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**Change history**

Version	Valid and binding as of:	Description, comments (by author)	Author's initials
7.0	01.07.2021	Clarification of process / procedure AAA	fg/gf/ru/zsa
6.0	01.04.2021	Accelerated Application Meeting replaces application for temporary authorisation.  Clarification in section 8 regarding retention of the "temporary" status when the indication extension with the complete data record is approved.	fg/gf/ru/zsa  stb
5.0	01.11.2020	Inclusion of a decision tree and criteria for demarcating between temporary authorisation and FTP in Annexes 12.5 and 12.6	stb
4.0	01.04.2020	Complete revision with explanations in sections 3, 6.1.1, 6.5, 7 (previously 6.7) and 9 (previously 6.8), and new sections 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 (Section 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 (Section 8).  Updates regarding the "ex officio" temporary authorisation (Section 7) and the temporary authorisation in accordance with Art. 13 TPA (Section 9).	fg / stb
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1.0	01.01.2019	Implementation of HMV4	sjo

## 1 Definitions, terms, abbreviations

### 1.1 Abbreviations

AAA	Accelerated Application Hearing
AE	Adverse Event
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
FTP	Fast-Track authorisation Procedure
IRB	Institutional Review Board
KAS	Medicinal product with known active substance
LoQ	List of Questions
NAS	New Active Substance
SAE	Serious Adverse Event
ST	Standard Treatment
TEAE	Treatment-Emergent Adverse Event
temp.auth.	Temporary authorisation
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. Under the temporary authorisation procedure (temp.auth.), the submitted clinical documentation does not have to be as complete as for an "ordinary" procedure. In contrast with the "ordinary" authorisation procedure, an application for temporary authorisation must be preceded by the submission to Swissmedic of a request for an Accelerated Application Hearing (AAA) during which a procedure for temporary authorisation is approved by Swissmedic.

**Section 5** of this guidance document describes the conditions that must be met before the request for an authorisation procedure for temp.auth. can be approved, and specifies the detailed procedure for the meeting with the applicant (AAA) scheduled for the processing of this application (see section 12 for the detailed AAA procedure). The formal and content requirements for an **application** for the temp.auth. of a medicinal product, as well as the evaluation procedure itself, are described in **section 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 new authorisations of human medicinal products containing a new active substance (NAS). It does not apply to additional indications or other extensions of an authorisation.

### 4 Legal framework

Temporary authorisation is regulated in Article 9a TPA.

Articles 18 - 22 TPLO set out in detail the conditions for the granting of temp.auth.

## 5 Preconditions for the implementation of a temporary authorisation procedure and procedural issues

### 5.1 Principle

Temp.auth. should be granted if the conditions detailed in section 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 Material preconditions

Art. 18 letters a to e TPLO require the following criteria to be fulfilled **cumulatively** to qualify a human medicinal product for temp.auth.:

- a) *The product is 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 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) *No alternative and equivalent medicinal product is authorised 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; and
    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.
  - Based on the clinical documentation submitted with the application for an AAA, it should be possible, even without an evaluation of the detailed data, to assess whether the therapeutic

benefit is superior to that of the current authorised treatment/standard therapy to a clinically relevant extent (comparative basis). The evaluation of the clinical data considers not just the control arm of the clinical trial as a basis for comparison, but also all treatments with authorised medicinal products (used as monotherapy or in combination) that are available in Switzerland at the time of submission of the application for an AAA for a temp.auth. for the proposed indication(s). In a tabular overview, the company must compare the study results on efficacy (endpoints accepted from the regulatory standpoint) and safety (in addition to TEAEs, a table of grade 3-5 TEAEs; SAEs and TEAEs that resulted in death) with the existing treatments with authorised medicinal products that are available in Switzerland. This applies particularly if the submitted clinical trial was not randomised and therefore lacks a control arm. A standard treatment (ST) is considered to be the treatment with the ordinarily or temporarily authorised medicinal products that are available in Switzerland for the corresponding indication. The AAA application submission date is considered to be the key date for the evaluation of the high therapeutic benefit. If the ST changes between the implementation of the study and the time of the application for an AAA, the applicant must demonstrate that the medicinal product proposed for temp.auth. offers a greater therapeutic benefit than the new (current) ST.

- The assessment of the clinical relevance depends on the individual clinical presentation and the corresponding clinical and scientific practice.
- d) *The applicant is expected to be able to supply the necessary data 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 temp.auth. expires, and 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 temp.auth., together with confirmation of the above-mentioned undertaking to submit documentation *post hoc* should temp.auth. 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 takes 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. Diseases that are associated with an increased risk, but classified as 'chronic' are not within the scope of temp.auth.

