Furoscix (furosemide) Prior Authorization with Quantity Limit Program Summary

This program applies to Medicaid.

The BCBS MN Step Therapy Supplement also applies to this program for Medicaid.

POLICY REVIEW CYCLE

Effective Date
11/1/2023

Date of Origin
7/1/2023

FDA APPROVED INDICATIONS AND DOSAGE

Agent(s)	FDA Indication(s)	Notes	Ref#
Furoscix® (furosemide) Subcutaneous cartridge kit	Treatment of congestion due to fluid overload in adults with NYHA Class II/III chronic heart failure		1

See package insert for FDA prescribing information: https://dailymed.nlm.nih.gov/dailymed/index.cfm

CLINICAL RATIONALE

Management of Heart Failure

The 2022 AHA/ACC/HFSA Guidelines for the Management of Heart Failure (HF) recommends the following on diuretic and decongestion strategies in patient with HF (Strong evidence):(8)

- In patients with HF who have fluid retention, diuretics are recommended to relieve congestion, improve symptoms, and prevent worsening HF
- For patients with HF and congestive symptoms, addition of a thiazide (eg, metolazone) to treatment with a loop diuretic should be reserved for patients who do not respond to moderate or high-dose loop diuretics to minimize electrolyte abnormalities

Commonly Used Oral Loop Diuretics in Treatment of Congestion for Chronic HF include the following:(8)

Loop Diuretic	Duration of Action	Starting Dose	Maximum Dosage
Bumetanide	4-6 hours	0.5–1.0 mg once or twice	10mg
Furosemide	6-8 hours	20–40 mg once or twice	600 mg
Torsemide	12-16 hours	10–20 mg once	200mg

Effective diuretic action in HF requires four discrete steps: 1) ingestion and gastrointestinal absorption (if given orally), 2) delivery to the kidney, 3) secretion into the tubule lumen; and 4) binding to the transport protein.(5) Controlled trials with diuretics showed their effects to increase urinary sodium excretion, decrease physical signs of fluid retention, and improve symptoms, quality of life, and exercise tolerance. Recent data from the nonrandomized OPTIMIZE-HF (Organized Program

