drink warm tea 3-times a day. In sleep disorders: place two tea bags in one cup before retiring to sleep. The tea must always be prepared fresh and just before consumption.	

*The active substances must add up to at least 70% (m/m) of the herbal tea combination. Other ingredients – if they are used- can be Anisi fructus, Foeniculi amari fructus, Carvi fructus, Rosmarini folium (spasmolytic, carminative), Matricariae flos, Millefolii herba, Calendulae flos (spasmolytic, carminative, anti-inflammatory), Aurantii amari flos, Rosae pseudofructus, Liquiritiae radix (improving aroma or taste). Each other ingredient must not be more than 5% of the herbal tea combination.

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

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 compared to fine cut material for tea bags. However, in Wichtl - Teedrogen und Phytopharmaka (Blaschek 2016) the following information is given:

Lavendulae flos: 1 teaspoon = about 0.8 g

Lupuli flos: 1 teaspoon = about 0.4 g

Melissae folium: 1 teaspoon = about 1.0 g

Passiflorae herba: 1 teaspoon = about 2.0 g

Valerianae radix: 1 teaspoon = about 2.5 g

Therefore, as a mean 1 teaspoon is calculated as 1 gram for tea combinations without Valerianae radix and 1.3 gram for tea combinations with Valerianae radix. On condition that 1 tablespoon corresponds to 3 teaspoons (Blaschek 2016) 1 tablespoon is calculated as 3 to 4 grams of herbal tea combination without or with Valerianae radix.

Table 2: Overview of historical data

	Herbal preparation	Documented use / Traditional use	Pharmaceutical form, posology	Reference
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	Herbal preparation	Documented use / Traditional use	Pharmaceutical form, posology	Reference
1	Valerianae radix 30 parts (Menthae piperitae folium 30 parts) Melissae folium 30 parts (Foeniculi fructus 10 parts)	Species valerianae	Herbal tea	Czechoslovak Pharmacopoeia (Pharmacopoea Bohemoslovenica) second edition, 1954
2	Valerianae radix 30 parts (Menthae piperitae herba 30 parts) Melissae herba 30 parts (Foeniculi fructus 10 parts)	Species valerianae	Herbal tea Single dose 2 g as an infusion in 1 teacup (150ml) 2 cups per day, 1 in the morning and 1 in the evening	Karmazin et al 1984
3	Valerianae rhizoma 40 parts (Menthae folium 15 parts) Melissae folium 15 parts (Millefolii herba 20 parts) (Chamomillae anthodium 10 parts)	Species sedativae	Herbal tea	Polish Pharmacopoeia (Pharmacopoea Polonica) III, 1954
4	Valerianae radix 60 parts Melissae folium 10 parts (Menthae piperitae folium 10 parts) (Aurantii flos 10 parts) (Aurantii endocarpium and mesocarpium 10 parts)	Species sedativae	Herbal tea Single dose 1.5 g as an infusion in 1 teacup (150ml)	Austrian Pharmacopoeia IX, 1960
5	Rhizoma valerianae 25g Herba passiflorae 20g Folium melissae 10g (Flos aurantii 20g) (Folium menthae piperitae 10g) (Fructus anisi 15g)	Species sedativae	Herbal tea Single dose 2 g	Swiss Pharmacopoeia (Pharmacopoea Helvetica) VI, 1972
6	Valerianae rhizoma 5g (10%) (Menthae piperitae folium 10g (20%)) (Menyanthis folium 5g (10%)) (Centaurii herba 5g (10%)) Farfae folium 5g (10%) Juniperi galbulus 5g (10%) Coriandri fructus 5g (10%) Cynosbati pseudofructus 10g (20%) (corrigens))	Species valerianae compositae	Herbal tea Posology: infusion of 3-3.5 g of the herbal tea in 0.25l of boiling water used 3 times a day	Hungary: Formulae Normales, 1987 (not considered for assessment: only one active ingredient)
7	Valerianae radix 40.0 g Lupuli flos 20.0 g Melissae folium 15.0 g (Aurantii amari pericarpium 10.0 g) (Menthae piperitae folium 15.0 g)	Species sedativae Beruhigungstee I	Herbal tea 1 tablespoon (=3-4 g) of herbal tea + 150 ml boiling water, 15 min steeping time, 2-3 times daily and before bedtime	Germany: Standard marketing authorisation, 1987 according to section 36 of the German Medicinal Products Act, cited in Braun 2011
8	Valerianae radix 30.0-40.0 % Lupuli flos 20.0-30.0 % Melissae folium 20.0-30.0 %	Species sedativae Beruhigungstee II		Germany: Standard marketing authorisation, 1988, according to section 36 of the German Medicinal Products
9	Valerianae radix 30.0-	Species sedativae		