In any case, a positive evaluation for the application for an authorisation procedure for temp.auth. is possible only if the applicant can demonstrate, separately for each proposed indication, that the criteria a to e are all fulfilled. Criteria a to e per Art. 18 TPLO must be fulfilled throughout the period of temp.auth. Swissmedic can withdraw the authorisation at any time if any of the conditions are no longer fulfilled or the authorisation holder does not fulfil the special conditions specified in Art. 21 para. 1 TPLO.

## **5.2 Formal preconditions for the implementation of an AAA**

An AAA is generally mandatory before an authorisation procedure for a temp.auth. can be accepted. The application for an AAA should be submitted between 2 and 12 months before the authorisation application.

### **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 for an AAA must be made in writing by the applicant or one of its legal representatives to Swissmedic. The application must be substantiated scientifically and be backed up by the required documentation. 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 temp.auth. are fulfilled (5 to a maximum of 15 pages). Specific position statements on all criteria stated in Art. 18 let. a to e TPLO should be provided (see point 5.1.1). 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) If several indications are proposed for the medicinal product, the applicant must demonstrate that the criteria stated in Art. 18 let. a to e TPLO are all fulfilled for each individual indication.
- d) Supportive information in the form of available relevant top-line<sup>1</sup> results of ongoing studies (see also criterion c in section 5.1.1).
- e) Overview of the data package intended for the application for temp.auth. 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.
- f) Confirmation that the complete data for pharmaceutical quality (module 3) are available and will be submitted with the application for temp.auth. This refers to the medicinal products for which temporary authorisation is being requested.
- g) Draft of the risk management plan (RMP) for the medicinal product scheduled for temp.auth. 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 temp.auth. 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".
- h) Draft version of the Information for healthcare professionals or the Summary of Product Characteristics.

The process for requesting a procedure for temp.auth. is shown in [Annex 12.1](#).

### 5.3 Processing the application for an AAA

The applicant will receive confirmation of receipt of the application for an AAA, and the documentation will then be formally checked. Swissmedic will decide within 30 days of completion of the formal checks of the application whether the criteria for an AAA are met. The applicant will be informed of the decision on an AAA with, if applicable, confirmation of the date no later than 10 days before the meeting is due to take place. The AAA is conducted on Swissmedic premises or, if applicable, in the form of a teleconference.

If, after receiving the applicant's application, Swissmedic unconditionally agrees to review its authorisation application in the context of a temp.auth. and if the evaluation of the submitted documentation does not reveal any aspects requiring clarification, Swissmedic can dispense with the implementation of an AAA. In this case, Swissmedic will directly issue an official decision to approve the application for an authorisation procedure for temp.auth. The approval is recorded in the decision minutes. These are enclosed as an integral part of the official order.

<sup>1</sup> Available results evaluated statistically as per study protocol, but no complete studies or interim reports as per ICH-E3 available

## 5.4 Presubmission Meeting (optional)

If the application for a procedure for temp.auth. has been approved, a Presubmission Meeting can be held if required between one and two months before the application for temp.auth. 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 Section 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 Procedure for an AAA (see the annex for the detailed procedure)

During the AAA, Swissmedic discusses with the applicant whether, on the basis of the submitted documents, the preconditions of Art. 18 let. a to e TPLO are satisfied and whether a temp.auth. is possible. The applicant can issue a position statement on Swissmedic's line of reasoning and, if applicable, present counterarguments that justify the implementation of a temp.auth.

Based on the provisional result of the review of the documents submitted with the application for an AAA and the supplementary reasons presented to the applicant during the hearing, Swissmedic will reach a binding decision during the AAA on the acceptance or otherwise of an authorisation procedure for a temp.auth.

The decision taken by Swissmedic is recorded in writing in the minutes and a legal justification supplied as necessary. The applicant signs (electronically if applicable) the decision minutes to confirm that it has been informed of all the reasons for Swissmedic's decision during the AAA. The applicant confirms that it has orally presented its position statement on the intended decision and has therefore been granted a fair hearing in accordance with the law.

The decision minutes are signed both by Swissmedic and the applicant. Swissmedic therefore assumes that at least one authorised signatory with decision-making powers will represent the applicant at the AAA.

Following the AAA, the applicant will receive the decision in writing in the form of an official order. The signed decision minutes (i.e. the rationale for the decision) produced at the AAA and signed by Swissmedic and the applicant will be enclosed as an appendix and as an integral part of the official order concerning the application for an authorisation procedure for a temporary authorisation.

