EU Risk Management Plan for Betamethasone 500 microgram Soluble Tablets

RMP version to be assessed as part of this application:

RMP Version number: 1

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Rationale for submitting an updated RMP: Not applicable for initial marketing authorisation application submission

Summary of significant changes in this RMP: Not applicable

Other RMP versions under evaluation: Not applicable

Details of the currently approved RMP: Not applicable

QPPV name:

QPPV signature:

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Part I: Product(s) Overview

Table Part I.1 – Product Overview

Active substance(s) **(INN or common name)**	Betamethasone sodium phosphate
Pharmacotherapeutic group(s) (ATC Code)	Corticosteroids for systemic use, plain, Glucocorticoids ATC: H02A B01
Marketing Authorisation Applicant	
Medicinal products to which this RMP refers	Betamethasone 500 microgram Soluble Tablets
Invented name(s) in the European Economic Area (EEA)	Betamethasone 500 microgram Soluble Tablets
Marketing authorisation procedure	National
Brief description of the product	Chemical class Corticosteroid/Glucocorticoid
	Summary of mode of action Betamethasone sodium phosphate is an active corticosteroid with topical anti-inflammatory activity. Betamethasone is a glucocorticoid which is about eight to ten times as active as prednisolone on a weight-for-weight basis. The vast majority of corticosteroids, including betamethasone, are absorbed from the gastrointestinal tract.
	Important information about its composition The medicinal product is manufactured in the form of a soluble tablet containing the active substances and conventional pharmacopoeial excipients, which are present at typical levels.
Hyperlink to the Product Information	Hyperlink to SmPC Hyperlink to PIL
Indication(s) in the EEA	Current (if applicable):
	Proposed (if applicable): A wide variety of diseases may sometimes require corticosteroid therapy. Some of the principal indications are: Bronchial asthma, severe hypersensitivity reactions, anaphylaxis, rheumatoid arthritis, systemic lupus erythematosus,

	dermatomyositis, mixed connective tissue disease (excluding systemic sclerosis), polyarteritis nodosa; Inflammatory skin disorders, including pemphigus vulgaris, bullous pemphigoid and pyoderma gangrenosum; Minimal change nephrotic syndrome, acute interstitial nephritis; Ulcerative colitis, Crohn's disease, sarcoidosis, rheumatic carditis; Haemolytic anaemia (autoimmune), acute and lymphatic leukaemia, malignant lymphoma, multiple myeloma, idiopathic thrombocytopenic purpura; Immunosuppression in transplantation.
Dosage in the EEA	Current (if applicable):
	Proposed (if applicable): Posology: The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. During prolonged therapy, dosage may need to be increased temporarily during periods of stress or in exacerbations of illness. *Adults:* The dose used will depend on the disease, its severity and the clinical response obtained. The following regimens are for guidance only. Divided dosage is usually employed. *Short term treatment:* 2-3mg daily for the first few days, then reducing the daily dose by 250 or 500mcg (0.25 or 0.5mg) every two to five days, depending upon the response. *Rheumatoid arthritis:* 500mcg (0.5mg) to 2mg daily. For maintenance therapy the lowest effective dosage is used. *Most other conditions:* 1.5 to 5mg daily for one to three weeks, then reducing to the minimum effective dosage. Larger doses may be needed for mixed connective tissue diseases and ulcerative colitis. *Paediatric population:* A proportion of the adult dosage may be used (e.g. 75% at 12 years, 50% at 7 years and 25% at 1 year) but clinical factors must be given due weight.

	Method of Administration: For oral use. Betamethasone Soluble Tablets are best taken dissolved in water, but they can be swallowed whole without difficulty. **If the patient breaks the tablet in half, the part of the tablet that is not administered should be discarded. Once dissolved in water, the solution should be administered immediately.**
Pharmaceutical form(s) and strengths	Current (if applicable):
	Proposed (if applicable): Pink, flat, round tablet, diameter 6mm and thickness 2.2mm, scored on one side and engraved 'B0.5' on the other. Each tablet contains 500 micrograms (0.5mg) betamethasone as betamethasone sodium phosphate.
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 relevant as betamethasone is a generic medicinal product.

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

Not applicable.

Part II: Module SIII - Clinical trial exposure

Not applicable.

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

Not applicable.

Part II: Module SV - Post-authorisation experience

Not applicable.

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

Not applicable for this generic 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

Not applicable.

