swissmedic

Guidance document
Criteria Annexes 4–10 KPTPO

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1 Terms, definitions, abbreviations

1.1 Definitions and terms

Notification procedure	Authorisation of medicinal products on the basis of a notification (Chap. 7 KPTPO)

1.2 Abbreviations

Art.	Article
GLP	Good Laboratory Practice
HMPC	Committee on Herbal Medicinal Products
KPTPO	Ordinance of the Swiss Agency for Therapeutic Products of 7 September 2018 on the Simplified Licensing of Complementary and Phytotherapeutic Products (SR 812.212.24)
HAS List	List of homeopathic and anthroposophic substances
Let.	Letter
MT	Mother tincture
No.	Number
Para.	Paragraph
Ph. Eur.	European Pharmacopoeia
Ph. Helv.	Pharmacopoeia Helvetica
p.i.	per iniectionem (by injection)
SC List	List of Schüssler salts
TAS List	List of traditional Asian substances

2 Introduction

Among other things, Annexes 4 to 10 KPTPO provide the basis for both the notification procedures referred to in KPTPO and some of the simplified medicinal product authorisation procedures referred to in KPTPO.

3 Objective

This guidance document describes the requirements that a substance (or standard work in the case of Annex 9 KPTPO) must fulfil to qualify for inclusion in or addition to the lists in Annexes 4 to 10 KPTPO.

4 Scope

Appropriate documentation to support or provide evidence for the addition or updating of a substance or the addition of a standard work can be submitted at any time via the Complementary and Herbal Medicines department (Anhaenge_KPAV@swissmedic.ch).

5 Description

5.1 List criteria

The lists in Annexes 4 to 10 KPTPO are regularly reviewed to ensure they reflect current scientific knowledge (e.g. new toxicological findings) and findings in the school of therapy in question and are updated as necessary. In the course of its review, Swissmedic will consider any modifications proposed by external sources that are supported by authoritative documentation.

Documents to support the addition of a substance to one of the lists or the updating of its entry

a. Literature (extracts)

Where literature is cited, the citations must be taken from published specialist literature such as pharmacopoeias, text books or journal articles.

If the substance is the subject of a monograph in the Pharmacopoeia or another pharmacopoeia recognised by the Ordinance of the Swiss Agency for Therapeutic Products on the issuing of the Pharmacopoeia and recognition of other pharmacopoeias, a reference to the relevant monograph will be sufficient.

In all other cases, the relevant pages, title page and publishing details page of the work in question must be provided as a minimum requirement. Paragraphs that are specifically cited must be marked. Simple literature references, references to websites and transcripts are not sufficient.

Applicants may be required to provide additional information to demonstrate that the cited literature is genuinely specialist in nature and has been published by a specialist publishing house. Literature will be recognised as specialist in nature if the traditional knowledge, the experience acquired over a protracted period of years and the established application of that knowledge and experience through to the present day and in accordance with the relevant therapeutic principles have been handed down in traceable fashion. As part of this process, authors, publishing house, year, number of issues, etc. will be assessed for the purposes of judging whether the literature is an established and known work in the relevant school of therapy. Secondary literature can only be recognised if it is a reappraisal or treatment (which may be historical criticism) of primary sources and includes the mandatory citation of associated literature references.

Literature not published by a specialist publishing house but, for example, by a non-fiction publisher, private publisher or company will not be recognised.

b. Trials

Where trials are cited – to cover toxicological aspects, for example – they must be submitted and their results evaluated in such a way that they are suitable for an audit should the need arise.

c. Other documents

Depending on the list to be updated, other documents may be suitable for submission to back up the reasoning presented. These should be comparable in scope to literature extracts and be prepared in the same way.

5.2 Annexes 4 to 10 KPTPO

5.2.1 Tea drugs list (Annex 4 KPTPO)

The tea drugs list comprises herbal drugs that can be authorised on the basis of a notification as individual teas in combination with the health claim formulated in the list.

Herbal drugs in the tea drugs list have a pharmacopoeia monograph. The health claim associated with the drug in question must fulfil the requirements for assigning the individual tea to dispensing category E.

5.2.1.1 Requirements pertaining to herbal drugs on the tea drugs list

For any herbal drug on the tea drugs list, a reference to the underlying Ph. Eur. or Ph. Helv. monograph must be provided.

The health claim associated with the herbal drug is intended for use in adults only, and must be adequately backed up.

Where an HMPC monograph – for example – exists for a drug submitted for addition to the list, the health claim must refer to this where possible. If there is no relevant monograph, the health claim chosen must be adequately backed up by specialist literature.
The reasons for the dosage associated with the drug must be stated and proof of the toxicological innocuousness of the dosage must be provided.

