Guidance document
Authorisation of antidote

Identification number:	ZL000_00_031
Version:	1.2
Valid from:	23.05.2023

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1 Terms, definitions, abbreviations

1.1 Definitions

1.1.1 Important and rarely used antidotes

Important and rarely used antidotes are preparations for the treatment of incidents of poisoning

a) the substances and dosages of which are mentioned in the tox info suisse (formerly STIZ: Swiss toxicology information centre) or Armed Forces Pharmacy lists
b) that are intended for the type of use specified in the documents prepared by the bodies mentioned under a) above (e.g. indications and dosage) and
c) that do not affect more than five in 10,000 people in Switzerland annually or which are intended for use in crisis situations (e.g. armed conflict, attack or nuclear accident)

To qualify as an important and rarely used antidote, a medicinal product must fulfil all three criteria above (a to c).

1.2 Abbreviations

AApot	Swiss Armed Forces Pharmacy
ADR	Adverse Drug Reaction
AW	Instruction (from German *Anweisung*)
CEP	Certificate of suitability to the monographs of the European Pharmacopoeia
CTD	Common Technical Document for the Registration of Pharmaceuticals for Human Use
DMF	Drug Master File
EDQM	European Directorate for the Quality of Medicines and HealthCare
FeeO-Swissmedic	Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products of 14 September 2018 (SR 812.214.5)
FOPH	Federal Office of Public Health
GMP	Good Manufacturing Practice
GSASA	Swiss Association of Public Health Administration and Hospital Pharmacists
NAS	New Active Substance
NTA	Notice to Applicants
Ph. Eur.	European Pharmacopoeia
PMS	Post Marketing Surveillance
TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, SR 812.21)
TPLO	Ordinance of the Swiss Agency for Therapeutic Products of 22 June 2006 on the Simplified Licensing of Therapeutic Products and the Authorisation of Therapeutic Products by the Notification Procedure (SR 812.212.23)
TPLRO	Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (Therapeutic Products Licensing Requirements Ordinance, SR 812.212.22)

2 Introduction

This document describes the conditions that applications for authorisation of important and rarely used antidotes have to fulfil in order to qualify for the simplified procedure and defines the associated requirements. Since this is a guidance document aimed at administrative bodies, it does not directly specify the rights and obligations of private individuals. It provides Swissmedic first and foremost with a resource for applying the legal provisions governing authorisation of rarely used antidotes in a uniform and equitable manner. The intention of publishing this Instruction is to show private individuals what requirements have be fulfilled under Swissmedic practice to ensure that corresponding authorisation applications are processed as quickly and efficiently as possible.

2.1 Legal framework

The simplified procedure for the authorisation of important and rarely used antidotes is governed by the:
Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, TPA):

- Art. 10 Conditions for granting a marketing authorisation
- Art. 14 Simplified authorisation procedures

Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (Therapeutic Products Licensing Requirements Ordinance, TPLRO):

- Art. 3 Documentation of analytical, chemical and pharmaceutical investigations
- Art. 12 Information and text on containers and packaging materials

Ordinance of the Swiss Agency for Therapeutic Products of 22 June 2006 on the Simplified Licensing of Therapeutic Products and the Licensing of Therapeutic Products by the Notification Procedure (TPLO):

- Art. 27a Radiopharmaceuticals and antidotes in general medical use

3 Objective

In its bulletin, the Federal Office of Public Health (FOPH) publishes an annual list for public pharmacies, hospitals and the regional antidote centres specifying a range of antidotes. The list is produced and updated by the antidotes working group of tox info suisse and the Swiss Association of Public Health Administration and Hospital Pharmacists (GSASA). The Armed Forces Pharmacy (AApot) also keeps a range of antidotes for crisis situations. Many important and rarely used antidotes do not have marketing authorisation for Switzerland. To ensure cost-effective supply of these medicinal products at all times, Swissmedic has decided to simplify the authorisation conditions to which they are subject.

4 Scope

The Instruction applies to the authorisation of important and rarely used antidotes (Sec. 1.1.1) and their extensions.
Swissmedic will also apply this Instruction to important antidotes that are used frequently but are difficult to procure – i.e. non-specific antidotes such as activated charcoal and economically unviable preparations – if this is the only way to guarantee supply to the Swiss market.
This Instruction does not apply to frequently used antidotes such as naloxone or flumazenil or to rarely used antidotes that do not appear on the tox info suisse or AApot lists or whose recommended uses diverge from those specified in the lists mentioned (e.g. other indications). In such cases the standard authorisation procedure, which is based on appropriate technical, preclinical and clinical documentation, must be followed. Swissmedic reserves the right to allow simplified authorisation on the basis of suitable bibliographic documentation.

5 Description

5.1 Fees

It is overwhelmingly in the public interest to waive fees for the authorisation of important and rarely used antidotes. Accordingly, Swissmedic will not charge any fees for applications for authorisation of these antidotes in accordance with Article 12 of the Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products (FeeO-Swissmedic).

