Instructions to applicants for submitting variations to the terms of Marketing Authorisations

Commission Regulation (EU) No 712/2012 of 3 August 2012 amending Regulation (EC) No 1234/2008 of 24 November 2008 was published in August 2012. Among other changes, this regulation extended the scope of the Regulation on Variations to the national procedure from 4 August 2013.

The purpose of this document is to clarify aspects related to the submission to Infarmed – Autoridade Nacional do Medicamento e Produtos de Saúde, I.P. of variation to the terms of Marketing Authorisations (MAs) by national procedure and by Mutual Recognition and Decentralised procedure, and it should be used as a supplement to the European Commission Guidelines on the details of the various types of variations, on the operation of the procedures laid down in Chapters II, IIa, III and IV of Commission Regulation (EC) No 1234/2008 of 24 November 2008, and the documentation that must be submitted in accordance with those procedures.

Regardless of the type of variation or procedure, these applications must be submitted exclusively online using the Medicinal Products for Human Use Management System – Variations (SMUH-ALTER) available at the Infarmed website at Medicamentos Uso Humano> Autorização de Introdução no Mercado> Alterações aos Termos de AIM / Transferência de Titular> Submissão eletrónica de alterações.

This document **does not cover** the following applications:

- MA extensions
- MAH ownership transfers
- Notifications under article 31 (4) of Decree Law no. 176/2006 of 30 August, transposing article 61 (3) of Directive 2001/83/EC of 6 November

Contents

Purely National Procedure

1. Variation Procedure Numbering System

Infarmed considered it was necessary to develop a numbering system for variation procedures based on the mutual recognition/decentralised procedure (MR/DC) numbering system currently in effect.

Applicants should be aware of the numbering system's rules in order to assign the correct procedure number to variation applications when submitting them through SMUH-ALTER.

Similar to the numbering system applicable to the MR/DC procedure, the variation procedure number is comprised of:

- **Base structure**, which identifies the procedure number of the medicinal products, assigned under the MA application;
- **Additional information**, identifying the type of variation application submitted and its sequential number.

The base structure used by Infarmed to identify MA applications submitted by national procedure since 1999 is the following:

AA/H/nnnn/sss	AA =	Year the MA application was submitted
	H =	Medicinal product for human use
	nnnn =	Application sequential no. for each year
	sss =	Strength/pharmaceutical form identifying no.

Examples:

Name of medicinal product	MA no.
Paracetamol XPTO 1000 mg Tablets	99/H/0999/001
Paracetamol XPTO 40 mg/ml Syrup	06/H/0999/001
Sinvastatin XPTO 20 mg Tablets	05/H/0999/001
Sinvastatin XPTO 40 mg Tablets	05/H/0999/002

Note: Sinvastatin XPTO – To make reference to all strengths/pharmaceutical forms, the abbreviated form 05/H/0999/001-002 may be used.

For MAs prior to 1999, the numbers of MA applications submitted by national procedure follow various base structures, including:

n/nnn/AA or AA/n/nnn		
n/nnn/Lxx or Lxx/n/nnn		
nnn/AA		
Gn/nnn/AA or nnn/AG/AA	G =	Generic medicinal product
	AG =	Generic medicinal product
nnn/NC/AA	NC =	National
ME/nnn	ME =	Multi-states
RX/nnn/AA or nnn/RX/AA	RX =	Radiopharmaceuticals
nnnn		MA revision

Examples:

Name of medicinal product	MA Number
Paracetamol XPTO 500 mg Tablets	9/099/89
Paracetamol XPTO 125 mg Suppositories	G9/099/93
Paracetamol XPTO 250 mg Suppositories	G9/099/93

For certain medicinal products, the numbers of the MA applications submitted by the national procedure follow the base structures below:

MTBP/nnnn/AA	MTBP = Traditional Herbal Medicinal Product
nnnn/HOM/AA	HOM = Homeopathic Medicinal Product
AA/PI/CC/nnn	PI = Parallel Imports CC = A two letter code identifying the Member State of Origin

When submitting variations online, applicants will be required to insert the **Variation Procedure Number** and the **MRP/National Variation Number** (corresponding to an individual variation number associated to each medicinal product included in the application) pertaining to each submitted variation application.

MA Number:
This number is shown on the first page of the variation application form and is used to identify the application in communications between the applicant and the Medicinal Product Evaluation Department (DAM - Direção de Avaliação de Medicamentos).
The MA Number shall refer to the sequential number of the variation application by national procedure, by applicant and for each year.

