EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

11 March 2010
EMA/HMPC/CHMP/CVMP/287539/2005 Rev.1
Committee on Herbal Medicinal Products (HMPC)
Committee for medicinal products for human use (CHMP)
Committee for medicinal products for veterinary use (CVMP)

Guideline on declaration of herbal substances and herbal preparations[1] in herbal medicinal products[2] /traditional herbal medicinal products

Final

Draft agreed by HMPC drafting group on quality	February 2006
Adoption by HMPC for release for consultation	March 2006
Draft agreed by quality working party	May 2006
Adoption by CHMP for release for consultation	1 June 2006
Adoption by CVMP for release for consultation	22 June 2006
End of consultation (deadline for comments)	31 December 2006
Final agreed by HMPC drafting group on quality	12 April 2007
Adoption by HMPC	8 May 2007
Final agreed by quality working party	7 June 2007
Adoption by CHMP	18 June 2007

[1] The term "herbal substance" should be considered as equivalent to the term "herbal drug" as defined in the European Pharmacopoeia and the term "herbal preparation" should be considered as equivalent to the term "herbal drug preparation" as defined in the European Pharmacopoeia

[2] Throughout the guideline and unless otherwise specified, the term "herbal medicinal product" includes "traditional herbal medicinal product"

[3] SmPC: Summary of Product Characteristics.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7523 7455
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

Adoption by CVMP	12 July 2007
Date for coming into effect	1 February 2008
Draft rev 1 agreed by HMPC drafting group on quality	June 2008
Adoption by HMPC for release for consultation of rev 1	July 2008
Draft rev 1 agreed by quality working party	September 2008
Adoption by CVMP for release for consultation of rev 1	16 October 2008
Adoption by CHMP for release for consultation of rev 1	23 October 2008
End of consultation (deadline for comments)	30 April 2009
Final rev 1 agreed by HMPC drafting group on quality	14 October 2009
Adoption by HMPC	12 November 2009
Adoption by CVMP	10 December 2009
Adoption by CHMP	17 December 2009
QRD-review agreed by HMPC drafting group on quality	10 February 2010
Adoption by HMPC	11 March 2010
Date for coming into effect	1 October 2010

Keywords	Herbal medicinal products; traditional herbal medicinal products; herbal substances; herbal preparations; extracts; declaration; SmPC; package leaflet; labelling; HMPC

INTRODUCTORY NOTE TO REVISION 1 (2008)

The guideline EMEA/HMPC/CHMP/CVMP/287539/2005 was limited to guidance on the declaration in the SmPC. It was revised to integrate the declaration in package leaflet and labelling. The revision is in line with the "Concept paper on the declaration of herbal substances/herbal preparations in finished herbal medicinal products" (EMEA/HMPC/241953/2005).

The main chapters that have been revised are the following:

- Executive summary: Declaration in the package leaflet and labelling has been introduced, besides declaration in the SmPC
- Definitions: Definitions for the terms "declaration" and "strength" have been added
- Annex 1: This new annex has been added to the guideline, providing guidance specifically on declaration in the package leaflet and labelling.

There are only editorial changes in the guidance on declaration in the SmPC (chapter 5 and 6).

Guideline on declaration of herbal substances and herbal preparations in herbal medicinal products/traditional herbal medicinal products

Table of contents

Executive summary

The guideline EMEA/HMPC/CHMP/CVMP/287539/2005 was limited to guidance on the declaration in the SmPC. It was revised to integrate the declaration in package leaflet and labelling. The revision is in line with the "Concept paper on the declaration of herbal substances/herbal preparations in finished herbal medicinal products" (EMEA/HMPC/241953/2005).
This revised guideline outlines the principles for uniform declaration of herbal substances/preparations in herbal medicinal products as well as in traditional herbal medicinal products. It focuses on the different types of herbal substances/preparations in relation to the quality documentation given. Examples of declaration of such active substances are provided. The main guideline describes declaration in the SmPC. Guidance on package leaflets, labelling and other herbal specific provisions, for SmPC, package leaflets and labelling, have been added in Annex 1.
The guideline should be read in conjunction with current EU/(V)ICH guidelines.

