Guidance document
Orphan Drug

Identification number:	ZL100_00_002
Version:	3.2
Valid from:	01.05.2023

List of contents

1 Terms, definitions, abbreviations

1.1 Definitions

1.1.1 Important medicinal product for rare diseases (Orphan Drug)

A human medicinal product which has been demonstrated to:

- identify, prevent or treat a life-threatening or chronic debilitating disease which, at the time the application is submitted, affects no more than 5 in 10,000 people in Switzerland (Art. 4 para. 1 letter a^{decies} no. 1 TPA)
  or
- is a medicinal product / contains an active pharmaceutical ingredient which has been recognised as an important medicinal product for rare diseases in another country with equivalent medicinal product control as stipulated in Art. 13 TPA (Art. 4 para. 1 letter a^{decies} no. 2 TPA).

1.2 Abbreviations

FeeO-Swissmedic	Ordinance on the Fees charged by the Swiss Agency for Therapeutic Products of 14 September 2018 (SR 812.214.5)
LoQ	List of Questions
NAS	New Active Substance
ODS	Orphan Drug Status
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 Licensing of Therapeutic Products by the Notification Procedure (SR 812.212.23)

2 Introduction

In accordance with Art. 14 para. 1 letter f TPA, important medicinal products for rare diseases are eligible for the simplified authorisation procedure. The relevant provisions for implementation are laid down in the TPLO. A distinction is made therein between recognition of the status as an important medicinal product for rare diseases (Art. 4 - 7 TPLO) and the authorisation of a medicinal product that has been granted ODS by Swissmedic (Art. 24 - 26 TPLO).

3 Objective

Swissmedic uses this guidance document first and foremost as a resource for applying the legal provisions in a uniform and equitable manner. For applicants, the document is intended to make clear the specific requirements that must be fulfilled so that corresponding applications can be processed by Swissmedic as quickly and efficiently as possible.

Section 6.3 of the guidance document describes various aspects relating to ODS (requirements relating to an application for ODS, recognition, transfer and withdrawal of ODS, etc.); section 6.4 contains information about applications for authorisation of medicinal products with ODS to treat rare diseases.

4 Scope

The explanations in this guidance document apply only to human medicinal products.

5 Description

5.1 Time limits

The processing times stated in the guidance document *Time limits for authorisation applications HMV4* apply both to applications for ODS and associated applications for authorisation of medicinal products.

Applications for authorisation of medicinal products with ODS will be given priority.

5.2 Fees

The fees stated in FeeO-Swissmedic. The flat-rate fees for the new authorisation application of medicinal products with orphan drug status are waived in accordance with Art. 9 letter a FeeO-Swissmedic.

5.3 Application for recognition of ODS (Art. 4 – 7 TPLO)

5.3.1 Principle

A human medicinal product is granted the status of important medicinal product for rare diseases (Orphan Drug) on application if the applicant can demonstrate that the medicinal product meets the criteria in accordance with Art. 4 para. 1 letter a^{decies} TPA (Art. 4 TPLO).

The criterion for the rarity of the disease always applies to the disease in its entirety, including all stages of it, and not to an isolated stage in the course of the disease or to a sub-group defined by molecular genetic markers, unless the subgroup is so limited as a result of another medical condition that it is recognised and classified as a separate disease. A sub-group (e.g. Her-2 positive breast cancer) does not qualify as an independent, rare disease; neither, for example, does the restriction of an indication to second-line treatment.

5.3.2 Formal aspects, documents to be submitted and examination

Unlike applications for authorisation, applicants do not have to have a manufacturing, import or wholesale trading licence at the time they submit their application for recognition of ODS. Neither do they have to have registered offices in Switzerland; in such cases an invoice address as well as a Swiss address for postal deliveries must be provided.

The application for recognition of ODS must be accompanied by scientific documentation demonstrating that the medicinal product fulfils the criteria as laid down in Art. 4 para. 1 and 2 TPLO. If the applicant is applying for recognition of ODS on the basis of recognition in a country with comparable medicinal product control as stipulated in Art. 13 TPA, all the administrative and scientific documentation submitted to the foreign authority in order to gain recognition of ODS must be submitted to this authority, as must a copy of the official decision by the foreign medicinal products authority granting the *Orphan Drug Designation*. If this status was granted in more than one country with a comparable control system for medicinal products, Swissmedic requires the status decisions of all the authorities concerned. However, the administrative and scientific documentation only need be submitted for the reference authority. In addition, documentary evidence must be provided that the medicinal product that is the subject of the application for ODS is identical to (or contains the same active substance as) the medicinal product (or active substance) that is recognised abroad as an orphan drug.

5.3.3 Timing of the submission of the application for ODS

The applicant may decide whether to submit the application for recognition of ODS either in advance of the authorisation application, simultaneously, or after the authorisation has been granted (Art. 4 para. 3 TPLO). The application for ODS is processed independently of the authorisation application. Since the processing times for the application for ODS are shorter than those for processing the authorisation, the status may be recognised before authorisation is granted.

5.3.4 ODS and indication extensions

Additional indications for medicinal products with/without ODS can be authorised in the following situations and subject to the rules described:

5.3.4.1 Medicinal product with ODS

Case 1):
The disease underlying the new additional indication fulfils the criteria for ODS in accordance with Art. 4 para. 1 and 2 TPLO. In addition to the application for recognition of ODS for the disease underlying the additional indication, an application for an indication extension (major variation, type II) must also be submitted. The name of the medicinal product and the authorisation number can stay the same. The medicinal product retains ODS.