Individual Variation Number:
This is the number shown on the table of medicinal products in the variation application form corresponding to the application. It identifies the medicinal product / strength / pharmaceutical form, in particular when dealing with grouped applications.
The individual variation number shall refer to the chronological application sequence number, by national procedure, and by medicinal product.

For the purpose of defining the submission of single variation applications versus grouped variation applications within the **national procedure**, medicinal products should be considered as part of the same market authorisation when they have:

- the same MA Holder (same legal entity)
- the same INN;
- the same name (notwithstanding product name differences attributable to acronyms or qualitative terms).

1.1. MA Number/Individual Variation Number for single applications

The MA Number shall use a year/applicant structure plus two additional elements, as shown in the example below:

AAAA/[Applicant]/QQ/vvvv	AAAA = Year the application was submitted [Applicant] = Applicant's abbreviated name or acronym QQ = IA, IB or II, according to the type of variation vvvv = Chronological number of the application submitted to Infarmed by applicant and by year

The Individual Variation Number shall use the base structure of the MA number plus two additional elements, as shown in the example below:

[Base structure]/QQ/vvv	QQ = IA, IB or II, according to the type of variation vvv = Chronological number of the variation

Examples:

Variation type	MA no.	Individual variation no.
Type IA Sinvastatin XPTO	2013/XPTO/IA/0001	20 mg Tablets: 05/H/0999/001/IA/001 40 mg Tablets: 05/H/0999/002/IA/001
Type IB Sinvastatin XPTO	2013/XPTO/IB/0002	20 mg Tablets: 05/H/0999/001/IB/002
Type II Sinvastatin XPTO	2013/XPTO/II/0003	20 mg Tablets: 05/H/0999/001/II/003 40 mg Tablets: 05/H/0999/002/II/002
Type IA Paracetamol XPTO	2013/XPTO/IA/0004	500 mg Tablets: 9/099/89/IA/001 1000 mg Tablets: 99/H/0999/001/IA/001 125 mg Suppositories: G9/099/93/IA/001 250 mg Suppositories: G9/099/93/IA/001
Type IB Paracetamol XPTO	2013/XPTO/IB/0005	500 mg Tablets: 9/099/89/IB/002 1000 mg Tablets: 99/H/0999/001/IB/002 40 mg/ml Syrup: 06/H/0999/001/IB/001 125 mg Suppositories: G9/099/93/IB/002
Type II Paracetamol XPTO	2013/XPTO/II/0006	500 mg Tablets: 9/099/89/II/003 125 mg Suppositories: G9/099/93/II/003 250 mg Suppositories: G9/099/93/II/002

1.2. MA number/Individual variation number for grouped applications

For the national procedure, the following types of grouped variations can be submitted:

- Type IA/IB/II grouped variations concerning a MA.
- Type IA/IB/II grouped variations concerning more than one MA of the same holder, authorised by the same competent national authority, i.e. Infarmed.

Type IA/IB/II grouped variations concerning one MA

The MA number shall use the year/applicant structure plus three additional elements, as shown in the example below:

AAAA/[Applicant]/QQ/vvvv/G	AAAA = Year the application was submitted [Applicant] = Applicant's abbreviated name or acronym QQ = IA, IB or II, according to main type of variation vvvv = Chronological number of the application

	submitted to Infarmed by applicant and by year G = Grouped variation identifier

The Individual Variation Number shall use the base structure of the MA Number plus three additional elements, as shown in the example below:

[Base structure]/QQ/vvv/G	QQ = IA, IB or II, according to main type of variation vvv = Chronological number of the variation G = Grouped variation identifier

Examples:

Variation type	MA no.	Individual variation no.
Type IA Group Sinvastatin XPTO	2013/XPTO/IA/0007/G	20 mg Tablets: 05/H/0999/001/IA/004/G 40 mg Tablets: 05/H/0999/002/IA/003/G
Type IB Group Sinvastatin XPTO	2013/XPTO/IB/0008/G	20 mg Tablets: 05/H/0999/001/IB/005/G
Type II Group Sinvastatin XPTO	2013/XPTO/II/0009/G	20 mg Tablets: 05/H/0999/001/II/006/G 40 mg Tablets: 05/H/0999/002/II/004/G
Type IA Group Paracetamol XPTO	2013/XPTO/IA/0010/G	500 mg Tablets: 9/099/89/IA/004/G 1000 mg Tablets: 99/H/0999/001/IA/003/G
Type IB Group Paracetamol XPTO	2013/XPTO/IB/0011/G	500 mg Tablets: 9/099/89/IB/005/G 1000 mg Tablets: 99/H/0999/001/IB/004/G 40 mg/ml Syrup: 06/H/0999/001/IB/002/G 125 mg Suppositories: G9/099/93/IB/004/G
Type II Group Paracetamol XPTO	2013/XPTO/II/0012/G	500 mg Tablets: 9/099/89/II/006/G 125 mg Suppositories: G9/099/93/II/005/G 250 mg Suppositories: G9/099/93/II/003/G

