	Special warnings and precautions for use presented in Section 4.4; Undesirable effects presented in Section 4.8; Pharmacokinetic properties 5.2	

VI.2 Elements for a Public Summary

VI.2.1 Overview of disease epidemiology

Furosemide is a loop diuretic indicated whenever parenteral therapy is required to treat:

- oedema
- hypertensive crisis
- acute or chronic renal failure

Furosemide as a loop diuretic is used in the treatment of oedema associated with heart failure (e.g. left ventricular failure), including pulmonary oedema, and with renal and hepatic disorders (e.g. cirrhotic ascites) [1].

Pulmonary oedema occurs in about 1% to 2% of the general population. Between the ages of 40 and 75 years, males are affected more than females. After the age of 75 years, males and females are affected equally. The incidence of pulmonary oedema increases with age and may affect about 10% of the population over the age of 75 years. Risk factors include exposure to inhaled toxins, aspirated toxins, substances affecting caliber of blood vessels (histamines, kinins), dense smoke, and the abuse of certain drugs such as cocaine or heroin may increase an individual's risk of pulmonary oedema [2].

Ascites is the most common complication from cirrhosis of the liver, developing in around 50 % of patients observed over a 10-year period. The occurrence of ascites usually portends a poor prognosis and heralds the onset of other complications of portal hypertension, such as variceal hemorrhage and hepatic encephalopathy. Thus, uncontrolled ascites is often the reason for hospital admission in patients with decompensated cirrhosis [3].

Oedema is a common clinical symptom in patients with nephrotic syndrome. The nephrotic syndrome is one of the best known presentations of adult or paediatric kidney disease. The term describes the association of (heavy) proteinuria with peripheral oedema, hypoalbuminaemia, and hypercholesterolaemia. Nephrotic syndrome has an incidence of three new cases per 100 000 each year in adults. It is a relatively rare way for kidney disease to manifest compared with reduced kidney function or microalbuminuria as a complication of systemic diseases, such as diabetes and raised blood pressure. Idiopathic nephrotic syndrome is a common renal disease in children. Children with severe oedema are usually hospitalised [4,5].

The worldwide prevalence of hypertension is around 26%, totalling 1 billion people. Of these, 1% to 2% will suffer a hypertensive crisis in their lifetime. Men may be more likely than women to suffer a hypertensive emergency [6]. Hypertensive emergency is also more common in older patients and in black people while Caucasian patients are reported to have higher rates of emergencies as opposed to the more benign urgency equivalent [6,7]. In the US, 30% of people suffer from hypertension; lack of insurance or a primary care doctor and non-adherence to treatment all predispose toward development of hypertensive emergency. As the average age of the global population increases, the prevalence of hypertension and therefore hypertensive emergency is expected to increase [6].

Acute kidney injury (formerly known as acute renal failure) may increase the risk for chronic kidney disease and end-stage renal disease. The incidence of acute kidney injury (AKI) has been increasing over time. The proportion of patients surviving after AKI has also been increasing over time [8].

The most common underlying risk factors for acute kidney injury include: previous acute kidney injury, pre-existing chronic kidney disease, age (patients aged 65 years or over), congestive heart failure, atherosclerotic peripheral vascular disease, diabetes, liver disease. AKI can be triggered by: sepsis or infection, hypovolemia (dehydration, bleeding), hypotension (e.g. after a serious heart attack) and certain medicines [9]. About 80% of cases of AKI are caused by pre-renal issues and acute tubular necrosis, 10% are due to obstruction (post-renal) and 10% are due to intrinsic renal causes [10].

AKI has been identified as an independent risk factor for chronic kidney failure, end-stage renal disease, death, and other important non-renal outcomes, implying significant public health concerns.

Chronic kidney disease is defined by indicators of kidney damage—imaging or proteinuria (commonly using albumin to creatinine ratio, ACR)—and decreased renal function (below thresholds of GFR estimated from serum creatinine concentration). Chronic kidney disease has a high global prevalence with a consistent estimated global chronic kidney disease prevalence of between 11 to 13% with the majority stage 3. Chronic kidney disease is associated with age-related renal function decline accelerated in hypertension, diabetes, obesity and primary renal disorders. Cardiovascular disease (CVD) is the primary cause of morbidity and mortality where chronic kidney disease is regarded as an accelerator of CVD risk and an independent risk factor for CVD events. There is a graded inverse relationship between CVD risk and glomerular filtration rate (GFR) that is independent of age, sex and other risk factors. Decreased renal function is a predictor of hospitalisation, cognitive dysfunction and poor quality of life. The healthcare burden is highest in early stages due to increased prevalence, affecting around 35% of those over 70 years. While this high (and rising) prevalence is in part due to the ageing population, it is also associated with increases in hypertension and diabetes mellitus. However, conversely a UK manuscript published in 2014 examined nationally representative cross-sectional studies within the UK and found that the prevalence

estimates reported declined over time [11]. Chronic kidney failure is recognised as having changed from a subspecialty issue to a global health concern.

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