EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Guideline on core SmPC, Labelling and Package Leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells.

Draft

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Comments should be provided using this template. The completed comments form should be sent to QRD@ema.europa.eu

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Guideline on core SmPC, Labelling and Package Leaflet for advanced therapy medicinal products (ATMPs) containing genetically modified cells.

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Executive summary

This guideline describes the information to be included in the Summary of Products Characteristics (SmPC), Labelling and Package Leaflet for Advanced Therapy Medicinal Products (ATMPs) containing genetically modified cells.

1. Introduction (background)

The purpose of this core SmPC, Labelling and Package Leaflet (hereby referred to as core SmPC) is to provide applicants and regulators with harmonised guidance on the information to be included in the Product Information (PI) of ATMPs containing genetically modified cells.

2. Scope

This core SmPC only covers medicinal products containing genetically modified cells, allogeneic or autologous, including viral vector modified and genome edited cells.

Examples for Chimeric Antigen Receptor T (CAR-T) cells and Cluster of Differentiation 34+ (CD34+) modified cells are given in more detail. These can be used as model wording for other types of genetically modified cells.

3. Legal basis

This guideline should be read in conjunction with Article 11 and Annex V of Directive 2001/83/EC as amended, and Annexes II, III and IV of Regulation 1394/2007 on ATMPs. The guideline on SmPC and QRD product information templates and other reference documents should be read in the context of this guideline.

4. Glossary of terms and abbreviations

A	cell surface structures e.g. CD19, BCMA
Aph ID	apheresis identification number
ATMP	advanced therapy medicinal product
B	co-stimulatory domain e.g. CD28
C	signalling domain e.g. CD3-zeta
COI ID	chain of identity identification number
DIN	donor identification number
DOB	date of birth
JOIN	nomenclature for lot number
LIS	lot information sheet
n	a number of cells indicating dose or dose range
RfIC	release for infusion certificate

T	temperature
X	name of the medicinal product

5. Core SmPC, Labelling and Package Leaflet for ATMPs containing genetically modified cells.

ANNEX I

SUMMARY OF PRODUCT CHARACTERISTICS

<▼This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions. See section 4.8 for how to report adverse reactions.>

1. NAME OF THE MEDICINAL PRODUCT

[The strength should be expressed on the basis of the general term 'cells', which in this section is considered to define cells which contribute to the therapeutic effect.

e.g. CAR-T cells = total number of viable transduced cells
e.g. total number of CD34+ cells including the transduced cells: in addition to the therapeutic effect of the progeny of genetically modified stem/progenitor cells, the hematopoietic and immune reconstitution of the whole population is clinically relevant.

The specific cell type contributing to the therapeutic effect should be specified in section 2 of the SmPC, and in section 1 of Annex IIIA and IIIB in brackets beside the INN.

In those cases where there are two types of cells responsible for the therapeutic effect the strengths should be separated by a slash '/' as would be done for a fixed dose combination product
e.g. {X} $\geq 4 \times 10^6$ cells / $\geq 4.5 \times 10^6$ cells dispersion for infusion.

In line with the SmPC guideline, for containers where content is **delivered in full,** with no additional preparation step which would warrant a calculation of the cells on the basis of the volume, *the* ***total amount in the container(s)*** **(total use)** *would be the most meaningful expression*.

For containers where content may not be delivered in full and **calculation of total number of cells based on volume** may be needed, or dose is calculated on the basis of patient body weight, it would be more meaningful to express the strength on the basis of the ***amount per volume*** **(partial use).**

The term 'container' is understood as the 'immediate' container e.g. infusion bag, vial..etc.]

{(Invented) name strength pharmaceutical form}
[No ® ™ symbols included here and throughout the text; "cells" and "viral genomes" in plural.]

2. QUALITATIVE AND QUANTITATIVE COMPOSITION

[A detailed description of the cells or tissues contained in the product and their specific origin shall be provided, including the species of animal in cases of non-human origin. The following sub-headings shall be included:]

2.1 General description

[For CAR-T cell products the following wording should be included:]

{X} {<(INN)><(common name)>} is a genetically modified <autologous><allogeneic> cell-based product containing T cells <transfected><transduced><edited> *ex vivo* using a <{name of editing method}><{type of vector}> expressing an anti-{A} chimeric antigen receptor (CAR) comprising a <murine><human> <anti-{A} single chain variable fragment (scFv) linked to {B} co-stimulatory domain and {C} signalling domain>.

[For CD34+ cell products the following wording should be included:]

{X} {<(INN)><(common name)>} is a genetically modified autologous CD34+ cell enriched population

that contains haematopoietic stem <and progenitor> cells (HS<P>C) <transduced><edited> *ex vivo* using a **<**{name of editing method}**>** <{type of vector}> expressing the {gene name} <gene>.

2.2 Qualitative and quantitative composition

[Explanatory illustrations may be included, if necessary.

