EU Risk Management Plan for Folic acid Vitabalans (Folic acid)

RMP version to be assessed as part of this application:

RMP Version number: 0.2

Data lock point for this RMP: 31 Aug 2018

Date of final sign off: 5 Sep 2018

Rationale for submitting an updated RMP: not applicable

Summary of significant changes in this RMP: not applicable

Other RMP versions under evaluation: not applicable

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Table of content

Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) (INN or common name)	Folic acid
Pharmacotherapeutic group(s) (ATC Code)	B03BB01
Marketing Authorisation <Holder> <Applicant>	Vitabalans Oy
Medicinal products to which this RMP refers	Folic acid tablets
Invented name(s) in the European Economic Area (EEA)	Folic acid Vitabalans 1 mg and 5 mg tablets
Marketing authorisation procedure	Decentralised procedure
Brief description of the product	Chemical class: Pteroylglutamic acid
	Summary of mode of action: Folic acid is a part of the coenzymes involved in certain transmethylation processes e.g. synthesis of deoxyribonucleic acid and ribonucleic acid. Folic acid is a component of the B croup of vitamins and is necessary for the normal production and maturation of red blood cells. Folic acid deficiency is one of the causes of megaloblastic anaemia.
	Important information about its composition: Cellulose, microcrystalline Starch, pregelatinized Croscarmellose sodium Sodium ascorbate Silica colloidal anhydrous Magnesium stearate
Hyperlink to the Product Information	2018-10-08-spc-folicacidvb-1mg-common 2018-10-08-spc-folicacidvb-5mg-common 2018-10-08-pl-folicacidvb-1mg-common 2018-10-08-pl-folicacidvb-5mg-pom-common 2018-10-08-pl-folicacidvb-5mg-otc-common
Indication(s) in the EEA	Current (if applicable): Not applicable

	Proposed: Folate deficiency. Treatment of folate deficiency states confirmed by blood test including vitamin B12 status. During treatment with drugs that inhibit folate absorption or folate metabolism such as methotrexate. For the prevention of neural tube defects in the foetus for women planning a pregnancy.
Dosage in the EEA	Current (if applicable): Not applicable
	Proposed: <u>Adults (including elderly)</u> In folate deficiency: 1 mg daily Treatment of folate deficiency states confirmed by blood test including vitamin B12 status: Remission treatment: 5 mg daily for about 2 weeks. Maintenance: 1 mg daily, possibly higher dose in case of persistent folate deficiency. In drug induced folate deficiency: 5 mg weekly. Prevention of neural tube defects in the foetus for women planning a pregnancy: 5 mg daily started at least 4 weeks before conception and at least 12 weeks thereafter.
Pharmaceutical form(s) and strengths	Current (if applicable):
	Proposed (if applicable): Tablets 1 mg and 5 mg
Is/will the product be subject to additional monitoring in the EU?	No

Part II: Safety specification

Part II: Module SI - Epidemiology of the indication(s) and target population(s)

Not applicable – well established medicinal use product

Part II: Module SII - Non-clinical part of the safety specification

Not applicable – well established medicinal use product

Part II: Module SIII - Clinical trial exposure

Not applicable – well established medicinal use product

Part II: Module SIV - Populations not studied in clinical trials

Not applicable – well established medicinal use product

Part II: Module SV - Post-authorisation experience

Not applicable – well established medicinal use product

Part II: Module SVI - Additional EU requirements for the safety specification

Not applicable – well established medicinal use product

Part II: Module SVII - Identified and potential risks

SVII.1 Identification of safety concerns in the initial RMP submission

SVII.1.1. Risks not considered important for inclusion in the list of safety concerns in the RMP

Known risks that require no further characterisation and are followed up via routine pharmacovigilance namely through signal detection and adverse reaction reporting, and for which the risk minimisation messages in the product information are adhered by prescribers (e.g. actions being part of standard clinical practice in each EU Member state where the product is authorised):

- allergic reactions: frequency rare (≥ 1/10 000 to <1/1000)
- anorexia: frequency rare (≥ 1/10 000 to <1/1000)
- nausea: frequency rare (≥ 1/10 000 to <1/1000)
- abdominal distension and flatulence: frequency rare (≥ 1/10 000 to <1/1000)
- masking and exacerbation of neurological symptoms due to vitamin B12 (cobalamin) deficiency
- drug interactions with antiepileptics
- use in patients with malignant disease

SVII.1.2. Risks considered important for inclusion in the list of safety concerns in the RMP

Important identified risks:

None

Important potential risks:

None

Missing information:

None

SVII.2 New safety concerns and reclassification with a submission of an updated RMP

This is the first version of the RMP, there are no newly identified safety concerns to present in this section.