## 5.6 Submission of the authorisation application following the approval of the application for a temporary authorisation

The application for temp.auth. can be submitted at the earliest two months, and must be submitted at the latest, twelve months after the official decision to approve the application for an authorisation procedure for a temp.auth. Applicants must inform Swissmedic in writing of the date on which they intend to 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 temp.auth. application 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 temp.auth. is carried out as described in [Annex 12.1](#). 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 Review time limits

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 temp.auth. 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 temp.auth. 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 temp.auth., together with an application for the granting of ordinary authorisation. If Swissmedic receives the documentation on the fulfilment of conditions within this period, the temp.auth. 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 temp.auth. 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 temp.auth. cannot be submitted within the specified period of two years, it may be possible to extend the temp.auth. 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 temp.auth. 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 temp.auth. into an ordinary authorisation. If this application is subsequently approved, the authorisation will then be valid for five years, and the 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" temp.auth. (see Annex 12.2). If, on the basis of a summary review of the application, Swissmedic believes that the preconditions for granting a temp.auth. will probably be fulfilled, Swissmedic will inform the applicant of this option in the preliminary notification of rejection of the application for new authorisation. In its reply to this preliminary notification of rejection, the applicant then informs Swissmedic whether it agrees or not with a temp.auth. This reply must be received by Swissmedic within 30 CD (see Annex 12.2.1).

If the applicant **agrees** with the granting of a temp.auth., Swissmedic shall have a period of 90 CD in which to issue the preliminary notification of approval of the temp.auth., see route B) in Annex 12.2.1.

If the applicant **does not agree** with the granting of a temp.auth., the following options exist:

- Route A) in Annex 12.2.1:  
The applicant withdraws its application for the ordinary authorisation of the medicinal product.
- Route C) in Annex 12.2.1:  
Along with its statement, the applicant explains to Swissmedic why it wishes to pursue its application for ordinary authorisation and why the application should be approved.
  - i) If Swissmedic agrees with the company's reasons, it can issue a preliminary notification to approve the ordinary authorisation.
  - ii) If Swissmedic still considers that the data provided are not adequate for an ordinary authorisation, taking the company's reasons into account, it will issue the contestable rejection decision.

Only Swissmedic is entitled to switch from an ordinary to a temporary authorisation procedure. The applicant can make this switch only if it has been suggested by Swissmedic. If the company wishes to switch from an ongoing ordinary authorisation procedure to a temporary procedure and this has **not** been suggested by Swissmedic, it must discontinue the ongoing application by withdrawal, and

initiate a procedure for the granting of temp.auth. by means of a prior application for an authorisation procedure for a temp.auth. in connection with an AAA (see section 5) along with a subsequent application (see section 6).

## 8 Variations and extensions for temporarily authorised medicinal products

After temp.auth. has been approved for the medicinal product, the authorisation holder is required to submit any variations to Swissmedic in accordance with Art. 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 (FTP), then – once the application for an FTP 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.

If an application for an indication extension with a complete data record is approved before the temporary authorisation of the medicinal product expires, i.e. before all the conditions are met and it is converted to a regular authorisation, the product will retain its temporary authorisation. So even if a medicinal product with temporary authorisation is approved for another fully documented indication, it remains temporarily authorised, and this status applies to all indications.

## 9 Application of 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 temp.auth. 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 temp.auth. 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:

- 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 an authorisation procedure for temp.auth. in connection with an AAA. 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 FeeO-Swissmedic apply.

For conducting an AAA Swissmedic invoices the applicant for its administrative and scientific costs. The costs are calculated on the basis of Art. 4 FeeO-Swissmedic.

The fees for reviewing the documentation for the removal of conditions attached to the temp.auth. will be calculated according to the work involved.

## 12 Annex 1

### 12.1 Instruction Accelerated Application Hearing (AAA) procedure

#### Before the AAA

- The Hearing takes place 6-8 weeks following receipt of the application for an AAA. The AAA lasts up to 2 hours, including two time-outs. Confirmation of the date on which the AAA will be held is sent to the applicant in writing at least 10 days before the Hearing takes place. Swissmedic provides the applicant with instructions on applying for access to the SharePoint platform.
- The applicant's line of reasoning to substantiate fulfilment of the criteria set out in Art. 18 let. a to e TPLO for the planned procedure for temp.auth. must be presented on slides. The presentation slides are uploaded to the SharePoint platform by the applicant at least 5 days before the AAA.
- Shortly before the AAA begins, Swissmedic makes the draft decision minutes available in Word format on the SharePoint platform so that the applicant can work on them during the AAA.

