VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Basocare® (other brand names include Bicafres®, Azidofres® and Fresonorm®) is indicated for treatment of metabolic acidosis in patients with chronic renal failure.

Metabolic acidosis is characterised primary by reduction of the bicarbonate serum concentration including a reduction in blood pH value. Bicarbonate is an important part of the acid-base homeostasis in the human body maintaining the blood pH within the narrow range of 7.35 to 7.45. Any shift of the blood pH value under 7.35 due to increase in the production of non-volatile acids or a loss of bicarbonate from the body for example due to renal dysfunction may lead to a metabolic acidosis. Untreated metabolic acidosis may cause decreased cardiac output due to decreased myocardial contractility, slowing of the heart rate, and an increased risk for dysrhythmias. The hyperkalaemia that usually accompanies metabolic acidosis increases the risk for decreased cardiac output, dysrhythmias, and even death. Even mild metabolic acidosis associated with renal disease may have diverse deleterious effects including effects on organ function.

Metabolic acidosis is commonly associated with chronic kidney disease (CKD) (e.g. Kraut et al. 2005, Kopple et al. 2005). As the number of functioning nephrons declines in CKD, acid excretion is initially maintained by an increase in the ammonium excreted per nephron. Due to the insufficient function of the kidneys in relation to the important part in the acid-base homeostasis regulation an unintentionally shift of the blood pH value occurs.

VI.2.2 Summary of treatment benefits

Basocare® and other oral bicarbonate preparations are effective in increasing blood pH and bicarbonate levels in acidotic patients with chronic kidney disease and therefore avoiding any complications associated with metabolic acidosis.

VI.2.3 Unknowns relating to treatment benefits

The product is well known and the use is well established. Sodium hydrogen carbonate has been used for many decades by physicians and patients world-wide in a variety of conditions, comprehensive information exists on its biochemistry, pharmacology, toxicology, and clinical use.

No sufficient clinical data is available for children and pregnant or breast feeding women. It is unknown whether sodium hydrogen carbonate affects fertility.

There is only little evidence from clinical trials with sodium hydrogen carbonate regarding the efficacy and safety of this treatment in children. Due to the lack of adequate data and as a precautionary measure, the product is not recommended in paediatric patients under the age of 14 years.

Bicarbonate readily passes the placental barrier (e.g. Aarnoudse et al.1984); it is unknown whether bicarbonate can cause foetal harm when administered to pregnant women. Therefore, sodium

hydrogen carbonate should be used during pregnancy only when clearly needed. A thorough risk-to-benefit evaluation and cautious use is recommended when sodium hydrogen carbonate is used during breast feeding due to insufficient data. Sodium hydrogen carbonate is a physiological substance and undesired effects during pregnancy and breast feeding overall appear unlikely when the pH is restored at normal values. However, physiological imbalances of arterial pressure or respiratory alkalosis may be increased during pregnancy, which must be considered during treatment with sodium hydrogen carbonate.

VI.2.4 Summary of safety concerns

Important identified risks

Table 16

Risk	What is known	Preventability
Increased pH blood value (Alkalosis)	The product contains the active ingredient bicarbonate which is an alkaline substance. It is responsible to shift the acidic blood pH which is symptomatic for metabolic acidosis to a normal range. However an overdose of bicarbonate can raise the blood pH value to the alkali side including the occurrence of alkalosis.	Weekly control of sodium hydrogen carbonate effects are required to ensure that the blood pH value is within the tolerated range.
Decrease in blood potassium levels (Hypokalaemia)	The product contains bicarbonate which activates certain shifts of electrolytes in the intra- and extracellular area. This includes decrease of potassium concentration outside of the cells in the intercellular space.	Constant controls of the blood potassium levels are necessary to ensure that the blood potassium levels are within the tolerated ranges. However sodium hydrogen carbonate should not be taken by patients with pre-existing hypokalaemia.
Increased in blood sodium levels (Hypernatraemia)	The product contains bicarbonate bound to sodium. This additional intake of sodium and the limited balance control function of the kidney due to the underlying disease can cause an increase of the sodium blood concentration.	Constant controls of the blood sodium levels are necessary to ensure that the sodium levels are within the tolerated ranges. However sodium hydrogen carbonate should not be taken by patients with pre-existing hypernatraemia and low-sodium diet.
Decrease in blood calcium levels (Hypocalcaemia)	In case of bicarbonate overdose even without symptoms the blood plasma hydrogen ion concentration decreases, caused by respiratory or metabolic alkalosis. This has a decreased	Constant monitoring of the blood pH are recommended during treatment with sodium hydrogen carbonate. This is already included in the

Risk	What is known	Preventability
	impact on the concentration of freely ionized calcium which is the biologically active component of blood calcium. This is because, since a portion of both hydrogen ions and calcium are bound to serum albumin, the blood becomes alkalotic. Bound hydrogen ions dissociate from albumin, freeing up the albumin to bind with more calcium, and thereby decreasing the freely ionized portion of total serum calcium	SmPC. It is contraindicated for patient with pre-existing low calcium blood levels (hypocalcaemia)
Kidney stones (Renal urolithiasis)	Sodium hydrogen carbonate has an impact on the blood pH value and therefore as well impact on the electrolytes solubility. In addition to the underlying disease of the patients with less control on the electrolytes concentration due to the impaired renal function a potential risk of kidney stones occurrence exists.	Constant monitoring of the blood pH recommended during treatment with sodium hydrogen carbonate. This is already included in the SmPC.
Interaction: Altered elimination of weak acids and bases (e.g. sympathomimetics, anticholinergics, tricyclic antidepressants, barbiturates, H_2-blockers, captopril, and quinidine) via an increase of the pH in urine by sodium hydrogen carbonate	Sodium hydrogen carbonate may have an effect on the elimination of certain substance due to their chemical properties in relation to the increase of pH in the urine. Due to potential shift of the pH value in the gastrointestinal tract an impact on the absorption of certain substance may take place.	Sodium hydrogen carbonate should be used carefully together with these medications. To ensure that the treating physicians are aware of it, a warning statement is placed in the product information.
Interaction: Decrease in blood potassium levels (hypokalaemia) with drugs increasing the potassium	Drugs that have impact on the potassium excretion can have an intensifying effect in	Sodium hydrogen carbonate should be used carefully together with these medications.

Risk	What is known	Preventability
excretion, e.g. gluco- and mineralcorticoids, androgens, and diuretics.	combination with sodium hydrogen carbonate.	To ensure that the treating physicians are aware of it, a warning statement is placed in the product information.

Missing information

Table 17

Risk	What is known
There are limited data on the use of sodium hydrogen carbonate in children and adolescent under 14-years.	The potential risk for humans is unknown. The product should not be taken in this particular patient group.
No data is available for fertility impact during the use of sodium hydrogen carbonate	It is unknown whether sodium hydrogen carbonate affects fertility
No or limited data is available on the use of sodium hydrogen carbonate during pregnancy and by women who are breastfeeding.	Sodium hydrogen carbonate should be used with caution and only if clearly needed during pregnancy. High dose and long term use of the product is not recommended during breastfeeding.
Treatment with Basocare® in other indications which are not stated in the product information.	Currently no information for use of the product in other indications and patient populations is available.

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 can be found on the web pages of the national competent authorities in the EU.

This medicine has no additional risk minimisation measures.

VI.2.6 Planned post authorisation development plan

No post authorisation development plan is required as the product is well known and the use is well established.

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

Not applicable as this is the first RMP.