Type IA/IB/II grouped variations concerning more than one MA of the same holder

The MA number shall use the year/applicant structure plus three additional elements, as shown in the example below:

AAAA/[Applicant]/QQ/vvvv/G	AAAA = Year the application was submitted [Applicant] = Applicant's abbreviated name or acronym QQ = IA, IB or II, according to main type of variation vvvv = Chronological no. of the application submitted to Infarmed by applicant and by year G = Grouped variation identifier

The Individual Variation Number shall use the base structure of the MA Number plus three additional elements, as shown in the example below:

[Base structure]/QQ/vvv/G	QQ = IA, IB or II, according to main type of variation vvv = Chronological no. of the application submitted to Infarmed by applicant and by year G = Grouped variation identifier

Examples:

Variation type	MA no.	Individual variation no.
Type IA Group Sinvastatin XPTO Paracetamol XPTO	2013/XPTO/IA/0013/G	20 mg Tablets: 05/H/0999/001/IA/007/G 40 mg Tablets: 05/H/0999/002/IA/005/G
		500 mg Tablets: 9/099/89/IA/008/G 1000 mg Tablets: 99/H/0999/001/IA/005/G 40 mg/ml Syrup: 06/H/0999/001/IA/003/G 125 mg Suppositories: G9/099/93/IA/006/G 250 mg Suppositories: G9/099/93/IA/004/G
Type IB Group Sinvastatin XPTO Paracetamol XPTO	2013/XPTO/IB/0014/G	20 mg Tablets: 05/H/0999/001/IB/008/G
		1000 mg Tablets: 99/H/0999/001/IB/006/G 40 mg/ml Syrup: 06/H/0999/001/IB/004/G 125 mg Suppositories: G9/099/93/IB/007/G 250 mg Suppositories: G9/099/93/IB/005/G
Type II Group Sinvastatin XPTO Paracetamol XPTO	2014/XPTO/II/0001/G	20 mg Tablets: 05/H/0999/001/II/009/G 40 mg Tablets: 05/H/0999/002/II/006/G
		40 mg/ml Syrup: 06/H/0999/001/II/005/G

1.3. MA number/individual variation number for worksharing procedures

The worksharing procedure entails the grouping of several MAs owned by the same holder, authorised by MR/DC procedure or national procedure, in different Member States by the respective competent national authorities. One of the competent authorities will act as the reference authority in the worksharing procedure.

The MA number shall use the structure defined for the MR/DC procedure without reference to the strength/pharmaceutical form identifier plus three additional components, as shown in the example below:

CC/H/xxxx/WS/vvvv	CC = Two-letter code identifying the Reference Authority Member State H = Medicinal product for human use WS = Worksharing vvvv = Application sequential no. assigned by the Reference Authority

NOTE: When Infarmed is the reference authority, the worksharing procedure number will be assigned prior to submission.

The individual variation number shall use the base structure of the MA number plus two additional components, as shown in the example below:

[Base structure]/WS/vvv	WS = *Worksharing* vvv = Chronological no. of variation

Examples of worksharing including at least one MA by national procedure:

Variation type	MA no.	Individual variation no.
Worksharing PT/H/0999/001-002 NO/H/ 0999/001 Sinvastatin XPTO	PT/H/xxxx/WS/0001	PT/H/0999/001/WS/038 PT/H/0999/002/WS/038
		NO/H/0999/001/WS/022
		20 mg Tablets: 05/H/0999/001/WS/010 40 mg Tablets: 05/H/0999/002/WS/007
Worksharing PT/H/0999/001-002 CZ/H/0999/001-002 Sinvastatin XPTO Paracetamol XPTO	PT/H/xxxx/WS/0002	PT/H/0999/001/WS/039 PT/H/0999/002/WS/039
		CZ/H/0999/001/WS/008 CZ/H/0999/002/WS/008
		20 mg Tablets: 05/H/0999/001/WS/011 40 mg Tablets: 05/H/0999/002/WS/008
		500 mg Tablets: 9/099/89/WS/009 1000 mg Tablets: 99/H/0999/001/WS/007