In cases where the quantitative information may vary between individual patient batches, separate batch/patient specific documentation should accompany the product e.g. Lot information sheet (LIS) or Release for infusion certificate (RfIC). The placement of this document should be mentioned in section 2.2.]

[For CAR-T cell products the following wording should be included:]

Each patient-specific {container} of {X} contains {<(INN)><(common name)>} at a batch-dependent concentration of <autologous><allogeneic>T cells genetically modified to express an anti-{A} chimeric antigen receptor (CAR-positive viable T cells). The medicinal product is packaged in one or more {container(s)} overall containing a cell {<pharmaceutical form>} of {n} [dose or dose range] CAR-positive viable T cells suspended in a <cryopreservative> solution.

Each {container}contains {volume} of {pharmaceutical form}.

<The quantitative information of medicinal product, including the number of {containers} (see section 6) to be administered, is presented in the <Lot information sheet (LIS)><Release for infusion certificate (RfIC)> located <inside the lid of the cryoshipper used for transport>>.

[For CD34+ cell products the following wording should be included:]

Each patient-specific {container} of {X} contains {<(INN)><(common name)>} at a batch-dependent concentration of genetically modified autologous CD34+ cell enriched population. The medicinal product is packaged in one or more {container(s)} overall containing a {pharmaceutical form}of {n} [total amount of cells/mL or range of cells/mL] of viable CD34+ enriched cell population suspended in a <cryopreservative> solution.

Each {container} contains {volume} of {X}.

<The quantitative information of medicinal product, including the number of {containers} (see section 6) to be administered, is presented in the <Lot information sheet (LIS)><Release for infusion certificate (RfIC)> located <inside the lid of the cryoshipper used for transport>>.

<Excipient(s) with known effect:>

[Cryopreservative content should be listed here.]

<For the full list of excipients, see section 6.1.>

3. PHARMACEUTICAL FORM

[Product specific]

4. CLINICAL PARTICULARS

4.1 Therapeutic indications

[Product specific]

4.2 Posology and method of administration

Posology

[For CAR-T cell products the following wording should be included:]

Treatment consists of a <single><multiple> dose(s) for infusion containing a {pharmaceutical form}> of CAR-positive viable T cells in <one><or more>{container(s)}.
The target dose is {total amount of cells per dose} CAR-positive viable T cells within a range of {n} [dose or dose range] CAR-positive viable T cells. See the accompanying <Lot information sheet (LIS)><Release for infusion certificate (RfIC)> for additional information pertaining to dose.

[For CD34+ cell products the following wording should be included:]

Treatment consists of a <single><multiple> dose(s) for infusion containing a {pharmaceutical form} of viable CD34+ cells in <one><or more> {container(s)}.

The minimum recommended dose of {X} is {*n*} CD34+ cells/kg.
In clinical studies, doses up to {*n*} CD34+ cells/kg have been administered.
See the accompanying < Lot information sheet (LIS)>< Release for infusion certificate (RfIC)> for additional information pertaining to dose.

The dose of {X} should be determined on the patient's body weight at the time of infusion.

Paediatric population

Method of administration

[Product specific]

For detailed instructions on preparation, administration, accidental exposure and disposal of {X}, see section 6.6.

4.3 Contraindications

<Hypersensitivity to the active substance(s) or to any of the excipients listed in section 6.1 <or {name of the residue(s)}>.>

4.4 Special warnings and precautions for use

[The order of warnings and precautions should in principle be determined by the importance of the safety information provided and the chronology of their occurrence.]

Traceability

The traceability requirements of cell-based advanced therapy medicinal products must apply. To ensure traceability the name of the product, the batch number and the name of the treated patient should be kept for a period of 30 years after expiry date of the product.

<Autologous use

{X} is intended solely for autologous use and should under no circumstances be administered to other patients. {X} must not be administered if the information on the product labels <and><lot information sheet><release for infusion certificate> <do><does> not match the patient's identity.>

<Transmission of an infectious agent

Although {X} is tested for sterility <and mycoplasma>, a small risk of transmission of infectious agents exists. Healthcare professionals administering {X} should, therefore, monitor patients for signs and symptoms of infections after treatment and treat appropriately, if needed.>

Blood, organ, tissue and cell donation

Patients treated with {X} should not donate blood, organs, tissues and cells for transplantation. <This information is provided in the Patient <Alert> Card which should be given to the patient after treatment.>

[Statements on screening for HBV, active HIV and active HCV should be included, when relevant.

For products containing a cryopreservant (e.g. DMSO) when administered, please include the following statement:]

<Hypersensitivity reactions

Serious hypersensitivity reactions, including anaphylaxis, may be due to <cryopreservant> [e.g. dimethyl sulfoxide (DMSO)] in {X}.>

[If patients are expected to enrol in a post-authorisation registry or registry based study to understand the long-term safety and efficacy of the product, include the following statement.]