1. Introduction

Common criteria for the declaration shall ensure clear differentiation between different types of herbal substances/preparations and proper description of their qualitative and quantitative particulars. As a result, a precise and consistent description of active substances of herbal medicinal products will be guaranteed within the Community.
The complex composition of herbal substances/preparations, which is essentially determined by various factors like the production process, the extraction solvent, the genuine drug extract ratio (DER genuine), and the type/physical state of the herbal substances/preparations, needs to be stated to guarantee identification and facilitate comparison of herbal substances/preparations. However, it is not feasible to provide full characterisation in the declaration as the declaration should be kept as short and precise as possible.
The declaration is primarily intended to describe the identity and quantity of the herbal substance/preparation, being the active substance of the herbal medicinal product and should focus on those characteristics found to be useful in ensuring the safety and efficacy of the herbal substance/preparation and herbal medicinal product.
Therefore, a declaration system has been established which reflects the main characteristics of herbal substances/preparations as defined in the respective specifications. For this purpose, general guidance as given in the European Pharmacopeoia (particularly the monographs "Extracts", "Herbal Drugs", "Herbal Drug Preparations", and "Herbal Teas") as well as in the guidelines listed under *References*, should be followed.

2. Scope

This guideline addresses the declaration of herbal substances/preparations when being the active substance of a herbal medicinal product. Examples of standardised, quantified, and other herbal substances/preparations are given.
The main guideline addresses only the declaration of herbal substances/preparations in herbal medicinal products (including fixed combinations) in the SmPC, whereas declaration in package leaflet and labelling is addressed in *Annex 1*. It shall apply to herbal medicinal products both for human and veterinary use and to traditional herbal medicinal products for human use. Traditional herbal medicinal products may additionally contain vitamins and/or minerals. Declaration of these chemically defined substances is not covered by this guideline. Reference is given to the INN-system and to "A guideline on summary of product characteristics".
This guideline reflects the current state of the art at the time it has been written. If necessary, the national regulatory authority/HMPC should be asked for additional guidance, especially in those cases not covered by examples in the guideline.

3. Legal basis

This guideline supports applications for marketing authorisations or registrations according to Directive 2001/83/EC and Directive 2001/82/EC as amended.
A simplified registration procedure was established for traditional herbal medicinal products for human use under Directive 2001/83/EC as amended by Directive 2004/24/EC. The principals for declaration of

herbal substances/preparations in herbal medicinal products apply equally to such traditional herbal medicinal products for human use.

4. Main guideline text

This guideline presents a brief definition of each concept and gives examples of the declaration in the SmPC. Generally, if the classification of a herbal preparation is not unambiguous, alternative proposals should be justified by the applicant and approved by the regulatory authority before being put into effect.
In the different chapters the characteristics, which are generally needed for the declaration of the different kinds of herbal substances/preparations, are given, followed by examples. The examples in the guideline are for illustration purposes only and not intended to reflect binding specifications. Within each example it is shown, what information is needed to form the specific declaration of the active substance of the herbal medicinal product in section 2 of the SmPC. In this context it is pointed out that both excipients for adjustment (valid for standardised herbal preparations only) and/or other excipients (e.g. carrier substances) must be declared in section 6.1 of the SmPC, preferably listed with a subtitle “excipients of the herbal substance/preparation”. Extraction solvents are to be declared in section 2 of the SmPC only. Furthermore, section 5.3 of the (human) SmPC provides for the possibility to inform on limits of unwanted (i. e. toxicologically relevant) constituents of herbal substances/preparations for safety reasons, provided that these limits are laid down in the specification as part of the quality documentation.

5. Declaration of herbal substances in the SmPC

It should be noted that this section does not apply to a herbal substance being the starting material of a herbal preparation.
The declaration of a herbal substance should cover the name and the quantity of the herbal substance. The name of the herbal substance is the scientific Latin name of the plant species according to the binomial system (genus, species, variety and author) with the Latin term of the plant part, followed by the [translated] common name of the monograph of the European Pharmacopoeia if available, or else of the Pharmacopoeia of a Member State, if available, or else the common name of the herbal substance (in brackets). In those special cases, where many different Latin plant species apply to the same herbal substance, the list of Latin names could be shortened to the genus name followed by the word “species”, e.g. “*Crataegus* species”. This option is only applicable in cases, where no restrictions concerning the species used are known from the quality documentation. In special cases, where necessary, only the scientific Latin name of the plant species may be used together with the [translated] common term for the plant part. For specific types of herbal substances (e.g. standardised, quantified) additional information may be necessary.

The following characteristics have to be stated in the declaration:
1. Name of the herbal substance.
2. Quantity of the genuine herbal substance.
3. Name and quantity of the constituent(s) with known therapeutic activity (standardised herbal substances), if applicable.
4. Name and quantity (given as a range) of the active markers (quantified herbal substances), if applicable.

5.1. Standardised herbal substances

Standardised herbal substances are adjusted within an acceptable tolerance to a given content of constituents with known therapeutic activity; standardisation is achieved by adding excipients for adjustment to the herbal substance or by blending batches of the herbal substance.
For such herbal substances the name and content of the constituent(s) with known therapeutic activity should be stated. The equivalent quantity of the genuine herbal substance should be given (as a range, if applicable).

