Contents

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Change history

Version	Valid and binding as of:	Description, comments (by author)	Author's initials
4.0	**01.04.2020**	**Complete revision with explanations in chapters 3, 6.1.1, 6.5, 7 (previously 6.7) and 9 (previously 6.8), and new chapters 8 (Variations and extensions for temporarily authorised medicinal products) and 10 (Time limits). In addition, new flowchart 12.2.1. in Annex:** - **All documents for the fulfilment of conditions must be submitted to Swissmedic together with the submission of an application for ordinary authorisation (conversion) within a maximum of two years following the official approval decision for temporary authorisation (Chapter 6.5.2).** - **Variations and extensions for temporarily authorised medicinal products are possible (particularly applications for additional indications). However, all clinical trial data must be available, i.e. the data situation must be definitive (Chapter 8).** **Updates regarding the "ex officio" temporary authorisation (Chapter 7) and the temporary authorisation in accordance with Art. 13 TPA (Chapter 9).**	**fg / stb**
3.0	**23.09.2019**	**Clarification inserted in Chapter 6.3 Ex officio temporary authorisation** **Chapters 5.1.1 and 8.4: SMC position on tissue agnostic indications**	**fg** **ru**
2.0	**12.06.2019**	**Chapter 6.3, Time limits for assessment: Addition regarding time windows for submitting answers to the List of Questions**	**sjo**
1.1	19.02.2019	Chapter 8.1, Procedure / application for temporary authorisation: Response to prelim. decision max. 60 CD.	sjo
1.0	**01.01.2019**	**Implementation of TPO4**	**sjo**

1 Definitions, terms, abbreviations

1.1 Abbreviations

AI	Additional indication
COMP	Committee for Orphan Medicinal Products
EMA	European Medicines Agency
FC	Formal check
FDA	Food and Drug Administration
FDHA	Federal Department of Home Affairs
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
IRB	Institutional Review Board
KAS	Medicinal product with known active substance
LoQ	List of Questions
NAS	New Active Substance

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TPA	Federal Act of 15 December 2000 on Medicinal Products and Medical Devices (Therapeutic Products Act, SR 812.21)
TPO	Ordinance of 21 September 2018 on Therapeutic Products (Therapeutic Products Ordinance, TPO) (SR 812.212.21)
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)
TPLRO	Ordinance of the Swiss Agency for Therapeutic Products of 9 November 2001 on the Licensing Requirements for Therapeutic Products (SR 812.212.22)

2 Introduction and objective

It is possible for temporary authorisation to be granted under certain conditions defined by law in order to make medicinal products for the treatment of life-threatening diseases available to patients as quickly as possible.
The requirements concerning the completeness of the clinical documentation are reduced for temporary authorisation in comparison with a normal procedure.

Chapter 5 of this guidance document describes the conditions that must be met for a positive outcome from the **application** for a procedure for temporary authorisation, as well as the procedure for an application of this type.
Formal and content requirements for an **application** for temporary authorisation of a medicinal product, as well as the evaluation procedure itself, are described in Chapter 6.
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.

3 Scope

Temporary authorisation is possible only for medicinal products that contain a new active substance (NAS). It does not apply to additional indications or other extensions of an authorisation.

4 Legal framework

The conditions for temporary authorisation are listed in Art. 9a TPA.
Temporary authorisation is possible as per Art. 18 TPLO.

Arts. 18–22 TPLO set out in detail the conditions for the granting of temporary authorisation.

5 Application for a procedure for temporary authorisation

5.1 Conditions for temporary authorisation

Temporary authorisation should be granted if the conditions detailed in Chapter 5.1.1. are met cumulatively. The clinical documentation that was incomplete when the authorisation application was assessed should be supplemented only after the official decision. This information, required in connection with the conditions imposed, will subsequently be reviewed by Swissmedic; if the documentation is approved the temporary authorisation, if duly requested, can be converted into an ordinary authorisation.