5.2.2 "Lozenges" list (Annex 5 KPTPO)

In addition to synthetic substances, the "lozenges" list includes herbal drugs and essential oils. Substances on the "lozenges" list have a known toxicological profile and are considered innocuous when used at the normal dosages. In combination with the permissible health claims (also specified in Annex 5 KPTPO), cough and throat sweets and pastilles can be authorised in dispensing category E on the basis of a notification.

5.2.2.1 Requirements pertaining to herbal drugs and essential oils on the "lozenges" list

For any herbal drug or essential oil on the "lozenges" list, a reference to the underlying Ph. Eur. or Ph. Helv. monograph must be provided.

For herbal drugs – and thus also for preparations of them – comprehensive evidence from literature sources must be provided to demonstrate that use in connection with the health claims specified in the list is customary and, above all, innocuous.

Where an essential oil is to be added to the list, a minimum content per unit must be specified. This must be chosen in such a way that the indication is justified, and this must be demonstrated by literature.

Where an essential oil is to be added to the "lozenges" list, toxicity issues, particularly genotoxicity and reproductive toxicity, must be considered. This can be done experimentally (in compliance with GLP) or bibliographically. Care must be taken to ensure that the data were obtained with an essential oil that is qualitatively comparable to the one submitted for addition.

5.2.3 HAS list (Annex 6 KPTPO)

The HAS list contains the substances for which Swissmedic has proof of familiarity in homeopathy or anthroposophic medicine. The “reduced dossier without documents on safety and innocuousness” column gives the potencies or concentrations from which there is no requirement to submit safety or innocuousness documents relating to authorisation with a reduced dossier under Art. 25 para. 1 KPTPO. The “Notification procedure as of” columns give the potencies or concentrations from which the relevant medicinal products can be notified to Swissmedic for authorisation provided they meet the conditions set out in Art. 27 KPTPO.

Furthermore, the HAS list defines the scope of documents required for the authorisation of spagyric medicinal products (Art. 39 para. 1 let. d KPTPO).

5.2.3.1 Requirements pertaining to substances and potencies/dilutions on the HAS list

Documentation must be provided to demonstrate the familiarity of every new substance in homeopathy or anthroposophic medicine in accordance with Annex 3 no. 2 KPTPO. Additional designations for the same substance can be used as a synonym if necessary.

The starting material must be clearly defined in the specialist publications or other documents used as evidence.

If there is only evidence for familiarity but no documents on safety, the substance can still generally be added to the HAS list for oral administration from a potency of D12/C6.

For lower potencies or different routes of administration (e.g. p.i.), further documents must be provided:

- A potency of less than D12/C6, a new substance or a change to a lower potency (or higher concentration) for a substance that is already on the HAS list requires documents as specified in Annex 3 no. 3 and 4 KPTPO that demonstrate the safety, innocuousness and tolerability of the requested potency in homeopathy or anthroposophic medicine. These documents must relate to the route of administration (oral, external or p.i.) and reflect current scientific knowledge at the time in question. They could include the current edition of a toxicological text book, for example. The recommended potencies given in older homeopathic specialist literature are not adequate evidence of safety and innocuousness.
- For routes of administration other than oral (p.i., for example), evidence must be available that these routes of administration are customary in homeopathy or anthroposophic medicine for the substance in question.

In certain cases, comparability with a substance already on the HAS list can be deduced. However, this is only possible if the substances are genuinely comparable in terms of composition (e.g. salts of the same metal) or in terms of constituent spectrum (type and quantity) and there is no additional risk arising from the particular nature of the substance (e.g. certain salt or compound).

If other substances already on the HAS list are cited for a new potency, the substance in question must be specified and reasons why it is considered comparable in terms of safety and innocuousness must be provided on the basis of the substance composition.

5.2.4 SC list (Annex 7 KPTPO)

The SC list contains the substances and potencies used in Schüssler therapy (Art. 4 para. 2 let. h KPTPO). All substances and potencies used in accordance with the recognised literature on Schüssler therapy are on the SC list.

5.2.4.1 Requirements pertaining to substances on the SC list

Evidence from the specialist literature must be provided for each substance to prove that it belongs to the closed system of Schüssler therapy. The SC list specifies the potencies defined in the therapy.

5.2.5 Gemmotherapy list (Annex 8 KPTPO)

The gemmotherapy list in Annex 8 KPTPO contains the starting materials for medicinal products for gemmotherapy with and without an indication (see Art. 27 let. b and Art. 35 para. 2 KPTPO).