	Herbal preparation	Documented use / Traditional use	Pharmaceutical form, posology	Reference
	40.0 % Lavandulae flos 15.0-25.0 % Melissae folium 10.0-20.0 % (Menthae piperitae folium 10.0-30.0 %)	Beruhigungstee III		Act, cited in Braun 2011
10	Lupuli flos 25.0-40.0 % Lavandulae flos 20.0-30.0 % Melissae folium 20.0-30.0 %	Species sedativae Beruhigungstee IV		
11	Valerianae radix 30.0-40.0 % Lupuli flos 15.0-30.0 % Melissae folium 10.0-20.0 % (Menthae piperitae folium 10.0-30.0 %)	Species sedativae Beruhigungstee V		
12	Valerianae radix 30.0-40.0 % Lupuli flos 15.0-25.0 % Passiflorae herba 10.0-20.0 % (Menthae piperitae folium 10.0-30.0 %)	Species sedativae Beruhigungstee VI		
13	Valerianae radix 30.0-40.0 % Melissae folium 15.0-40.0 % Passiflorae herba 10.0-20.0 % (Menthae piperitae folium 10.0-30.0 %)	Species sedativae Beruhigungstee VII		
14	Valerianae radix 15.0-40.0 % Lupuli flos 15.0-25.0 % Lavandulae flos 15.0-25.0 % Melissae folium 15.0-25.0 %	Species sedativae Beruhigungstee VIII		
15	Valeriane radix 30 parts Crataegi inflorescentia 20 parts Melissae folium 15 parts Lupuli strobulus 15 parts (Menthae piperitae folium 10 parts) (Chamomillae anthodium 10 parts)	Species sedativae	Herbal tea	Polish Pharmacopeia (Pharmacopoea Polonica) V, Supl. I, 1995
16	Valeriane radix 30 parts Crataegi inflorescentia 20 parts Melissae folium 15 parts Lupuli strobulus 15 parts (Menthae piperitae folium 10 parts) (Chamomillae anthodium 10 parts)	Species sedativae	Herbal tea single dose 3-4 g, 1-4 x daily	Polish Pharmacopeia (Pharmacopoea Polonica) VI, 2002

The concept of use of herbal tea combinations in nervous complaints derives from older composed herbal teas in dispensaries and handbooks in Germany in the 19th century, e.g. Heim's Species nervinae or Species nervinae Heim. This formula contained originally 6 parts of Menthae piperitae folium, 3 parts of Menyanthidis folium and 1 part of Valerianae radix. Later the Valerianae radix

content was increased to 22% and 33% (Fischer & Hartwich: Hagers Handbuch 1919). Species nervinae present in German Pharmacopoeia DAB 6 (1926) contained 30% Valerianae radix, 30% Menthae piperitae folium and 40% Menyanthidis folium. This herbal tea combination was included in the Polish Pharmacopoeia II as Species sedativae in 1937. Melissa folium was added in socialistic countries after the Second World War. In 1954, a monograph for Species sedativae was included to the Polish pharmacopoeia (Pharmacopoea Polonica III) containing 40% Valerianae radix, 15% Melissa folium, 15% Menthae piperitae folium, 20% Millefolii herba and 10% Matricariae flos. Also in DAB 7 (1964) in the German Democratic Republic (East Germany), the combination Species nervinae was substituted by the newly created combination Species sedativae containing 50% Valerianae radix, 25% Melissa folium and 25% Menthae piperitae folium. In Species sedativae in Austrian pharmacopoeia (ÖAB, 1960) Aurantii flos and Aurantii pericarpium were included. In the quantitative composition, the main accent of the combination was placed on 60% of Valerianae radix as an active ingredient. Species sedativae in Swiss pharmacopoeia (Pharmacopoea Helvetica, 1972) contained in addition to Aurantii flos also Passiflorae herba. In Germany in 1987 typical recipes I and in 1988 further II-VIII were published (Standard marketing authorisations: Beruhigungstee I 1987, Beruhigungstees II-VIII 1988) where compositions were presented in a form of ranges of components. The standard tea combinations were composed of Valerianae radix 15-40%, Melissa folium 10-40%, Lupuli flos 15-40%, Lavandulae flos 15-30% or Passiflorae herba 10-20%. The combinations I, III, V, VI, VII contained Menthae piperitae folium 10-30%. Further ingredients introduced for the first time in the combinations of Species sedativae were Crataegi folium cum flore 1988 and Hyperici herba 1989 in Hungary, and Leonuri cardiaca herba in Poland in 1991. Species Valerianae compositae described in Hungarian Formulae Normales (1987) contained only one active ingredient Valerianae radix in a quantity of 10%. It does not meet the criterion of an herbal tea combination.