5.1.1 Details of the conditions for temporary authorisation

Art. 18 - 22 TPLO require the following conditions to be fulfilled **cumulatively** to qualify a human medicinal product for temporary authorisation:

a) The product must be used *"to identify, prevent or treat a disease that can lead to serious invalidity, severe suffering possibly resulting in death or to the death of a patient in the short term"*.
- The target population should comprise patients with an established clinical presentation. Reference may also be made to a subgroup that is at a certain stage of the underlying disease

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or that exhibits a recognised molecular pathogenic entity with specific characteristics in terms of course, prognosis or therapy. Please refer to Annex 12.4 for information on tissue agnostic or tissue independent indications, which are relevant owing to the growing significance of molecular diagnostics, particularly in oncology.
- The risk of serious invalidity or a possible fatal outcome is intended to apply to all the patients in the target population.
- The target population should be reflected explicitly in the indication.

b) *There must be no alternative and equivalent medicinal product authorised or available in Switzerland.*
- Applies to diseases for which no prophylactic or treatment options with authorised medicinal products exist and where non-medicinal treatments (such as surgery) are not curative.
- The existing treatment options with authorised medicinal products do not adequately reduce the risk of serious invalidity or a possible fatal outcome.

c) *Major therapeutic benefit is expected from use of the product for which authorisation is being requested.*
- Major therapeutic benefit should be demonstrated in clinical studies in the target population in a clinically and scientifically convincing manner.
  The following three aspects must be fulfilled in this respect:
  1. The selected trial end point(s) must be clinically relevant, i.e. survival rates, or surrogate markers for survival or the prevention of serious invalidity that are validated and recognised in the target population should be available.
  2. The events attributed to the trial endpoints(s) must occur with sufficient frequency in order to permit an assessment of the effect size.
  3. Causality between treatment and clinical effect must be evident: prevention or therapy of the disease achieves a relevant reduction in the risk of invalidity or threat to life.
- The clinical documentation submitted with the application for the procedure should, even without the detailed data being evaluated, demonstrate the likelihood of the therapeutic benefit being significantly superior to the current therapy standard.
- The assessment of the clinical relevance depends on the individual clinical presentation and the corresponding clinical and scientific practice.

d) *The applicant will probably be in a position to submit the required data as per section 2 of the TPLO before the temporary authorisation expires with a view to achieving ordinary authorisation.*
- One or more studies decisive for authorisation will be completed before the temporary authorisation expires, and the corresponding reports will be submitted to Swissmedic (in accordance with ICH E3).
- The final study protocol (i.e. the version approved by the Ethics Committee/IRB) for the pivotal study must be submitted with the application for temporary authorisation, together with confirmation of the above-mentioned undertaking to submit documentation *post hoc* should temporary authorisation be granted. The expected date of the *data cut-off point* and the date on which the report will be submitted should be stated with binding effect.

e) *It would take so long to compile all the required data and to process and evaluate the data under letter d in an ordinary authorisation procedure as per Art. 11 TPA that irreversible damage in patients would result or worsen or this would be associated with severe suffering.*
- The above-mentioned target population must be in immediate danger of invalidity or imminent death in the short term. Diseases that are associated with an increased risk but termed ‘chronic’ are not within the scope of temporary authorisation.

5.2 Application for a procedure for temporary authorisation

A procedure for temporary authorisation for a medicinal product must be requested from Swissmedic in advance.
The applicant should demonstrate in this application that the conditions for an application for temporary authorisation as per Art. 18 TPLO are fulfilled.

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5.2.1 Scientific Advice

If required, the applicant can request a pre-submission meeting with Swissmedic in the form of a Scientific Advice Meeting to discuss the available data (see the guidance document *Meeting for applicants held with the Authorisation sector HMV4*).

5.2.2 Documentation to be supplied

The application must be made in writing by the applicant or one of its legal representatives / companies to Swissmedic with the notice: “Application for a procedure for temporary authorisation”.

The following documents should be submitted:

a) Covering letter stating the indication(s) requested for Switzerland. The wording of the scheduled indication should be based on the patient populations that have been or are being investigated and documented by the results of studies.
   If applicable, the covering letter must also refer to authorisation applications pending in other countries and the existence of questions or decisions from other authorities where these exist.
b) Justification of why the applicant believes the conditions for temporary authorisation are fulfilled (5 to a maximum of 15 pages). The argumentation must be documented (e.g. summary of the data from the pivotal studies that are available or will be submitted *post hoc*).
c) Supportive information in the form of available relevant top-line[1] results of ongoing studies.
d) Overview of the data package intended for the application for temporary authorisation at the time of submission, with a tabular listing and brief overview of the ongoing studies, number of patients for efficacy and safety results. The CTD module 5.2 "Table of All Clinical Studies" can be used as a template for this listing.
e) Confirmation that the complete data for pharmaceutical quality (module 3) are available and will be submitted with the application for temporary authorisation. This refers to the formulations for which temporary authorisation is being requested.
f) Draft of the risk management plan (RMP) for the medicinal product scheduled for temporary authorisation with the risk aspects of the medicinal product, the planned pharmacovigilance activities and risk-mitigation measures. The principles of the RMP that must be submitted in the context of temporary authorisation are described in the documents “ICH E2E Guideline - Pharmacovigilance Planning”, the European Medicines Agency (EMA) Guideline “Good pharmacovigilance practices (GVP): Module V – Risk management systems” and the Swissmedic information sheet “RMP / ICH E2E - Information for submission”.
g) Draft version of the Information for healthcare professionals or the Summary of Product Characteristics.