<Long-term follow-up

Patients are expected to be enrolled in a <registry><long-term follow-up scheme> in order to better understand the long-term safety and efficacy of {X}.>

<Paediatric population>

4.5 Interaction with other medicinal products and other forms of interaction

<No interaction studies have been performed.>

[Please consider including the following statement as applicable:]

<Live vaccines

The safety of immunisation with live viral vaccines during or following treatment with {X} has not been studied. Vaccination with live viral vaccines is not recommended <for at least 6 weeks><{specified time}> prior to the start of <conditioning regimens><lymphodepleting chemotherapy >, during {X} treatment, and until <immune>< haematological> recovery following treatment.>

<Paediatric population>
<Interaction studies have only been performed in adults.>

4.6 Fertility, pregnancy and lactation

<Pregnancy>
<Breast-feeding>
<Fertility>

4.7 Effects on ability to drive and use machines

<{Invented) name} has <no or negligible influence> <minor influence> <moderate influence> <major influence> on the ability to drive and use machines.> [describe effects where applicable.]

<Not relevant.>

4.8 Undesirable effects

[Immunogenicity must be addressed in the subsection "Description of selected adverse reactions". Data from clinical studies should be summarised in this subsection.]

<Paediatric population>

Reporting of suspected adverse reactions
Reporting suspected adverse reactions after authorisation of the medicinal product is important. It allows continued monitoring of the benefit/risk balance of the medicinal product. Healthcare professionals are asked to report any suspected adverse reactions via the national reporting system listed in Appendix V*.

[*For the printed material, please refer to the guidance of the annotated QRD template.]

4.9 Overdose

<Paediatric population>

5. PHARMACOLOGICAL PROPERTIES

5.1 Pharmacodynamic properties

Pharmacotherapeutic group: {group}, ATC code: <{code}> <not yet assigned>

<Mechanism of action>
<Pharmacodynamic effects>
<Clinical efficacy and safety>
<Paediatric population>

[If the European Medicines Agency has waived or deferred a paediatric development, the information should be given as follows:]

[For waivers applying to all subsets:]
<The European Medicines Agency has waived the obligation to submit the results of studies with <{(Invented) name}> in all subsets of the paediatric population in {condition as per paediatric investigation plan (PIP) decision, for the granted indication} (see section 4.2 for information on paediatric use).>

[For deferrals applying to at least one subset:]
<The European Medicines Agency has deferred the obligation to submit the results of studies with {(Invented) name}> in one or more subsets of the paediatric population in {condition as per paediatric investigation plan (PIP) decision, for the granted indication} (see section 4.2 for information on paediatric use).>

[For medicinal products approved under "conditional approval", include the following statement:]
<This medicinal product has been authorised under a so-called 'conditional approval' scheme.
This means that further evidence on this medicinal product is awaited.
The European Medicines Agency will review new information on this medicinal product at least every year and this SmPC will be updated as necessary.>

[For medicinal products approved under "exceptional circumstances", include the following statement:]
<This medicinal product has been authorised under 'exceptional circumstances'.
This means that <due to the rarity of the disease> <for scientific reasons> <for ethical reasons> it has not been possible to obtain complete information on this medicinal product.
The European Medicines Agency will review any new information which may become available every year and this SmPC will be updated as necessary.>

5.2 Pharmacokinetic properties

<Absorption>
<Distribution>
<Biotransformation>
<Elimination>
<Linearity/non-linearity>
<Pharmacokinetic/pharmacodynamic relationship(s)>

5.3 Preclinical safety data

<Non-clinical data reveal no special hazard for humans based on conventional studies of safety pharmacology, repeated dose toxicity, genotoxicity, carcinogenic potential, toxicity to reproduction and development.>

<Effects in non-clinical studies were observed only at exposures considered sufficiently in excess of the maximum human exposure indicating little relevance to clinical use.>

<Adverse reactions not observed in clinical studies, but seen in animals at exposure levels similar to clinical exposure levels and with possible relevance to clinical use were as follows:>

<Environmental risk assessment (ERA)>
[Not applicable for medicinal products containing genetically modified cells.]

6. PHARMACEUTICAL PARTICULARS

6.1 List of excipients

[The excipients should be listed in the language of the text, expressed qualitatively only. Preservative systems should also be described.]

<None.>

6.2 Incompatibilities

<Not applicable.>

<In the absence of compatibility studies, this medicinal product must not be mixed with other medicinal products.>

<This medicinal product must not be mixed with other medicinal products except those mentioned in section <6.6> <and> <12>.>

6.3 Shelf life

[Information on the finished product shelf life and on the in-use stability after thawing and/or reconstitution/dilution should appear here. Only one overall shelf life for the finished product is to be given even if different components of the product may have a different shelf life.]

<...> <6 months> <...> <1 year> <18 months> <2 years> <30 months> <3 years> <...>

6.4 Special precautions for storage

[For storage condition statements, see Appendix III.]
[General storage conditions of the finished medicinal product should appear here, together with a cross-reference to section 6.3 where appropriate.