Example:

Where a herbal medicinal product contains:

Senna leaf, cut.

Constituents with known therapeutic activity: 2.55 % hydroxyanthracene glycosides, calculated as sennoside B.
Quantity of the genuine herbal substance as a range: 85 - 96 %.
Excipients for adjustment: 4 - 15 %.
Quantity of the standardised herbal substance (herbal substance and excipients for adjustment) in the herbal medicinal product: 1.3 g/tea sachet.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each tea sachet contains 1.10 g - 1.25 g *Cassia senna* L. (*C. acutifolia* Delile) and/or *Cassia angustifolia* Vahl, folium (Senna leaf), corresponding to 33 mg hydroxyanthracene glycosides, calculated as sennoside B.

5.2. Quantified herbal substances

Quantified herbal substances are adjusted to a defined range of constituents; adjustments are made by blending batches of herbal substances used in the manufacturing process.
For quantified herbal substances the name of the active markers should be stated and their content should be given in a range. The equivalent quantity of the genuine herbal substance should be given.

Example:

Where a herbal medicinal product contains:

Willow bark, cut.

Quantification: 1.5 - 1.7 % of total salicylic derivatives calculated as salicin.
Quantity of the herbal substance in the herbal medicinal product: 3.0 g/tea sachet.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each tea sachet contains 3 g of various species of genus *Salix* including *S. purpurea* L., *S. daphnoides* Vill. and *S. fragilis* L., cortex (Willow bark), corresponding to 45 mg to 51 mg of total salicylic derivatives, calculated as salicin.

5.3. Other herbal substances

For other herbal substances neither constituents with known therapeutic activity nor active markers are generally known. Therefore these herbal substances are essentially defined by their production process and their specifications.
For other herbal substances the name and content of the analytical marker(s) should not be stated. The quantity of the genuine herbal substance should be given.

Example:

Where a herbal medicinal product contains:

100 g Linseed.
Quantity of the herbal substance in the herbal medicinal product: 1 g/g.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 g herbal medicinal product contains 1 g *Linum usitatissimum* L., semen (Linseed).

6. Declaration of herbal preparations in the SmPC

Herbal preparations are diverse in character ranging from simply processed, comminuted plant material to complex processed preparations such as refined extracts. The declaration of a herbal preparation should cover the name of the herbal substance and the definition of the herbal preparation including the physical state, ratio of herbal substance to genuine herbal preparation (DER genuine, also named native DER), and extraction solvent(s) if appropriate. The name of the herbal substance is the scientific Latin name of the plant species according to the binomial system (genus, species, variety and

author) with the Latin term of the plant part, followed by the [translated] common name of the monograph of the European Pharmacopoeia if available, or or else of the Pharmacopoeia of a Member State, if available, or else the common name of the herbal substance (in brackets). In those special cases, where many different Latin plant species apply to the same herbal substance, the list of Latin names could be shortened to the genus name followed by the word "species", e.g. "*Crataegus* species". This option is only applicable in cases, where no restrictions concerning the species used are known from the quality documentation. In special cases, where necessary, only the scientific Latin name of the plant species may be used together with the [translated] common term for the plant part.

In addition, the declaration of herbal preparations needs to reflect the different extract type (type of herbal preparation) as described in the European Pharmacopoeia.

(i) '**Standardised herbal preparations'**: are adjusted within an acceptable tolerance to a given content of constituents with known therapeutic activity; standardisation is achieved by adding excipients for adjustment to the herbal preparations or by blending batches of herbal preparations/herbal substances used in the manufacturing process.
For such preparations the name and content of the constituent(s) with known therapeutic activity should be stated. The equivalent quantity of the genuine herbal preparation should be given (as a range, if applicable).

(ii) **'Quantified herbal preparations'**: are adjusted to a defined range of constituents (active markers); adjustments are made by blending batches of herbal preparations/herbal substances used in the manufacturing process.
For such preparations the name and content of the active markers should be stated in a range. The equivalent quantity of the genuine herbal preparation should be stated, quoting either the corresponding amount of herbal substance (given as a range) or the DER genuine.

(iii) **'Other herbal preparations'**: are essentially defined by their production process and their specifications.
For such preparations the name and content of the analytical marker(s) should not be stated. The quantity of the genuine herbal preparation should be stated, quoting either the corresponding amount of herbal substance (given as a range) or the DER genuine.