The process for applying for a procedure for temporary authorisation is shown in Annex 12.1.

5.2.3 Application fee

The assessment of the application for a procedure for temporary authorisation is charged on the basis of the work involved as per FeeO-Swissmedic.

5.3 Processing the application for a procedure for temporary authorisation

Swissmedic will decide within 30 days whether the criteria for temporary authorisation are met or not. The applicant will be informed of the decision in a preliminary notification or, in the case of an approval and if there is no need for clarification, directly with an official approval decision. If a preliminary notification is issued, the applicant has the option to submit a statement on the preliminary notification within 30 days. The corresponding official decision will subsequently be issued.

5.4 Presubmission Meeting (optional)

If the application for a procedure for temporary authorisation has been approved, a Presubmission Meeting can be held if required between one and two months before the application for temporary

[1] Available results evaluated statistically as per study protocol, but no complete studies or interim reports as per ICH-E3 available

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authorisation is submitted. The aim of the meeting is to establish whether all the documentation required to process the application is available. In particular, the following formal aspects of the authorisation application to be submitted will be considered:

- Index of scientific and administrative documentation
- Any unresolved questions concerning incomplete clinical documentation and the times at which it will be submitted

The definitive submission date is established at the Presubmission Meeting.

The following information / documentation must be sent to Swissmedic, with an appropriate covering letter, at the latest 2 weeks before the Presubmission Meeting:

- List of questions: Presentation of the issues to be clarified during the Presubmission Meeting, usually in the form of a Briefing Book (see Chapter 3.2 List of questions / documentation in the guidance document *Meeting for applicants held with the Authorisation sector HMV4*)
- Draft agenda with the points to be discussed
- Proposal for the type of meeting: in person, teleconference or videoconference
- List of participants and their functions

The guidance document Meeting for applicants held with the Authorisation sector HMV4 also applies.

5.5 Planning the submission after approval of the application

The application for temporary authorisation must be submitted no sooner than two months before and no later than six months after the official approval decision has been issued.
Applicants must inform Swissmedic in writing of the date on which they will submit the authorisation application (exact date) as soon as possible but at least one month before submitting the authorisation application.

6 Submission of the application for temporary authorisation

6.1 Formal aspects and the documentation to be submitted

The applicant must submit the application for temporary authorisation together with all documentation required according to the application type to Swissmedic by the agreed date. If submission in eCTD format is planned, it is advisable for applicants with limited or no experience with eCTD to submit a test sequence in good time (at least 3 weeks before submitting the application) in order to avoid exceeding the time limits due to technical problems.

6.1.1 Labelling in the Information for healthcare professionals

The requirements to be fulfilled by the Information for healthcare professionals are derived from the guidance document *Product information for human medicinal products HMV4*. This guidance document only refers to the special circumstances for temporarily authorised medicinal products.
The note concerning additional monitoring (▼ *This medicinal product is subject to additional monitoring….) must be followed by the following sentence:*

"NAME" is temporarily authorised – see "Properties/Effects" section.
In the "Properties/Effects" section of Annex 4, section 3 TPLRO, the following note must be added for temporarily authorised medicinal products under the title "Temporary authorisation":
The medicinal product "NAME" has been granted temporary authorisation as the clinical data was incomplete at the time the authorisation application was assessed (Art. 9a TPA). The temporary authorisation is contingent on the timely fulfilment of conditions. After they have been met, the temporary authorisation can be transformed into an ordinary authorisation.

6.2 Review phases

The process of assessing an application for temporary authorisation is carried out as described in Annex 12.1.

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The assessment is performed using process ZL 101 for human medicinal products (see guidance document *Authorisation of human medicinal product with new active substance HMV4*).

6.3 Time limits for assessment

The time limits are based on the guidance document *Time limits for authorisation applications HMV4*. Answers to the LoQ must be submitted within the time windows published on the Swissmedic website. To ensure that applications are processed promptly, the applicant must also notify Swissmedic in advance of the date on which the responses to the preliminary decision will be submitted.

6.4 Grant of the temporary authorisation

- No document protection is granted when an application for temporary authorisation is approved, and the following is stated on the authorisation certificate: “Temporary authorisation as per Art. 9a TPA”.

