EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

25 July 2013
EMA/465933/2013 Rev.1[1]
Patient Health Protection

Guidance on format of the risk management plan (RMP) in the EU for Generics

Active substance(s) (INN or common name):	
Pharmaco-therapeutic group (ATC Code):	
Name of Marketing Authorisation Holder or Applicant:	
Number of medicinal products to which this RMP refers:	Choose one of the following: • 1 • 2 • 3 • 4 • 5 • 6
Product(s) concerned (brand name(s)):	

Data lock point for this RMP	<Enter a date>	Version number	<Enter a version no>
Date of final sign off	<Enter a date>		

[1] Please note that under section VI.1.4 Summary table of Risk Minimisation Measures "Copy table from Part V: 5.2" should have read "Copy table from Part V: V.3"

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This guidance covers the Parts and modules of the RMP which may be required for applications concerning generics in the EU. Some sections of this guidance may not always apply to generics but have been provided for completeness. Parts III and IV many not be required and applicants are encouraged to discuss the need with the competent authority prior to submission of the RMP.

Part I: Product(s) Overview

Administrative information on the RMP

Part	**Module / annex**	**Date last updated for submission (sign off date)**	***Version number of RMP when last submitted / or** **Not Applicable**
Part II Safety Specification	SV Post authorisation experience Only required for updates to the RMP	<Enter a date>	
	SVIII Summary of the safety concerns	<Enter a date>	
Part III Pharmacovigilance Plan	Only needed if reference product has additional PhV activities	<Enter a date>	
Part IV Plan for post-authorisation efficacy studies	Only needed if reference product has imposed post-authorisation efficacy studies	<Enter a date>	
Part V Risk Minimisation Measures		<Enter a date>	
Part VI Summary of RMP		<Enter a date>	
Part VII Annexes	ANNEX 2 Current or proposed SmPC/PIL	<Enter a date>	
	ANNEX 3 Worldwide marketing status by country	<Enter a date>	
	ANNEX 5 Synopsis of pharmacoepidemiological study programme	<Enter a date>	
	ANNEX 6 Protocols for proposed and on-going studies in Part III	<Enter a date>	

Part	Module / annex	Date last updated for submission (sign off date)	*Version number of RMP when last submitted / or Not Applicable
	ANNEX 7 Specific adverse event follow-up forms	<Enter a date>	
	ANNEX 8 Protocols for studies in Part IV	<Enter a date>	
	ANNEX 9 Synopsis of newly available study reports in Parts III-IV	<Enter a date>	
	ANNEX 10 Details of proposed additional risk minimisation activities	<Enter a date>	
	ANNEX 11 Mock up examples	<Enter a date>	
	ANNEX 12 Other supporting data	<Enter a date>	

** A new RMP version number should be assigned each time any Parts/modules are updated*

Some modules of the RMP may be omitted (for eligible types of products see GVP V table V.2) if the RMP relates only to products falling into these categories. In these circumstances leave the date field blank and write "Not applicable" or "NA" in the version field

QPPV name ……

QPPV signature ……

Contact person for this RMP ……

E-mail address or telephone

number of contact person ……

There can only ever by ONE agreed RMP for a product or products. Wherever possible there should only be one additional submitted RMP version under evaluation. To facilitate this, MAHs are reminded that where possible "routine" updates of a RMP should NOT be submitted when there is already a version of a RMP being evaluated as part of an on-going procedure. A cover letter should be submitted instead stating that there is no change to the RMP version xx dated yy submitted as part of procedure.

Where a procedure would normally require the submission of an updated RMP as part of the dossier, but there is already another version under evaluation because of another procedure, it is also possible to submit a letter as stated above.

In some circumstances there may be a need to submit a third RMP which is a different version from both the agreed RMP and a second RMP version currently undergoing evaluation e.g. if new safety concerns have been recently identified or if a new indication requires different risk minimisation measures. In this case different versions of a RMP will be simultaneously under evaluation. The purpose of this section is to provide oversight.

Overview of versions:

Version number of last agreed RMP:

Version number	<Enter a version no>
Agreed within	<Indicate procedure>

Current RMP versions under evaluation:

RMP Version number	Submitted on	Submitted within
<Insert number>	<Enter a date>	<indicate procedure number>
… etc.		