The gemmotherapy list comprises substances and potencies that are established and customary in gemmotherapy and also suitable for the notification procedure from a toxicological perspective.

5.2.5.1 Requirements pertaining to substances and/or additional potencies on the gemmotherapy list

Documentary evidence demonstrating familiarity, safety and innocuousness in gemmotherapy must be provided for substances on the gemmotherapy list.

Familiarity in gemmotherapy must be proven by appropriate specialist literature and by means of an appropriately long period of at least 30 years (as for homeopathy, spagyrics, etc., Annex 3 no. 2.1 let. c and d KPTPO). This must be done using specialist literature or company documents proving manufacture and use for at least 30 years. The starting material must be clearly defined in the documents. If a medicinal product is authorised as a homeopathic medicinal product containing a substance from the HAS list as a glycerine extract, this does not constitute proof of familiarity in gemmotherapy.

Safety and innocuousness may be demonstrated by reference to the substance listed in the HAS list provided it can also be demonstrated that the plant material in the HAS list and gemmotherapy list is qualitatively and quantitatively comparable in terms of safety-relevant constituents.

A demonstration of familiarity and safety in gemmotherapy is required for each individual substance. For this reason, it is not sufficient to simply list substances in the specialist literature.

The notification procedure only makes allowance for potencies TM and D1 and for the oral pharmaceutical forms of drops or sprays, since adequate proof to support use in gemmotherapy does not currently exist for other potencies and pharmaceutical forms.

5.2.6 List of standard works (Annex 9 KPTPO)

The list of standard works comprises literature references that contain traditional and established classic formulations for the authorisation of fixed medicinal product combinations from Asian medicine without an indication in the simplified procedure and on the basis of a notification.

5.2.6.1 Requirements pertaining to works on the list of standard works

For a work to be included in the list of standard works, proof must have been provided that the work is known and established in the school of Asian therapy in question and that it contains traditional or classic formulations that have been handed down in the school of therapy in question for several decades (so that the use, safety and innocuousness of the formulations can be considered to have been empirically proven). The work in question must also contain information on contraindications, adverse drug reactions and dosage recommendations.

The standard work in question must be available and must not be out of print.

5.2.7 TAS list (Annex 10 KPTPO)

The TAS list contains substances that are established and customary in the schools of Asian therapy defined in KPTPO. The substances listed are crude drugs, i.e. substances of plant origin and substances of mineral origin. They are used as starting materials that are worked up into active substances and ready-to-use medicinal products. The list includes both prepared and unprepared substances. None of the listed substances is of animal or human origin.

5.2.7.1 Requirements pertaining to substances on the TAS list

The requirements are prescribed in Art. 32 KPTPO. If the substance is the subject of a monograph in the Pharmacopoeia or another pharmacopoeia recognised by the Ordinance of the Swiss Agency for Therapeutic Products on the issuing of the Pharmacopoeia and recognition of other pharmacopoeias, a reference to the relevant monograph will be sufficient.

However, if a monograph from a different pharmacopoeia is to be used as a quality reference for a substance, the monograph must be available in English or an official language of Switzerland and submitted to Swissmedic. The pharmacopoeia monograph in question must satisfy the requirements of the Pharmacopoeia. The content and scope must comply with the Ph. Eur. monograph *Herbal Drugs / Plantae medicinales*. In particular, the monograph cited for a substance must include tests for the identity, purity and, where necessary, content of relevant constituents.

Evidence of the customary use of a new substance – and thus also of its use over a protracted number of years – must be provided. The traditional indications must be documented and appropriately demonstrated by literature.

The necessary information about a new substance must still include a customary dosage recommendation.

Use of the substance on its own or in combination must have been documented.

Contraindications, possible adverse drug reactions and, where applicable, restrictions on use referred to in the principles of the school of Asian therapy in question must also have been documented.

In addition, up-to-date toxicology data and data on constituents or groups of constituents that may be relevant from a toxicological perspective must be submitted. Consideration must be given to whether possible toxic effects can be prevented by restricting the dosage (maximum dosage) or duration of dosage (preventing overdosage). The aim should be to provide evidence of the innocuousness of the substance to be added to the TAS list.

Full, traceable referencing is required for the aspects set out above. Ideally, several different authors should be cited as sources to ensure that the application can be evaluated in consolidated and adequately documented form.

Change history

Version	Change	sig
1.2	New layout, no content adjustments to the previous version.	dei
1.1	List of abbreviations streamlined	stb, lap
1.0	New document	spm, lap, heb, moj