1.4. Chronological number of variation

The following rules should be followed with regard to the **chronological number of the variation**:

- Sequential number, regardless of the type of variation to be submitted
- There can be no gaps in the sequence
- The numbering system for variations to the terms of the MA is separate from other numbering rules/systems applicable to renewal applications or notices under article 31 (4) of Decree Law no. 176/2006 of 30 August, which have their own chronological sequence

2. Validation of Type IB/II variations

In order to validate type IB and type II variation applications Infarmed shall check the application's completeness with regard to:

- Proper completion of application form
- Type of procedure (single variation, grouped variations or worksharing)
- Correct type/classification of variations included in the application
- Validation of applicable fee

In accordance with Commission Communication — Guidelines on the operation of the procedures laid down in Chapters II, III and IV of Commission Regulation (EC) No 1234/2008 concerning the examination of variations to the terms of marketing authorisations for medicinal products for human use and veterinary medicinal products, when involving the submission of **type IB or type II variations**, the applicant will be notified with regard to:

- result of the validation
- procedure start date, or day 0 (zero)
- variation schedule

3. Classification of purely national variations

Variations to the terms of a MA comprising exclusively national procedures should be submitted according to the type/classification shown below.

3.1. Change to generic medicinal product applications

In accordance with article 31 of Decree Law no. 176/2006 of 30 August, change to generic medicinal product applications should be submitted as a type II variation.

The category C.I.z) *Variations to safety, efficacy and pharmacovigilance. Other variation*. should be used.

The application should be completed by using the variation application form, which should include the following information:

REFERENCE MEDICINAL PRODUCT
Note: The reference medicinal product chosen should be authorised in the Community based on a complete dossier, in compliance with the provisions of article 8 of Directive 2001/83/EC.

- **Medicinal product which is or has been authorised in accordance with Community provisions in force for not less than 6/10 years in the EEA:**
  - Name of medicinal product, strength(s), pharmaceutical form(s):
  - Marketing Authorisation Holder:
  - Date of authorisation (yyyy-mm-dd):
  - Marketing Authorisation granted by:
    - Community
    - Member State (EEA)
  - Marketing Authorisation number(s):

  Note: This section defines the reference medicinal product chosen to establish the end date of the data protection period.

- **Medicinal product authorised in the Community/Member State (EEA) where the application is submitted or European Reference Medicinal Product:**
  - Name of medicinal product, strength(s), pharmaceutical form(s):
  - Marketing Authorisation Holder:
  - Marketing Authorisation number(s):
  - Marketing Authorisation granted by:
    - Community
    - Member State (EEA)

- **Medicinal product which is or has been authorised in accordance with Community provisions in force and to which bioequivalence has been demonstrated by appropriate bioavailability studies:**
  Note: It must agree with the global marketing authorisation notion, if different from the medicinal product identified above.
  - Name of medicinal product, strength(s), pharmaceutical form(s):
  - Marketing Authorisation Holder *:
  - Date of authorisation (yyyy-mm-dd):
  - Marketing Authorisation granted by:

- Community
- Member State (EEA)

- Marketing Authorisation number(s):
- Member State of origin:
- bioavailability study number(s)/EudraCT number:

Note: A copy of this section should be provided for each medicinal product used to demonstrate bioequivalence.

**Shall be taken as the "same" as that referred to above, in accordance with Commission Communication 98/C 299/03 (i.e. belonging to the same parent company, group of companies or "licensees").*

DOCUMENTS making up change to generic medicinal product application

- ☐ Authorisation letter to contact on behalf of MA holder, if applicable
- ☐ Identification of quantitative and qualitative composition in terms of active substances and excipients of the medicinal product covered by the application
- ☐ Summary of Product Characteristics (SmPC) and Package Information Leaflet (PIL) of the reference medicinal product, in force
- ☐ SmPC, PIL and labelling plans for the medicinal product covered by the application, in accordance with the SmPC and PIL of the reference medicinal product
- ☐ Copy of the last approved version of the SmPC, PIL and labelling for the medicinal product covered by the application
- ☐ Copy of MA certificate and notices of variations to the terms of the MA of the medicinal product covered by the application
- ☐ Statement from the holder of the MA for the medicinal product covered by the application declaring that the test medicinal product used in the bioequivalence study is the same as that submitted for the change to generic medicinal product
- ☐ Statement from sponsor of the bioequivalence study authorising the holder of the MA for the medicinal product covered by the application to use the bioequivalence study in question
- ☐ Justification for not submitting a bioequivalence study, with reference to the terms of the applicable regulation(s)
- ☐ Proposed payment form for the fee

3.2. Classification variation applications for dispensing to the public

Classification variation applications for dispensing to the public should be submitted as a type II variation.