When solvent(s) are used in the manufacture of a herbal preparation (extraction solvent(s)), the name and composition of the solvent(s) used in the first extraction step should be included in the declaration of the herbal medicinal product. If purification procedures are used in the manufacture of a herbal preparation, the word "refined" should be added to the name of the herbal preparation, where applicable.

In the SmPC the following wording can be used, as appropriate: "Extraction solvent: <NAME> <COMPOSITION> % V/V" (or % m/m, as applicable).
If a fresh herbal substance is used as a starting material for manufacture of the herbal preparation, this should be added to the name of the herbal preparation, as appropriate.

6.1. Herbal preparations consisting of comminuted or powdered herbal substances

The following characteristics have to be stated in the declaration:
1. Name of the herbal substance used.
2. Physical state of the herbal preparation, if relevant.
3. Quantity of the genuine herbal preparation.
4. Name and quantity of the constituent(s) with known therapeutic activity (standardised herbal preparations), if applicable.
5. Name and quantity (given as a range) of the active markers (quantified herbal preparations), if applicable.

6.1.1. Standardised herbal preparations

Example a): Standardisation by adding excipients for adjustment

Where a herbal medicinal product contains:

Senna leaf, powdered.
Tinnevelly Senna pods, powdered.
Constituents with known therapeutic activity: 3.5 % hydroxyanthracene glycosides, calculated as sennoside B.
Quantity of the genuine herbal preparation as a range: 70 - 95 % (mixture of both senna preparations).
Excipients for adjustment: 5 - 30 %.
Other excipients: 0 %.
Quantity of the standardised herbal preparation (genuine herbal preparation + excipients for adjustment) in the herbal medicinal product: 1 g/g (200 mg Senna leaf, 500 mg - 750 mg Tinnevelly Senna pods and 50 mg - 300 mg excipients for adjustment).

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 g powder contains 200 mg *Cassia senna* L. (*C. acutifolia* Delile) and/or *Cassia angustifolia* Vahl, folium (Senna leaf) and 500 mg - 750 mg *Cassia angustifolia* Vahl, fructus (Tinnevelly Senna pods), corresponding to 35 mg hydroxyanthracene glycosides, calculated as sennoside B .

Example b): Standardisation by mixing herbal preparations

Where a herbal medicinal product contains:

Senna leaf, powdered.
Tinnevelly Senna pods, powdered.
Alexandrian Senna pods, powdered.
Constituent(s) with known therapeutic activity: 2.7 % hydroxyanthracene glycosides, calculated as sennoside B.
Quantity of the genuine herbal preparation (as a range): 100 % genuine herbal preparation (mixture of all three senna preparations).
Other excipients: 0 %.
Quantity of the genuine standardised herbal preparation in the herbal medicinal product: 1 g/g (200 mg Senna leaf, 500 mg - 750 mg Tinnevelly Senna pods, and 50 mg - 300 mg Alexandrian Senna pods).

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 g powder contains 200 mg *Cassia senna* L. (*C. acutifolia* Delile) and/or *Cassia angustifolia* Vahl, folium (Senna leaf), 500 mg - 750 mg *Cassia angustifolia* Vahl, fructus (Tinnevelly Senna pods) and 50 mg - 300 mg *Cassia senna* L. (*C. acutifolia* Delile), fructus (Alexandrian Senna pods), corresponding to 27 mg hydroxyanthracene glycosides, calculated as sennoside B.

6.1.2. Quantified herbal preparations

Example:

Where a herbal medicinal product contains:

Willow bark, powdered.
Quantification: 1.5 - 1.7 % of total salicylic derivatives, calculated as salicin.
Other excipients: 0 %.
Quantity of the genuine herbal preparation in the herbal medicinal product: 2.5 g/tea sachet.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 tea sachet contains 2.5 g of various species of genus *Salix* including *S. purpurea* L., *S. daphnoides* Vill. and *S. fragilis* L, cortex (Willow bark), corresponding to 37.5 mg to 42.5 mg of total salicylic derivatives, calculated as salicin.

6.1.3. Other herbal preparations

Example:

Where a herbal medicinal product contains:

Valerian root, powdered.
Other excipients: 0 %.

Quantity of the genuine herbal preparation in the herbal medicinal product: 300 mg/capsule.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each capsule contains 300 mg of *Valeriana officinalis* L. s.l., radix (Valerian root).

6.2. Herbal preparations produced by steps which exceed comminution/powdering (e.g. extracts)

The following characteristics have to be stated in the declaration:
1. Name of the herbal substance used.
2. Type/physical state of the herbal preparation.
3. Quantity of the genuine herbal preparation.
4. Name and quantity of the constituent(s) with known therapeutic activity (standardised herbal preparations), if applicable.
5. Name and quantity (given as a range) of the active markers (quantified herbal preparations), if applicable.
6. Drug extract ratio (DER genuine) or equivalence in the quantity of the herbal substance (as a range) (quantified and other herbal preparations).
7. Name and composition of extraction solvent(s).