#### During the AAA

- During the Hearing, the person authorised by the applicant to manage the application presents the prepared presentation of the application for a temp.auth. procedure.
- If Swissmedic has asked for any clarification regarding the data submitted, the applicant must provide this information on a differentiated basis during the AAA. However, no additional or new data are accepted during the AAA.
- Swissmedic informs the applicant whether the preconditions of Art. 18 let. a to e TPLO are satisfied on the basis of its provisional review result, and whether the temp.auth. procedure requested by the applicant can be accepted.
- The applicant can issue a position statement on Swissmedic's line of reasoning and, if applicable, present counterarguments that justify the implementation of the requested temp.auth. procedure.
- During the AAA the applicant documents its opinion and relevant points for discussion in the decision minutes on SharePoint.
- Before the AAA ends, Swissmedic reaches a binding decision on the basis of the provisional result of the documentation review and the supplementary line of reasoning presented by the applicant at the Hearing. Swissmedic will allow itself a 15-minute time-out for decision-making after discussing the data with the applicant.
- After the time-out, Swissmedic will present its decision to the applicant by word of mouth. The decision will be recorded in the decision minutes. If the application for a temp.auth. procedure is rejected, Swissmedic can recommend the applicant to submit an application for authorisation via an alternative procedure.
- Once Swissmedic has communicated its decision, the applicant is granted a 15-minute time-out. The applicant then has the chance to discuss the decision and, where required, to discuss

the proposal for the submission of another authorisation procedure without Swissmedic being present.

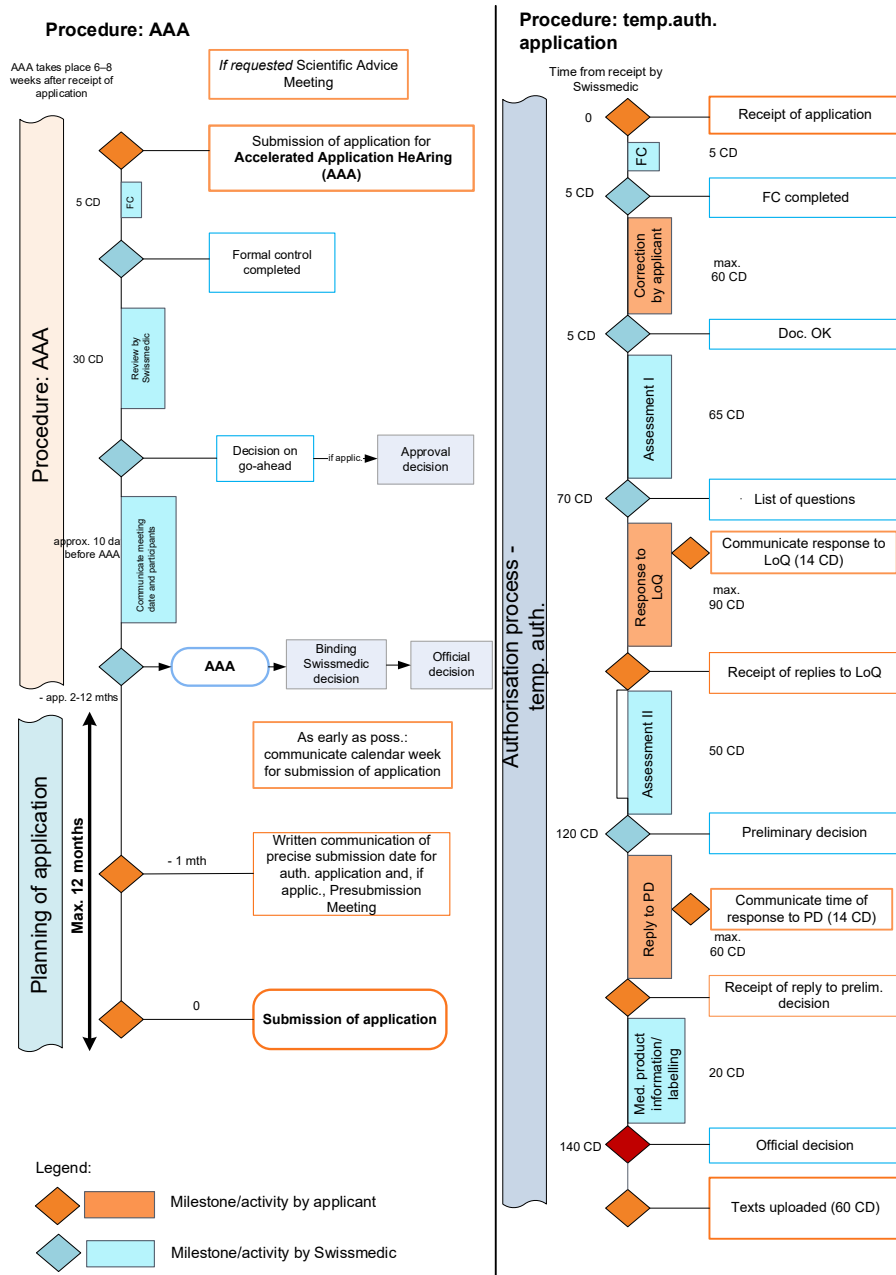
- The decision minutes written up by the applicant during the AAA are read and supplemented as necessary by Swissmedic. The final decision minutes are signed by the applicant and Swissmedic before the AAA ends.