The category C.I.z) *Variations to safety, efficacy and pharmacovigilance. Other variation.* should be used.

The application should be completed using the variation application form, in accordance with the rules of Circular Letter no. 103/CD of 27 May 2009.

Mutual Recognition/Decentralised and National Procedures

4. Online submission of variation applications

Regardless of the type and applicable procedure, all variations to the terms of a MA must be submitted exclusively online using the Medicinal Products for Human Use Management System – Variations platform (SMUH-ALTER) available at the Infarmed website at Medicamentos Uso Humano> Autorização de Introdução no Mercado> Alterações aos Termos de AIM / Transferência de Titular> Submissão eletrónica de alterações.

Before submitting variation applications, the variation application submission handbook should be consulted in the SMUH-ALTER platform available at the Infarmed website in the same area to ensure that applications are properly submitted and to streamline their validation.

The following applications are **excluded** from the scope of online submission through the SMUH-ALTER platform:

- MA extensions
- MA transfers of ownership
- Notices under article 31 (4) of Decree Law no. 176/2006 of 30 August, transposing article 61 (3) of Directive 2001/83/EC of 6 November

These applications should continue to be submitted via case file.

5. User registration

For each MA holder, Infarmed assigns only one user and one password to access the SMUH platform.

To request access (user and/or password), MA holders should go to the "User Registration" platform at the Infarmed website in the area Medicamentos Uso Humano> Autorização de Introdução no Mercado> Alterações aos Termos de AIM / Transferência de Titular> Submissão eletrónica de alterações, accept the terms of use and properly fill in the request form (including mandatory attached documentation).

The User Registration handbook available at the Infarmed website in the same area should be consulted.

6. Manufacturing flowchart confirmation/updating

Outdated information in the Infarmed database on the manufacturing flowchart of medicinal products may restrict the submission of variation applications impacting the manufacturing flowchart through the SMUH-ALTER platform.

To view the information in the Infarmed database for medicinal products authorised by MR/DC and national procedures, applicants should access the "Manufacturing Flowchart Confirmation/Updating" platform available at the Infarmed website in the area Medicamentos Uso Humano> Autorização de Introdução no Mercado> Alterações aos Termos de AIM /

Transferência de Titular> Submissão eletrónica de alterações and submit online applications to update/correct the information, if applicable.

The Manufacturing Flowchart Confirmation/Update application submission handbook available at the Infarmed website in the same area should be consulted.

7. Communications exclusively online

With a view to streamlining communications between Infarmed and applicants with regard to validation, starting the evaluation procedure, notification of information requests and notification of the decision on variations to the terms of MAs, the Medicinal Product Evaluation Department (DAM) will make communications exclusively by email.

At the time of submitting variation applications, the document "*Declaration form for the use of e-mail communications with Infarmed"* must be attached, identifying the e-mail address for Infarmed to send its communications.

The attached form for this declaration (Annex I) should be filled in, bearing in mind the following:

- Wherever possible, the applicant should indicate a shared e-mail (proxy) for institutional communications with Infarmed.
- The document "*Declaration form for the use of e-mail communications with Infarmed"* should be signed by the MA holder or a duly authorised representative.

Communications for the purposes of Commission Regulation (EC) No 1234/2008 of 24 November, as amended by Regulation (EU) No 712/2012 of 3 August, and Decree Law no. 176/2006 of 30 August, within the scope of variations to the terms of a MA, should be sent to the following Infarmed e-mail addresses:

- submissao.alteracoes@infarmed.pt for variation applications submitted for medicinal products authorised by national procedure.
- rms.procedures@infarmed.pt for variation applications submitted for medicinal products authorised by MR/DC procedure in which Portugal acts as a Reference Member State.
- cms.post_MA@infarmed.pt for variation applications submitted for medicinal products authorised by MR/DC procedure in which Portugal acts as a Concerned Member State.