In summary it can be stated, that the main ingredients of the herbal tea combinations indicated as sedative are the following herbal substances: Valerianae radix, Lupuli flos, Lavandulae flos, Melissa folium, and Passiflorae herba. For all these herbals an HMPC assessment has been performed. Often used additives are essential oil-containing herbs such as Anisi fructus, Carvi fructus, Foeniculi amari fructus, Matricariae flos, Menthae piperitae folium, Millefolii herba (spasmolytic, carminative) and/or Aurantii amari flos, Rosae pseudofructus and Liquiritiae radix (improving aroma or taste). These additional herbal substances which may be combination partners but are not linked to the therapeutic area are considered as excipients.

The main indication of Crataegi folium cum flore is the relief of symptoms of temporary nervous cardiac complaints (EMA/HMPC/159075/2014); the second part of the indication 'for relief of mild symptoms of mental stress and to aid sleep' does not refer to comminuted herbal substance as herbal tea for oral use. For Leonuri cardiaca herba, there is also an indication with focus on symptoms of nervous cardiac complaints; furthermore, the herbal tea combination in Poland does not fulfil the criteria for traditional use. Hyperici herba has a long tradition in folk medicine for the treatment of low mood, anxiety, to 'strengthen the nerves' (EMA/HMPC/244315/2016), but is not a typical combination partner in herbal tea combinations such as Species sedativae (Schulz and Hänsel 2004, Fintelmann and Weiss 2009, Schilcher 2016). Therefore, these herbal substances are not included in this assessment report.

2.3 Overall conclusions on medicinal use

Table 3: Valerianae radix in combinations

Combination partner	Single dose of herbal tea combination (excl. excipients)	Content of Valerianae radix in combination (excl. excipients)	Single dose of Valerianae radix/ Daily dose of Valerianae radix/ Frequency	Reference (in table 1)
Melissae folium	2.8 g	37%	1g/3-4g/3-4 x	8
	3.0 g	53%	1.6g/4.8-6.4g/3-4x	9
	4.0 g	30-40%	1.2-1.6g/3.6-6.4g/3-4x	10
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4 x	11
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4 x	13
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4x	15
	4.0 g	15-40%	0.6-1.6g/1.8-6.4g/3-4x	16
Lupuli flos	3.0 g	53%	1.6g/4.8-6.4g/3-4x	9
	4.0 g	30-40%	1.2-1.6g/3.6-6.4g /3-4x	10
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4x	11
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g /3-4x	13
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4x	14
	4.0 g	15-40%	0.6-1.6g/1.8-6.4g /3-4x	16
Lavandulae flos	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g/3-4x	11
	4.0 g	15-40%	0.6-1.6g/1.8-6.4g /3-4x	16
Passiflorae herba	2.8 g	37%	1g/3-4g /3-4 x	8
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g /3-4x	14
	2.8-3.6 g	33-57%	0.9-2.0g/2.7-8.0g /3-4x	15
Summary	2.8-4.0 g	15-57%	Single doses: 0.60 – 2.0 g Daily doses: 1.8 to 8.0 g Frequency: 3-4 x daily	Traditional use
			Single dose 0.3 - 3.0 g Daily dose: up to 9.0 g Frequency: up to 3 x daily	EU Monograph on Valerianae radix