6.2.1. Standardised extracts

Example:

Where a herbal medicinal product contains:

Dry extract from Horse chestnut seed
Constituent(s) with known therapeutic activity: 19 % triterpene glycosides, calculated as anhydrous ß-aescin.
Quantity of the genuine extract (as a range): 70 - 95 % genuine extract.
DER genuine: 5 – 8 : 1.
Excipients for adjustment: 30 - 5 %.
Other excipients: 0 %.
Extraction solvent: Methanol 80 % V/V.
Quantity of the standardised extract (genuine herbal preparation and excipients for adjustment) in the herbal medicinal product: 200 mg/capsule.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each capsule contains 140 mg - 190 mg of extract (as dry extract) from *Aesculus hippocastanum* L., semen (Horse chestnut seed) corresponding to 38 mg triterpene glycosides, calculated as anhydrous ß-aescin.
Extraction solvent: Methanol 80 % V/V.

6.2.2. Quantified extracts

Example:

Where a herbal medicinal product contains:

Dry extract from Ginkgo leaf, refined.
Quantity of the genuine extract: 100 % genuine extract.
DER genuine: 35 – 67 : 1.
Quantification: 22.0 to 27.0 % of flavonoids expressed as flavone glycosides.
2.8 to 3.4 % of ginkgolides A, B and C.
2.6 to 3.2 % of bilobalide.
Other excipients: 0 %.
First extraction solvent: Acetone 60 % m/m.
Quantity of the genuine quantified extract in the herbal medicinal product: 60 mg/capsule.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each capsule contains 60 mg of extract (as dry extract, refined) from *Ginkgo biloba* L., folium (Ginkgo leaf) (35 – 67 : 1), corresponding to:
13.2 mg to 16.2 mg of flavonoids expressed as flavone glycosides

1.68 mg to 2.04 mg of ginkgolides A, B and C
1.56 mg to 1.92 mg of bilobalide.
First extraction solvent: Acetone 60 % m/m.

or

Each capsule contains 60 mg of extract (as dry extract, refined) from *Ginkgo biloba* L., folium (equivalent to 2.1 g – 4.0 g of Ginkgo leaf), corresponding to:
13.2 mg to 16.2 mg of flavonoids expressed as flavone glycosides
1.68 mg to 2.04 mg of ginkgolides A, B and C
1.56 mg to 1.92 mg of bilobalide.
First extraction solvent: Acetone 60% m/m.

6.2.3. Other extracts

Example a: Other extracts such as dry extracts

Where a herbal medicinal product contains:

Dry extract from Valerian root.
Quantity of the genuine extract: 80 % genuine extract.
DER genuine: 3 – 6 : 1
Other excipients: 20 %.
Extraction solvent: Ethanol 70 % V/V.
Quantity of the dry extract (genuine herbal preparation and other excipients) in the herbal medicinal product: 200 mg/capsule.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each capsule contains 160 mg of extract (as dry extract) from *Valeriana officinalis* L. s.l., radix (Valerian root) (3 – 6 : 1).
Extraction solvent: Ethanol 70 % V/V.

or

Each capsule contains 160 mg of extract (as dry extract) from *Valeriana officinalis* L. s.l., radix (equivalent to 480 mg – 960 mg of Valerian root).
Extraction solvent: Ethanol 70 % V/V.

Example b): Other extracts such as liquid extracts

Where a herbal medicinal product contains:

Liquid extract from Matricaria flower..
Quantity of the genuine extract: 100 % genuine extract.
DER genuine: 1 : 1.
Other excipients: 0 %.
Extraction solvent: 2.5 parts ammonia solution 10 % m/m
50 parts of ethanol 96 % V/V
47.5 parts of water.
Quantity of the genuine liquid extract in the herbal medicinal product: 1 ml/ml.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 ml [corresponding to ... g] of oral liquid contains 1 ml of liquid extract from *Matricaria recutita* L. (*Chamomilla recutita* (L.) Rauschert), flos (Matricaria flower) (1 : 1).
Extraction solvent: Ammonia solution 10 % m/m / ethanol 96 % V/V / water (2.5/50/47.5).

or

1 ml [corresponding to ... g] of oral liquid contains 1 ml of liquid extract from *Matricaria recutita* L. (*Chamomilla recutita* (L.) Rauschert), flos (equivalent to 1 g Matricaria flower).
Extraction solvent: Ammonia solution 10 % m/m / ethanol 96 % V/V / water (2.5/50/47.5).