8. Instructions on applicable variation application fees

For variation applications submitted from 5 August 2013 onwards, the applicable fee will be paid after the DAM's validation of the proposed payment form accompanying the online submission of the variation application.

In addition, **for applicants paying fees from the national territory**, the payment will only be available via **"Multibanco" (ATM) reference**.

8.1. List of applicable variation applications fees

Upon submitting a variation application online, the applicant must identify, in the proposed payment form, the fee applicable to each variation for each strength/pharmaceutical form of the medicinal product(s) included in the application.

The list of fees applicable to variations to the terms of MAs is available at the online submission platform, in accordance with the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April, and includes the following options:

Variations	Applicable law	Descrição da alínea de taxa aplicável (PT)	Description of applicable fee item (EN)	Value (€)
Variations with no impact on PT or Repeated strength/PhF	.	Isento ou Repetição de dosagem ou forma farmacêutica	Free of charge or Repeated strength or pharmaceutical form	0,00
Type I Variations (IA, IA_{IN} e IB) MR/DC	Ordinance 377/2005	5.a) i) Por cada alteração tipo I, incluindo uma dosagem e uma forma farmacêutica	5.a) i) For each type I variation, including one strength and one pharmaceutical form	797,94
	Ordinance 377/2005	5.a) ii) Por cada alteração tipo I, cada dosagem ou forma farmacêutica suplementar	5.a) ii) For each type I variation, each additional strength or pharmaceutical form	271,10
Type I Variations (IA, IA_{IN} e IB) MR /DC Categories A.1 ou A.7	Ordinance 377/2005	5.a) iii) Por cada alteração tipo I, relativa a alteração do nome, firma, sede ou representação do titular AIM ou da retirada de empresas envolvidas no fabrico, incluindo a libertação de lote, do medicamento e da(s) substância(s) ativa(s)	5.a) iii) For each type I variation concerning the change of the name, company, head-office or representation of the MA holder or the deletion of companies involved in the manufacturing, including the batch release, of the medicine and of the active substance(s)	184,14
Type II Variations MR /DC	Ordinance 377/2005	5.b) i) Por cada alteração tipo II, incluindo uma dosagem e uma forma farmacêutica	5.b) i) For each type II variation, including one strength and one pharmaceutical form	1585,65
	Ordinance 377/2005	5.b) ii) Por cada alteração type II, cada dosagem ou forma farmacêutica suplementar	5.b) ii) For each type II variation, each additional strength or pharmaceutical form	511,50
Type I Variations (IA, IA_{IN} e IB) National	Ordinance 377/2005	5.a) i) + d) Por cada alteração nacional tipo I, incluindo uma dosagem e uma forma farmacêutica	5.a) i) + d) For each national type I variation, including one strength and one pharmaceutical form	478,76
	Ordinance 377/2005	5.a) ii) + d) Por cada alteração nacional tipo I, cada dosagem ou forma farmacêutica suplementar	5.a) ii) + d) For each national type I variation, each additional strength or pharmaceutical form	162,66
Type I Variations (IA, IA_{IN} e IB) National Categories A.1 ou A.7	Ordinance 377/2005	5.a) iii) + d) Por cada alteração nacional tipo I, relativa a alteração do nome, firma, sede ou representação do titular AIM ou da retirada de empresas envolvidas no fabrico, incluindo a libertação de lote, do medicamento e da(s) substância(s) ativa(s)	5.a) iii) + d) For each national type I variation concerning the change of the name, company, head-office or representation of the MA holder or the deletion of companies involved in the manufacturing, including the batch release, of the medicine and of the active substance(s)	110,48
Type II Variations National	Ordinance 377/2005	5.b) i) + d) Por cada alteração nacional tipo II, incluindo uma dosagem e uma forma farmacêutica	5.b) i) + d) For each national type II variation, including one strength and one pharmaceutical form	951,39
	Ordinance 377/2005	5.b) ii) + d) Por cada alteração nacional tipo II, cada dosagem ou forma farmacêutica suplementar	5.b) ii) + d) For each national type II variation, each additional strength or pharmaceutical form	306,90
Variations Categories A.1, A.4 e A.5	Ordinance 377/2005	9.a) Por cada alteração tipo I que consista apenas na alteração do nome, firma, residência, sede ou representação do fabricante ou do titular AIM, em todas as AIM de que o requerente seja titular: Um conjunto inicial de 1 a 10 medicamentos, incluindo uma dosagem e uma forma farmacêutica	9.a) For each type I variation consisting only in the change of the name, company, address, head-office or representation of the manufacturer or of the MA holder, in every MA of which the applicant is holder: An initial set of 1 to 10 medicines, including one strength and one pharmaceutical form	383,63