5.2 Review principles

5.2.1 Acknowledgement of “well established use” for important and rarely used antidotes

Under Article 27a TPLO, any antidote containing an active substance not contained in any medicinal product authorised by Swissmedic now or in the past is eligible for simplified authorisation if the active substance has been used for the requested indication and administration route for at least 10 years and its safety and efficacy are generally acknowledged on the basis of accumulated experience in use (Art. 27a para. 1. let. a TPLO) or if the preparation is, or was, authorised for the requested indication and administration route in a country with a comparable regulatory system for medicinal products, or if the preparation has been approved by the competent foreign authority or by Swissmedic for the treatment of specific patients (Art. 27a para. 1. let. b TPLO). Antidotes intended for addition to the Armed Forces Pharmacy can be authorised under the simplified procedure if they meet the requirement set out in paragraph 1 letter a of TPLO (Art. 27a, para. 2).
Swissmedic will waive the requirement for preclinical and clinical documentation – including documentation in bibliographical form – for rarely used antidotes that satisfy the criteria of the tox info suisse or AApot list.
Applications for authorisation should be based on complete quality documentation. To compensate for the fact that preclinical and clinical trial data does not have to be submitted, conditions (Sec. 8) require adverse drug reactions to be monitored more strictly as part of documentation of incidents of poisoning.

5.2.2 Dispensing category

The preparations should always be assigned to dispensing category A. Dispensing and use should be restricted to clearly defined situations under the supervision of competent physicians by means of a corresponding warning on the packaging (“ANTIDOTE: only to be used in emergencies under supervision of a doctor. Indication to be ascertained by prescribing physician.”)
In justified exceptions, specifically if safety in use is guaranteed and there is no other way of ensuring the necessary rapid supply, antidotes can also be classified in dispensing category D. This applies to non-specific antidotes such as activated charcoal, for example.

5.3 Requirements for documents to be submitted

5.3.1 Administrative documents (Module 1)

The formal requirements regarding applications in general and the formal requirements for Module 1 and the cover letter are laid down in the guidance document *Formal requirements HMV4* and in the associated table, *Overview of documents to be submitted*.

5.3.2 Quality overall summary (Module 2, section 2.3)

A summary of all the data from Module 3 must be submitted.

5.3.3 Analytical, chemical and pharmaceutical documentation (Module 3)

5.3.3.1 Active substance quality.

Full quality documentation (complete Module 3.2.S or Drug Master File (DMF)) with corresponding Letter of Access should be submitted, or, if available, a Certificate of Suitability (CEP) from the EDQM and a GMP certificate for the manufacturing site.
Active substances have to meet pharmacopoeia requirements, particularly those of General Monograph 2034 “Substances for pharmaceutical use” of Ph. Eur. (see also Art. 8 TPA). The right to make exceptions in accordance with paragraph 4 is reserved.
Non-pharmaceutical quality active substances can be employed if they are not used as a medication. Such active substances should be used in the highest possible commercially available purity. The documentation to be submitted should include at least the test specification, a brief description of the key test methods (e.g. identity and assay), the analytical certificate for at least one representative batch with quantitative analytical results, a brief description of the manufacturing process and an assessment of possible critical impurities. If there are any safety concerns, e.g. if potentially critical impurities are present, toxicological data must be submitted in addition to the assessment mentioned above.

If no GMP certificate is available for an active substance because it is produced for use in foodstuffs, cosmetics or as an excipient, for example, and not as an active substance for medicinal products, the applicant's Responsible Person must additionally carry out an evaluation of the production process for the "non-typically pharmaceutical" active substance. This evaluation should discuss the extent to which GMP rules are respected, and provide a risk-centred basis for justifying the lack of a GMP certificate. The applicant's Responsible Person must sign and date the risk-based justification (see also Information sheet *GMP compliance by foreign manufacturers of active pharmaceutical ingredients and/or ready-to-use medicinal products*).

5.3.3.2 Finished product quality

The finished product must be manufactured and tested in accordance with the rules of Good Manufacturing Practice (see also Art. 7 TPA). The applicable pharmacopoeia monographs must be observed (for example the monograph on pharmaceutical forms; see also Art. 8 TPA). Any deviations must be justified.

5.4 Conditions

5.4.1 General

To compensate for the fact that applications for authorisation of antidotes are exempt from the obligation to submit preclinical and clinical trial data, adverse reactions must be intensively monitored every time the antidote is administered, and incidents of poisoning must be documented accordingly.

5.4.2 Pharmacovigilance

The authorisation holder must ensure that:

a) every pack of antidote contains a copy of the pharmacovigilance form and
b) whenever an antidote is delivered, dispensing outlets are requested to notify tox info suisse every time they dispense the antidote, naming the preparation and recipient.

This condition does not apply to antidotes with a non-specific effect (e.g. activated charcoal).

Change history

Version	Change	sig
1.2	New layout, no content adjustments to the previous version.	dei
1.1	Formal adjustments to the header and footer No content adjustments to the previous version.	dei
1.0	Implementation of TPO4	dei