As an example, for frozen cell products the following wording could be included:]

<{X} must be stored in <the vapour phase of liquid nitrogen {(≤ − {T} °C)}><…> and must remain frozen until the patient is ready for treatment to ensure viable cells are available for patient administration. Do not re-freeze after thawing.>

<For storage conditions after <thawing><reconstitution><dilution> of the medicinal product, see section 6.3.>

6.5 Nature and contents of container <and special equipment for use, administration or implantation>

[Explanatory illustrations may be included, if necessary.]

<Not all pack sizes may be marketed.>

6.6 Special precautions for disposal and other handling

[Instructions for the transport, handling and preparation prior to administration, thawing, administration, disposal and accidental exposure should be included:]

Precautions to be taken before handling or administering the medicinal product

<{X} should be transported within the facility in closed, break-proof, leak-proof containers.>

This medicinal product contains human <blood> cells. Healthcare professionals handling {X} should take appropriate precautions (wearing <gloves><protective clothing><and><eye protection>) to avoid potential transmission of infectious diseases.

[Information to verify prior to administration e.g. number of infusions bags, volume to be infused, patient identity, breaches of integrity etc. should be included]

Preparation prior to administration

[If applicable, the thawing process must be detailed in full in the following section:]

<Thawing>

Administration

Precautions to be taken for the disposal of the medicinal product
Unused medicinal product and all material that has been in contact with {X} (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling of human-derived material.

Accidental exposure
In case of accidental exposure local guidelines on handling of human-derived material should be followed. Work surfaces and materials which have potentially been in contact with {X} must be decontaminated with appropriate disinfectant.

<Use in the paediatric population>

7. MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

8. MARKETING AUTHORISATION NUMBER(S)

9. DATE OF FIRST AUTHORISATION/RENEWAL OF THE AUTHORISATION

<Date of first authorisation: {DD month YYYY}>
<Date of latest renewal: {DD month YYYY}>

10. DATE OF REVISION OF THE TEXT

<{MM/YYYY}>
<{DD/MM/YYYY}>
<{DD month YYYY}>

<11. DOSIMETRY>

<12. INSTRUCTIONS FOR PREPARATION OF RADIOPHARMACEUTICALS>

<Any unused medicinal product or waste material should be disposed of in accordance with local requirements.>

<Detailed information on this medicinal product is available on the website of the European Medicines Agency http://www.ema.europa.eu<, and on the website of {name of MS Agency (link)}>.

ANNEX III

LABELLING AND PACKAGE LEAFLET

A. LABELLING

PARTICULARS TO APPEAR ON <THE OUTER PACKAGING> <AND> <THE IMMEDIATE PACKAGING>

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT

[A description of the type of cell as per section 2 of the SmPC should be included in this section beside the INN in brackets e.g. (CAR + viable T cells) or (CD34+ cells)]
{(Invented) name strength pharmaceutical form}
{active substance(s)}

2. STATEMENT OF ACTIVE SUBSTANCE(S)

[Where the advanced therapy medicinal product contains cells or tissues, the statement "This medicine contains cells of human/animal {as appropriate} origin" together with a short description of these cells or tissues and of their specific origin, including the species of animal in cases of non-human origin should be included.]
This medicine contains cells of <human> <animal> origin.

3. LIST OF EXCIPIENTS

[Preservative systems should be described.]

4. PHARMACEUTICAL FORM AND CONTENTS

5. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

6. SPECIAL WARNING THAT THE MEDICINAL PRODUCT MUST BE STORED OUT OF THE SIGHT AND REACH OF CHILDREN

Keep out of the sight and reach of children.

7. OTHER SPECIAL WARNING(S), IF NECESSARY

[In the case of advanced therapy medicinal products for autologous use, the unique patient identifier and the statement "For autologous use only" shall be included.]
<For autologous use only.>

8. EXPIRY DATE

[The expiry date may specify the day, or day and time for non-cryopreserved products.]

9. SPECIAL STORAGE CONDITIONS

10. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains human <blood> cells. Unused medicine or waste material must be disposed of in compliance with the local guidelines on handling of waste of human-derived material.

11. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}><{fax}>
<{e-mail}>

12. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

13. BATCH NUMBER, DONATION AND PRODUCT CODES

[The following donation and product codes should be included if applicable. The Single European Code (SEC), a technical requirement laid down in Commission Directive (EU) 2015/565, should be included on the outer packaging, or when there is no outer packaging on the immediate packaging. If this is not possible it should always be included in the accompanying Lot information sheet (LIS) or Release for infusion certificate (RfIC).]

{SEC}:
<{First name}:>
<{Last name}:>
<{Patient DOB}:>
<{Patient ID}:>
<{Aph ID/DIN}:>
<{COI ID}:>
<{JOIN}:>
<{Bag ID}:>
<{Order ID}:>

14. GENERAL CLASSIFICATION FOR SUPPLY

15. INSTRUCTIONS ON USE

16. INFORMATION IN BRAILLE

Justification for not including Braille accepted.