#### After the AAA

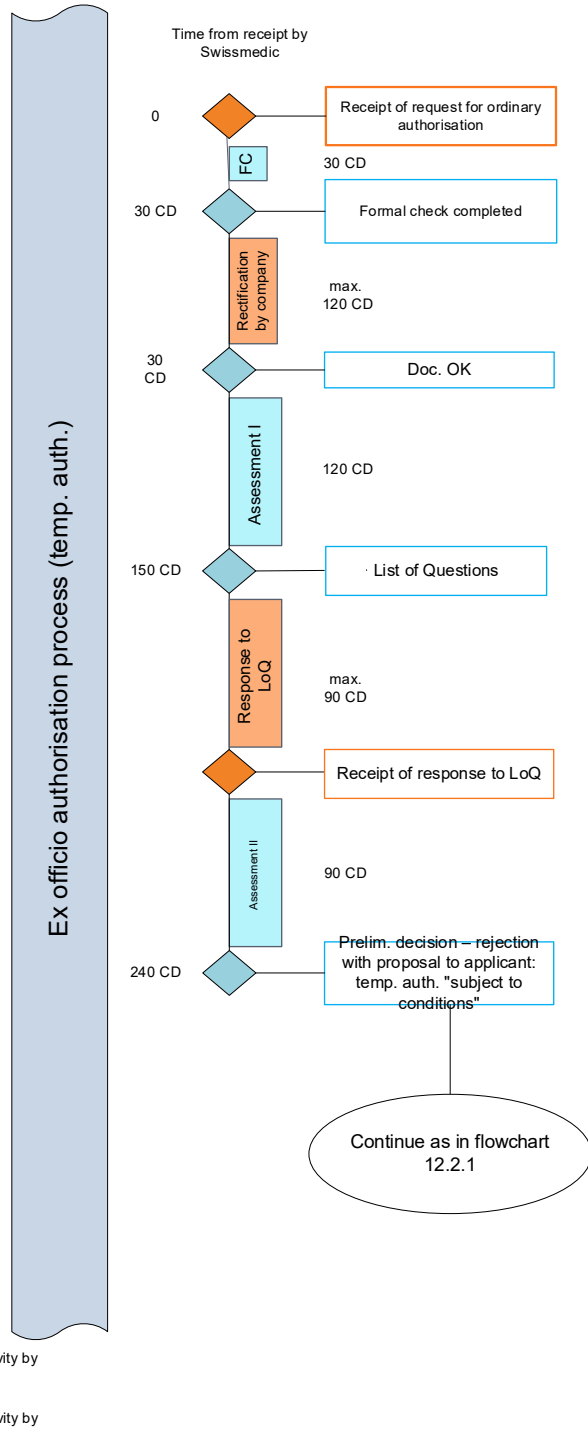
- After the AAA, Swissmedic informs the applicant of the binding decision taken at the AAA in the form of a written official order. The decision minutes produced and signed at the AAA are enclosed as an appendix and as an integral part of the official order concerning the application for a temp.auth. procedure.

