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Patient Health Protection

Guidance on format of the risk management plan (RMP) in the EU part III: Pharmacovigilance Plan

Active substance	
Product(s) concerned (brand name(s)):	
MAH/Applicant name	

Data lock point for this module	<Enter a date>
Version number of RMP when this module was last updated	<Enter a version no>

This guidance should be used in conjunction with the information in Good Pharmacovigilance Practices: Risk Management Systems.

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8668
E-mail info@ema.europa.eu **Website** www.ema.europa.eu
An agency of the European Union

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 1. 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	<Enter a date>

	Description of activity (or study title if known)	Milestone(s)	Due Date(s)
		submission)	
		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 2. 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 3. 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 4. 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>