Case 2):
The disease underlying the new additional indication **does not** fulfil the criteria for ODS in accordance with Art.4 para. 1 and 2 TPLO. Two options are available:

a) The new indication (not uncommon) is added to the existing medicinal product and the medicinal product loses ODS or
b) The medicinal product with the indication(s) which has/have already been authorised (uncommon) retains ODS and a new, separate medicinal product with the new indication (not uncommon) is authorised independently (without ODS) as a KAS with innovation.

5.3.4.2 Medicinal product without ODS

If an application is to be made for a new, additional indication for a rare disease for an already authorised medicinal product **without ODS**, an application for recognition of ODS must be submitted for the new indication. The authorisation holder must submit an application for authorisation of a medicinal product (KAS) with innovation that covers solely the indication for the rare disease (Art. 24 para.2 TPLO). This product will be given a new name, a new authorisation number and the corresponding document protection.

5.3.5 Authorisation extensions

For a new dosage form of an already authorised medicinal product with ODS, submission of a separate application for recognition of ODS is not required. The cover letter accompanying the authorisation application for the new dosage form should, however, refer to the ODS of the already authorised dosage form.

5.3.6 Grant of status; notification obligation

Swissmedic grants ODS if the requirements stipulated in Art. 4 TPLO are fulfilled. That status may be subject to restrictions and conditions. If a medicinal product has been granted ODS on the basis of this status having been granted abroad, the applicant or the authorisation holder must submit to Swissmedic all the decisions relating to this status issued by all the countries with comparable medicinal product control as stipulated in Art. 13 TPA that have granted ODS (Article 5 para. 2 TPLO). Swissmedic must be notified immediately of any changes to the status abroad (e.g. impending withdrawal, voluntary discontinuation or initiation of a review procedure).

5.3.7 Withdrawal of status

The ODS can be withdrawn on application or *ex officio*. If the ODS is withdrawn at the request of the applicant or authorisation holder (Art. 6 letter a TPLO), the procedure will be carried out analogously to the procedure for discontinuation of the authorisation (cf. guidance document *Renewal and discontinuation of authorisation on change of status (main authorisation/export licence) HMV4)*. If, however, the ODS is to be withdrawn because the criteria in accordance with Art. 4 TPLO are no longer fulfilled (Art. 6 letter b TPLO), Swissmedic will perform a review.

Swissmedic will withdraw the ODS if it cannot be demonstrated on request that the sum of all the authorised and requested indications with ODS for the same active substance within the same medical condition, including all the stages of the disease, affects a maximum of five per ten thousand people in Switzerland (Art. 6 letter c and d TPLO).

5.3.8 Transfer of status

In order to transfer the ODS to another company, the future status holder must submit a written application to Swissmedic. The application must mention the current and the new ODS holder (applicants). In addition, the following two confirmations signed by authorised signatories must be submitted:

- a declaration of assignment bearing the legally valid signature of the previous status holder, stating the name of the medicinal product to be transferred and the wording of the orphan disease
- a declaration bearing the legally valid signature of the new status holder, confirming that it will accept the ODS with all the associated rights and obligations at the time stated

5.4 Applications for authorisation of a medicinal product with ODS (Art. 24–26 TPLO)

5.4.1 General

A medicinal product that has been granted ODS in accordance with Art. 4 TPLO is eligible for the simplified authorisation procedure (Art. 24 para. 1 TPLO). In essence, the authorisation procedure for a medicinal product with ODS is the same as the authorisation procedure applicable to the relevant category of medicinal product. The provisions of the corresponding guidance documents *Authorisation of human medicinal product with new active substance HMV4*, *Authorisation of human medicinal product with known active pharmaceutical substance HMV4*, etc. are therefore also applicable to the authorisation of a medicinal product with ODS.

The present guidance document therefore only refers to those areas where the authorisation of a medicinal product with ODS differs from a normal authorisation application.

5.4.2 Evaluation of the authorisation application

In order to authorise a medicinal product with ODS, evidence of its quality, efficacy and safety must be provided. When evaluating the preclinical and clinical data, however, the rarity of the disease will be taken into account. In particular, the limited number of patients and the increased difficulty of carrying out trials must be taken into consideration. In justified cases, Swissmedic therefore accepts published results instead of complete trial data for orphan drugs. This does not mean, however, that a dossier lacking in scientific substance may be submitted for the authorisation of an orphan drug.

5.4.3 Document protection for medicinal products with ODS

According to Art. 11b para. 4 TPA, an important medicinal product for rare diseases is granted document protection for 15 years, unless document protection already exists for another medicinal product containing the same active substance that has been authorised by Swissmedic for the same use (cf. section 5.6 of the guidance document *Document protection HMV4*).

5.4.4 Listings

Swissmedic publishes online a list of medicinal products which have orphan drug status in Switzerland (Art. 7 TPLO). This list is updated on a monthly basis and contains the following information:

- Active substance(s)
- Applicant / authorisation holder
- Rare disease to be treated
- Date on which status was granted
- Where appropriate, date on which status was withdrawn
- Authorisation status of the medicinal product (notified/authorised)
- Authorisation number
- Name of the medicinal product
- Date of first authorisation of the medicinal product
- Where appropriate, date on which the temporary authorisation of the medicinal product expires
- Authorised indication for the medicinal product (with reference to the current information for healthcare professionals containing full details of the indication)

Change history

Version	Change	sig
3.2	New layout, no content adjustments to the previous version.	dei
3.1	Formal adjustments to the header and footer No content adjustments to the previous version.	dei
3.0	Correction, supplement an explanation in chapter 6.2 (Fees), 6.3.4 (ODS and indication extensions) and 6.3.8 (Transfer of status).	stb
2.0	Chapter 6.3.2 “Formal aspects, documents to be submitted and examination”: Swissmedic will cancel the advance payment of the application fee.	gf
1.0	Implementation of TPO4	stb