6.5 Phase after temporary authorisation

The phase after temporary authorisation is characterised by the following:

6.5.1 Risk management plan and post-marketing activities

The risk management plan (RMP) describes the risk aspects of the medicinal product, the planned pharmacovigilance activities and the risk-mitigation measures. The pharmacovigilance activities and the risk-mitigation measures cannot be planned or assessed definitively yet since knowledge of the risk aspects is still incomplete at the time the authorisation application is assessed. Specific conditions regarding safety specifications, the further collection of pharmacovigilance data and implementation of risk-mitigation measures may therefore be imposed.

6.5.2 Timetable, conditions and ex officio extension

The temporary authorisation is granted for a maximum of two years. The conversion to an ordinary authorisation is contingent on the fulfilment of the conditions imposed. All documentation on the fulfilment of conditions must be submitted to Swissmedic for review within two years of the official approval decision for the temporary authorisation, together with an application for the granting of ordinary authorisation. If Swissmedic receives the documentation on the fulfilment of conditions within this period, the temporary authorisation is extended until the new documentation has been reviewed (generally 540 CD). The process for the fulfilment of the conditions relating to temporarily authorised medicinal products is the same as that for ordinarily authorised medicinal products.
If, after reviewing the documentation on the fulfilment of conditions, Swissmedic concludes that the documentation is incomplete, the temporary authorisation is revoked or lapses, since conversion to an ordinary authorisation is not possible.

6.5.3 Extension of the temporary authorisation by the authorisation holder

If the documentation on the fulfilment of conditions for a temporary authorisation cannot be submitted within the specified period of two years, it may be possible to extend the temporary authorisation in scientifically justified exceptional cases, subject to an application being submitted (stating reasons), in accordance with Art. 21 para. 3 TPLO. This application for the extension of the temporary authorisation must be submitted by the authorisation holder at least three months before the end of the temporary authorisation period or, at the latest, together with a statement on any negative preliminary notification concerning the fulfilment of conditions and must include an interim report on the status and progress of the fulfilment of the special conditions imposed.

6.5.4 Fulfilment of conditions and conversion

At the same time as the documentation on the fulfilment of conditions, the authorisation holder must also submit an application for converting the temporary authorisation into an ordinary authorisation. If this application is subsequently approved, the authorisation will then be valid for five years, and the

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corresponding document protection will be granted. The authorisation number and packaging codes will be taken over.

7 "Ex officio" temporary authorisation

If, during its review of an ordinary new authorisation, Swissmedic determines that the clinical documentation does not adequately support the requested indication(s), Swissmedic will always consider the possibility of an "ex officio" temporary authorisation. If, on the basis of a summary review of the application, Swissmedic believes that the preconditions for granting a temporary authorisation will probably be fulfilled, Swissmedic will inform the applicant of this option in the preliminary notification of rejection.
In its statement on the preliminary notification to reject the application for an ordinary new authorisation, the applicant must inform Swissmedic whether it **agrees** or disagrees with the granting of a temporary authorisation (see "Ex officio temporary authorisation" flowchart in the Annex).
If the applicant **does not agree** with the granting of a temporary authorisation, the following options exist:
Along with its statement on the preliminary notification to reject ordinary authorisation, the applicant explains to Swissmedic why it wishes to pursue its application for ordinary authorisation and why the application should be approved. If Swissmedic agrees with the applicant's reasons, it can issue a preliminary notification to approve the ordinary authorisation. If Swissmedic still considers that the data provided are not adequate for an ordinary authorisation, taking the company's reasons into account, the application for ordinary authorisation will be rejected.
The applicant withdraws its application for ordinary authorisation of the medicinal product.
The applicant requests the issuing of a contestable rejection decision.

If the applicant would like a temporary new authorisation rather than an ordinary one, the current application should be withdrawn and a procedure for the granting of a temporary authorisation should be initiated using the aforementioned application (see Chapter 5) along with a subsequent application (see Chapter 6).

8 Variations and extensions for temporarily authorised medicinal products

After a temporary authorisation has been approved for the medicinal product, the authorisation holder is required to submit any variations to Swissmedic in accordance with Articles 21 to 24 TPO. Applications for additional indications (AI, C.I.6, Type II variation) may also be submitted for a temporarily authorised medicinal product. The clinical development must have been concluded for these AIs, and the complete study data (incl. the corresponding final reports) must be available. If the AI qualifies for the fast-track authorisation procedure, then – once the application is approved accordingly – the review period will be shortened. Likewise for the AI, a procedure with prior notification (PPN) can be submitted so that this procedure can be applied if appropriate.