17. UNIQUE IDENTIFIER – 2D BARCODE

[As per Annex I of Commission Regulation 2016/161 advanced therapy medicinal products which contain or consist of tissues or cells are exempt from the requirement to bear the safety features on their packaging pursuant to Article 54a(1) of Directive 2001/83/EC. The following statement should be included in this section in grey-shading:]

Not applicable.

[When this template is used for immediate labelling, this section must be included and left blank.]

18. UNIQUE IDENTIFIER - HUMAN READABLE DATA

[As per Annex I of Commission Regulation 2016/161 advanced therapy medicinal products which contain or consist of tissues or cells are exempt from the requirement to bear the safety features on their packaging pursuant to Article 54a(1) of Directive 2001/83/EC. The following statement should be included in this section in grey-shading:]

Not applicable.

[When this template is used for immediate labelling, this section must be included and left blank.]

MINIMUM PARTICULARS TO APPEAR ON BLISTERS OR STRIPS

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT

[A description of the type of cell as per section 2 of the SmPC should be included in this section beside the INN in brackets e.g. (CAR + viable T cells) or (CD34+ cells)]

{(Invented) name strength pharmaceutical form}
{active substance(s)}

2. NAME OF THE MARKETING AUTHORISATION HOLDER

{Name}

3. EXPIRY DATE

4. BATCH NUMBER, DONATION AND PRODUCT CODES

[The following donation and product codes should be included if applicable. The Single European Code (SEC), a technical requirement laid down in Commission Directive (EU) 2015/565, should be included on the outer packaging, or when there is no outer packaging on the immediate packaging. If this is not possible it should always be included in the accompanying Lot information sheet (LIS) or Release for infusion certificate (RfIC).]

{SEC}:
<{First name}:>
<{Last name}:>
<{Patient DOB}:>
<{Patient ID}:>
<{Aph ID/DIN}:>
<{COI ID}:>
<{JOIN}:>
<{Bag ID}:>
<{Order ID}:>

5. OTHER

[In the case of advanced therapy medicinal products for autologous use, the unique patient identifier and the statement “For autologous use only” shall be included.]
<For autologous use only.>

MINIMUM PARTICULARS TO APPEAR ON SMALL IMMEDIATE PACKAGING UNITS

{NATURE/TYPE}

1. NAME OF THE MEDICINAL PRODUCT AND ROUTE(S) OF ADMINISTRATION

[A description of the type of cell as per section 2 of the SmPC should be included in this section beside the INN in brackets e.g. (CAR + viable T cells) or (CD34+ cells)]
{(Invented) name strength pharmaceutical form}
{active substance(s)}
{Route of administration}

2. METHOD OF ADMINISTRATION

3. EXPIRY DATE

4. BATCH NUMBER, DONATION AND PRODUCT CODES

[The following donation and product codes should be included if applicable. The Single European Code (SEC), a technical requirement laid down in Commission Directive (EU) 2015/565, should be included on the outer packaging, or when there is no outer packaging on the immediate packaging. If this is not possible it should always be included in the accompanying Lot information sheet (LIS) or Release for infusion certificate (RfIC).]

{SEC}:
<{First name}:>
<{Last name}:>
<{Patient DOB}:>
<{Patient ID}:>
<{Aph ID/DIN}:>
<{COI ID}:>
<{JOIN}:>
<{Bag ID}:>
<{Order ID}:>

5. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT

6. OTHER

[In the case of advanced therapy medicinal products for autologous use, the unique patient identifier and the statement “For autologous use only” shall be included.]
<For autologous use only.>

PARTICULARS TO APPEAR ON THE <LOT INFORMATION SHEET (LIS)><RELEASE FOR INFUSION CERTIFICATE (RfIC)> INCLUDED WITH EACH SHIPMENT FOR ONE PATIENT

[When the medicinal product is accompanied by a lot information sheet or release for infusion certificate which completes the patient-specific information provided in the outer/immediate labelling with batch specific information, the content of this document will be included as the last element of Annex IIIA. The data should be presented according to the template below, irrespective of their sequence and their position in the printed materials.]

1. NAME OF THE MEDICINAL PRODUCT

[A description of the type of cell as per section 2 of the SmPC should be included in this section beside the INN in brackets e.g. (CAR + viable T cells) or (CD34+ cells)]

{(Invented) name strength pharmaceutical form}

2. STATEMENT OF ACTIVE SUBSTANCE(S)

3. CONTENTS BY WEIGHT, BY VOLUME OR BY UNIT, AND DOSE OF THE MEDICINAL PRODUCT

[The particulars needed for the correct dosing and administration of the product should be included here such as volume per container, total number of container(s), total number of cells per container, total dose etc.]

4. METHOD AND ROUTE(S) OF ADMINISTRATION

Read the package leaflet before use.

5. OTHER SPECIAL WARNING(S), IF NECESSARY

Save this document and have it available when preparing for administration of {X}.

<For autologous use only.>

6. SPECIAL STORAGE CONDITIONS

7. EXPIRY DATE AND OTHER BATCH SPECIFIC INFORMATION

[Additional batch specific information should be included in this section as necessary, e.g. date of manufacture, time for transportation, time for expiry etc.")]