Table 4: Melissae folium in combinations

Combination partner	Single dose of herbal tea combination (excl. excipients)	Content of Melissae folium in combination (excl. excipients)	Single dose of Melissae folium/ Daily dose of Melissae folium/ Frequency	Reference (in table 1)
Valerianae radix	2.8 g	28%	0.8g/2.4-3.2g /3-4x	8
	3.0 g	20%	0.6g /1.8-2.4g/3-4x	9
	4.0 g	20-30%	0.8-1.2g/2.4-4.8g/3-4x	10
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	11
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	13
	2.8-3.6 g	27-57%	0.76-2.0g/2.28-8.0g/3-4x	15
	4 g	15-25%	0.6-1.0g/1.8-4.0g/3-4x	16
Lupuli flos	3.0 g	20%	0.6g /1.8g-2.4g/3-4x	9
	4.0 g	20-30%	0.8-1.2g/2.4-4.8g/3-4x	10
	3.0 g	20-30%	0.6-0.9g/1.8-3.6g/3-4x	12
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	13
	4.0g	15-25%	0.6-1.0g/1.8-4.0g/3-4x	16
Lavandulae flos	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	11
	3.0 g	20-30%	0.6-0.9g/1.8-3.6g/3-4x	12
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g/3-4x	16
Passiflorae herba	2.8 g	28 %	0.8g/2.4-3.2g/3-4x	8
	2.8-3.6 g	27-57%	0.76-2.0g/2.28-8.0g /3-4x	15

Summary	2.8-4.0 g	11-57%	Single dose: 0.3 -2.0 g Daily doses: 0.9-8.0 g Frequency: 3-4x daily	Traditional use
			Single dose: 1.5 – 4.5g Daily dose: 1.5 – 13.5g Frequency: up to 3 times daily	EU Monograph on Melissae folium

Table 5: Lupuli flos in combinations

Combination partner	Single dose of herbal tea combination (excl. excipients)	Content of Lupuli flos in combination (excl. excipients)	Single dose of Lupuli flos / Daily dose of Lupuli flos/ Frequency	Reference (in table 1)
Valerianae radix	3.0 g	27%	0.8g/2.4-3.2g/3-4x	9
	4.0 g	20-30%	0.8-1.2g/2.4-4.8g /3-4x	10
	2.8-3.6 g	21-43%	0.6-1.5g/1.8-6.0g/3-4x	13
	2.8-3.6 g	21-36%	0.6-1.3g/1.8-5.2g/3-4x	14
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g /3-4x	16
Melissae folium	3.0 g	27%	0.8g/2.4-3.2g/3-4x	9
	4.0 g	20-30%	0.8-1.2g/2.4-4.8g /3-4x	10
	3.0 g	25-40%	0.7-1.2g/2.1-4.8g /3-4x	12
	2.8-3.6 g	21-43%	0.6-1.5g/1.8-6.0g/3-4x	13
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g /3-4x	16
Lavandulae flos	3.0 g	25-40%	0.7-1.2g/2.1-4.8g/3-4x	12
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g /3-4x	15
Passiflorae herba	2.8-3.6 g	21-36%	0.6-1.3g/1.8-5.2g /3-4x	14
Summary	2.8-4.0 g	15-43%	Single doses: 0.6–1.5 g Daily dose: 1.8–6.0 g Frequency: 3-4x daily	Traditional use
			Single dose: 0.5 g Daily dose: up to 2.0 g Frequency: up to 4x daily	EU Monograph on Lupuli flos

Remark: In the traditional use of herbal tea combinations, single and daily doses of Lupuli flos are higher than single and daily doses in the EU monograph. This discrepancy is probably due to the fact that besides Lupuli flos (=Strobuli lupuli) another herbal substance, namely Lupulinum (=Glandulae lupuli) has been used in the past in several countries. Lupulinum was regarded to have twice the content of biologically active substances compared to Lupuli flos and lower single doses were considered sufficient. Although Lupulinum was no longer used later on, its dosage was often transferred unchanged to Lupuli flos. No safety concerns however have arisen from the traditional use of herbal tea combinations containing Lupuli flos in the documented traditional posologies. A rationale to limit the content of Lupuli flos cannot be derived from the available data.