Example c: Other extracts such as tinctures

Where a herbal medicinal product contains:

Tincture from Valerian root.
Quantity of the genuine extract: 100 % genuine extract.
DER genuine: 1 : 4.0 - 4.5.
Other excipients: 0 %.
Extraction solvent: Ethanol 70 % V/V.
Quantity of the tincture in the herbal medicinal product: 1 ml/ml.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 ml [corresponding to ... g] of oral liquid contains 1 ml of tincture from *Valeriana officinalis* L. s.l., radix (Valerian root) (1 : 4.0 - 4.5).
Extraction solvent: Ethanol 70 % V/V.

or

1 ml [corresponding to ... g] of oral liquid contains 1 ml of tincture from *Valeriana officinalis* L. s.l., radix (equivalent to 220 mg - 250 mg Valerian root).
Extraction solvent: Ethanol 70 % V/V.

Example d: Other extracts such as dry extracts from a mixture

Where a herbal medicinal product contains:
Dry extract from 3 parts Valerian root
2 parts Hop strobile
2 parts Melissa leaf.
Quantity of the genuine extract: 80 % genuine extract.
DER genuine: 4 – 7 : 1.
Other excipients: 20 %.
Extraction solvent: Ethanol 70 % V/V.
Quantity of the dry extract (genuine herbal preparation and other excipients) in the herbal medicinal product: 200 mg/capsule.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

Each capsule contains 160 mg of extract (as dry extract) (4 – 7 : 1) from *Valeriana officinalis* L. s.l., radix (Valerian root) / *Humulus lupulus* L., flos (Hop strobile) / *Melissa officinalis* L., folium (Melissa leaf) (3/2/2).
Extraction solvent: Ethanol 70 % V/V.

or

Each capsule contains 160 mg of extract (as dry extract) (equivalent to 0.64 g – 1.1 g mixture of the herbal substances) from *Valeriana officinalis* L. s.l., radix (Valerian root) / *Humulus lupulus* L., flos (Hop strobile) / *Melissa officinalis* L, folium (Melissa leaf) (3/2/2).
Extraction solvent: Ethanol 70 % V/V.

6.3. Herbal preparations not covered by 6.1 or 6.2

The following characteristics have to be stated in the declaration:
1. Name of the herbal substance used.
2. Type of the herbal preparation.
3. Quantity of the genuine herbal preparation.
4. Drug extract ratio (DER genuine) or equivalent quantity of the herbal substance (as a range), if applicable.
5. Name and composition of extraction solvent(s), if applicable.

6.3.1. Other herbal preparations such as essential oils

Example:

Where a herbal medicinal product contains:

Peppermint oil.

Quantity of the essential oil: 100 % essential oil.
Other excipients: 0 %.
Quantity of the essential oil in the herbal medicinal product: 81 mg/ml oral liquid.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 ml [corresponding to … g] of oral liquid contains 81 mg of *Mentha* × *piperita* L., aetheroleum (peppermint oil).

6.3.2. Other herbal preparations such as expressed juices

Example:

Where a herbal medicinal product contains:

Expressed juice from fresh purple coneflower herb.
Quantity of the genuine expressed juice:100% genuine expressed juice.
DER genuine: 1.2 - 1.5 : 1.
Other excipients: 0 %.
Quantity of the genuine expressed juice in the herbal medicinal product: 1 ml/ml oral liquid.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 ml [corresponding to ... g] of oral liquid contains 1 ml of expressed juice from *Echinacea purpurea* (L.) Moench, herba (fresh purple coneflower herb) (1.2 - 1.5 : 1)

or

1 ml [corresponding to ... g] of oral liquid contains 1 ml of expressed juice from *Echinacea purpurea* (L.) Moench, herba (equivalent to 1.2 g – 1.5 g fresh purple coneflower herb).

6.3.3. Other herbal preparations such as processed exudates

Example:

Where a herbal medicinal product contains:

Tincture from Myrrh.
Quantity of the processed exudate: 100 % processed exudate.
DER genuine: 1 : 4.0 - 4.5.
Other excipients: 0 %.
Extraction solvent: Ethanol 90 % V/V.
Quantity of the tincture in the herbal medicinal product: 25 mg/ml oral liquid.