9 Temporary authorisation in accordance with Art. 13 TPA

Swissmedic basically performs its own comprehensive scientific assessment of applications for authorisation of a medicinal product with new active substance on the basis of all the available documentation (Art. 18 para. 1 TPO). In justified cases, Swissmedic may reduce the assessment accordingly on application or *ex officio* on the basis of corresponding outcomes of foreign reviews (Art. 18 para. 2 TPO). Reduced assessment under application of Art. 13 TPA for an application for temporary authorisation is possible, on the one hand, for medicinal products that have been classified as an orphan drug by the Committee for Orphan Medicinal Products (COMP) of the EMA or under the Orphan Drug Act of the FDA and have been authorised. On the other hand, and in application of Art. 13 TPA in conjunction with Art. 18 para. 2 TPO, Swissmedic may, on request, scale back its assessment of an application for the temporary authorisation of a medicinal product that has already been authorised by the EU Commission or US FDA if the product in question fulfils all the following conditions:

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a) The medicinal product is intended to prevent a transmissible infectious disease that may cause severe harm or serious suffering with potentially fatal consequences.
b) The medicinal product's indication is identical to the indication approved by the reference authority.

In addition, Swissmedic must have approved the preceding application for a procedure for temporary authorisation. Furthermore, the statements in the guidance document *Authorisation of human medicinal product as per Art. 13 TPA HMV4* apply.

10 Time limits

The time limits are based on the guidance document *Time limits for authorisation applications HMV4*.

11 Fees

The fees specified in the Ordinance on Fees Levied by the Swiss Agency for Therapeutic Products apply. The fees for assessment of documentation for the removal of conditions attached to the temporary authorisation will be calculated according to the work involved.

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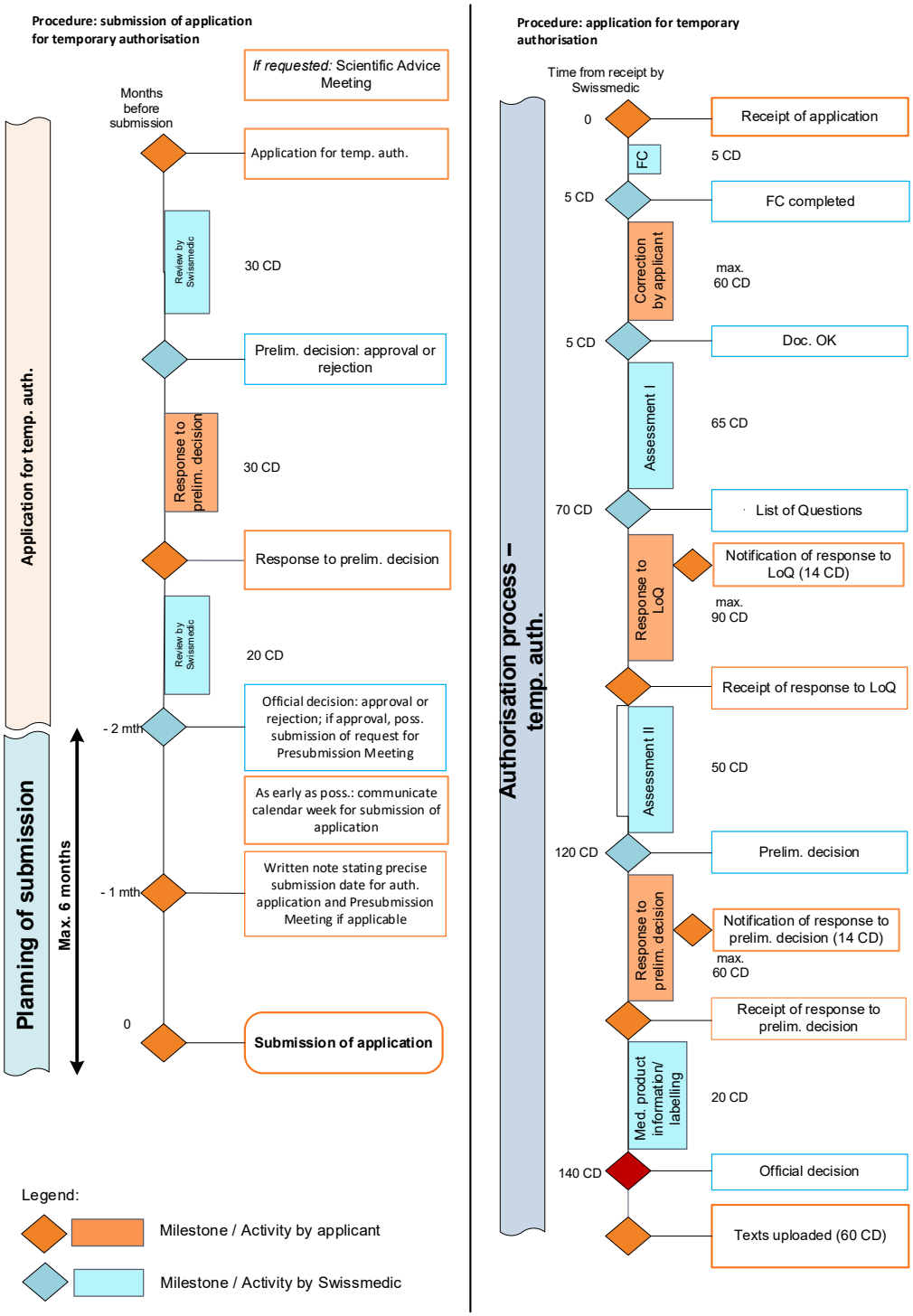
12 Annex