Table 6: Lavandulae flos in combinations

Combination partner	Single dose of herbal tea combination (excl. excipients)	Content of Lavandulae flos in combination (excl. excipients)	Single dose of Lavandulae flos/ Daily dose of Lavandulae flos/ Frequency	Reference (in table 1)
Valerianae radix	2.8-3.6 g	17-36%	0.5-1.3g/1.5-5.2g /3-4x	11
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g /3-4x	16
Melissae folium	2.8-3.6 g	17-36%	0.5-1.3g/1.5-5.2g/3-4x	11
	3.0 g	20-30%	0.6-0.9g/1.8-3.6/3-4x	12
	4.0 g	15-25%	0.6-1.0g/1.8-4.0g /3-4x	16

Lupuli flos	3.0 g 4.0 g	20-30% 15-25%	0.6-0.9g/1.8-3.6/3-4x 0.6-1.0g/1.8-4.0g /3-4x	12 16
Summary	2.8-4 g	15-36%	Single dose: 0.5-1.3 g Daily dose: 1.5-5.2 g Frequency: 3-4x daily	Traditional use
			Single dose: 1.0 – 2.0 g Daily dose: 3.0 – 6.0 g Frequency: 3 x daily	EU Monograph on Lavandulae flos

Table 7: Passiflorae herba in combinations

Combination partner	Single dose of herbal tea combination (excl. excipients)	Amount of Passiflorae herba in combination (excl. excipients)	Single dose of Passiflorae herba/ Daily dose of Passiflorae herba/ Frequency	Reference (in table 1)
Valerianae radix	2.8 g	34%	1g/3-4g/3-4x	8
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	14
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g/3-4x	15
Melissae folium	2.8 g	34%	1g/3-4g /3-4x	8
	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g /3-4x	15
Lupuli flos	2.8-3.6 g	11-28%	0.3-1.0g/0.9-4.0g /3-4x	14
Summary	2.8-3.6 g	11-34%	Single dose: 0.3-1.0 g Daily dose: 0.9-4.0 g Frequency: 3-4 x daily	Traditional use
			Single dose: 1.0 – 2.0 g Daily dose: 1.0 – 8.0 g Frequency: 1 – 4 x daily	EU Monograph on Passiflorae herba

Table 8: Combination of an herbal substance (left row) with other herbal substances (excipients excluded) based on documented traditional medicinal use. The numbers indicate the percentage of the herbal substance in combination with other herbal substances.

Example: When Valerianae radix is combined with Lupuli flos and Melissae folium then 15-57% of Valerianae radix is traditionally used in combinations. This combination contains 15-43% Lupuli flos and 11-30% Melissae folium.

	Valerianae radix	Melissae folium	Lupuli flos	Lavandulae flos	Passiflorae herba	Range
Amount of Valerianae radix in combination with:	-	15-57%	15-57%	15-57%	33-57%	15-57%
Amount of Melissae folium in combination with:	11-30%	-	11-30%	11-30%	27-57%	11-57%
Amount of Lupuli flos in combination with:	15-43%	15-43%	-	15-40%	21-36%	15-43%
Amount of Lavandulae flos in combination with:	15-36%	15-36%	15-30%	-	-	15-36%
Amount of Passiflorae herba in combination with:	11-34%	11-34%	11-28%	-	-	11-34%

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

Evidence for combination: The grey shaded fields in Table 8 indicate combinations with evidence of traditional medicinal use. Example: *Lavandulae flos* has evidence of combination with *Valerianae radix*, *Melissae folium*, and *Lupuli flos*. The combination partners for an application for a traditional herbal medicinal product may be chosen out of these documented combinations.

Number of combination partners: The number of active substances in an herbal tea combination should be 3 or 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. Usually, the sum of all excipients should not exceed 30% in the final combination and no more than 3 excipients should be used (see also Regulatory Q&A on herbal medicinal products, EMA/HMPC/345132/2010 - Rev.4).

Example:

Combination of *Valerianae radix* + *Melissae folium* + *Lavandulae flos*. The combination should contain 15–57% *Valerianae radix*, 11–30% *Melissae folium*, and 15–36% *Lavandulae flos*. Therefore, a combination of 50% *Valerianae radix*, 25% *Melissae folium* and 25% *Lavandulae flos* 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

Indications

<i>Valeriana officinalis</i> L., radix	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep.
<i>Melissa officinalis</i> L., folium	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep.
	Traditional herbal medicinal product for symptomatic treatment of mild gastrointestinal complaints including bloating and flatulence.
<i>Humulus lupulus</i> L., flos	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep.
<i>Lavandula angustifolia</i> Miller, flos	Traditional herbal medicinal product for relief of mild symptoms of mental stress and exhaustion and to aid sleep.
<i>Passiflora incarnata</i> L., herba	Traditional herbal medicinal product for relief of mild symptoms of mental stress and to aid sleep.

