Simplified authorisation procedure for herbal medicines according to Art. 14 para. 1 let. c^{bis} and $a^{bis\text{-}quater}$ TPA

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Authorisation procedure for herbal medicinal products (human medicinal products)

Ordinary authorisation / New active substance
Art. 11 TPA

Medicinal products and procedures authorised in foreign countries
Art. 13 TPA

Simplified authorisation procedure
Art. 14 TPA

- **Simplified authorisation**
  Art. 14 para. 1 let. a bis-quater TPA
- **Herbal medicinal products**
  Art. 14 para. 1 let. c^{bis} TPA and Art. 8 – 11 KPTPO
  - **Herbal medicinal products with known active substance**
  - **Herbal medicinal products with well-established use**
  - **Herbal medicinal products with traditional use**

Authorisation on the basis of a notification
Art. 15 TPA

- **Notification procedure for teas**
  Art. 15 para. 1 let. b TPA
  Art. 12 KPTPO

Co-marketing medicinal products
Art. 34 ff. TPLO

Herbal medicinal products with known active substance

- Herbal medicinal products comparable to a medicinal product that is already authorised in **Switzerland** can be authorised in a simplified procedure according to **Art. 14 para. 1 let. c^{bis} TPA** and Art. 8-11 KPTPO.

- **Precondition**: Evidence of comparability with the Swiss comparator product

  *Note: Medicinal products that are already authorised in a foreign country but have not yet been authorised in Switzerland do **not** count as **"known active substances"** in Switzerland*

  Does NOT have to have been authorised in Switzerland for 10 years as is the case with herbal medicinal products with "well-established use" (beware: document protection)

- **Herbal medicinal products with known active substance are not generics!**

  Note: The guidance document "Authorisation of human medicinal product with known active substance HMV4" and Art. 12 TPA and Art. 14 para.1 let. a TPA in conjunction with Art. 12 ff TPLO do NOT apply to herbal medicinal products because of the specific nature of herbal medicinal products as complex mixtures with many substances.

  The specific requirements for herbal medicinal products are described in Chapter 7.1.1 of the "Guidance document Authorisation of herbal medicinal products HMV4".

Herbal medicinal products with known active substance

Requirements → **Guidance document Authorisation of herbal medicinal products HMV4,**

Chapter 7.1.1 ff:

- Complete quality documentation
- Complete toxicology and pharmacology documentation
  - including mutagenicity, carcinogenicity and reproductive toxicity aspects (Chap. 7.3.2) → **AMES TEST**
- Complete clinical documentation – usually in the form of bibliographic data/supplementary monographs –
  - Evidence of therapeutic and pharmaceutical equivalence with Swiss comparator product
  - Reference can be made to the authorised comparator product for the known aspects
  - For new aspects that have not yet been authorised in Switzerland: Evidence in keeping with an "ordinary authorisation procedure according to Art. 11 TPA" (usually own clinical and preclinical studies; rarely bibliographical evidence)
  - A literature search must not be older than 12 months
  - A Clinical Safety Summary (Module 2.7.4) is mandatory (PSUR data, exposure to patient population)

The Clinical Safety Summary must present safety data from the clinical trials and/or tolerability data from post-marketing experience (PSUR)

Herbal medicinal products with well-established use

- **Art. 14 para. 1 let. c^{bis} TPA** describes, in conjunction with Art. 8-11 KPTPO, the option of simplified authorisation on the basis of bibliographical documentation for herbal medicinal products with “well-established use”

- **Precondition:** the herbal active substance must have been “authorised” in the EU/EFTA in a medicinal product for the proposed indication and use for at least 10 years.

  Note: Since the definition of 10 years refers to the herbal active substance, refinements of the pharmaceutical form or dosage, for example, may be approved if the corresponding data is available in the literature.

- **Sufficient bibliographical documentation** must exist:

  For herbal medicinal products with well-established use, evidence of the efficacy of the medicinal product in the proposed indication must be documented **by at least a good-quality controlled clinical (literature) study**.