Reason for not including an identified or potential risk in the list of safety concerns in the RMP:

Not applicable.

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

Important Identified Risk 1:

Hypothalamo-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome in patients on therapy over 3 weeks, and in some cases under 3 weeks (e.g. previous therapy within past year or for longer than 3 weeks; high dose therapy, non-drug related adrenocortical insufficiency).

Risk-benefit impact:

The lowest dosage that will produce an acceptable result should be used; when it is possible to reduce the dosage, this must be accomplished by stages. Undesirable effects may be minimised by using the lowest effective dose for the minimum period and by administering the daily requirement as a single morning dose, or whenever possible as a single morning dose on alternate days.

Frequent patient review is required to appropriately titrate the dose against disease activity (see "Posology and Method of Administration"). Adrenal cortical atrophy develops during prolonged therapy and may persist for years after stopping treatment. Frequency of endocrine disorder reports is unknown.

Important Identified Risk 2:

Eye disorders (increased risk of glaucoma and cataracts)

Risk-benefit impact:

Frequency of eye disorders, including increased intraocular pressure (IOP) and glaucoma, is unknown. Patients with glaucoma or a family history of glaucoma should be monitored frequently. Visual disturbance may be reported with systemic and topical corticosteroid use. If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Important Identified Risk 3:

Opportunistic infections (including bacterial, fungal and viral cutaneous infections), exposure to live vaccines or exposure to chicken pox, herpes zoster or measles if a definite history of disease or immunisation is uncertain.

Risk-benefit impact:

Suppression of the inflammatory response and immune function increases the susceptibility to infections and their severity. The clinical presentation may often be atypical and serious infections such as septicaemia and tuberculosis may be masked and may reach an advanced stage before being recognised. Chickenpox is of particular concern since this normally minor illness may be fatal in immunosuppressed patients. Patients (or parents of children) without a definite history of chickenpox should be advised to avoid close personal contact with chickenpox or herpes zoster and if exposed they should seek urgent medical attention. Passive immunisation with varicella zoster immunoglobulin (VZIG) is needed for exposed non-immune patients who are receiving systemic corticosteroids or who have used them within the previous 3 months; this should be given within 10 days of exposure to chickenpox. If a diagnosis of chickenpox is confirmed, the illness warrants specialist care and urgent treatment. Corticosteroids should not be stopped and the dose may need to be increased. The frequency of reports of increased susceptibility to and severity of infections with suppression of clinical symptoms and signs, opportunistic infections, or recurrence of dormant tuberculosis is unknown.

Important Identified Risk 4:

Pre-existing conditions (current or history of), such as: osteoporosis; hypertension or congestive heart failure; severe affective disorders; diabetes mellitus; tuberculosis; glaucoma; previous corticosteroid-induced myopathy; liver failure; renal insufficiency; epilepsy; peptic ulceration.

Risk-benefit impact:

Use in patients with or with a history of certain pre-existing conditions requires care and frequent monitoring to ensure undesirable effects are discovered early. The frequency of reports of all adverse events is unknown with the exception of psychiatric disorders, which is common.

Important Identified Risk 5:

Conditions particularly associated with more serious consequences in elderly patients, such as osteoporosis; hypertension; hypokalaemia; diabetes; susceptibility to infection and thinning of the skin.

Risk-benefit impact:

The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin. Close clinical supervision is required to avoid life-threatening reactions. The frequency of these effects occurring in elderly patients is not known.

Important Potential Risk 1:

Use in pregnancy (due to potential effects on the embryo: intra-uterine growth retardation and decreased adrenal gland function)

Risk-benefit impact:

The ability of corticosteroids to cross the placenta varies between individual drugs, however, betamethasone readily crosses the placenta. Administration of corticosteroids to pregnant animals can cause abnormalities of foetal development including cleft palate, intra-uterine growth retardation and effects on brain growth and development. There is no evidence that corticosteroids result in an increased incidence of congenital abnormalities, such as cleft palate/lip in man. However, when administered for prolonged periods or repeatedly during pregnancy, corticosteroids may increase the risk of intra-uterine growth retardation. Hypoadrenalism may, in theory, occur in the neonate following prenatal exposure to corticosteroids but usually resolves spontaneously following birth and is rarely clinically important. Myocardial hypertrophy and gastroesophageal reflux have been reported in association with in-utero exposure to betamethasone. As with all drugs, corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks. When corticosteroids are essential however, patients with normal pregnancies may be treated as though they were in the non-gravid state. Patients with pre-eclampsia or fluid retention require close monitoring. Betamethasone, systemically administered to a woman during pregnancy may result in a transient suppression of the foetal heart rate parameters and biophysical activities that are widely used for the assessment of foetal well–being. These characteristics can include a reduction in foetal breathing movements, body movements and heart rate.