For each product in the RMP

Invented name(s) in the European Economic Area (EEA)	
Authorisation procedure	<indicate procedure>
Brief description of the product including: • chemical class • summary of mode of action • important information about its composition (e.g. origin of active substance of biological, relevant adjuvants or residues for vaccines	
Indication(s) in the EEA Current (if applicable)	
Proposed (if applicable)	
Posology and route of administration in the EEA Current (if applicable)	
Proposed (if applicable)	
Pharmaceutical form(s) and strengths Current (if applicable)	
Proposed (if applicable)	

Country and date of first authorisation worldwide	<Enter a country> <Enter a date>
Country and date of first launch worldwide	<Enter a country> <Enter a date>
Country and date of first authorisation in the EEA	<Enter a country> <Enter a date>

Is the product subject to additional monitoring in the EU? Yes ☐ No ☐

Part II: Module SV - Post-authorisation experience

Only required for updates to the RMP

The purpose of this RMP module is to provide information on the number of patients exposed post authorisation; how the medicinal product has been used in practice and labelled and off-label use. It should also include brief information on the number of patients included in any completed or on-going observational studies conducted either to elucidate a safety issue or for drug utilisation purposes. It is appreciated that detailed data may not be available. These tables provide guidance on how the data might be provided when available. Details of significant actions taken to update information on the safety of the medicinal product should also be provided in this module.

SV.1 Action taken by regulatory authorities and/or marketing authorisation holders for safety reasons

List any significant regulatory action (including those initiated by the MAH in any market in relation to a safety concern. Significant regulatory action would include a restriction to the approved indication, a new contra-indication, a new or strengthened warning in section 4.4 of the SPC (or equivalent) or any action to suspend or revoke a marketing authorisation.

The list should be cumulative but newly taken action (since last update to the module) should be presented separately first, as well as being in the cumulative list. Roll-out in multiple countries of a new safety statement initiated by the MAH can be presented as one action (but list all countries and range of dates e.g. March-September 2011.) Comments may be added if the regulatory action is not applicable to certain products/formulations as authorised in the EU.

Table 1. Detailed description of action taken since last update to this module

Safety issue	
Background to issue	
Evidence source	
Action taken	
Countries affected	
Date(s) of action	

Table 2. Cumulative list

Safety concern 1			
Country(ies)	Action taken	Comment	Date(s)

Safety concern 2 etc.			
Country(ies)	Action taken	Comment	Date(s)

SV.2 Non-study post-authorisation exposure

Where possible, data on patients exposed post marketing should be provided based on market research. When the number of persons is calculated on the basis of sales data, details and justification should be provided of the measure used to calculate exposure. Tables should be provided for each indication and route of administration where possible.

SV.2.1 Method used to calculate exposure

If different methods have been used to calculate exposure for some tables, this section should be repeated before the relevant table(s).

SV.2.2 Exposure

By age group and gender				
Indication				
Age Group	Persons		Exposure (e.g. packs or person years)	
	M	F	M	F
Age group 1				
Age group 2				
Etc.				

By indication		
	Persons	Exposure (e.g. packs or person years)
Indication 1		
Indication 2		
Etc.		

By route of administration		
	Persons	Exposure (e.g. packs or person years)
Oral		
intravenous		
Etc.		

By dose		
Indication		
	Persons	Exposure (e.g. packs or person years)
Dose level 1		
Dose level 2		
Etc.		

By country		
Indication		
	Persons	Exposure (e.g. packs or person years)
EU		
Non-EU		

If possible, EU use should be broken down into country or sales area. Note the categories provided, are suggestions only and other relevant variables can be used e.g. oral versus i.e., duration of treatment etc.

SV.3 Post-authorisation use in special populations

Where there are data on post-authorisation use in the special populations mentioned below, estimation of the numbers exposed and the method of calculation should be provided whether or not the usage is on- or off-label. Comment on any differences in benefit or risk seen between the special population and the target population as a whole.

Paediatric use		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• Pre-term new-borns • Neonates (birth to 27 days) • Infants and toddlers (1 month to 23 months) • Children (2 years to e.g. 11 years) • Adolescents (e.g. 12 years to 18 years)		
Data source		
Method of calculation		

Elderly use		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• 65 – 74 years • 75 – 84 years • 85+ years		
Data source		
Method of calculation		

Pregnant or breast feeding women		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• Pregnant • Breast feeding		
Data source		
Method of calculation		

Hepatic impairment		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• Mild • Moderate • Severe		
Data source		
Method of calculation		

Renal impairment		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• Mild • Moderate • Severe		
Data source		
Method of calculation		

Other use (specify)		
Estimated use	Number	Comment on any variation in benefit or risk from overall target population
• Specify category • Specify category • Specify category		
Data source		
Method of calculation		

SV.4 Post-authorisation off-label use

Post marketing, updates to the safety specification, should include information on EU off-label use; i.e. the intentional use, for a medical purpose, which is not in accordance with the authorised product information for a medicinal product. Off-label use includes use in non-authorised paediatric age categories.