	Ordinance 377/2005	9.b) Por cada alteração tipo I que consista apenas na alteração do nome, firma, residência, sede ou representação do fabricante ou do titular AIM, em todas as AIM de que o requerente seja titular: 11 a 50 medicamentos - Cada conjunto adicional de 1 a 5 medicamentos	9.b) For each type I variation consisting only in the change of the name, company, address, head-office or representation of the manufacturer or of the MA holder, in every MA of which the applicant is holder: 11 to 50 medicines - Each additional set of 1 to 5 medicines	204,60
	Ordinance 377/2005	9.c) Por cada alteração tipo I que consista apenas na alteração do nome, firma, residência, sede ou representação do fabricante ou do titular AIM, em todas as AIM de que o requerente seja titular: 51 a 120 medicamentos - Cada conjunto adicional de 1 a 5 medicamentos	9.c) For each type I variation consisting only in the change of the name, company, address, head-office or representation of the manufacturer or of the MA holder, in every MA of which the applicant is holder: 51 to 120 medicines - Each additional set of 1 to 5 medicines	179,03
	Ordinance 377/2005	9.d) Por cada alteração tipo I que consista apenas na alteração do nome, firma, residência, sede ou representação do fabricante ou do titular AIM, em todas as AIM de que o requerente seja titular: Mais de 120 medicamentos - Cada conjunto adicional de 1 a 5 medicamentos	9.d) For each type I variation consisting only in the change of the name, company, address, head-office or representation of the manufacturer or of the MA holder, in every MA of which the applicant is holder: More than 120 medicines - Each additional set of 1 to 5 medicines	153,45

8.2. Applicable grouped variations and worksharing procedures fees

The fee applicable to grouped variations and worksharing procedures is the sum of the fees applicable to each variation for each strength/pharmaceutical form of the medicinal product(s) included in the application.

When submitting grouped variations or worksharing procedures, there is no reduction to the total applicable fee.

Note that for grouped variations to the name and/or address of the MA holder in Portugal (category A.1) or the name and/or address of the manufacturer (e.g. categories A.4 and A.5), submitted simultaneously for all MAs held by the applicant, the reduced fee in no. 9 of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April shall apply.

8.3. 40% fee reduction for medicinal products authorised by national procedure

Under no. 5.d) of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April, for medicinal products authorised by national procedure and not subject to a Mutual Recognition procedure, the cost of the acts referred to in no. 5.a) and 5.b) (Type I and Type II variations, respectively) are reduced by 40%.

As regards filling in the proposed payment form in the online submission of variation applications for medicinal products authorised by national procedure, the applicant should select options including the reference “+ d)” from the list of available fees.

8.4. Variations without impact in Portugal

Variations without impact in Portugal are defined as variations submitted by MR/DC procedure in which Portugal acts as a Concerned Member State ("PT-CMS") and which do not involve Portugal (e.g. variation to the name and/or address of a MA holder in France). In these cases, the variation application is free of charge.

Variation applications involving the addition, deletion or replacement of manufacturers or finished product packaging sizes are not free of charges, even when the holder does not wish to implement the variation in Portugal.

As regards filling in the proposed payment form in the online submission of PT-CMS variation applications without impact in Portugal, the applicant should select the option "*Free of charge or Repeated strength or pharmaceutical form*" from the list of available fees.

When Portugal acts as a Reference Member State ("PT-RMS"), even though the variation may not have an impact in Portugal, the application is not free of charge, since the validation/evaluation will be performed by Infarmed.

8.5. Fee applicable to additional strength or pharmaceutical form included in the same application

Nos. 5.a) ii) or 5.b) ii) of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April shall apply when the same variation application includes additional strengths or pharmaceutical forms belonging to the same MA.