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 for relief of mild symptoms of mental stress and to aid sleep*” appears suitable for 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 4 g. The single and daily dosages of most herbal substances are below the

dosages stated in the monographs for the single herbal substances, except for Lupuli flos (please see remark under Table 5). The single dose for new combinations should be set to about 2 to 4 g (active herbal substances, excluding excipients).

The mean dosage frequency is 3-4 times daily, the last dose before going to bed. Most 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 times daily' dosage frequency, in case of 'Species sedativae' with an additional dose before going to sleep. Therefore, the dosage frequency is set to 3–4 times daily for all combinations.

Table 11: Comparison of the daily dose in the combinations with the upper limit according to the EU herbal monographs

	Range in combinations	Daily dose in combinations	Maximum daily dose EU herbal monograph
<i>Valeriana officinalis</i> L., radix	15-57%	1.8 to 8.0 g	9 g
<i>Melissa officinalis</i> L., folium	11-57%	0.9-8.0 g	13.5 g
<i>Humulus lupulus</i> L., flos	15-43%	1.8–6.0 g	2.0 g
<i>Lavandula angustifolia</i> Miller, flos	15-36%	1.5-5.2 g	6 g
<i>Passiflora incarnata</i> L., herba	11-34%	0.9-4.0 g	8 g

Age limits

<i>Valeriana officinalis</i> L., radix	Adolescents, adults and elderly
<i>Melissa officinalis</i> L., folium	Adolescents, adults and elderly
<i>Humulus lupulus</i> L., flos	Adolescents, adults and elderly
<i>Lavandula angustifolia</i> Miller, flos	Adolescents, adults and elderly
<i>Passiflora incarnata</i> L., herba	Adolescents, adults and elderly

Assessment for combinations: The information in the EU herbal monographs is reflected in the traditional use of the tea combinations in adolescents, adults and elderly.

Duration of use

<i>Valeriana officinalis</i> L., radix	If symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Melissa officinalis</i> L., folium	If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Humulus lupulus</i> L., flos	If the symptoms persist longer than two weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Lavandula angustifolia</i> Miller, flos	If the symptoms persist during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Passiflora incarnata</i> L., herba	If the symptoms persist longer than 2 weeks during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Assessment for combinations: A duration of use of 2 weeks is justified.

Contraindications

<i>Valeriana officinalis</i> L., radix	Hypersensitivity to the active substance
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<i>Melissa officinalis</i> L., folium	Hypersensitivity to the active substance
<i>Humulus lupulus</i> L., flos	Hypersensitivity to the active substance
<i>Lavandula angustifolia</i> Miller, flos	Hypersensitivity to the active substance(s)
<i>Passiflora incarnata</i> L., herba	Hypersensitivity to the active substance

Assessment for combinations: All combinations have to include hypersensitivity to the active substances as contraindication.

Special warnings and precautions for use

<i>Valeriana officinalis</i> L., radix	The use in children under 12 years of age has not been established due to lack of adequate data. If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Melissa officinalis</i> L., folium	The use in children under 12 years of age has not been established due to lack of adequate data. If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.
<i>Humulus lupulus</i> L., flos	The use in children under 12 years of age has not been established due to lack of adequate data. If the symptoms worsen during the use of the medicinal product, a doctor or qualified health care practitioner should be consulted.
<i>Lavandula angustifolia</i> Miller, flos	The use in children under 12 years of age has not been established due to lack of adequate data.
<i>Passiflora incarnata</i> L., herba	The use in children under 12 years of age has not been established due to lack of adequate data. If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Assessment for combinations: Based 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. All combinations have to include the warning: If the symptoms worsen during the use of the medicinal product, a doctor or a qualified health care practitioner should be consulted.

Interactions

<i>Valeriana officinalis</i> L., radix	None reported
<i>Melissa officinalis</i> L., folium	No data available
<i>Humulus lupulus</i> L., flos	None reported
<i>Lavandula angustifolia</i> Miller, flos	None reported
<i>Passiflora incarnata</i> L., herba	None reported

Assessment for combinations: All combinations have to include the statement: None reported.