  Note: The wording of the indication, the dosage, interactions, etc. are guided by the submitted bibliographical documentation or the recognised monographs for the herbal active substance

Herbal medicinal products with well-established use

Requirements → **Guidance document Authorisation of herbal medicinal products HMV4, Chapter 7.1.2 ff:**

- Complete quality documentation
- Complete toxicology and pharmacology documentation
  - including mutagenicity, carcinogenicity and reproductive toxicity aspects (Chap. 7.3.2) → **AMES TEST**
- Complete clinical documentation – usually in the form of bibliographical documentation –
  - Evidence that the herbal active substance has been used medically in the proposed indication and use for at least 10 years in a medicinal product in the EU/EFTA.
  - Here the evidence of efficacy and/or safety may additionally refer to recognised monographs (HMPC, ESCOP, WHO, etc.).
  - A literature search must not be older than 12 months
  - A Clinical Safety Summary (Module 2.7.4) is mandatory (PSUR data, exposure to patient population)

The Clinical Safety Summary must present safety data from the clinical trials and/or tolerability data from post-marketing experience (PSUR)

Herbal medicinal products with traditional use

- **Art. 14 para. 1 let. c^{bis} TPA** describes, in conjunction with Art. 8-11 KPTPO, the option of simplified bibliographical documentation of the plausibility of the efficacy and safety of herbal medicinal products with traditional use.
- **Precondition:** The proposed herbal medicinal product – or a comparable medicinal product (comparator product) – has been used medically for at least 30 years, and for at least 15 years in an EU/EFTA country. **(Protection of the "treasury of medicinal products")**
  Note: The emphasis in traditional use is on the specific herbal comparator medicinal product and not, as is the case in WEU, on the herbal active substance. There must have been no refinements or major changes (e.g. active substance composition, dispensing category, changes of indication, relevant change of pharmaceutical form) to the comparator product during the 30 years.
- **No relevant safety signals/risks** have been documented during the 30 years of medical use (see Guidance document "Authorisation of phytotherapeutic products HMV4")
- The procedure is only available for **non-prescription medicinal products**
  This means that this procedure cannot be used for medicinal products for injection or List B medicinal products
- **The wording of the indication**: must contain traditional use and must be comprehensible to lay persons.
  Verbatim: "Use of this medicinal product in the specified indication is based entirely on traditional practice."

Herbal medicinal products with traditional use

Requirements → **Guidance document Authorisation of herbal medicinal products HMV4, Chapter 7.1.3 ff:**

- Complete quality documentation
- Complete toxicology and pharmacology documentation
  - including mutagenicity, carcinogenicity and reproductive toxicity aspects (Chap. 7.3.2) → **AMES TEST**
- Complete clinical documentation – usually in the form of bibliographic data/supplementary monographs –
  - instead of documenting efficacy by submitting clinical trials, emphasis is placed on evidence of the plausibility of 30 years of medical use of a specific (comparator) medicinal product.
  - It is therefore mandatory to name a specific comparator medicinal product and to demonstrate/discuss (SmPC, rote Liste (Germany), sales figures, foreign authorisation decision, etc.) that is has been used medically (or was “registered”/”authorised”) for at least 30 years in the proposed indication/dosage, and for at least 15 years during this period in an EU/EFTA country.
  - Reference may be made to recognised monographs containing specific details of traditional use (HMPC, ESCOP, WHO, etc.).
  - Tolerability and safety on the basis of post-marketing experience with the comparator product (including sales figures and number of patients exposed) in the Clinical Safety Summary (Module 2.7.4)

Which of the procedures in Art. 14 para. 1 let. c^{bis} TPA is suitable?

It depends on how well-known the herbal active substance, the pharmaceutical form and the indication are!

- Herbal active substance in a comparable medicinal product authorised in **Switzerland** with the same indication
  → **Herbal medicinal product with "known active substance"**
- Herbal active substance has been authorised in the EU/EFTA for >10 years (known or new active substance in Switzerland)
  → **Herbal medicinal product with "well-established use"**
- Herbal medicinal product used medically for >30 years, including >15 years in the EU/EFTA (known or new active substance in Switzerland)
  → **Herbal medicinal product with "traditional use"**
- New herbal active substance (including non-comparable extracts), or new indication for a known active substance, or non-comparable pharmaceutical form, etc.
  → **Ordinary new authorisation** (or documentation of the new aspects by analogy with an ordinary new authorisation) → no simplifications specific to herbal medicinal products

Art. 14 para. 1 letter a^{bis} TPA

- Use of the procedure has been described in detail in Art. 14a para. 1 let. a TPA and in Art. 17a and 17b TPLO **since 1 January 2019**.
- **Precondition:** Reference to a specific foreign comparator medicinal product, the active substance in which has been authorised in an EU/EFTA country for at least 10 years **and** which is comparable in terms of indication, dosage and method of administration.
- The **procedure is not specific to herbal medicinal products**, it can basically be used for all medicinal product categories.
- Efficacy and safety are only **summarily reviewed** by Swissmedic.
- The **authorisation fee** is reduced (70%).

