13 Part VI: Summary of the risk management plan of Valsartan

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

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

This summary of the RMP for valsartan should be read in the context of all this information including the assessment report of the evaluation and its plain-language summary, all which is part of the European Public Assessment Report (EPAR).

Important new concerns or changes to the current ones will be included in updates of valsartan's RMP.

13.1 Part VI: I. The medicine and what it is used for

Valsartan is authorized for treatment of hypertension in children and adolescents 6 to 18 years of age and it is also proposed for the treatment of hypertension in children 1 to <6 years. It contains valsartan as the active substance and it is given orally either as oral solution or film coated tablet.

Further information about the evaluation of valsartan's benefits can be found in valsartan's EPAR, including in its plain-language summary, available on the EMA website, under the medicine's webpage link to product's EPAR summary landing page on the EMA webpage: <Pre-authorization RMP (this line should be only edited by EMA): link to the EPAR summary landing page. Post-authorization RMP (this line should be edited by the Applicant/MAH): link to product's EPAR summary landing page on the EMA webpage.>

13.2 Part VI: II. Risks associated with the medicine and activities to minimize or further characterize the risks

Important risks of valsartan together with measures to minimize such risks are outlined below.

Measures to minimize 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 minimize its risks.

Together, these measures constitute routine risk minimization 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.

13.2.1 Part VI – II A: List of important risks and missing information

Important risks of valsartan are risks that need special risk management activities to further investigate or minimize the risk, so that the medicinal product can be safely administered. 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 valsartan. 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);

Table 13-1 List of important risks and missing information

List of important risks and missing information	
Important identified risks	None
Important potential risks (for pediatric population)	Elevation of liver function values Renal impairment Hypersensitivity including angioedema and serum sickness Medication error including overdose
Missing information	None

13.2.2 Part VI - II B: Summary of important risks

Table 13-2 Important potential risk Elevation of liver function values

Evidence for linking the risk to the medicine	About 70% of the absorbed dose is excreted in the bile, mainly as unchanged compound. Valsartan does not undergo extensive biotransformation, and, as expected, systemic exposure to valsartan is not correlated with the degree of liver dysfunction. No dose adjustment for valsartan is therefore necessary in patients with hepatic insufficiency of non-biliary origin and without cholestasis.
Risk factors and risk groups	Valsartan is mostly eliminated unchanged in the bile, and patients with biliary obstructive disorders showed lower valsartan clearance. Particular caution should be exercised in patients with biliary obstructive disorders.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.2 (Posology and method of administration), section 4.3 (Contraindications), section 4.4 (Special warnings and precautions for use), section 4.8 (Undesirable effects), section 5.2 (Pharmacokinetic properties) (Film coated tablets). SmPC section 4.2 (Posology and method of administration), section 4.4 (Special warnings and precautions for use), section 5.2 (Pharmacokinetic properties) - Pediatric hypertension (Oral solution). Additional risk minimization measures: None

Table 13-3 Important potential risk Renal impairment

Evidence for linking the risk to the medicine	As expected for a compound where renal clearance accounts for only 30% of total plasma clearance, no correlation was seen between renal function and systemic exposure to valsartan. Dose adjustment is

	therefore not required in patients with renal impairment. However, no data is available for severe cases (creatinine clearance <10 mL/min.) and caution is therefore advised.
Risk factors and risk groups	No dosage adjustment is required for patients with renal impairment. However, no data is available for severe cases (creatinine clearance <10 mL/min) and caution is therefore advised.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.2 (Posology and method of administration), section 4.4 (Special warnings and precautions for use), section 4.5 (Interactions), section 4.8 (Undesirable effects), section 4.9 (Overdose), section 5.2 (Pharmacokinetic properties) (Film coated tablets). SmPC section 4.2 (Posology and method of administration), section 4.4 (Special warnings and precautions for use), section 5.2 (Pharmacokinetic properties) - Pediatric hypertension (Oral solution) Additional risk minimization measures: None

Table 13-4 Important potential risk Hypersensitivity including angioedema and serum sickness

Evidence for linking the risk to the medicine	Angioedema, including swelling of the larynx and glottis, causing airway obstruction and/or swelling of the face, lips, pharynx, and/or tongue has been reported in patients treated with valsartan; some of these patients previously experienced angioedema with other drugs including ACE inhibitors.
Risk factors and risk groups	Patient with history of hypersensitivity and/or previously experienced angioedema with other drugs including ACE inhibitors are at risk. Diovan should be immediately discontinued in patients who develop angioedema, and Diovan should not be re-administered.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.3 (Contraindications), section 4.8 (Undesirable effects) (Film coated tablets). SmPC section 4.4 (Special warnings and precautions for use) - Pediatric hypertension (Oral solution). Additional risk minimization measures: None

Table 13-5 Important potential risk Medication error including overdose

Evidence for linking the risk to the medicine	Overdose with Diovan may result in marked hypotension, which could lead to depressed level of consciousness, circulatory collapse and/or shock
Risk factors and risk groups	During overdose, if the ingestion is recent, vomiting should be induced. Otherwise, the usual treatment would be intravenous infusion of normal saline solution. Valsartan is unlikely to be removed by hemodialysis.
Risk minimization measures	Routine risk minimization measures: SmPC section 4.2 (Posology and method of administration) section 4.4 (Special warnings and precautions for use), section 4.9 (Overdose) (Film coated tablets).

	SmPC section 4.2 Posology and method of administration - Pediatric hypertension (solution), section 4.4 (Special warnings and precautions for use), section 4.9 (Overdose) (Oral solution). Additional risk minimization measures: None

13.2.3 Part VI – II C: Post-authorization development plan

13.2.3.1 II.C.1 Studies which are conditions of the marketing authorization

There are no studies which are conditions of the marketing authorization or specific obligation of valsartan.

13.2.3.2 II.C.2. Other studies in post-authorization development plan

There are no studies required for valsartan.