The declaration in section 2 of the SmPC of the herbal medicinal product is:

1 ml [corresponding to ... g] of oral liquid contains 25 mg of tincture from *Commiphora molmol* Engler and/or other species of *Commiphora* (Myrrh) (1 : 4.0 - 4.5).
Extraction solvent: Ethanol 90 % V/V.

or

1 ml [corresponding to ... g] of oral liquid contains 25 mg of tincture from *Commiphora molmol* Engler and/or other species of *Commiphora* (equivalent to 5.5 mg - 6.3 mg Myrrh).
Extraction solvent: Ethanol 90 % V/V.

Definitions

Constituents with known therapeutic activity: are chemically defined substances or groups of substances which are generally accepted to contribute substantially to the therapeutic activity of a herbal substance, a herbal preparation or a herbal medicinal product.

Declaration: A statement of the content of the active substance(s) expressed qualitatively and quantitatively per dosage unit, per unit of volume or weight according to the dosage form.

Drug extract ratio (DER): means the ratio between the quantity of herbal substance used in the manufacture of a herbal preparation and the quantity of herbal preparation obtained. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the herbal preparation obtained.

Excipients: In general, excipients may be defined as constituents of the medicinal product other than the active substance(s). However, in the context of this guideline only two categories of excipients are addressed:

Excipients for adjustment are used for standardisation of herbal substances/preparations.

Other excipients are technological excipients (e.g. carrier substances) which may be part of herbal preparations.

Extraction solvents: are solvents which are used for the extraction process.

Genuine (Native) herbal preparation: refers to the preparation without excipients, even if for technological reasons the genuine herbal preparation is not available. However, for soft and liquid herbal preparations the genuine herbal preparation may contain variable amounts of (extraction) solvent.

Ratio of herbal substance to genuine herbal preparation (DER genuine): is the ratio of the quantity of the herbal substance to the quantity of the resulting genuine herbal preparation. The number (given as the actual range) written before the colon is the relative quantity of the herbal substance; the number written after the colon is the relative quantity of the genuine herbal preparation obtained.

Herbal medicinal products: any medicinal product, exclusively containing as active substances one or more herbal substances or one or more herbal preparations, or one or more such herbal substances in combination with one or more such herbal preparations.

Herbal preparations: are obtained by subjecting herbal substances to treatments such as extraction, distillation, expression, fractionation, purification, concentration or fermentation. These include comminuted or powdered herbal substances, tinctures, extracts, essential oils, expressed juices and processed exudates.

Herbal substances: all mainly whole, fragmented or cut plants, plant parts, algae, fungi, lichen in an unprocessed, usually dried form but sometimes fresh. Certain exudates that have not been subjected to a specific treatment are also considered to be herbal substances. Herbal substances are precisely defined by the plant part used and the botanical name according to the binomial system (genus, species, variety and author).

Herbal teas: consist exclusively of one or more herbal substance(s) intended for oral aqueous preparations by means of decoction, infusion or maceration. The preparation is prepared immediately before use. Herbal teas are usually supplied in bulk form or in sachets (tea bags).

Markers: are chemically defined constituents or groups of constituents of a herbal substance, a herbal preparation or a herbal medicinal product which are of interest for control purposes independent of whether they have any therapeutic activity. Markers serve to calculate the quantity of herbal substance(s) or herbal preparation(s) in the herbal medicinal product if the marker has been quantitatively determined in the herbal substance or herbal preparation.

There are two categories of markers:

Active markers are constituents or groups of constituents which are generally accepted to contribute to the therapeutic activity.

Analytical markers are constituents or groups of constituents that serve for analytical purposes.

Quantification: means adjusting the herbal substance or herbal preparation to a defined range of constituents (active markers) exclusively achieved by blending different batches of herbal substances and/or herbal preparations (e.g. quantified extract).

Specification: A list of tests, references to analytical procedures, and appropriate acceptance criteria which are numerical limits, ranges, or other criteria for the tests described. It establishes the set of criteria to which a herbal substance/preparation or herbal medicinal product should conform to be considered acceptable for its intended use. "Conformance to specifications" means that the herbal substance/preparation and/or herbal medicinal product, when tested according to the listed analytical procedures, will meet the listed acceptance criteria. Specifications are binding quality standards that are agreed to between the appropriate governmental regulatory agency and the applicant.

Standardisation: means adjusting the herbal substance/preparation to a defined content of a constituent or a group of constituents with known therapeutic activity respectively either by adding excipients or by blending batches of the herbal substance and/or herbal preparation (e.g. standardised extracts).

Strength: The content of the active substance(s) expressed quantitatively per dosage unit, per unit of volume or weight according to the dosage form.

Traditional herbal medicinal products: are medicinal products for human use that fulfil the conditions laid down in article 16a (1) of Directive 2001/83/EC, as amended.

