NEW DRUG APPROVAL

Brand Name	Soaanz®
Generic Name	torsemide
Drug Manufacturer	Sarfez Pharmaceuticals Inc

New Drug Approval

FDA Approval Date: June 14, 2021

Review Designation: Standard

Review Type: Type 5 - New Formulation or New Manufacturer; New Drug Application (NDA): 213218

Dispensing Restrictions: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Edema is defined as a palpable swelling on the body produced by expansion of the interstitial fluid volume. This accumulation of fluid in the interstitial space occurs as the capillary filtration exceeds the amount of fluid take out by lymphatic drainage. When Edema is massive and generalized, it is called anasarca. It is caused by a variety of clinical conditions like heart failure, renal failure, liver failure, or problems with the lymphatic system. Edema usually becomes clinically apparent as the interstitial volume exceeds 2.5 -3 liters.

Congestive heart failure is one of the most important causes of peripheral edema seen in clinical practice. Edema in congestive heart failure is the result of the activation of a series of humoral and neurohumoral mechanisms that promote sodium and water reabsorption by the kidneys and expansion of the extracellular fluid. These mechanisms, in concert with abnormal Starling forces such as increased venous capillary pressure and decreased plasma oncotic pressure, promote fluid extravasation and edema formation.

Fluid retention is a major clinical problem in individuals with advanced chronic kidney disease (CKD), also known as stage 5 CKD or end-stage renal disease and is associated with morbid conditions such as lower-extremity edema, anasarca, ascites, pulmonary vascular congestion or edema, hypertension, and worsening heart failure.

During the past decade, the worldwide medical community has become increasingly aware of the fact that chronic kidney disease (CKD) is a strong and independent risk factor for cardiovascular disease (CVD). In the US, for example, the prevalence of CVD in CKD patients reaches 63%, in contrast with only 5.8% in people without CKD, and this prevalence is directly correlated with the severity of CKD. In dialysis-dependent end-stage renal disease (ESRD) patients, the risk of cardiovascular (CV) mortality is 10-fold to 20-fold higher than in age- and gender-matched control subjects without CKD. This remarkable association of CKD with CVD is commonly explained by a typical clustering of several CV risk factors in patients with CKD; these factors may be classified as “traditional” (including advanced age, hypertension, diabetes, and dyslipidemia) and “nontraditional” (CKD-specific) ones (such as anemia, volume overload, mineral metabolism abnormalities, proteinuria, malnutrition, oxidative stress, and inflammation).

Heart failure (HF) is the leading CV complication in CKD patients and its prevalence increases with declining kidney function. In the Atherosclerosis Risk in Communities (ARIC) study, a large, population-based study of US adults, the incidence of HF was 3-fold higher in individuals with an estimated glomerular filtration rate (GFR) <60 mL/min/1.73 m^2, compared with the reference group with an estimated GFR ≥90 mL/min/1.73 m^2. In dialysis patients, the presence of HF at the start of dialysis is a strong and independent predictor of short-term and long-term mortality, in both hemodialysis (HD) and peritoneal dialysis (PD) patients. The median survival of dialysis

patients with baseline HF has been estimated to be 36 months, in contrast with 62 months for those without baseline HF. Over 80% of ESRD patients who are recently diagnosed with HF are expected to die within only three years from the time of this diagnosis.

Efficacy

N/A

Safety

ADVERSE EVENTS

The following risks are given below,

- Hypotension and Worsening Renal Function.
- Electrolyte and Metabolic Abnormalities.
- Ototoxicity

Discontinuation of therapy due to adverse reactions occurred in 6% of patients treated with Soaanz®

WARNINGS & PRECAUTIONS

- Non-steroidal anti-inflammatory drugs (NSAIDs): Reduced diuretic, natriuretic, and antihypertensive effects; risk of renal impairment.
- CYP2C9: Concomitant use with CYP2C9 inhibitors can decrease torsemide clearance. Torsemide may affect the efficacy and safety of sensitive CYP2C9 substrates or of substrates with a narrow therapeutic range, such as warfarin or phenytoin.
- Cholestyramine: Decreased exposure of Soaanz®.
- Organic anion drugs: may decrease diuretic activity of Soaanz®.
- Lithium: Risk of lithium toxicity.
- Renin-angiotensin inhibitors: Increased risk of hypotension and renal impairment.
- Radiocontrast agents: Increased risk of renal toxicity.
- Corticosteroids and ACTH: Increased risk of hypokalemia.

CONTRAINDICATIONS

Hypersensitivity to Soaanz®, anuria, and hepatic coma.

Clinical Pharmacology

MECHANISMS OF ACTION

Micropuncture studies in animals have shown that torsemide acts from within the lumen of the thick ascending portion of the loop of Henle, where it inhibits the Na+/K+/2Cl--carrier system. Clinical pharmacology studies have confirmed this site of action in humans, and effects in other segments of the nephron have not been demonstrated. Diuretic activity thus correlates better with the rate of drug excretion in the urine than with the concentration in the blood. Torsemide increases the urinary excretion of sodium, chloride, and water, but it does not significantly alter glomerular filtration rate, renal plasma flow, or acid-base balance.

Dose & Administration

ADULTS

The recommended initial dose is 20 mg orally once daily. Titrate dose by approximately doubling until desired diuretic response is obtained.

PEDIATRICS

The safety and effectiveness of Soaanz® in pediatric patients have not been established.

GERIATRICS

Refer to adult dosing.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Tablets: 20 mg, 40 mg, and 60 mg.