EU off-label use			
Off label category	Country	Source of information	Comment
<E.g. Use in dysmenorrhoea (non-authorised indication)>	<E.g. Italy>	<E.g. Poseidon: Drug utilisation study using Emilia Romagna NHS drug prescription in general practice, Italy>	<E.g. Epidemiological study in electronic health care records found 15 women (1.7%) prescribed painoprofen for dysmenorrhoea out of total of 975 users>

SV.5 Epidemiological study exposure (if applicable)

Marketing authorisation holders should provide a listing of epidemiological studies which are, or have been, conducted to elucidate safety or efficacy issues, study drug utilisation or measure effectiveness of risk minimisation measures. This listing should include studies undertaken by the marketing authorisation holder itself or funded by them via a grant, whether specific or unconditional. Studies undertaken by a marketing partner, or where the MAH has been sent the results by a third party, should also be included.

Study title and study type (e.g. cohort or case/control)	**Objectives**	**Population studied (data source and country)**	**Duration (study period)**	**Number of persons (in each group or of cases and controls) and person time (if appropriate)**	**Comment**
<E.g. Poseidon (cross sectional DUS)>	<E.g. Investigate utilisation of painoprofen in General Practice in Italy>	<E.g. Emilia Romagna NHS drug prescription in general practice, Italy>	<E.g. 3 month time window>	<E.g. 975 users from study population of 3.5M>	<E.g. Study report in annex 5>
Study 2 etc.					

Part II: Module SVIII - Summary of the safety concerns

A summary should be provided of the safety concerns. A safety concern may be an:

- important identified risk;
- important potential risk; or
- missing information.

For RMPs covering multiple products where there may be significant differences in the important identified and important potential risks for different products, it may be appropriate to subdivide the summary of safety concerns under specific headings with the relevant identified and potential risks under each heading. Headings which could be considered include:

- safety concerns relating to the active substance;
- safety concerns related to a specific formulation or route of administration;
- safety concerns relating to the target population;
- risks associated with switch to non-prescription status.

Division of safety concerns by headings should only be considered when the risks clearly do not apply to some products and inclusion as a single list could cause confusion.

Table 3. Summary of safety concerns

Summary of safety concerns	
Important identified risks	<> List
Important potential risks	<> List
Missing information	<> List

Part III: Pharmacovigilance Plan

(Only required if reference product has additional PhV activities)

The Pharmacovigilance plan (PhV Plan) provides details of pharmacovigilance activities/ studies which are intended to identify and/or characterise safety concerns. What is required will depend upon the nature of the medicine, the target population, the number of safety concerns and where the medicine is in its life-cycle. A PhV Plan may also include details of studies to measure the effectiveness of risk minimisation measures for important measures where a formal study is required.

Some safety concerns may be well characterised in which case routine PhV will be sufficient. Depending upon the safety concern, and areas to be investigated, a PhV Plan will often include epidemiological (non-interventional) studies (such as cohort, case control, registries, drug utilisation etc.) but may also include interventional studies or more rarely pre-clinical activities (such as PK/PD, clinical trials, in vivo or in vitro studies). Further information on post authorisation safety studies is given in GVP Module VIII.

In the PhV Plan, section III.1 reviews each safety concern and what areas need investigation whereas III.4 gives details of the individual studies and milestones. Section III.2 provides details of any activities aimed at measuring the effectiveness of risk minimisation activities. The results of any studies in the PhV Plan should be briefly summarised in section III.3. If the study results concern the effectiveness of risk minimisation, brief results should be provided in section III.3. If the results suggest that the risk minimisation measure is failing in its objectives, this should be discussed with the root cause analysis and proposal for rectification in Part V of the RMP. Section III.5 summarises the entire PhV plan – both completed, on-going and planned activities.

III.1 Safety concerns and overview of planned pharmacovigilance actions

For each safety concern in Part II SVIII, provide details of specific areas that still need confirmation or further investigation – e.g. confirmation of incidence, investigation of risk factors. It may be that for a well characterised safety concern that there are no areas which need investigating in which case "none" should be written in column 1 and the only proposed action will be "routine pharmacovigilance". Some areas may need more than one activity to characterise a safety concern with different activities having different objectives. If a specific questionnaire is planned for collecting structured data on a safety concern of special interest this is still considered to be routine but should be mentioned and a mock up provided in RMP annex 7. A requirement to report on a specific adverse drug reaction at defined intervals resulting from a previous evaluation (e.g. PSUR/PBER) will be considered as routine pharmacovigilance but should be detailed in the table against the specific safety concern. Outstanding additional pharmacovigilance activities should be detailed in section III.4.