12.1 Application for temporary authorisation



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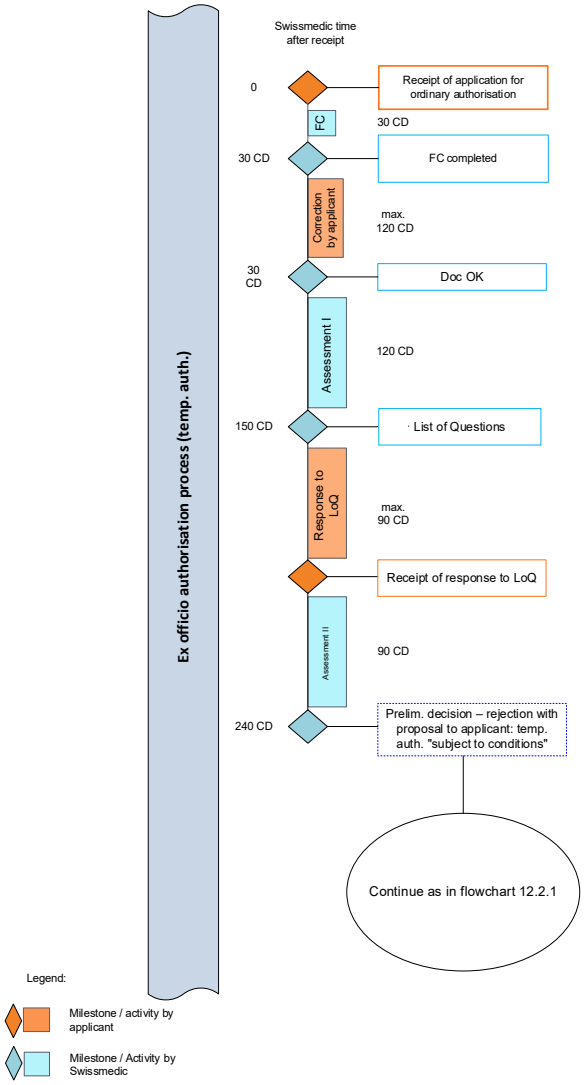
12.2 Ex officio temporary authorisation