Missing information 1:

Use in lactation

Risk-benefit impact:

Corticosteroids may pass into breast milk, although no data are available for betamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

Missing information 2:

Use in children under 1 year

Risk-benefit impact:

Dosing adjustments are not given for children under 1 year. Age and weight are considered when determining dose, which is not known for this age group. Additionally, Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimise suppression of the HPA axis and growth retardation, consideration should be given to administration of a single dose on alternate days. The frequency of growth suppression in infancy is unknown.

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

Not applicable.

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 Risk 1:

Hypothalamo-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome in patients on therapy over 3 weeks, and in some cases under 3 weeks (e.g. previous therapy within past year or for longer than 3 weeks; high dose therapy, non-drug related adrenocortical insufficiency).

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:
Frequency of endocrine disorders is unknown. The impact on quality of life is variable dependent upon severity of reactions and whether treatment is given early. Ranges from mild symptoms to potentially acute, life-threatening symptoms.

Risk factors and risk groups:
Patients taking betamethasone longer than three weeks or for less than three weeks, but in high doses, previously within the past year, or previously at high doses; additionally, patients with non-drug related adrenal insufficiency.

Preventability:
Using with caution in patients with known risk factors after careful benefit/risk evaluation, avoiding long-term use or abrupt discontinuation when possible.

Impact on the risk-benefit balance of the product:
The frequency of endocrine disorders is unknown. The degree and duration of adrenocortical insufficiency produced by the drugs is highly variable among patients and depends on the dose, frequency and time of administration, and duration of glucocorticoid therapy. This effect may be minimized by use of alternate-day therapy[1].

Public health impact:
Variable dependent upon severity of reaction. Main impact is utilisation of emergency and general health care resources for severe reactions.

Important Identified Risk 2:

Eye disorders (increased risk of glaucoma and cataracts)

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:
Frequency of eye disorders is unknown. The impact on quality of life is variable dependent upon severity of reactions and whether treatment is given early. Ranges from mild symptoms to potentially acute, sight-threatening symptoms.

Risk factors and risk groups:
Patients with a history of glaucoma may have increased risk; however, patients without known history may also be at risk.

Preventability:
If a patient presents with symptoms such as blurred vision or other visual disturbances, the patient should be considered for referral to an ophthalmologist for evaluation of possible causes which may include cataract, glaucoma or rare diseases such as central serous chorioretinopathy (CSCR) which have been reported after use of systemic and topical corticosteroids.

Impact on the risk-benefit balance of the product:
The frequency of eye disorders is unknown. Prolonged use of glucocorticoids may result in posterior subcapsular and nuclear cataracts (particularly in children), exophthalmos, or increased intraocular pressure which may result in glaucoma or may occasionally damage the optic nerve[1].

Public health impact:
Variable. Main impact is utilisation of general health care resources for serious eye disorder issues.

Important Identified Risk 3:

Opportunistic infections (including bacterial, fungal and viral cutaneous infections), exposure to live vaccines or exposure to chicken pox, herpes zoster or measles if a definite history of disease or immunisation is uncertain.

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:
Frequency of increased susceptibility to and severity of infections is unknown. The impact on quality of life is variable dependent upon severity of reactions and whether treatment is given early. Ranges from mild symptoms to potentially acute, life-threatening symptoms.

Risk factors and risk groups:

All patients may be at risk for increased susceptibility to infections with increased severity; however, elderly patients or patients without a definite history of infections such as chickenpox or measles may be at increased risk from these infections as well as patients with a history of or exposure to tuberculosis.

Preventability:
Patients without a history of chickenpox should avoid close contact with chickenpox or herpes zoster; patients should avoid exposure to infections, such as tuberculosis, measles, or other infections, which may lead to septicaemia due to masked symptoms.