Note:

- Under a **MR/DC recognition procedure**, the following definition of "same MA" covers: all strengths and/or pharmaceutical forms of a given medicinal product (as defined in *CMDh Best Practice Guide for the Allocation of MRP Variation Numbers, CMDh/291/2013, Rev. 19, February 2013)*. For example, all medicinal products belonging to AT/H/1234/001-n shall be taken as belonging to the same MA.
- Under a **national procedure**, for the purposes of paying applicable variation application fees, medicinal products with:
  - same MA holder (same legal entity);
  - same INN;
  - same name (notwithstanding different medicinal product names attributable to qualifying terms or acronyms).

  may be taken as additional strengths/pharmaceutical forms

8.6. Repeated strength/pharmaceutical form of medicinal product

In the Infarmed database, there are medicinal products in which the same strength/pharmaceutical form is shown in more than one record.

As regards filling in the proposed payment form in the online submission of variation applications for a repeated strength/pharmaceutical form of a medicinal product, the applicant should select the option "*Free of charge or Repeated strength or pharmaceutical form*" from the list of available fees.

For example, the medicinal product XPTO 40000 IU/ml solution for injection in pre-filled syringe, corresponding to procedure no. PT/H/9990/001, is shown in three records in the internal Infarmed database: 20000 IU/0.5 ml, 30000 IU/0.75 ml and 40000 IU/1 ml. In this case, the applicant should select the fee corresponding to the variation application for one of the PT/H/9990/001 records, and select the option "*Free of charge or Repeated strength or pharmaceutical form*" for the two records repeating the strength 001.

8.7. Fees applicable to variation applications in categories A.1 and A.7

No. 5.a) iii) of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April applies to variation applications submitted in the categories A.1 and A.7.

As regards filling in the proposed payment form in the online submission of variation applications in the categories A.1 and A.7, the applicant should select for all the medicinal product's strength/pharmaceutical forms, the option 5.a) iii) or 5.a) iii) + d) from the list of available fees, as applicable.

Note that for grouped variations to the name and/or address of the MA holder in Portugal (category A.1) submitted simultaneously for all MAs held by the applicant, the reduced fee in no. 9 of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April shall apply.

8.8. Fees applicable to variation applications in categories A.1, A.4 and A.5

No. 9 of the Table referred to in no. 1 of Ordinance no. 377/2005 of 4 April applies to variation applications submitted in the categories A.1, A.4 and A.5, when submitted simultaneously for all MAs held by the applicant.

The amounts shown in the table below should be taken into account.

As regards filling in the proposed payment form in the online submission of variation applications, for the first medicinal product of each set, the applicant should select the applicable amount from no. 9 from the list of available fees; for the remaining medicinal products of each set, the applicant should select the option "*Free of charge or Repeated strength or pharmaceutical form*" from the list of available fees.

No. of medicinal products **(including one strength and one pharmaceutical form)**	**Cost (€)**	**Fee payable (€)**
1-10	383.63	383.63
11-15	204.60	588.23
16-20	204.60	792.83
21-25	204.60	997.43
26-30	204.60	1202.03
31-35	204.60	1406.63
36-40	204.60	1611.23
41-45	204.60	1815.83
46-50	204.60	2020.43
51-55	179.03	2199.46
56-60	179.03	2378.49

No. of medicinal products (including one strength and one pharmaceutical form)	**Cost (€)**	**Fee payable (€)**
61-65	179.03	2557.52
66-70	179.03	2736.55
71-55	179.03	2915.58
76-80	179.03	3094.61
81-85	179.03	3273.64
86-90	179.03	3452.67
91-95	179.03	3631.70
96-100	179.03	3810.73
101-105	179.03	3989.76
106-110	179.03	4168.79
111-115	179.03	4347.82
116-120	179.03	4526.85
121-125	153.45	4680.30
126-130	153.45	4833.75
131-135	153.45	4987.20
136-140	153.45	5140.65
141-145	153.45	5294.10
146-150	153.45	5447.55
...	153.45	5601.00
...	...	...

Annex I Declaration form for the use of e-mail communications with Infarmed – E-mail address identification form

<*MA holder*>, legal entity/taxpayer identification no. <*taxpayer identification number*>, with its registered office at <*address*>, represented herein by <*name of MA holder representative*>, in the capacity of <*director, manager, legal representative, etc.*> and duly authorised to act, hereby declares, for the purposes of Commission Regulation (EC) No 1234/2008 of 24 November, as amended by Regulation (EU) No 712/2012 of 3 August, and Decree Law no. 176/2006 of 30 August, that all of its communications with Infarmed, I.P. relating to applications for variations to the terms of MAs, shall be done using the following e-mail addresses:

- <*MA holder e-mail address(es)*>.

Signature _____