Art. 14 para. 1 letter a^{bis} TPA

Requirements → **Guidance document Authorisation according to Art. 14 para. 1 let. a$^{bis-quater}$ TPA HMV4, Chapter 6 ff:**

- Complete quality documentation → **Swissmedic reviews in full.**
- **Complete bibliographical documentation** of pharmacological, toxicological and clinical testing – including the corresponding expert reports by analogy with simplified authorisation according to Art. 14 para 1 let. c^{bis} → **Swissmedic reviews only summarily.**
- Evidence of EU/EFTA authorisation, e.g. **authorisation decision from a foreign country**.
- It is mandatory to use the medicinal product information texts of the specific named foreign comparator product.
- Swissmedic reserves the right to make safety-relevant modifications to the medicinal product information.

The efficacy and safety of NAME OF THE MEDICINAL PRODUCT X have only been summarily reviewed by Swissmedic. The authorisation of NAME OF THE MEDICINAL PRODUCT X is based on NAME OF THE MEDICINAL PRODUCT Y, date of revision of the text MONTH YYYY, which contains the same active substance(s) and is authorised in COUNTRY Z.

Art. 14 para. 1 letter a^{bis} TPA

- Throughout the period in which the authorisation is valid, it must be possible for all internationally recorded safety signals concerning the named comparator medicinal product to be submitted promptly and unprompted (Art. 14a para. 2 let. a TPA). **Summary: Only possible for companies operating internationally.**

Variation applications

- Indication, dosage, warnings, side effects, dispensing category, etc. CANNOT be adapted independently for Switzerland → **dead end**
- Variations of the Swiss medicinal product information that are based on an adaptation of the medicinal product information for the foreign comparator product must be proposed using an A.100 type IB variation (NOT C.I.x), by analogy with co-marketing.

- **Expiry/discontinuation of a foreign authorisation**
  Must be reported and may lead to the expiration of the authorisation in Switzerland

Art. 14 para. 1 letter a^{ter} TPA

- Use is detailed in Art. 14a para. 1 let. b TPA and in Art. 17c TPLO
- *Prescription-free medicinal products used medically for 30 years (including 15 years in the EU/EFTA)*
- **See the Guidance document Authorisation in accordance with Art. 14 para. 1 let. a$^{bis-quater}$ TPA HMV4, Chapter 7 ff**
  → Safety and efficacy are NOT reviewed

Art. 14 para. 1 letter a^{quater} TPA

- Use is detailed in Art. 14a para. 1 let. c TPA and in Art. 17d TPLO
- *Medicinal product authorised in a canton for 15 years*
- **See the Guidance document Authorisation in accordance with Art. 14 para. 1 let. a$^{bis-quater}$ TPA HMV4, Chapter 8 ff**

→ Safety and efficacy are NOT reviewed

Status of applications: To date no authorisation according to Art. 14 para. 1 a$^{bis-quater}$ TPA has been granted for herbal medicinal products.

Art. 14 para. 1 let. a^{bis} TPA for herbal medicinal products?

- A simplified authorisation procedure has been available for herbal medicinal products for **many** years (→ Art. 14 para. 1 let. c^{bis} TPA) → For herbals "a^{bis}" does not represent an innovation/advantage compared with "c^{bis}"
- Simplified authorisation procedures according to the relatively new Art. 14 para. 1 let. a$^{bis-quater}$ TPA are **NOT specific to herbal medicinal products** (e.g. also for chemical synthetic MP)
- According to Art. 14a para. 2 let. a TPA, the holder of an authorisation for a medicinal product authorised under Art. 14 para. 1 let. a^{bis} TPA is required to submit all the safety signals concerning the product recorded internationally **throughout** the duration of the **authorisation/life-cycle** of the product. → This simplified authorisation procedure is therefore effectively available **only to internationally operating companies** (dependence on a foreign country/parent company?)
- **Dependence of the medicinal product information:** Indication, dosage, warnings, side effects, dispensing category, etc. CANNOT be adapted specifically for Switzerland. It is mandatory to adopt the European texts VERBATIM (with the exception of safety-relevant modifications by Swissmedic).
- All EU modifications must be adopted in Switzerland → **Dependence on the EU**
- Problem: This means that the current state of knowledge is not always reflected.