8. SPECIAL PRECAUTIONS FOR DISPOSAL OF UNUSED MEDICINAL PRODUCTS OR WASTE MATERIALS DERIVED FROM SUCH MEDICINAL PRODUCTS, IF APPROPRIATE

This medicine contains human <blood> cells. Unused medicine or waste material must be disposed of in

compliance with the local guidelines on handling of waste of human-derived material.

9. BATCH NUMBER, DONATION AND PRODUCT CODES

[The following donation and product codes should be included if applicable. The Single European Code (SEC) should always appear in the Lot information sheet (LIS) or Release for infusion certificate (RfIC) if it cannot be placed on the outer packaging or immediate packaging.]

{SEC}:
<{First name}:>
<{Last name}:>
<{Patient DOB}:>
<{Patient ID}:>
<{Aph ID/DIN}:>
<{COI ID}:>
<{JOIN}:>
<{Bag ID}:>
<{Order ID}:>

10. NAME AND ADDRESS OF THE MARKETING AUTHORISATION HOLDER

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

11. MARKETING AUTHORISATION NUMBER(S)

EU/0/00/000/000

B. PACKAGE LEAFLET

[**NOTE**: The following items which must appear in the package leaflet are listed in Annex IV of Regulation (EC) 1394/2007.

Guidance notes in orange cross-refer to the section/information of the SmPC which is to be reflected in that particular section of the package leaflet.]

Package leaflet: Information for the <patient> <user>

{(Invented) name strength pharmaceutical form}
{active substance(s)}

[A description of the type of cell as per section 2 of the SmPC should be included in this section beside the INN in brackets e.g. (CAR + viable T cells) or (CD34+ cells)]

< ▼This medicine is subject to additional monitoring. This will allow quick identification of new safety information. You can help by reporting any side effects you may get. See the end of section 4 for how to report side effects. > [For medicinal products subject to additional monitoring ONLY]

<**Read all of this leaflet carefully before you start <taking> <using> this medicine because it contains important information for you.**
- Keep this leaflet. You may need to read it again.
- If you have any further questions, ask your <doctor> <,> <or> <pharmacist> <or nurse>.
<- This medicine has been prescribed for you only. Do not pass it on to others. It may harm them, even if their signs of illness are the same as yours.> [Do not include this statement in case of hospital use.]
- If you get any side effects, talk to your <doctor> <,> <or> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. See section 4.>

What is in this leaflet

1. What X is and what it is used for

[(Invented) name, active substance(s) and pharmacotherapeutic group]

[Therapeutic indications]

[If appropriate, specify that:
- if the medicine is an advanced therapy medicine which contains cells or tissues, a description of those cells or tissues and of their specific origin, including the species of animal in cases of non-human origin, should be provided in line with section 2.1 of the SmPC.
- if the medicine is an advanced therapy medicine which contains medical devices or active implantable medical devices, a description of those devices and their specific origin should be provided in line with section 2.2 of the SmPC.]

[Information on the benefits of using this medicine]

<You must talk to a doctor if you do not feel better or if you feel worse <after {number of} days>.>

2. What you need to know before you <receive> <are given> X

[Contraindications]
Do not <take> <use> X
- <if you are allergic to {active substance(s)} or any of the other ingredients of this medicine (listed in section 6).>

[Appropriate precautions for use; special warnings]
Warnings and precautions
Talk to your doctor <or> <,> <pharmacist> <or nurse> before <taking> <using> X

[All warnings and precautions for use included in section 4.4 of the SmPC should be provided here (as in the SmPC, the order should be in principle determined by the importance of safety information provided) and it should also be made clear for each warning or precaution for use, what action the patient should take to minimise the potential risk. In the case of advanced therapy products containing genetically modified cells the order will also be determined by the chronology of occurrence of the adverse drug reaction.]

Children <and adolescents>

[Interactions with other medicines]
Other medicines and X
<Tell your <doctor> <or> <pharmacist> if you are <taking> <using>, have recently <taken> <used> or might <take> <use> any other medicines.>

[Interactions with food and drink]
X with <food> <and> <,> <drink> <and> <alcohol>

[Use by pregnant or breast-feeding women, information on fertility]
Pregnancy <and> <,> breast-feeding <and fertility>
<If you are pregnant or breast-feeding, think you may be pregnant or are planning to have a baby, ask your <doctor> <or> <pharmacist> for advice before taking this medicine.>

[Effects on the ability to drive or to use machines]
Driving and using machines

[Excipients warnings]
<X contains {name the excipient(s)}>

3. How X is given

[Dose (SmPC section 4.2)]

<The recommended dose is...>

<Use in children <and adolescents>>

[Route(s) and/or method of administration (SmPC section 4.2)]

< Other medicines you will be given before X>

<How X is given>

<After X is given>

<If you <are given> more X than you should>

<If you miss an appointment>

< Call your doctor or the treatment centre as soon as possible to make another appointment.>

[Duration of treatment (SmPC section 4.2)]

<If you stop <taking> <using> X>
<If you have any further questions on the use of this medicine, ask your <doctor> <,> <or> <pharmacist> <or nurse>.>

4. Possible side effects

[Description of side effects]
[Begin this section with]
Like all medicines, this medicine can cause side effects, although not everybody gets them.