References

"Guideline on specifications: Test procedures and acceptance criteria for herbal substances, herbal preparations and herbal medicinal products/traditional herbal medicinal products" (CPMP/QWP/2820/00 Rev.1 and EMEA/CVMP/815/00 Rev.1).

"Guideline on quality of herbal medicinal products/traditional herbal medicinal products" (CPMP/QWP/2819/00 Rev.1 and EMEA/CVMP/814/00 Rev.1).

"A Guideline on Summary of Product Characteristics (SmPC)" (Human Medicinal Products) Eudralex Vol. 2C, current version.

Guideline on "Summary of Product Characteristics (SPC) – Pharmaceuticals" (Veterinary Medicinal Products) Eudralex Volume 6C, current version.

"Concept paper on the declaration of herbal substances/herbal preparations in finished herbal medicinal products" (EMEA/HMPC/241953/2005).

Annex 1 Declaration in the package leaflet and labelling

1. Introduction

Suitable declaration of herbal substances and herbal preparations in herbal medicinal products should be included in the package leaflets and product labelling. The declaration should follow the regulations of Directive 2001/83/EC and Directive 2001/82/EC as amended, and it should be consistent with the declaration given in the SmPC. Therefore, overall the declaration in the SmPC should form the basis of the declaration in the package leaflet and labelling.

The main guideline on declaration in the SmPC was developed to obtain an agreed view in the harmonisation process for herbal medicinal products. Likewise, harmonisation of the declaration in package leaflet and labelling is desirable. As the declaration should be as precise as possible, satisfactory declaration of a herbal medicinal product is most often extensive and requires much space in writing. Therefore, declaration in labelling could be abbreviated, although still in line with the principles of the main guideline for the SmPC.

This annex focuses on acceptable abbreviation in the declaration in the package leaflet and labelling compared to the declaration in the SmPC.

In general, due to different national traditions, the exact wording and the order of the elements of the declaration could be different from the SmPC. However, it should be ensured that the information and meaning is the same as in the SmPC. No new information is allowed to be added compared to the SmPC.

For requirements on Braille, see separate guidance documents ("Guideline on the readability of the labelling and package leaflet of medicinal products for human use").

2. Declaration of herbal medicinal products - in package leaflets

Because writing space is not a limiting factor for package leaflets, the declaration in the package leaflet should be the same as the one given in the SmPC section 2.

3. Declaration of herbal medicinal products - in labelling

As the size of the immediate and outer packaging is limited, the space on the label is likewise limited. Therefore the declaration may be abbreviated, provided that this will not affect the safe use of the product.

Examples of abbreviated declaration in labelling:

Wherever possible the labelling should include the plant name(s) stated in the SmPC unless otherwise authorised by the competent authority.

The extraction solvent may be omitted, if justified.

The physical state of a herbal preparation may be omitted, e.g. "extract (as dry extract)" may be abbreviated to "extract".

If justified for a herbal preparation, the equivalent quantity of the herbal substance may be replaced by the ratio of the herbal substance to the genuine herbal preparation and vice versa, in this case the SmPC should include both versions.

4. Strength of herbal medicinal products – in the SmPC, package leaflets and labelling

In general for a medicinal product, the (invented) product name should be followed by its strength, cf. Dir. 2001/83/EC; article 54, 55 and 59 and Dir. 2001/82/EC; article 58, 59, 60 and 61.

For herbal medicinal products this requirement is normally not appropriate: The declaration in the SmPC most often includes more than one quantity (mass). For e.g. a quantified extract the declaration includes both the quantity of active marker(s), the quantity of the genuine extract and the equivalent quantity of the herbal substance (or DERgenuine). So if the name is to be followed by the strength expressed as a single unspecified mass (e.g. 40 mg), the meaning will not be clear and could be misleading. This could create confusion to the patients and other readers. In conclusion, the 'invented' product name should not be followed by a designation 'strength', but the quantitive compostition would be fully detailed in the declaration of the product.

5. "Common names" of active substances – in the SmPC, package leaflets and labelling

In general, if the name of a medicinal product is an invented name, the product name should be followed by the international non-proprietary name (INN) for each active substance, cf. Article 54, 55 and 59 of Directive 2001/83/EC, as amended and Article 58, 59, 60 and 61 of Directive 2001/82/EC, as amended.

As no INN's for herbal substances or herbal preparations exist, it is recommended to use an abbreviated form of the name for the active substance, for example "valerian dry extract" or "valerian tincture" (for package leaflet when the product contains only one active substance; for labelling when

the product contains up to 3 active substances). The name of an active substance in the declaration of the product should be based on the name given in the declaration in section 2 of the SmPC.