NEW DRUG APPROVAL

Brand Name	Furoscix®
Generic Name	furosemide
Drug Manufacturer	SC Pharmaceuticals, Inc.,

New Drug Approval

FDA approval date: October 07, 2022

Review designation: Standard

Type of review: Type 3 - New Dosage Form; New Drug Application (NDA): 209988

Dispensing restriction: N/A

Place in Therapy

DISEASE DESCRIPTION & EPIDEMIOLOGY

Heart failure is a common clinical symptom resulting from different structural or cardiac disorders that impairs the ability of the ventricle to fill with or eject blood. It is a severe chronic disease. It occurs when the heart cannot pump sufficiently to maintain blood flow through-out the body. Both peripheral edema and pulmonary edema as well as ascites can occur.

Causes of heart failure: coronary artery disease, myocardial infarction, diabetes, valvular heart disease, cardiomyopathy, thyroid disease, kidney disease, heart defects, high blood pressure, atrial fibrillation, and excess alcohol use. Confirmation by echocardiogram, blood tests, electrocardiography, and chest radiography may help in identifying the underlying cause.

Classification of heart failure: There are three main types of HF: heart failure with reduced ejection fraction (HFrEF), heart failure with mildly reduced ejection fraction (HFmfEF) and heart failure with preserved ejection (HFpEF) fraction. Heart failure due to reduced ejection fraction is also known as heart failure due to left ventricular systolic dysfunction or systolic heart failure. Heart failure with reduced ejection fraction occurs when the ejection fraction is less than 40%. Heart failure with preserved ejection fraction is also known as diastolic heart failure, or heart failure with normal ejection fraction. Patients HFmrEF might present with mild systolic and diastolic dysfunction. It is important to distinguish between the types of heart failure since they are treated differently.

Prevalence: There are 6.7 million people living with heart failure in the United States, with about 670,000 people diagnosed each year. By 2030, the prevalence is expected to exceed 8 million.

Disease Progression: High mortality rate, 5 years = 50%; after hospitalization for heart failure, the 30-day and 1 year mortality rates are 10% and 22% respectively.

Efficacy

Phase 2, multicenter, randomized study that compared scPharmaceuticals' investigational product, Furoscix® (furosemide 80 mg/10 mL for subcutaneous administration), with a "treatment as usual" approach in chronic heart failure patients presenting to a heart failure clinic with worsening congestion and requiring augmented diuresis.

The study enrolled 51 subjects, of which 34 received Furoscix® and 17 received "treatment as usual."

Data highlights:

- There was a positive trend in the Finkelstein-Schoenfeld win ratio of the hierarchal primary composite endpoint consisting of cardiovascular death, heart failure hospitalizations, emergency department visits for heart failure and % change from baseline of NT-proBNP at day seven in the Furoscix® group compared to the "treatment as usual" group across multiple analysis populations.
- Subjects randomized to Furoscix® had a 37% reduction in the risk of a heart failure hospitalization relative to patients randomized to "treatment as usual" at day 30.
- All pre-defined secondary endpoints measuring symptoms of congestion, quality of life and functional status favored the Furoscix® group and included a two-kilogram greater weight loss at day three and a 12-point increase in the 12 item Kansas City Cardiomyopathy Questionnaire (KCCQ-12) summary scores at day 7 and day 30.

Safety

ADVERSE EVENTS

The following important adverse reactions are:

- Fluid, Electrolyte, and Metabolic Abnormalities.
- Ototoxicity

The following adverse reactions associated with the use of furosemide were identified in clinical trials or post-marketing reports. Because these reactions were reported voluntarily from a population of uncertain size, it is not always possible to estimate their frequency reliably, or to establish a causal relationship to drug exposure.

Adverse reactions are categorized below by organ system and listed by decreasing severity.

Gastrointestinal System Reactions: pancreatitis, jaundice (intrahepatic cholestatic jaundice), increased liver enzymes, anorexia, oral and gastric irritation, cramping, diarrhea, constipation, nausea, vomiting.

Systemic Hypersensitivity Reactions: severe anaphylactic or anaphylactoid reactions (e.g., with shock), systemic vasculitis, interstitial nephritis, necrotizing angiitis.

Central Nervous System Reactions: tinnitus and hearing loss, paresthesias, vertigo, dizziness, headache, blurred vision, xanthopsia.

Hematologic Reactions: aplastic anemia, thrombocytopenia, agranulocytosis, hemolytic anemia, leukopenia, anemia, eosinophilia.

Dermatologic Hypersensitivity Reactions: toxic epidermal necrolysis, Stevens-Johnson Syndrome, erythema multiforme, drug rash with eosinophilia and systemic symptoms, acute generalized exanthematous pustulosis, exfoliative dermatitis, bullous pemphigoid, purpura, photosensitivity, rash.

Cardiovascular Reactions: orthostatic hypotension, increase in cholesterol and triglyceride serum levels.
Administration Site and Skin Reactions: erythema, bruising, edema, infusion site pain.

Other Reactions: glycosuria, muscle spasm, weakness, restlessness, urinary bladder spasm, thrombophlebitis, transient injection site pain following intramuscular injection, fever.

WARNINGS & PRECAUTIONS

Fluid, Electrolyte, and Metabolic Abnormalities: Monitor serum electrolytes, CO2, BUN, creatinine, glucose, and uric acid.

Worsening Renal Function: Monitor for dehydration and azotemia.

Ototoxicity: Avoid higher than recommended doses.

Acute Urinary Retention: Monitor patients with symptoms of urinary retention.

CONTRAINDICATIONS

- Anuria
- Hypersensitivity to furosemide or medical adhesives.
- Hepatic cirrhosis or ascites

Clinical Pharmacology

MECHANISMS OF ACTION

Furosemide primarily inhibits the reabsorption of sodium and chloride in the proximal and distal tubules and in the loop of Henle. The high degree of diuresis is largely due to the unique site of action. The action on the distal tubule is independent of any inhibitory effect on carbonic anhydrase and aldosterone.

Dose & Administration

ADULTS

The single-use, on-body infusor is pre-programed to deliver 30 mg of Furoscix® over the first hour then 12.5 mg per hour for the subsequent 4 hours.

PEDIATRICS

Safety and efficacy for pediatric use have not been established.

GERIATRICS

Controlled clinical studies did not include sufficient numbers of subjects to determine whether subjects aged 65 and over respond differently from younger subjects.

RENAL IMPAIRMENT

N/A

HEPATIC IMPAIRMENT

N/A

Product Availability

DOSAGE FORM(S) & STRENGTH(S)

Injection: 80 mg per 10 mL in a single-dose prefilled cartridge co-packaged with a single-use on-body infusor.