Safety concern 1		
Areas requiring confirmation or further investigation	Proposed routine and additional PhV activities	Objectives
1		
2		
3 etc.		

Safety concern 2 etc.		
Areas requiring confirmation or further investigation	Proposed routine and additional PhV activities	Objectives
1		
2		
3 etc.		

III.2 Additional pharmacovigilance activities to assess effectiveness of risk minimisation measures

Where there are risk minimisation measures which require the use of non-routine pharmacovigilance activities to measure the effectiveness, details should be provided here.

Risk minimisation measure		
Component measured	Activity(ies)	Rationale
Component 1		
Component 2 etc.		

III.3 Studies and other activities completed since last update of Pharmacovigilance Plan

This is a summary of completed studies and/or activities since the last update of the Pharmacovigilance Plan. The concise study report should be provided in RMP annex 9.

Study/activity title	
Safety concern(s)/risk minimisation measure investigated	
Brief summary of results	
Implications	

III.4 Details of outstanding additional pharmacovigilance activities

The MAH should propose categories for new additional PhV studies/activities in the pharmacovigilance plan. These categories will be confirmed or recategorised during the evaluation of the RMP. Updates of the RMP should reflect the categorisation as agreed by CHMP/national competent authority (along with any proposed new studies).

III.4.1 Imposed mandatory additional pharmacovigilance activity (key to benefit risk)

Table 4. Imposed activities considered key to the benefit risk of the product

	Description of activity (or study title if known)	**Milestone(s)**	**Due Date(s)**
1		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>
2 etc.		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>

III.4.2 Mandatory additional PhV Activity (being a Specific Obligation)

Table 5. Specific obligations

	Description of activity (or study title if known)	**Milestone(s)**	**Due Date(s)**
1		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>
2 etc.		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>

Non-interventional studies included in categories 1 and 2 are subject to the supervision exercised under Articles 107 (m)-(q) of Directive 2001/83.

III.4.3 Required additional pharmacovigilance activities to address specific safety concerns or to measure effectiveness of risk minimisation measures

These are category 3 activities that are conducted or financed by the MAH to address particular safety concerns but do not include studies which are imposed or which are specific obligations (i.e. categories 1 or 2 above). These activities may include trials or studies which may be on-going (e.g. from clinical trials where the activity would be to provide a report) or be planned where the activity is to conduct the study. This would include studies or activities requested by another Regulatory authority where the results are expected to provide

information relevant to existing areas of uncertainty. Studies which have been specifically requested by the CHMP/PRAC (which are not conditions of the marketing authorisation) or which may be suggested by the MAH to investigate a safety concern should also be included here. Studies to measure the effectiveness of risk minimisation measures would normally fall into this category.

Table 6. Required additional pharmacovigilance activities

	Description of activity (or study title if known)	**Milestone(s)**	**Due Date(s)**
1		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>
2 etc.		1.(e.g. protocol submission)	<Enter a date>
		2.(e.g. study start)	<Enter a date>
		3.(e.g. study finish)	<Enter a date>
		4. (e.g. final report)	<Enter a date>

III.4.4 Stated additional pharmacovigilance activities

These are activities which may provide additional supporting evidence but are not primarily intended to investigate a specific safety concern. This would include drug utilisation studies being conducted as a condition for reimbursement, studies requested by other regulatory authorities for reasons not related to a specific safety concern or safety studies carried out by a third party which the MAH is aware of, but is not providing funding (unconditional or otherwise) or other support.

Table 7. Stated additional pharmacovigilance activities

	Description of activity (or study title if known)	**Expected date of report**
1		<Enter a date>
2		<Enter a date>
3 etc.		<Enter a date>

III.5 Summary of the Pharmacovigilance Plan

III.5.1 Table of on-going and planned additional PhV studies/activities in the Pharmacovigilance Plan

This should be a complete overview of all on-going and planned studies in categories 1-3.