<Additional side effects in children <and adolescents>>

Reporting of side effects
If you get any side effects, talk to your <doctor> <or> <,> <pharmacist> <or nurse>. This includes any possible side effects not listed in this leaflet. You can also report side effects directly via the national reporting system listed in Appendix V.* By reporting side effects you can help provide more information on the safety of this medicine.

[*For the printed materials: No reference to Appendix V should be included in the printed materials. The above grey-shaded terms will only appear in the published version of the approved product information annexes on the European Medicines Agency website. The actual details of the national reporting system (as listed in Appendix V) of the concerned Member State(s) shall be displayed on the printed version.

5. How to store X

Keep this medicine out of the sight and reach of children.

[Expiry date]
[The expiry date may specify the day, or day and time for non-cryopreserved products.]
Do not use this medicine after the expiry date which is stated on the <label> <carton> <bottle> <…> <after {abbreviation used for expiry date}.>

[Storage conditions]
[Information should be in accordance with section 6.4 of the SmPC; for storage conditions statements see Appendix III.]

[Where applicable, shelf life after reconstitution, dilution or after first opening the container]
[Information should be in accordance with section 6.3 of the SmPC; please also refer to "Note for Guidance on Maximum Shelf Life for Sterile Products for Human Use after First Opening or Following Reconstitution" (CPMP/QWP/159/96/corr).]

[Where appropriate, warnings against certain visible signs of deterioration]
<Do not use this medicine if you notice {description of the visible signs of deterioration}.>

6. Contents of the pack and other information

[Full statement of the active substance(s) and excipient(s)]

What X contains

- The active substance(s) is (are)…
- The other <ingredient(s)> <(excipient(s))> is (are)... [A cross-reference to section 2 "X contains {name of the excipients}" should be included when applicable.]

This medicine contains genetically modified human <blood> cells.

[Pharmaceutical form, nature and contents of container in weight, volume or units of dose]

What X looks like and contents of the pack

[Name and address of the MAH and of the manufacturer responsible for batch release, if different]

Marketing Authorisation Holder and Manufacturer

{Name and address}
<{tel}>
<{fax}>
<{e-mail}>

<For any information about this medicine, please contact the local representative of the Marketing Authorisation Holder:

België/Belgique/Belgien
{Nom/Naam/Name}
<{Adresse/Adres/Anschrift }
B-0000 {Localité/Stad/Stadt}>
Tél/Tel: +{N° de téléphone/Telefoonnummer/ Telefonnummer}
<{e-mail}>

Lietuva
{pavadinimas}
<{adresas}
LT {pašto indeksas} {miestas}>
Tel: + {telefono numeris}
<{e-mail}>

България
{Име}
<{Адрес}
{Град} {Пощенски код}>
Тел.: +{Телефонен номер}
<{e-mail}>

Luxembourg/Luxemburg
{Nom}
<{Adresse}
L-0000 {Localité/Stadt}>
Tél/Tel: +{N° de téléphone/Telefonnummer}
<{e-mail}>

Česká republika
{Název}
<{Adresa}
CZ {město}>
Tel: +{telefonní číslo}
<{e-mail}>

Magyarország
{Név}
<{Cím}
H-0000 {Város}>
Tel.: +{Telefonszám}
<{e-mail}>

Danmark
{Navn}
<{Adresse}
DK-0000 {by}>
Tlf: +{Telefonnummer}
<{e-mail}>

Malta
{Isem}
<{Indirizz}
MT-0000 {Belt/Raħal}>
Tel: +{Numru tat-telefon}
<{e-mail}>

Deutschland
{Name}
<{Anschrift}
D-00000 {Stadt}>

Nederland
{Naam}
<{Adres}
NL-0000 XX {stad}>

Tel: +{Telefonnummer}
<{e-mail}>

Eesti
{Nimi}
<{Aadress}
EE - {Postiindeks} {Linn}>
Tel: +{Telefoninumber}
<{e-mail}>

Ελλάδα
{Όνομα}
<{Διεύθυνση}
GR-000 00 {πόλη}>
Τηλ: +{Αριθμός τηλεφώνου}
<{e-mail}>

España
{Nombre}
<{Dirección}
E-00000 {Ciudad}>
Tel: +{Teléfono}
<{e-mail}>

France
{Nom}
<{Adresse}
F-00000 {Localité}>
Tél: +{Numéro de téléphone}
<{e-mail}>

Hrvatska
{Ime}
<{Adresa}
{Poštanski broj} {grad}>
Tel: +{Telefonski broj}
<{e-mail}>