SVII.3 Details of important identified risks, important potential risks, and missing information

SVII.3.1. Presentation of important identified risks and important potential risks

Important identified/Potential Risk:

Not applicable

SVII.3.2. Presentation of the missing information

Missing information:

Not applicable

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Summary of safety concerns	
Important identified risks	None
Important potential risks	None
Missing information	None

Part III: Pharmacovigilance Plan (including post-authorisation safety studies)

III.1 Routine pharmacovigilance activities

There are no important safety concerns to be included in the list of safety concerns of RMP. Risks of the product will be monitored in routine pharmacovigilance activities. No additional risk minimization measures are needed.

III.2 Additional pharmacovigilance activities

No additional pharmacovigilance activities are required for the product.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

Post authorisation efficacy studies have not been planned for Folic acid Vitabalans.

Part V: Risk minimisation measures (including evaluation of the effectiveness of risk minimisation activities)

Risk Minimisation Plan

V.1. Routine Risk Minimisation Measures

Not applicable

V.2. Additional Risk Minimisation Measures

Not applicable

V.3 Summary of risk minimisation measures

Not applicable

Part VI: Summary of the risk management plan

Summary of risk management plan for Folic acid Vitabalans (folic acid)

This is a summary of the risk management plan (RMP) for Folic acid Vitabalans. The RMP details important risks of Folic acid Vitabalans, how these risks can be minimised, and how more information will be obtained about Folic acid Vitabalans' risks and uncertainties (missing information).

Folic acid Vitabalans' summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Folic acid Vitabalans should be used.

I. The medicine and what it is used for

Folic acid Vitabalans is authorised for:

Treatment of folate deficiency, also folate deficiency states confirmed by blood test including vitamin B12 status. Usage during treatment with drugs that inhibit folate absorption or folate metabolism such as methotrexate. For the prevention of neural tube defects in the foetus for women planning a pregnancy (see SmPC for the full indication). It contains folic acid as the active substance and it is given by oral route of administration.

II. Risks associated with the medicine and activities to minimise or further characterise the risks

Important risks of Folic Acid Vitabalans, together with measures to minimise such risks and the proposed studies for learning more about Folic acid Vitabalans' risks, are outlined below.
Measures to minimise the risks identified for medicinal products can be:

- Specific information, such as warnings, precautions, and advice on correct use, in the package leaflet and SmPC addressed to patients and healthcare professionals;
- Important advice on the medicine’s packaging;
- The authorised pack size — the amount of medicine in a pack is chosen so to ensure that the medicine is used correctly;
- The medicine’s legal status — the way a medicine is supplied to the patient (e.g. with or without prescription) can help to minimise its risks.

Together, these measures constitute *routine risk minimisation* measures.

II.A List of important risks and missing information

Important risks of Folic acid Vitabalans are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely taken. Important risks can be regarded as identified or potential. Identified risks are concerns for which there is sufficient proof of

a link with the use of folic acid. Potential risks are concerns for which an association with the use of this medicine is possible based on available data, but this association has not been established yet and needs further evaluation. Missing information refers to information on the safety of the medicinal product that is currently missing and needs to be collected (e.g. on the long-term use of the medicine);

List of important risks and missing information	
Important identified risks	None
Important potential risks	None
Missing information	None

II.B Summary of important risks

There are no important identified or potential risks or missing information to summarise.

II.C Post-authorisation development plan

II.C.1 Studies which are conditions of the marketing authorisation

There are no studies which are conditions of the marketing authorisation or specific obligation of Folic acid Vitabalans.

II.C.2 Other studies in post-authorisation development plan

There are no studies required for Folic acid Vitabalans.

Part VII: Annexes

Table of contents

Annex 1 – EudraVigilance Interface

Annex 2 – Tabulated summary of planned, ongoing, and completed pharmacovigilance study programme

Not applicable.

Annex 3 - Protocols for proposed, on-going and completed studies in the pharmacovigilance plan

Not applicable.

Annex 4 - Specific adverse drug reaction follow-up forms

Not applicable.

Annex 5 - Protocols for proposed and on-going studies in RMP part IV

Not applicable

Annex 6 - Details of proposed additional risk minimisation activities (if applicable)

Not applicable.

Annex 7 - Other supporting data (including referenced material)

Not applicable.

Annex 8 – Summary of changes to the risk management plan over time

Version	**Approval date** **Procedure**	**Change**
0.1	Not applicable	First version of RMP
0.2	Not applicable (updated during marketing authorisation process)	Indications and dosage information updated according to the authority comments. Risks updated according to the authority comments: suggested risks are deleted as those did not required additional pharmacovigilance activities.