Study / activity Type, title and category (1-3)	Objectives	Safety concerns addressed	Status (planned, started)	Date for submission of interim or final reports (planned or actual)
<E.g. CRUCIAL Cancer Registry at University College IdAho Liver unit (non-interventional cohort, 3)>	<E.g. To investigate long term survival, time to progression, safety profile and QoL in patients with primary liver cancer or solid tumour metastases>	<E.g. Bradycardia, thrombosis, leukopenia, use in patients with renal impairment, long term safety>	<E.g. Protocol submitted to PRAC>	<E.g. Interim reports planned June 2013, 2017 Final study report Dec 2020>
<E.g. Validation of antibody test (non-clinical, 3)>	<E.g. Comparison of Supertest kit with current gold standard>	<E.g. Development of antibodies>	<E.g. Planned start March 2013>	<E.g. Final study report December 2013>

III.5.2 Table of completed studies / activities from the Pharmacovigilance Plan

This should be a complete overview of all completed studies in categories 1-3.

Study / activity Type, title and category (1-3)	Objectives	Safety concerns addressed	Status (Completed)	Date of submission of final study report
<E.g.ABC-124 (randomised controlled trial, 3)>	<E.g. Compare time to disease progression with 3 different doses of Compare safety profile of different doses>	<E.g. Bradycardia, development of antibodies, Use in patients with renal impairment.>	<E.g. Completed. Final study report submitted>	<E.g. Final study report submitted 31st March 2009>

Part IV: Plans for post-authorisation efficacy studies

(May only be required if reference product has imposed post-authorisation efficacy studies)

IV.1 Tables of post-authorisation efficacy studies

The MAH/Applicant should list any post authorisation efficacy studies which are proposed by the MAH/Applicant in relation to the above and also include those studies which have been imposed by the CHMP/NCA or which are Specific Obligations. A synopsis of the protocols should be provided in Annex 8.

Table 8. Efficacy studies which are specific obligations and/or conditions of the MA

Description of study (including objectives and study number)	**Milestone(s)**	**Due Date(s)**
	1.(e.g. protocol submission)	<Enter a date>
	2.(e.g. study start)	<Enter a date>
	3.(e.g. study finish)	<Enter a date>
	4. (e.g. final report)	<Enter a date>

Table 9. Other efficacy/effectiveness studies

Description of study (including objectives and study number)	**Milestone(s)**	**Due Date(s)**
	1.(e.g. protocol submission)	<Enter a date>
	2.(e.g. study start)	<Enter a date>
	3.(e.g. study finish)	<Enter a date>
	4. (e.g. final report)	<Enter a date>

IV.2 Summary of post authorisation efficacy development plan

This should be a complete overview of all studies (on-going, planned)

Study (type and study number)	**Objectives**	**Efficacy uncertainties addressed**	**Status (planned, started)**	**Date for submission of interim or final reports**

IV.4 Summary of completed post authorisation efficacy studies

Study (type and study number)	Objectives	Efficacy uncertainties addressed	Status (Completed, Study report submitted)	Date of submission of final study report

Part V: Risk minimisation measures

Each safety concern identified in module SVIII "summary of the safety specification" should be addressed. If no risk minimisation measures are proposed, then "none proposed" should be entered against the objective.

If several components make up one risk minimisation measure (e.g. a pregnancy prevention plan may have educational material for health care professionals and patients, algorithms for deciding on child-bearing potential, patient reminder cards etc.) these should be grouped together.

For each safety concern, provide details of what criteria will be used to judge whether risk minimisation measures are a success e.g. fewer than 2 pregnancy reports in period y, no cases of liver failure reported, drug utilisation study showing <5% off-label use etc.

Further guidance on risk minimisation measures can be found in GVP Module XVI and CIOMS IX.

V.1 Risk minimisation measures by safety concern

Safety concern	
Objective(s) of the risk minimisation measures	
Routine risk minimisation measures	(Proposed) text in SmPC <E.g. Dose reduction for ……. in section 4.2 of the SPC…….. Warning in sec tion 4.4 to…… Listed in section 4.8>
	Comment (e.g. on any differences between SmPCs)
	Other routine risk minimisation measures <E.g. Prescription only medicine Use restricted to physicians experienced in the treatment of…….>
Additional risk minimisation measure(s) (repeat as necessary)	Objective and justification of why needed.
	Proposed actions/components and rationale

Effectiveness of risk minimisation measures	
How effectiveness of risk minimisation measures for the safety concern will be measured	*If a study is planned, this should also be included in Part III.2 Additional PhV activities to assess effectiveness of risk minimisation measures*
Criteria for judging the success of the proposed risk minimisation measures	
Planned dates for assessment	
Results of effectiveness measurement	Provide latest assessment at each update of the RMP. For risk minimisation measures where formal studies are planned, any results should be mentioned in Part III.2 with the implications discussed here and any remedial actions in V.2
Impact of risk minimisation	
Comment	

V.2 Risk minimisation measure failure (if applicable)

List the safety concerns and risk minimisation measures which are judged to have failed.