	to Initiate Lifesaving Treatment in Hospitalized Patients with Heart Failure) registry revealed reduced 30-day all-cause mortality and hospitalization for HF with diuretic use compared with no diuretic use after hospital discharge for HF. The most commonly used loop diuretic for the treatment of HF is furosemide, but some patients respond more favorably to other agents in this category (eg, bumetanide, torsemide), potentially because of their increased oral bioavailability.(8) Parenteral loop diuretics form the cornerstone of treatment of acute decompensated HF when patients respond insufficiently to oral diuretics alone. HF syndrome is characterized by unpredictable periods of decompensation, which require escalation of oral diuretic doses and/or frequency of dosing. When such oral treatment adjustment fails, IV diuretics are usually prescribed. Furthermore, many patients appear to temporarily have a reduced response to oral medication due to impaired absorption because of fluid overload and other factors affecting gastric and intestinal absorptive functions.(6) For patients on long-term loop diuretic agents, it is suggested that patients hospitalized with HF and congestion initially start loop diuretic dosage at 2.5 times their outpatient dose on a mg per mg basis. For example, for patients taking 40 mg of oral furosemide twice daily as an outpatient, initial intravenous (IV) dosing would be 100 mg of furosemide IV twice daily. For patients not receiving long-term loop diuretic agents, 40-80 mg IV BID of furosemide or the equivalent is a reasonable, empiric, starting dose. Due to post-dosing sodium retention, IV loop-diuretic agents should usually be given at least twice daily.(5) The average bioavailability after oral administration of furosemide is highly variable and has been reported to range between 49% and 72%, while individual differences range from below 20% to over 90%. Parenteral furosemide therapy not only reduces hypervolemia, but in many patients, it also restores oral bioavailability, allowing them to transition more readily back to oral maintenance therapy.(6) Parenteral therapy routinely requires emergency room or inpatient care. A novel buffered furosemide formulation (Furoscix) with neutral pH was developed to offer diuresis for outpatient use, including self-administration at home. Subcutaneous infusion using a biphasic delivery profile resulted in complete bioavailability (99.65%) and equivalent diuresis when compared with intravenous administration. Subcutaneous administration of buffered furosemide was well tolerated with no evidence of any drug-induced skin reactions. Subcutaneous infusion of buffered furosemide in the outpatient setting or home may help to reduce the burden of heart failure.(6)
Efficacy	Furoscix is a proprietary furosemide solution formulated to a neutral pH, designed to allow for subcutaneous infusion via a wearable, pre-programmed on-body infusor, for outpatient self-administration. It was developed for the treatment of congestion due to fluid overload in adult patients with New York Heart Association (NYHA) Class II and Class III chronic heart failure who display reduced responsiveness to oral diuretics and who do not require hospitalization.(4) The PK/PD Pivotal (Crossover Study to Compare the Pharmacokinetics and Bioavailability of a Novel Furosemide Regimen Administered Subcutaneously vs. the Same Dose Administered Intravenously in Subjects With Chronic Heart Failure; NCT02329834) study compared the pharmacokinetics and bioavailability of an 80-mg buffered furosemide solution administered via the SC route with an equivalent 80-mg dose of IV furosemide in a similar subject population. The main findings of this study were: 1) typical therapeutic levels of furosemide were reached within 30 min of SC administration and maintained for more than 5 h; 2) absolute bioavailability of SC furosemide was complete at 99.65%; 3) SC furosemide was as effective as IV furosemide in achieving diuresis; and 4) SC furosemide was well tolerated, with minimal erythema and edema at the site of injection. These results suggest that SC furosemide administration may offer a "hospital-strength" diuretic option for patients with HF who require a shift of their oral diuretic treatment, when hospitalization is not strictly warranted. These results also suggest that the reformulation combined with the slow infusion rate has resulted in a product

	that is free from the stinging and discomfort that had been reported with the administration of conventional furosemide injection.(6) The AT HOME-HF Pilot study (NCT04593823), a Phase 2 multicenter, randomized study that compared Furoscix 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. Results indicated a 37% reduction in heart failure hospitalizations relative to 'treatment as usual' and improvement in congestion signs and symptoms.(11) The FREEDOM-HF was a multicenter, prospective adaptive clinical that included a prospective treatment arm (i.e., Furoscix administered via the Furoscix Infusor) administered outside the hospital that was compared to a propensity-matched historical control arm of patients admitted to the hospital for less than or equal to 72 hours (i.e., Treatment As Usual (TAU)) that was derived from administrative claims data. Eligible patients for the Furoscix arm had NYHA Class II or III heart failure and were exhibiting signs of volume expansion defined as: jugular venous distention, pitting edema (greater than or equal to 1+), abdominal distension, pulmonary congestion on chest x-ray, or pulmonary rales.(4) Results of the FREEDOM-HF study showed positive results demonstrating the average 30-day heart failure related costs were reduced in the Furoscix arm compared to historically matched comparators ($p<0.0001$). Comparators were hospitalized for less than or equal to 72 hours and were selected from a claims database matched to seven variables associated with HF-related hospitalization and severity. Analyses of additional secondary endpoints have been conducted that provide additional insights into the clinical effectiveness of Furoscix. Patients who received Furoscix had a median reduction of heart failure peptide biomarkers from study entry (day 0) to first visit (day 2 to 4), and to last visit (day 30), of 42.3% and 28%, respectively (p less than or equal to 0.01). Patients who received Furoscix had a 12.8-point improvement in the Kansas City Cardiomyopathy Questionnaire (KCCQ-12) Summary Score 30 days after study entry.(9, 10)
Safety	Furoscix is contraindicated in patients with: • anuria • a history of hypersensitivity to furosemide or medical adhesives • hepatic cirrhosis or ascites