13 Annex 2

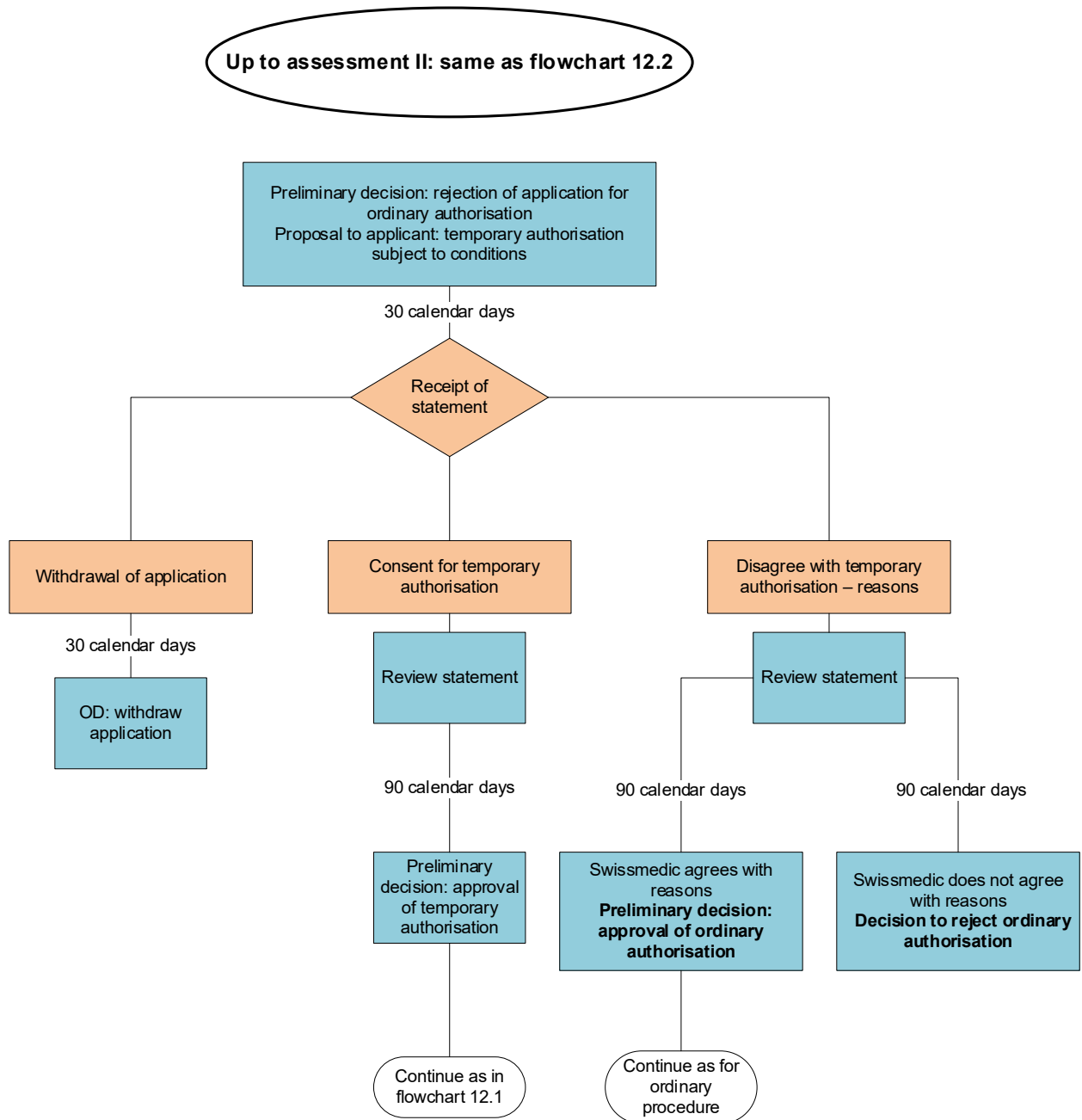
13.1 Procedure for an AAA / application for temp.auth.