Safety concern	**Risk minimisation measure**

V.2.1 Analysis of risk minimisation measure(s) failure

When risk minimisation measures for a safety concern are thought to be inadequate, a root cause analysis of where it is failing should be undertaken

Safety concern	
Risk minimisation measure(s)	
Component 1	Analysis
Component 2 etc.	Analysis
Discussion	

V.2.2 Revised proposal for risk minimisation

Based on the analysis of why the risk minimisation activities were inadequate, a proposal should be made for new (or revised) risk minimisation measures for the safety concern

Safety concern	
Objective(s) of the risk minimisation activities	
Routine risk minimisation activities	Synopsis of (proposed) text in SmPC
	Comment (e.g. on any differences between SmPCs)
	Other routine risk minimisation activities
Additional risk minimisation measure(s) (repeat as necessary)	Objective and justification of why needed.
	Proposed actions/components and rationale
Comment on how revised proposals will address failings	
Effectiveness of risk minimisation measures	
How effectiveness of risk minimisation measures for the safety concern will be measured	*If a study is planned, this should also be included in Part III: Additional PhV activities to assess effectiveness of risk minimisation measures*
Criteria for judging the success of the proposed risk minimisation measures	

V.3 Summary table of risk minimisation measures

Safety concern	**Routine risk minimisation measures**	**Additional risk minimisation measures**
	From V.1 “proposed text in SmPC” and “other routine risk minimisation measures”	From V.1 (list)
	<E.g. Dose reduction for ……. in section 4.2 of the SPC……. Warning in section 4.4 to…… Listed in section 4.8 Prescription only medicine Use restricted to physicians experienced in the treatment of……>	

Part VI: Summary of the risk management plan by product

A separate RMP Part VI should be provided for each product in the RMP.

VI.1 Elements for summary tables in the EPAR

VI.1.1 Summary table of Safety concerns

Copy table from Part I: SVIII

Summary of safety concerns	
Important identified risks	<> List
Important potential risks	<> List
Missing information	<> List

VI.1.2 Table of on-going and planned studies in the Post-authorisation Pharmacovigilance Development Plan

Copy table from III.5.1.

Study / activity Type, title and category (1-3)	**Objectives**	**Safety concerns addressed**	**Status (planned, started)**	**Date for submission of interim or final reports (planned or actual)**
<E.g. CRUCIAL Cancer Registry at University College IdAho Liver unit (non-interventional cohort, 3)>	<E.g. To investigate long term survival, time to progression, safety profile and QoL in patients with primary liver cancer or solid tumour metastases>	<E.g. Bradycardia, thrombosis, leukopenia, use in patients with renal impairment, long term safety>	<E.g. Protocol submitted to PRAC>	<E.g. Interim reports planned June 2013, 2017 Final study report Dec 2020>
<E.g. Validation of antibody test (non-clinical, 3)>	<E.g. Comparison of Supertest kit with current gold standard>	<E.g. Development of antibodies>	<E.g. Planned start March 2013>	<E.g. Final study report December 2013>

VI.1.3 Summary of Post authorisation efficacy development plan

Copy table IV.3 from Part IV

Study (type and study number)	Objectives	Efficacy uncertainties addressed	Status	Date for submission of interim or final reports

VI.1.4 Summary table of Risk Minimisation Measures

Copy table from Part V: V.3

Safety concern	Routine risk minimisation measures	Additional risk minimisation measures

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

(Maximum 150 words per indication)

Abbreviated lay language version of RMP Part II Module I.

VI.2.2 Summary of treatment benefits

The summary of treatment benefits should be in lay language and non-promotional. The text should not exceed a maximum of 200 words (up to 300 if multiple indications). The following should be considered for inclusion:

- *Describe briefly each pivotal study, including total participant numbers (randomised figure where applicable). Explain the primary endpoint in lay language.*
- *If there are multiple indications, use bullet points to separate the studies per indication. If there are several studies for one indication with a similar design, in some cases these may be described together and the total patient numbers combined to stay concise.*
- *For each study, describe the primary endpoint results directly after the description of the study (either in the same paragraph, or a separate paragraph if needed). When using percentages, give patient numbers in brackets.*

<E.g. The average survival time for patients in the main study treated with 475 mg of drug x in addition to drugs y and z increased by 19.5 months to 55.5 months compared with treatment 2 (36 months) and 17 months (57.5 months) compared with treatment 3 (40.5) months.>

VI.2.3 Unknowns relating to treatment benefits

(1 short paragraph per indication of 50 words maximum)

A short summary of the applicability of efficacy to all patients in the target population can be provided in lay language. This should be a précised version of Part IV IV.1 written for the lay reader. It should describe very briefly any relevant parts of the target population where experience is limited and whether efficacy is expected to be different in these people – e.g. factors such as age, sex, race, and organ impairment. If there is evidence that efficacy is either enhanced or reduced (e.g. ACE inhibitors and the Afro-Caribbean population) this should be stated.