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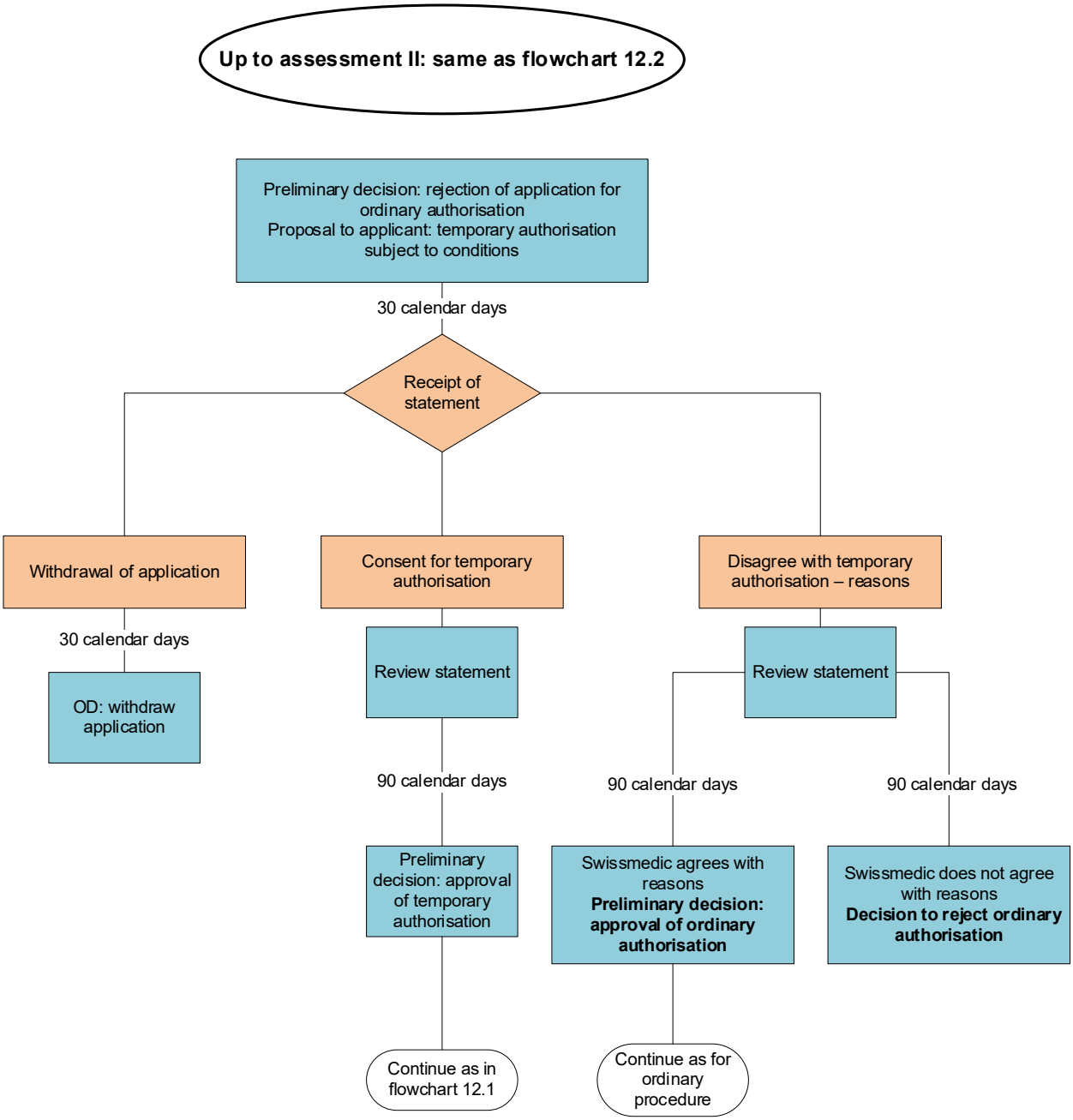
12.2.1 Procedure for "ex officio" temporary authorisation