Ireland
{Name}
<{Address}
IRL - {Town} {Code for Dublin}>
Tel: +{Telephone number}
<{e-mail}>

Ísland
{Nafn}
<{Heimilisfang}
IS-000 {Borg/Bær}>
Sími: +{Símanúmer}
<{Netfang }>

Italia
{Nome}
<{Indirizzo}

Tel: +{Telefoonnummer}
<{e-mail}>

Norge
{Navn}
<{Adresse}
N-0000 {poststed}>
Tlf: +{Telefonnummer}
<{e-mail}>

Österreich
{Name}
<{Anschrift}
A-0000 {Stadt}>
Tel: +{Telefonnummer}
<{e-mail}>

Polska
{Nazwa/ Nazwisko}
<{Adres:
PL-00 000{Miasto}>
Tel.: +{Numer telefonu}
<{e-mail}>

Portugal
{Nome}
<{Morada}
P-0000–000 {Cidade}>
Tel: +{Número de telefone}
<{e-mail}>

România
{Nume}
<{Adresă}
{Oraş} {Cod poştal} – RO>
Tel: +{Număr de telefon}
<{e-mail}>

Slovenija
{Ime}
<{Naslov}
SI-0000 {Mesto}>
Tel: +{telefonska številka}
<{e-mail}>

Slovenská republika
{Názov}
<{Adresa}
SK-000 00 {Mesto}>
Tel: +{Telefónne číslo}
<{e-mail}>

Suomi/Finland
{Nimi/Namn}
<{Osoite/Adress}

I-00000 {Località}>
Tel: +{Numero di telefono}
<{e-mail}>

Κύπρος
{Όνομα}
<{Διεύθυνση}
CY-000 00 {πόλη}>
Τηλ: +{Αριθμός τηλεφώνου}
<{e-mail}>

Latvija
{Nosaukums}
<{Adrese}
{Pilsēta}, LV{pasta indekss }>
Tel: +{telefona numurs}
<{e-mail}>

FIN-00000 {Postitoimipaikka/Stad}>
Puh/Tel: +{Puhelinnumero/Telefonnummer}
<{e-mail}>

Sverige
{Namn}
<{Adress}
S-000 00 {Stad}>
Tel: +{Telefonnummer}
<{e-mail}>

United Kingdom (Northern Ireland)
{Name}
<{Address}
{Town} {Postal code} – UK>
Tel: +{Telephone number}
<{e-mail}>

This leaflet was last revised in <{MM/YYYY}><{month YYYY}>.

[For medicines approved under "conditional approval", include the following statement:]
<This medicine has been given 'conditional approval'.
This means that there is more evidence to come about this medicine.
The European Medicines Agency will review new information on this medicine at least every year and this leaflet will be updated as necessary.>

[For medicines approved under "exceptional circumstances", include the following statement:]
<This medicine has been authorised under 'exceptional circumstances'.
This means that <because of the rarity of this disease> <for scientific reasons> <for ethical reasons> it has been impossible to get complete information on this medicine.
The European Medicines Agency will review any new information on this medicine every year and this leaflet will be updated as necessary.>

<Other sources of information>
Detailed information on this medicine is available on the European Medicines Agency web site: http://www.ema.europa.eu<, and on the website of {name of Member State Agency (link)}>.* <There are also links to other websites about rare diseases and treatments.> [the last part of the statement is applicable to orphan medicines only.]

[*This statement is optional and **it is only to be displayed on the final printed materials**. It will not be included in the product information annexes as applicants may choose to include it for one or more Member States but not for all of them.]

[For medicines having been granted an exemption of having English only package leaflet according to Art 63 of Directive 2001/83/EC, the following statement translated in all EU/EEA languages should be included here:
<This leaflet is available in all EU/EEA languages on the European Medicines Agency website.>
this information should appear prominently in the printed material.]

The following information is intended for healthcare professionals only:

[Instructions for the transport, handling and preparation prior to administration, thawing, administration, disposal and accidental exposure should be included as in section 6.6 of the SmPC:]

Precautions to be taken before handling or administering the medicinal product

<{X} should be transported within the facility in closed, break-proof, leak-proof containers.>

This medicinal product contains human <blood> cells. Healthcare professionals handling {X} should take appropriate precautions (wearing <gloves><protective clothing><and><eye protection>) to avoid potential transmission of infectious diseases.

[Information to verify prior to administration e.g. number of infusions bags, volume to be infused, patient identity, breaches of integrity etc.]

Preparation prior to administration

[If applicable, the thawing process must be detailed in full in the following section:]

<Thawing>

Administration

Precautions to be taken for the disposal of the medicinal product
Unused medicinal product and all material that has been in contact with {X} (solid and liquid waste) should be handled and disposed of as potentially infectious waste in accordance with local guidelines on handling of human-derived material.

Accidental exposure
In case of accidental exposure local guidelines on handling of human-derived material should be followed. Work surfaces and materials which have potentially been in contact with {X} must be decontaminated with appropriate disinfectant.