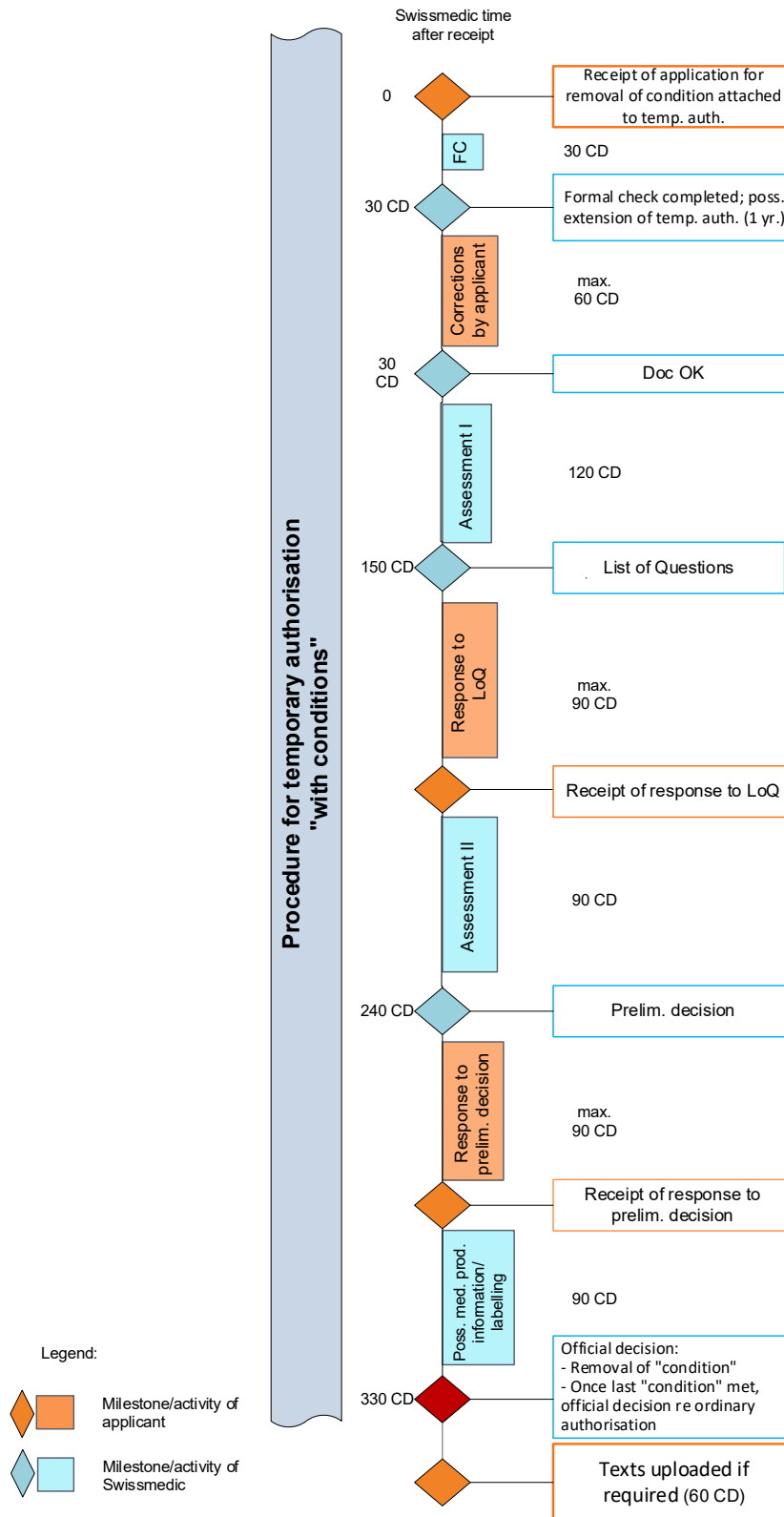
### 13.2 “Ex officio” temporary authorisation



13.2.1 Procedure for "ex officio" temporary authorisation



### 13.3 Application for removal of condition(s) attached to a temporary authorisation





## 13.4 Annex on tissue-independent or tumour-agnostic indications

### **Definition**

A tissue-independent or tumour-agnostic indication is characterised by the fact that its wording 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, an application for a procedure for temp.auth. can be submitted for oncologicals with tissue-independent or tumour-agnostic indication wording in connection with an AAA.

### **Guidance on the fulfilment of criteria of Art. 18 let. a to e. TPLO**

A disease or a subgroup of a disease may be deemed “recognised” or “established” in the context of a “tissue-independent” indication if it can be unequivocally distinguished from other subgroups within an entity by virtue of its prognosis, treatment and course, and by the fact that the medicinal product demonstrates general efficacy. 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.