Fertility, pregnancy and lactation

<i>Valeriana officinalis</i> L., radix	Safety during pregnancy and lactation has not been established. In the absence of sufficient data, use during pregnancy and lactation is not recommended. No fertility data available.
<i>Melissa officinalis</i> L., folium	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.
<i>Humulus lupulus</i> L., flos	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 are available.
<i>Lavandula angustifolia</i> Miller, flos	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.
<i>Passiflora incarnata</i> L., 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.

Assessment for combinations: All combinations 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.

Effects on ability to drive and use machines

<i>Valeriana officinalis</i> L., radix	May impair ability to drive and use machines. Affected patients should not drive or operate machinery.
<i>Melissa officinalis</i> L., folium	May impair ability to drive and use machines. Affected patients should not drive or operate machinery.
<i>Humulus lupulus</i> L., flos	May impair ability to drive and use machines. Affected patients should not drive or operate machinery.
<i>Lavandula angustifolia</i> Miller, flos	May impair ability to drive and use machines. Affected patients should not drive or operate machinery. No studies on the effect on the ability to drive and use machines have been performed.
<i>Passiflora incarnata</i> L., herba	May impair ability to drive and use machines. Affected patients should not drive or operate machinery.

Assessment for combinations: All combinations have to include the statement: May impair ability to drive and use machines. Affected patients should not drive or operate machinery.

Undesirable effects

<i>Valeriana officinalis</i> L., radix	Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur after ingestion of valerian root preparations. The frequency is not known.
<i>Melissa officinalis</i> L., folium	None known
<i>Humulus lupulus</i> L., flos	None known
<i>Lavandula angustifolia</i> Miller, flos	None known
<i>Passiflora incarnata</i> L., herba	None known

Assessment for combinations: Combinations containing Valerianae radix have to include: Gastrointestinal symptoms (e.g. nausea, abdominal cramps) may occur. The frequency is not known.

Overdose

<i>Valeriana officinalis</i> L., radix	Valerian root at a dose of approximately 20 g caused symptoms, such as fatigue, abdominal cramp, chest tightness, light-headedness, hand tremor and mydriasis, which disappeared within 24 hours. If symptoms arise, treatment should be supportive.
<i>Melissa officinalis</i> L., folium	No case of overdose has been reported.
<i>Humulus lupulus</i> L., flos	No case of overdose has been reported.
<i>Lavandula angustifolia</i> Miller, flos	No case of overdose has been reported.
<i>Passiflora incarnata</i> L., herba	No case of overdose has been reported.

Assessment for combinations: There are no relevant data on overdose of herbal tea combinations. Therefore, it is justified not to take into account the warning related to overdose of Valerianae radix. All combinations should include the statement: No case of overdose has been reported.

Preclinical safety data

<i>Valeriana officinalis</i> L., radix	AMES-tests on mutagenicity with extracts, representing the two extremes of the polarity range did not give any reason for concern. Tests on reproductive toxicity and carcinogenicity have not been performed.
<i>Melissa officinalis</i> L., folium	Not required as per Article 16c (1)(a)(i) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Adequate tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.
<i>Humulus lupulus</i> L., flos	Not required as per Article 16c(1)(a)(i) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Adequate tests on genotoxicity have not been performed. Tests on reproductive toxicity and carcinogenicity have not been performed.
<i>Lavandula angustifolia</i> Miller, flos	Not required as per Article 16c(1)(a)(i) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.
<i>Passiflora incarnata</i> L., herba	Not required as per Article 16c(1)(a)(i) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Tests on reproductive toxicity, genotoxicity and carcinogenicity have not been performed.

Assessment for combinations: Preclinical data are not required as per Article 16c (1)(a)(i) of Directive 2001/83/EC as amended, unless necessary for the safe use of the product. Tests on reproductive toxicity, genotoxicity and carcinogenicity for the combinations have not been performed.

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 Valerianae radix, Melissae folium, Lupuli flos, Lavandulae flos, and Passiflorae herba, for which EU herbal monographs have been established, are traditionally used in herbal tea combinations with the indication 'Traditional herbal medicinal product for the relief of mild symptoms of mental stress, to aid sleep'.

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.

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 adolescents and adults.

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

Annex

List of references