Impact on the risk-benefit balance of the product:
The frequency of opportunistic infections is unknown. Glucocorticoids, especially in large doses, increase susceptibility to and mask symptoms of infection. Infections with any pathogen, including viral, bacterial, fungal, protozoan, or helminthic infections in any organ system, may be associated with glucocorticoids alone or in combination with other immunosuppressive agents. These infections may be mild, but they can be severe or fatal, and localized infections may disseminate. Patients who become immunosuppressed while receiving glucocorticoids have increased susceptibility to infections compared with healthy individuals. Some infections such as varicella (chickenpox) and measles can have a more serious or even fatal outcome in such patients, particularly in children[1].

Public health impact:
Variable dependent upon severity of reaction. Main impact is utilisation of emergency and general health care resources for severe reactions.

Important Identified Risk 4:

Pre-existing conditions (current or history of), such as: osteoporosis; hypertension or congestive heart failure; severe affective disorders; diabetes mellitus; tuberculosis; glaucoma; previous corticosteroid-induced myopathy; liver failure; renal insufficiency; epilepsy; peptic ulceration.

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:
The frequency of reports of all adverse events is unknown with the exception of psychiatric disorders, which is common. The impact on quality of life is variable dependent upon severity of reactions and whether treatment is given early. Ranges from mild symptoms to chronic, disabling conditions, such as osteoporosis, or potentially acute, life-threatening symptoms.

Risk factors and risk groups:
All patients may be at risk; however, patients with a history of these disorders or elderly patients may be at increased risk.

Preventability:
Particular care is required when considering the use of systemic corticosteroids in patients with the following conditions and frequent patient monitoring is necessary.

Impact on the risk-benefit balance of the product:
The frequency of reports of all adverse events is unknown with the exception of psychiatric disorders, which is common.

Public health impact:
Variable dependent upon severity of reaction. Main impact is utilisation of emergency and general health care resources for severe and life-threatening reactions.

Important Identified Risk 5:

Conditions particularly associated with more serious consequences in elderly patients, such as osteoporosis; hypertension; hypokalaemia; diabetes; susceptibility to infection and thinning of the skin.

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:

The frequency of reports is unknown. The impact on quality of life is variable dependent upon severity of reactions and whether treatment is given early. Ranges from mild symptoms to chronic, disabling conditions, such as osteoporosis, or potentially acute, life-threatening symptoms.

Risk factors and risk groups:
The common adverse effects of systemic corticosteroids may be associated with more serious consequences in old age, especially osteoporosis, hypertension, hypokalaemia, diabetes, susceptibility to infection and thinning of the skin.

Preventability:
Close clinical supervision is required to avoid life-threatening reactions.

Impact on the risk-benefit balance of the product:
The frequency of these effects occurring in elderly patients is not known.

Public health impact:
Variable dependent upon severity of reaction. Main impact is utilisation of emergency and general health care resources for severe and life-threatening reactions.

Important Potential Risk 1:

Use in pregnancy (due to potential effects on the embryo: intra-uterine growth retardation and decreased adrenal gland function)

Potential mechanisms:
Drug class and mechanism of action.

Evidence source(s) and strength of evidence:
Post-marketing experience of comparator generic products based on spontaneous reporting and published literature.

Characterisation of the risk:
The frequency of pregnancy-related reports is unknown. Betamethasone, systemically administered to a woman during pregnancy may result in a transient suppression of the foetal heart rate parameters and biophysical activities that are widely used for the assessment of foetal well–being. These characteristics can include a reduction in foetal breathing movements, body movements and heart rate.

Risk factors and risk groups:
Patients who are or may become pregnant during use of betamethasone.

Preventability:
Corticosteroids should only be prescribed when the benefits to the mother and child outweigh the risks.

Impact on the risk-benefit balance of the product:
The frequency of potential effects occurring in pregnant patients is not known.

Public health impact:

Variable dependent upon severity of reaction. Main impact is utilisation of emergency and general health care resources for severe and life-threatening reactions.

SVII.3.2. Presentation of the missing information

Missing information 1:

Use in lactation

Evidence source:
Betamethasone may be prescribed to pregnant patients, patients who may become pregnant during treatment who subsequently may choose to breast-feed, or to patients already breast-feeding.

Anticipated risk/consequence of the missing information:
Corticosteroids may pass into breast milk, although no data are available for betamethasone. Infants of mothers taking high doses of systemic corticosteroids for prolonged periods may have a degree of adrenal suppression.

Missing information 2:

Use in children under 1 year

Evidence source:
The safety and efficacy of betamethasone oral solution in children below the age of 1 has not been established. The prescribing information does not give dosing for this age group.