REFERENCES

Number	Reference
1	Furoscix prescribing information. scPharmaceuticals, Inc. October 2022.
2	2013 ACCF/AHA Guideline for the Management of Heart Failure. Available at http://circ.ahajournals.org/.
3	2017 ACC/AHA/HFSA Focused Update on New Pharmacological Therapy for Heart Failure: An Update of the 2013 ACCF/AHA Guideline for the Management of Heart Failure. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. https://www.ahajournals.org/doi/pdf/10.1161/CIR.0000000000000509
4	Furoscix Real-World Evaluation for Decreasing Hospital Admissions in Heart Failure (FREEDOM-HF). Available at https://beta.clinicaltrials.gov/study/NCT03458325

Number	Reference
5	Felker GM, Ellison DH, Mullens W, Cox ZL, Testani JM. Diuretic Therapy for Patients With Heart Failure: JACC State-of-the-Art Review. J Am Coll Cardiol 2020;75:1178-1195.
6	Sica DA, Muntendam P, Myers RL, Ter Maaten JM, Sale ME, de Boer RA, Pitt B. Subcutaneous Furosemide in Heart Failure: Pharmacokinetic Characteristics of a Newly Buffered Solution. JACC Basic Transl Sci. 2018 Feb 7;3(1):25-34. doi: 10.1016/j.jacbts.2017.10.001. PMID: 30062191; PMCID: PMC6059009.
7	Daniel Bensimhon, MD, Tamas Alexy, MD, Kathleen L. Deering, PharmD. Effect of Subcutaneous Furosemide (Furoscix) On Natriuretic Peptides, Quality of Life and Patient/Caregiver Satisfaction in Heart Failure Patients: Secondary Outcomes of the Freedom-HF Trial. RESEARCH OR2| VOLUME 55, P171-172, SEPTEMBER 2022. DOI:https://doi.org/10.1016/j.hrtlng.2022.06.006
8	Heidenreich, Paul A. Heidenreich, MD, MS, FACC, FAHA, FHFSA, Chair, Bozkurt, Biykem Bozkurt, MD, PhD, FACC, FAHA, FHFSA, Vice Chair, et.al, 2022 AHA/ACC/HFSA Guideline for the Management of Heart Failure: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. 2022;145:e895–e1032. Available at: https://doi.org/10.1161/CIR.0000000000001063Circulation.
9	scPharmaceuticals Inc. Presents Late-breaking FREEDOM-HF Study Data at the Heart Failure Society of America Annual Scientific Meeting 2021. Available at: https://scpharmaceuticalsinc.gcs-web.com/news-releases/news-release-details/scpharmaceuticals-inc-presents-late-breaking-freedom-hf-study.
10	Effect of Subcutaneous Furosemide (Furoscix) on Natriuretic Peptides, Quality of Life and Patient/Caregiver Satisfaction in Heart Failure Patients: Secondary Outcomes of the FREEDOM-HF Trial. Presented at The American Association of Heart Failure Nurses 18thAnnual Meeting in Orlando, FL on June 18, 2022. Available at: http://ir.scpharma.com/static-files/0fdebb90-5032-4f86-afc1-a8279df9c74e
11	Avoiding Treatment in the Hospital With Furoscix for the Management of Congestion in Heart Failure - A Pilot Study (AT HOME-HF). Available at https://clinicaltrials.gov/ct2/show/NCT04593823

POLICY AGENT SUMMARY PRIOR AUTHORIZATION

Target Brand Agent(s)	Target Generic Agent(s)	Strength	Targeted MSC	Available MSC	Final Age Limit	Preferred Status
Furoscix	furosemide subcutaneous cartridge kit	80 MG/10ML	M ; N ; O ; Y	N		

POLICY AGENT SUMMARY QUANTITY LIMIT

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	QL Amount	Dose Form	Day Supply	Duration	Addtl QL Info	Allowed Exceptions	Targeted NDCs When Exclusions Exist
Furoscix	Furosemide Subcutaneous Cartridge Kit	80 MG/10ML	8	Kits	180	DAYS			