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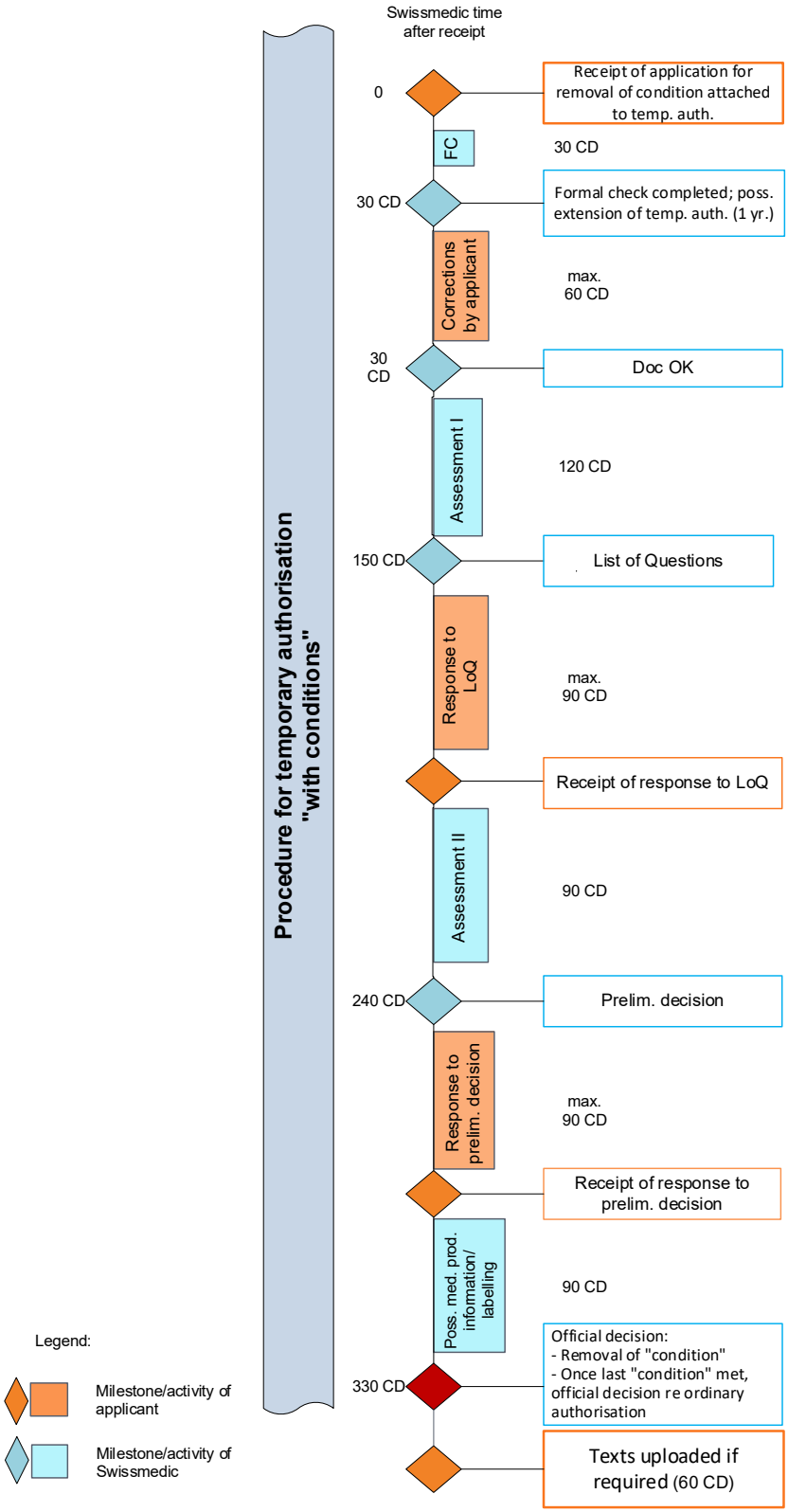
12.3 Application for removal of a condition attached to a temporary authorisation



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12.4 Annex on tissue-agnostic indications

Definition

A tissue-agnostic indication is characterised by the fact that the wording of the indication describes a patient population with a particular molecular abnormality that is not restricted to a localised, tissue-specific tumour entity, but that extends to all tumour entities regardless of their location (e.g.: “medicinal product A is indicated for all patients whose tumours display genetic abnormality xyz”.

Application

In principle, applications for temporary authorisation can be submitted for oncologicals with a tissue-agnostic indication.

Guidance on fulfilling criteria a to e of Article 18 in Section 3 TPLO

A disease or a subgroup of a disease may be deemed “recognised” or “established” in the context of a “tissue-agnostic” indication if it can be distinguished from other subgroups within an entity by virtue of its prognosis, treatment and course. It is incumbent on the applicant to demonstrate plausibly that in terms of prognosis and/or as a result of the treatment, the molecular tumour marker behaves differently in all tissue types, regardless of nature, when compared with histological subgroups without this marker. The relevant specialist guidelines should be consulted for this purpose.

Tissue-agnostic indications will be assessed for compliance with criteria a to c on a case-by-case basis using the evidence base submitted. For this purpose, convincing proof of efficacy obtained from an adequate number of patients for each case must be presented for tumours in peripheral and central nervous system locations and from different tissues of origin (sarcomas, carcinomas, or haematologic tumours if appropriate).

The temporary authorisation process will pay particular attention to the extent to which the applicant is able to subsequently supply such data as the Agency may require to ensure adequate case numbers in the above-mentioned different tumour locations and tissues of origin. The decision will also take account of this (criterion d). This approach is intended in particular to acknowledge the fact that – in contrast to applications for fast track authorisation (see Guidance document *Fast-track authorisation procedure HMV4* in Annex 6.2) – any review of an application for temporary authorisation is a provisional evaluation rather than one based on a final evidence base.

If an application for temporary authorisation is approved, a decision will be taken during the process of converting the temporary authorisation to an ordinary authorisation, and on the basis of the final submitted evidence base, as to whether the wording of the indication for the ordinary authorisation will be retained or has to be modified or, if applicable, whether the temporary authorisation must be withdrawn (without conversion to an ordinary authorisation) in accordance with Article 21a paragraph 1, TPLO.

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