Anticipated risk/consequence of the missing information:
Corticosteroids cause dose-related growth retardation in infancy, childhood and adolescence, which may be irreversible. Treatment should be limited to the minimum dosage for the shortest possible time. In order to minimise suppression of the HPA axis and growth retardation, consideration should be given to administration of a single dose on alternate days.

Part II: Module SVIII - Summary of the safety concerns

Table SVIII.1: Summary of safety concerns

Important Identified Risk	1. Hypothalamo-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome in patients on therapy over 3 weeks, and in some cases under 3 weeks (e.g. previous therapy within past year or for longer than 3 weeks; high dose therapy, non-drug related adrenocortical insufficiency). 2. Eye disorders (increased risk of glaucoma and cataracts). 3. Opportunistic infections (including bacterial, fungal and viral cutaneous infections), exposure to live vaccines or exposure to chicken pox, herpes zoster or measles if a definite history of disease or immunisation is uncertain. 4. Pre-existing conditions (current or history of), such as: osteoporosis; hypertension or congestive heart failure; severe affective disorders; diabetes mellitus; tuberculosis; glaucoma; previous corticosteroid-induced myopathy; liver failure; renal insufficiency; epilepsy; peptic ulceration. 5. Conditions particularly associated with more serious consequences in elderly patients, such as osteoporosis; hypertension; hypokalaemia; diabetes; susceptibility to infection and thinning of the skin.
Important Potential Risk	1. Use in pregnancy (due to potential effects on the embryo: intra-uterine growth retardation and decreased adrenal gland function).
Missing information	1. Use in lactation. 2. Use in children under 1 year.

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

III.1 Routine pharmacovigilance activities

The company performs routine pharmacovigilance activities including adverse reaction reporting and signal detection and is not aware of any additional PhV activities applied to the reference products.

III.2 Additional pharmacovigilance activities

Not applicable.

III.3 Summary Table of additional Pharmacovigilance activities

Not applicable.

Part IV: Plans for post-authorisation efficacy studies

None are proposed.

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

Risk Minimisation Plan

The safety information in the proposed product information is aligned to the reference medicinal product.

Part VI: Summary of the risk management plan

Summary of risk management plan for betamethasone

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

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

I. The medicine and what it is used for

Betamethasone is authorised for a variety of diseases that may sometimes require corticosteroid therapy, such as some inflammatory conditions and hypersensitivity reactions, certain autoimmune disorders, certain blood disorders, and immunosuppressive needs in transplantation (see SmPC for the full indications). It contains betamethasone as the active substance, and it is given orally as a tablet.

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

Important risks of betamethasone, together with measures to minimise such risks and the proposed studies for learning more about betamethasone's 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.

If important information that may affect the safe use of betamethasone is not yet available, it is listed under ‘missing information’ below.

II.A List of important risks and missing information

Important risks of betamethasone 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 betamethasone. 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).

Important Identified Risk	1. Hypothalamo-pituitary-adrenal (HPA) axis suppression and Cushing's syndrome in patients on therapy over 3 weeks, and in some cases under 3 weeks (e.g. previous therapy within past year or for longer than 3 weeks; high dose therapy, non-drug related adrenocortical insufficiency). 2. Eye disorders (increased risk of glaucoma and cataracts). 3. Opportunistic infections (including bacterial, fungal and viral cutaneous infections), exposure to live vaccines or exposure to chicken pox, herpes zoster or measles if a definite history of disease or immunisation is uncertain. 4. Pre-existing conditions (current or history of), such as: osteoporosis; hypertension or congestive heart failure; severe affective disorders; diabetes mellitus; tuberculosis; glaucoma; previous corticosteroid-induced myopathy; liver failure; renal insufficiency; epilepsy; peptic ulceration. 5. Conditions particularly associated with more serious consequences in elderly patients, such as osteoporosis; hypertension; hypokalaemia; diabetes; susceptibility to infection and thinning of the skin.
Important Potential Risk	1. Use in pregnancy (due to potential effects on the embryo: intra-uterine growth retardation and decreased adrenal gland function).
Missing information	1. Use in lactation. 2. Use in children under 1 year.

II.B Summary of important risks

The safety information in the proposed Product Information is aligned to the reference medicinal product.

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 obligations of betamethasone.

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

There are no studies required for betamethasone.

Part VII: Annexes

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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)

1. Betamethasone Sodium Phosphate 0.5mg Soluble Tablets Clinical Overview. V00_Jan_2019.

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

Not applicable.