CLIENT SUMMARY – PRIOR AUTHORIZATION

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Furoscix	furosemide subcutaneous cartridge kit	80 MG/10ML	Medicaid

CLIENT SUMMARY – QUANTITY LIMITS

Target Brand Agent Name(s)	Target Generic Agent Name(s)	Strength	Client Formulary
Furoscix	Furosemide Subcutaneous Cartridge Kit	80 MG/10ML	Medicaid

PRIOR AUTHORIZATION CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
PA	**Evaluation** **Target Agent(s)** will be approved when ALL of the following are met: 1. The patient has a diagnosis of New York Heart Association (NYHA) Class II or Class III chronic heart failure with congestion due to fluid overload **AND** 2. The patient has ONE of the following: A. An estimated creatinine clearance of >30 mL/min **OR** B. An estimated glomerular filtration rate of >20 mL/min/1.73m^2 **AND** 3. The requested agent will NOT be used in emergency situations **AND** 4. BOTH of the following: A. ONE of the following: 1. The patient is currently treated with a loop diuretic (e.g., bumetanide, furosemide, torsemide) equivalent to a total daily oral furosemide dose of at least 40-160 mg for 4 weeks **OR** 2. The patient has an intolerance or hypersensitivity to another loop diuretic (e.g., bumetanide, furosemide, torsemide) equivalent to a total daily oral furosemide dose of at least 40-160 mg **OR** 3. The patient has an FDA labeled contraindication to ALL other loop diuretics (e.g., bumetanide, furosemide, and torsemide) equivalent to a total daily oral furosemide dose of at least 40-160 mg **OR** 4. The patient is currently being treated with the requested agent as indicated by ALL of the following: A. A statement by the prescriber that the patient is currently taking the requested agent **AND** B. A statement by the prescriber that the patient is currently receiving a positive therapeutic outcome on requested agent **AND** C. The prescriber states that a change in therapy is expected to be ineffective or cause harm **OR** 5. The prescriber has provided documentation that ALL other loop diuretics (e.g., bumetanide, furosemide, and torsemide) equivalent to a total daily oral furosemide dose of at least 40-160 mg cannot be used due to a documented medical condition or comorbid condition that is likely to cause an adverse reaction, decrease ability of the patient to achieve or maintain reasonable functional ability in performing daily activities or cause physical or mental harm **AND** B. The patient will NOT be using the requested agent in combination with another loop diuretic agent and will be transitioned back to oral diuretic maintenance therapy after discontinuation of requested agent **AND** 5. If the patient has an FDA approved indication, then ONE of the following: A. The patient's age is within FDA labeling for the requested indication for the requested agent **OR** B. The prescriber has provided information in support of using the requested agent for the patient's age for the requested indication **AND** 6. The prescriber is a specialist in the area of the patient's diagnosis (e.g., cardiologist) or the prescriber has consulted with a specialist in the area of the patient's diagnosis **AND** 7. The patient does NOT have any FDA labeled contraindications to the requested agent **Length of Approval:** 12 months NOTE: If Quantity Limit applies, please refer to Quantity Limit Criteria.

QUANTITY LIMIT CLINICAL CRITERIA FOR APPROVAL

Module	Clinical Criteria for Approval
QL	**Quantity Limit for the Target Agent(s)** will be approved when ONE of the following is met: 1. The requested quantity (dose) does NOT exceed the program quantity limit **OR** 2. BOTH of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) does NOT exceed the maximum FDA labeled dose for the requested indication **OR** 3. ALL of the following: A. The requested quantity (dose) is greater than the program quantity limit **AND** B. The requested quantity (dose) is greater than the maximum FDA labeled dose for the requested indication **AND** C. The prescriber has provided information in support of therapy with a higher dose for the requested indication **Length of Approval**: 12 months