## VI.2 Elements for a Public Summary

### *VI.2.1 Overview of disease epidemiology*

Metolazone is to be used for oedema in patients with kidney disease, where no other therapy has helped. Nephropathy, also known as kidney disease, means damage to or disease of a kidney. This lead to renal failure (the kidneys do not function as efficiently) which leads to a number of secondary conditions in the body amongst them oedema, which is an increase of fluid in the space between the cells (interstitial fluid)

### *VI.2.2 Summary of treatment benefits*

Metolazone indirectly decreases the amount of water reabsorbed into the bloodstream by the kidney, so that blood volume decreases and urine volume increases. When the excess fluid in the body is excreted in the urine instead of being accumulated this will prevent oedema.

Specifically, Metolazone stops the function of the kidney to reabsorb water and electrolytes and as a result, water remains in the kidney and is excreted as urine, instead of being reabsorbed into the bloodstream.

### *VI.2.3 Unknowns relating to treatment benefits*

None

### *VI.2.4 Summary of safety concerns*

**Important identified risks**

**None**

**Important potential risks**

| **Risk** | **What is known (Including reason why it is considered a potential risk)** |
|---|---|
| Potential risk of overdose due to higher bioavailability than reference products leading to electrolyte disturbances. | Due to the nature of action of Metolazone, different tablets might have different bioavailability (the rate of absorption of a drug that reaches the body). It is important for health personnel to know that a similar dose with different types of metolazon medication can have different effect and precautions should be taken appropriately. |
| Potential risk of overdose due to impossibility to administer a dose corresponding to a 2.5 mg dose of the reference formulation. | Metolazon Abcur tablet cannot be administered to a 2.5mg dose of the reference formulation; this is equivalent to ¼ of the tablet. As the indication for Metolazon Abcur is oedema of kidney disease-which has a starting treating recommended dose of 5mg, the risk should be of no clinical relevance. |
| Potential risk of overdose due to variations in bioavailability and/or rate of absorption leading to electrolyte disturbances. | Metolazone Abcur tablet gives a higher maximum concentration in the body than the reference product at similar dosesIt cannot be excluded that the rate of absorption may vary due to factors such as gastric acid and food intake, or that food effect is different for different types of metolazone. |
| Potential risk of disturbances of the electrolyte balance (hypokalemia and/or hyponatremia). | Metolazon method of action in the body may cause disturbances in the electrolyte balance that could result in hyponatremia (low sodium ion concentration) and/or hypokalemia (low potassium ion concentration). Health care personnel should be aware of this possible effect and take appropriate actions. |
| Potential risk of renal insufficiency due to dehydration. | In dehydrated patients there is a risk of renal insufficiency, which in certain cases may be severe. Metolazone has been shown to apply a significant diuretic effect (promotes the production of urine) which might worsen the condition of a |

| Risk | What is known (Including reason why it is considered a potential risk) |
|---|---|
| | dehydrated patient causing or worsening of the renal insufficieny. Health care personnel should be aware of this possible effect and take appropriate actions. |
| Potential risk of Toxic Epidermal Necrolysis (TEN). | Toxic epidermal necrolysis (TEN) is a rare, life-threatening skin condition that is usually caused by a reaction to drugs. Cases of TEN have been reported after treatment with products containing metolazone. Health care personnel should be aware of this possible effect and take appropriate actions. |

**Missing information**

None

### *VI.2.5 Summary of risk minimisation measures by safety concern*

All medicines have a Summary of Product Characteristics (SmPC) which provides physicians, pharmacists and other health care professionals with details on how to use the medicine, the risks and recommendations for minimising them. An abbreviated version of this in lay language is provided in the form of the package leaflet (PL). The measures in these documents are known as routine risk minimisation measures.

The Summary of Product Characteristics and the Package leaflet for Metolazon can be found in FASS.

No additional risk minimisation measures are in effect for Metolazon Abcur.

### *VI.2.6 Planned post authorisation development plan*

Not applicable

### *VI.2.7 Summary of changes to the Risk Management Plan over time*

No major changes to the Risk Management Plan.

The RMP v1 dated 17 Nov 2009 is being update to the new format in this current version.