## VI.2 Elements for a Public Summary

### VI.2.1 Overview of disease epidemiology

Acute kidney injury (AKI) is defined as a rapid deterioration of kidney function, of various causes, resulting in the kidneys losing their filtering ability. When this happens, dangerous levels of wastes may accumulate in the body and substances (electrolytes) in the blood that have specific critical roles in keeping the body running well may get out of balance. This balance is important for things like hydration, nerve impulses, muscle function, and acid-base balance.

It estimated that 15% of adults admitted to hospital in developed countries develop AKI. It is particularly common in the elderly.

The population incidence in the UK has been found to be 486-630 per million population, depending on definition.

Duosol may be used in the treatment of AKI where harmful waste products and elevated substances in the blood are removed.

### VI.2.2 Summary of treatment benefits

The initial management of AKI involves treating the underlying cause, stopping drugs that are toxic to the kidneys, ensuring that the person is appropriately hydrated with an adequate control of blood pressure.

However, no specific treatments have been shown to reverse the course of AKI so renal replacement therapy (RRT) is the cornerstone of further management. During this process, the patient's blood is passed through a set of tubing (a filtration circuit) via a special machine with a filter where waste products and water are removed. Replacement fluid such as Duosol is added and the blood is returned to the patient. This process is individualised and thus it is necessarily has to take into consideration the particular clinical condition of each patient, i.e. prior to administration of the Duosol intense analysis of the patient's serum imbalances and electrolyte concentrations should be made.

Patients requiring RRT of any type are in a critical, usually life-threatening condition. Therefore, placebo-controlled studies, (where one group of patients receives an inactive medicinal product) are neither ethical nor feasible.

Accordingly, comparison was carried out on RRT containing substitution solution of substances such as bicarbonate or lactate. Essential substances in the blood in patients treated with bicarbonate were well controlled and remained within normal ranges, however, waste products (urea) in the blood, were significantly lower in the bicarbonate group (Olbricht 1990) compare to patients receiving lactate-based RRT.

This demonstrates that patients with AKI undergoing RRT can be adequately treated with bicarbonate-based substitution solutions such as Duosol.

### VI.2.3 Unknowns relating to treatment benefits

There are no significant unknowns about the treatment benefits. As the active substances contained within the product under question are naturally and physiologically present in the body in considerable amounts, new data emerging regarding unknown treatment benefit seems unlikely.

### VI.2.4 Summary of safety concerns

| **Important identified risks** | | |
|---|---|---|
| **Risk** | **What is known** | **Preventability** |
| Imbalance of potassium in your blood | Potassium is a substance (electrolyte) in your body that is critical to the proper functioning of nerve and muscles cells, particularly heart muscle cells. A small drop in potassium level may cause abnormal heartbeats (arrhythmia), especially if you have heart disease, fast heartbeats (palpitations), fatigue, muscle spasm, tingling or numbness. A large drop in potassium level may slow your heart and you may feel lightheaded. A very low potassium level may cause your heart to stop altogether. | Before and during administration of Duosol, the prescriber should closely monitor your blood pressure, blood flow, fluid balance, salt (electrolyte) balance, acid-base balance. The level of potassium in your blood must also be carefully monitored. If the potassium level becomes too low, the prescriber will ensure you receive extra potassium to compensate for the low level. |
| Abnormally low acid levels in the blood (metabolic alkalosis) | You may have a headache, feel sluggish, confused, or experience muscle spasm, fits (seizures). You may also be more prone to suffer for an angina attack (chest pain), or abnormal heartbeats (arrhythmia). You may also feel weak if the potassium level is low in your blood. | Before and during administration of Duosol, the prescriber should closely monitor your blood pressure, blood flow, fluid balance, salt (electrolyte) balance, acid-base balance. |

| **Important potential risk** | |
|---|---|
| **Risk** | **What is known (Including reason why it is considered a potential risk)** |
| None | - |

| **Missing information** | |
|---|---|
| **Risk** | **What is known** |
| None | - |

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

Not applicable. No additional risk minimisation measures are proposed for Duosol.

### VI.2.6 Planned post authorisation development plan

Not applicable

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

Major changes to the Risk Management Plan over time

| Version | Date | Safety Concerns | Comment |
|---|---|---|---|
| 01 | 28th July 2015 | Identified risks:<br>• Imbalance of potassium<br>• Abnormally low acid levels in the blood (metabolic alkalosis)<br><br>Potential risk:<br>• None<br><br>Missing information:<br>• None | None |