<E.g. In the main and supporting studies nearly all patients were white Caucasians aged between 52 and 86 with most patients aged over 65. There is no evidence to suggest that results would be any different in non-white patients or in younger patients unable to tolerate high dose chemotherapy.>

VI.2.4 Summary of safety concerns

Important identified risks

Risk	What is known	Preventability
<Safety concern in lay language (medical term)>	<Brief summary in lay language>	<Whether risk can be minimised or mitigated, and how>
<E.g. Damage to the nerves in hands and feet (peripheral neuropathy)>	<E.g. Approximately one in two people treated with x will experience some form of nerve damage which may increase to three out of four people after 12 months of treatment. The nerve damage varies from mild tingling and altered sensation to irreversible disabling damage in the most severe cases. Early symptoms usually resolve or improve upon dose adjustment or discontinuation of therapy. >	<E.g. Yes, by monitoring for early symptoms >
<E.g. Blood clots (thromboembolic events {TEE})>	<E.g. These may affect the arteries or veins. In the veins this may lead to a painful swelling of the legs (deep vein thrombosis) and very occasionally life threatening or fatal clots in the lungs. Clots in the arteries may lead to a heart attack or stroke – particularly in patients who already have problems with their arteries. Patients with cancer who are being treated with oestrogen are	<E.g. Yes with preventative anti-thrombotic medicines >

Risk	What is known	Preventability
	already at higher risk of blood clots so it is difficult to assess what extra risk is caused by x.>	

Important potential risks

Risk	What is known (Including reason why it is considered a potential risk)
<E.g. Secondary primary cancers>	<E.g. Patients treated with X may be at an increased risk of developing new cancers. There are theoretical mechanisms and more patients treated with X developed new cancers than those not treated with X, but this could also be due to the fact that they live longer.>

Missing information

Risk	What is known
<E.g. Limited information on use in patients with kidney impairment>	<E.g. X itself is not eliminated to any significant extent by the kidney so it is unlikely that kidney impairment will lead to problems. Some of its metabolites are eliminated by the kidney so it is recommended that patients with severe renal impairment are monitored carefully. >

VI.2.5 Summary of risk minimisation measures by safety concern

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for X can be found in the X's EPAR page

<This medicine has no additional risk minimisation measures>

<This medicine has special conditions and restrictions for its safe and effective use (additional risk minimisation measures). Full details on these conditions and the key elements of any educational material can be found in Annex II of the product information which is published in X's EPAR page; how they are implemented in each country however will depend upon agreement between the manufacturer and the national authorities.

These additional risk minimisation measures are for the following risks:

Safety concern in lay terms (medical term)

Risk minimisation measure(s)
Objective and rationale
• Summary description of main additional risk minimisation measures

Risk minimisation measure(s)
– key points
<E.g. Damage to the nerves in hands and feet (peripheral neuropathy) Healthcare Professional and patient education Objective and rationale Patients and HCPs to understand the risk of peripheral neuropathy and the procedures related to the appropriate management of this risk to minimise its occurrence and its severity. Proposed action: HCP educational materials to be provided to prescribing physicians and pharmacists including advice on: Use of electromyogram prior to and during treatment Importance of adherence to dosing recommendations Management of neuropathy including dose reduction and treatment discontinuation Direct HCP communication prior to launch ('Dear HCP' letter). Patient booklet will inform patients what the symptoms of nerve damage are and the importance of informing their HCP if any occur>

VI.2.6 Planned post authorisation development plan

From combined summary tables in Part III and Part IV

List of studies in post authorisation development plan

Study / activity (including study number)	Objectives	Safety concerns / efficacy issue addressed	Status	Planned date for submission of (interim and) final results

Studies which are a condition of the marketing authorisation

<None of the above studies are conditions of the marketing authorisation>

< <study(ies)> <is><are> <a> condition<s> of the marketing authorisation

Mention all studies in the table (including specific obligations) which are conditions of the MA.