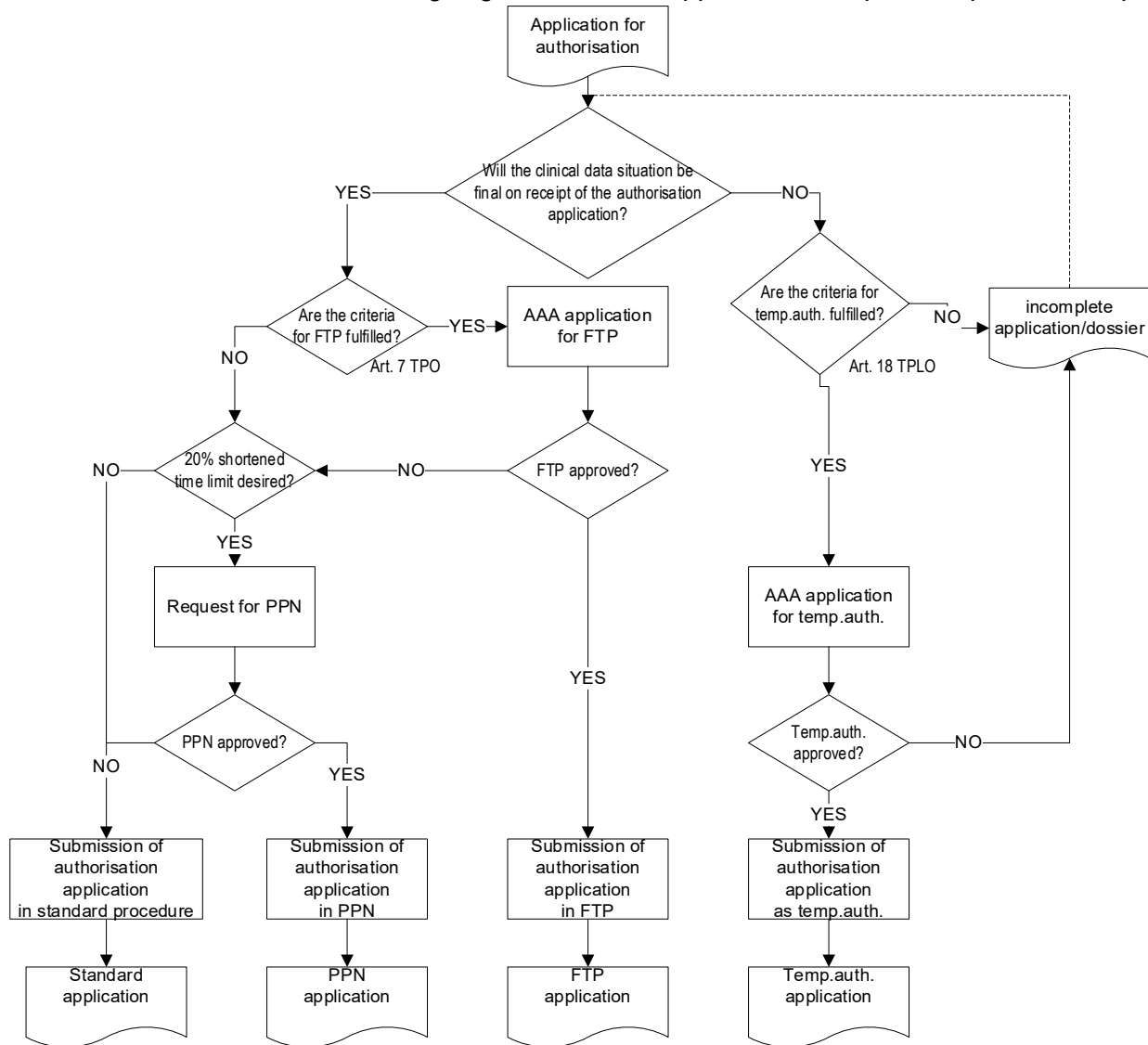
Tissue-agnostic indications will be assessed for compliance with criteria a to e on a case-by-case basis using the evidence base submitted. For this purpose, convincing proof of efficacy obtained from an adequate number of patients for each case must be presented for tumours in peripheral and central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

The temp.auth. 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 an authorisation procedure for temp.auth. 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 temp.auth. must be withdrawn (without conversion to an ordinary authorisation) in accordance with Article 21a paragraph 1, TPLO.

### 13.5 Decision tree

The key criterion for distinguishing temp.auth. and FTP is the **degree of finalisation of the clinical data package** on receipt of the authorisation application. If the pivotal clinical trials have been completed and evaluated (incl. CSR) at the time of application submission, then an FTP is possible. However, if clinical trials are still ongoing at the time of application receipt, a temp.auth. is required.



### 13.6 Interpretation in respect of the criterion of Art. 18 let. c TPLO when applying for temporary authorisation in connection with an AAA

Due to the differing degree of finalisation of the clinical data package on receipt of a temp.auth. application compared to an FTP application (see section 12.5), the requirement pertaining to the **point estimate** in respect of efficacy and safety and its **dispersion** (usually the 95% confidence interval) also differs.

- A.** An **approval of the application for an FTP** is probable if the point estimate is appreciably higher than that for the ST and the confidence intervals **do not overlap**.
- B.** A **rejection of the application for an FTP** is probable if the point estimate is higher but the confidence intervals **overlap**.
- C.** An **approval of the application for a temp.auth.** is probable if the point estimate for safety and efficacy is appreciably higher than that for the ST. However, the confidence intervals (ST – temp.auth.) may overlap in this case.
- D.** A **rejection of the application for a temp.auth.** is probable if the point estimate is only slightly higher and the confidence intervals overlap appreciably with those for the ST.

The efficacy and safety of the latest ST always form the basis for comparison in demonstrating the high therapeutic benefit (criterion c). Although the effect size for the temp.auth. candidate must be higher – to a clinically relevant extent – than that for the ST, the fact that the data situation is not yet final is taken into account and a larger confidence interval (possibly with overlapping with the ST) is acceptable (greater *uncertainty*).

The required difference in effect sizes (ST vs. proposed medicinal product for temp.auth.) in terms of safety and efficacy depend on the clinical situation, the currently marketed medicinal products for the respective indication and the prevalence and incidence of the illness.

Basically, statistically verified effects are basically expected at the time of the final data situation (FTP), whereas a conclusive statistical assessment – particularly from studies that are still in progress – might still be outstanding at the time of the prefinal data situation (temp.auth.).

