# Part VI: Summary of the risk management plan

## Summary of risk management plan for Vancomycin powder for concentrate for solution for infusion and oral solution (Vancomycin)

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

Vancomycin powder for concentrate for solution for infusion and oral solution's summary of product characteristics (SmPC) and its package leaflet give essential information to healthcare professionals and patients on how Vancomycin powder for concentrate for solution for infusion and oral solution should be used.

## I. The medicine and what it is used for

Vancomycin powder for concentrate for solution for infusion and oral solution is authorised for complicated skin and soft tissue infections (cSSTI), bone and joint infections, community acquired pneumonia (CAP), hospital acquired pneumonia (HAP), including ventilator-associated pneumonia (VAP) and infective endocarditis (see SmPC for the full indication). It contains Vancomycin hydrochloride as the active substance and it is given by intravenous and oral solution.

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

Important risks of Vancomycin powder for concentrate for solution for infusion and oral solution, together with measures to minimise such risks and the proposed studies for learning more about Vancomycin powder for concentrate for solution for infusion and oral solution'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.

In addition to these measures, information about adverse reactions is collected continuously and regularly analysed including PSUR assessment so that immediate action can be taken as necessary. These measures constitute routine pharmacovigilance activities.

## II.A List of important risks and missing information

Important risks of Vancomycin powder for concentrate for solution for infusion and oral solution are risks that need special risk management activities to further investigate or minimise the risk, so that the medicinal product can be safely administered via infusion and oral solution. 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 Vancomycin powder for concentrate for solution for infusion and oral solution 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** | |
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| Important identified risks | – Hypersensitivity to vancomycin<br>– Red man syndrome, vancomycin induced hypotension, pain and spasm syndrome<br>– Increased risk for patients with renal insufficiency<br>– Nephrotoxicity<br>– Ototoxicity<br>– Superinfection<br>– Pseudomembranous colitis<br>– Neutropenia and agranulocytosis<br>– Increased vancomycin serum concentrations in premature infants and children |
| Important potential risks | – Injection site necrosis / thrombophlebitis when injected intramuscularly<br>– Use in pregnancy and lactation |

| **List of important risks and missing information** | |
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| Missing information | – None |

## II.B Summary of important risks

| **Important identified risk - Hypersensitivity to vancomycin** | |
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| Evidence for linking the risk to the medicine | Reports of Hypersensitivity to vancomycin derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Vancomycin should be used with caution in patients with allergic reactions to teicoplanin, since cross hypersensitivity, including fatal anaphylactic shock, may occur. |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use”, Section 4.3 “Contraindication” and Section 4.8 “Undesirable effects”<br><br>Guidance in PL section 4 “Possible side effects”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Red man syndrome, vancomycin induced hypotension, pain and spasm syndrome** | |
| Evidence for linking the risk to the medicine | Reports of Red man syndrome, vancomycin induced hypotension, pain and spasm syndrome derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Rapid bolus administration (i.e. over several minutes) may be associated with exaggerated hypotension (including shock, and, rarely, cardiac arrest) histamine like responses and maculopapular or erythematous rash (“red man’s syndrome” or “red neck syndrome”). |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br><br>Guidance in PL section 4 “Possible side effects”<br>Additional risk minimisation measures |

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| | Not applicable |
| **Important identified risk - Increased risk for patients with renal insufficiency** | |
| Evidence for linking the risk to the medicine | Reports of Increased risk for patients with renal insufficiency derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | In adult and paediatric patients with renal impairment, consideration should be given to an initial starting dose followed by serum vancomycin trough levels rather than to a scheduled dosing regimen, particularly in patients with severe renal impairment or those who undergo renal replacement therapy (RRT) due to the many varying factors that may affect vancomycin levels in them. |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br><br>Guidance in PL section 4 “Possible side effects”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Nephrotoxicity** | |
| Evidence for linking the risk to the medicine | Reports of Nephrotoxicity derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | In adult and paediatric patients with renal impairment, consideration should be given to an initial starting dose followed by serum vancomycin trough levels rather than to a scheduled dosing regimen, particularly in patients with severe renal impairment or those who undergo renal replacement therapy (RRT) due to the many varying factors that may affect vancomycin levels in them. Concomitant use with nephrotoxic agents such as aminoglycoside antibiotics, NSAIDs (e.g., ibuprofen for closure of patent ductus arteriosus) or amphotericin B is associated with an increased risk of nephrotoxicity (and therefore more frequent monitoring of vancomycin serum levels and renal function is indicated. |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br><br>Guidance in PL section 4 “Possible side effects” |

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| | Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Ototoxicity** | |
| Evidence for linking the risk to the medicine | Reports of Ototoxicity derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Vancomycin should also be avoided in patients with previous hearing loss. Deafness may be preceded by tinnitus. The elderly are particularly susceptible to auditory damage. Monitoring of vestibular and auditory function in the elderly should be carried out during and after treatment. Concurrent or sequential use of other ototoxic substances should be avoided. |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use”and Section 4.8 “Undesirable effects”<br>Guidance in PL section 4 “Possible side effects”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Superinfection** | |
| Evidence for linking the risk to the medicine | Reports of Superinfection derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Prolonged use of vancomycin |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Pseudomembranous colitis** | |
| Evidence for linking the risk to the medicine | Reports of Pseudomembranous colitis derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Severe persistent diarrhoea |
| Risk minimisation measures | Routine risk minimisation measures |

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| | Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Neutropenia and agranulocytosis** | |
| Evidence for linking the risk to the medicine | Reports of Neutropenia and agranulocytosis derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | In patients receiving vancomycin over a longer-term period or concurrently with other medications which may cause neutropenia or agranulocytosis. |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br>Additional risk minimisation measures<br>Not applicable |
| **Important identified risk - Increased vancomycin serum concentrations in premature infants and children** | |
| Evidence for linking the risk to the medicine | Reports of Increased vancomycin serum concentrations in premature infants and children derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Premature neonates and young infants |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use”<br>Additional risk minimisation measures<br>Not applicable |
| **Important Potential risk - Injection site necrosis / thrombophlebitis when injected intramuscularly** | |
| Evidence for linking the risk to the medicine | Reports of Injection site necrosis / thrombophlebitis when injected intramuscularly derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Adverse clinical outcome might be associated with off-label use |

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| | (administered intramuscularly) |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC Section 4.4 “Special warnings and precautions for use” and Section 4.8 “Undesirable effects”<br>Guidance in PL section 4 “How to Vancomycin is given”<br>Additional risk minimisation measures<br>Not applicable |
| **Important Potential risk - Use in pregnancy and lactation** | |
| Evidence for linking the risk to the medicine | Reports of Use in pregnancy and lactation derived from multiple sources such as non-clinical findings confirmed by clinical data, clinical trials, epidemiological studies, and spontaneous data sources, including published literature. |
| Risk factors and risk groups | Pregnant and lactating women |
| Risk minimisation measures | Routine risk minimisation measures<br>Guidance in SPC section 4.6 “Fertility, pregnancy and lactation”<br>Guidance in PL section 2 What you need to know before you”<br>Additional risk minimisation measures<br>Not applicable |
| **Missing Information** | |
| None | None |

## 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 Vancomycin powder for concentrate for solution for infusion and oral solution.

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

There are no studies required for Vancomycin powder for concentrate for solution for infusion and oral solution.