VI.2.7 Summary of changes to the Risk Management Plan over time

Major changes to the Risk Management Plan over time

Version	Date	Safety Concerns	Comment
	At time of authorisation dd/mm/yyyy	Identified Risks Potential Risks Missing information	

Version	Date	Safety Concerns	Comment
<E.g. 7.0>	<E.g. 17/08/2012>	<E.g.Allergic conditions added as an identified risk Hypersensitivity removed as an identified risk Severe infection added as an identified risk Convulsions added as a potential risk>	<E.g. The previous term hypersensitivity was updated to allergic conditions to include angioedema and urticarial>

Part VII: Annexes

Table of contents

Annex 1 – EudraVigilance Interface

Available in electronic format only

Annex 2 - SmPC & Package Leaflet

Current (or proposed if product is not authorised) EU (centralised/mutual recognition/decentralised/national) summary of product characteristics (SmPC) and package leaflet(s) for each product in the RMP.

If multiple versions are included for a product, they should show in which Member State(s) they are applicable. In addition, if available, a core SmPC should be provided with an overview of the changes applicable to the SmPC in each Member State

Annex 3 - Worldwide marketing authorisation by country (including EEA)

For each product in the RMP provide:

A3.1 Licensing status in the EEA

Country	Current licence status	Date of licence action [1]	Date first marketed in country	Brand name(s)	Comments
	Choose one of the following: • Approved • Refused • Under review • Suspended • Expired • Withdrawn	<Enter a date>	<Enter a date>		If product has different routes of authorisation e.g. national + MRP in the EEA, note here which one applies

[1] Enter the date of the most recent change to the licence status: eg date of approval or date of suspension

A3.2 Licensing status in the rest of the world

Country	Current licence status	Date of licence action 1	Date first marketed in country	Brand name(s)	Comments
	Choose one of the following: • Approved • Refused • Under review • Suspended • Expired • Withdrawn	<Enter a date>	<Enter a date>		

Annex 4 - Synopsis of on-going and completed clinical trial programme

Study	**Description (Phase, short description of study (1 – 2 sentences including comparator name(s)/placebo))**	**Countries**	**Study design**	**Planned/actual number of patients**	**Duration of follow up**	**Estimated/ Actual completion date**
Main or pivotal studies						
<E.g. Study ABC>	<E.g. Study versus ibuprofen in adults with mild postoperative pain Phase III>	<E.g. Germany, USA, Chile>	<E.g. Randomised double-blind>	<E.g. 4075>	<E.g. 14 days>	<E.g. Jan 2005>
Further safety/efficacy studies						
Studies in special populations (e.g. paediatric, elderly)						

Annex 5 - Synopsis of on-going and completed pharmacoepidemiological study programme

Study	Research question	Study design	Population & study size	Duration of follow up	Milestones & dates	Status
						Choose one of the following: • Planned • Protocol under development • Protocol agreed • Data collection started • Data collection ended • Study completed

Annex 6 - Protocols for proposed and on-going studies in categories 1-3 of the section "Summary table of additional pharmacovigilance activities" in RMP part III

Overview of included protocols

Study title	**Protocol status** [1]	**Version of protocol**	**Date of protocol version**
	Choose one of the following: • Draft • Approved • Final		<Enter a date>

[1]Draft = not approved or final

Approved = when agreed by PRAC or CHMP as appropriate

Final = final version when PRAC/CHMP agreement not required

Annex 7 - Specific adverse event follow-up forms

Provide forms

Annex 8 - Protocols for proposed and on-going studies in RMP part IV

Study title	**Protocol status** [1]	**Version of protocol**	**Date of protocol version**
	Choose one of the following: • Draft • Approved • Final		<Enter a date>

[1]Draft = not approved or final

Approved = when agreed by CHMP

Final = final version when CHMP agreement not required

Annex 9 - Newly available study reports for RMP parts III & IV

Include the study abstract. For non-interventional studies use the abstract format detailed in Module: VIII Post Authorisation Safety Studies of Good Pharmacovigilance Safety Studies

Annex 10 - Details of proposed additional risk minimisation measures (if applicable)

Annex 11 - Mock-up of proposed additional risk minimisation measures (if applicable)

Mock up examples in English (or the National language if the product is only authorised in a single Member State) of the material provided to healthcare professionals and patients as a requirement of Annex II of the Commission Decision or as a requirement of national authorisations including those using the mutual recognition or decentralised procedure as applicable.

Annex 12 - Other supporting data (including referenced material)

Index of included material