

Loop Diuretic Use in Heart Failure

The chart below provides practical information on the use of loop diuretics in heart failure, presented in a “frequently asked questions” format. For information on loop diuretics use for other indications, and for other diuretics’ dosing, kinetics, cost, and place in therapy, see our chart, *Comparison of Commonly Used Diuretics*. For information on diuretic use in acute heart failure, see our chart, *Acute Heart Failure: FAQs*.

Abbreviations: ACEI = angiotensin-converting enzyme inhibitor; ARB = angiotensin receptor blocker; NYHA = New York Heart Association

Clinical Question	Pertinent Information or Resources
What is the role of loop diuretics in the treatment of heart failure?	<ul style="list-style-type: none"> • Loop diuretics are recommended for all volume overloaded patients with NYHA class II to IV heart failure to improve symptoms, exercise tolerance, and efficacy of other heart failure medications (e.g., beta-blockers).² <ul style="list-style-type: none"> • A thiazide could be used instead of a loop for patients with mild fluid retention and hypertension, for blood pressure control.² • Unlike potassium-sparing diuretics (e.g., spironolactone, eplerenone), loop diuretics have not been shown to reduce the risk of death.^{2,3}
How do loop diuretics compare ?	<ul style="list-style-type: none"> • Bioavailability: bumetanide and torsemide have better bioavailability (i.e., less erratic absorption) than furosemide, so some patients will respond better to them than to furosemide.² <ul style="list-style-type: none"> • Furosemide bioavailability is about 50% (range 10% to 90%).^{4,8} • Torsemide and bumetanide bioavailability is >80% to 90%. • Cost: furosemide is the least expensive loop diuretic • Efficacy: torsemide benefits over furosemide in regard to heart failure hospitalization and improvement in NYHA functional class have not been proven at equivalent doses [Evidence level A-2].^{6,7} There is not much data with bumetanide in heart failure.
What is the role of ethacrynic acid?	<ul style="list-style-type: none"> • Ethacrynic acid is rarely used because: <ul style="list-style-type: none"> • data on ethacrynic acid in heart failure is lacking. • it may be more ototoxic than other loops.¹³ • it is the most expensive loop diuretic (U.S.: ~\$9.98/each 25 mg tablet;^a Canada: \$1.04/each 25 mg tablet^a). • Ethacrynic acid does not contain a sulfa group and is a possible alternative in sulfonamide-allergic patients. For more information on use of loop diuretics in these patients, see our chart, <i>Sulfa Drugs and the Sulfa-Allergic Patient</i>.

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Clinical Question	Pertinent Information or Resources
<p>How do you dose loop diuretics in the treatment of heart failure?</p>	<p>--For information on diuretic use in acute heart failure, see our chart, <i>Acute Heart Failure: FAQs</i>--</p> <p>General concepts:</p> <ul style="list-style-type: none"> • High sodium intake and NSAID use reduces diuretic efficacy.² • In heart failure with preserved ejection fraction, diuretics must be dosed cautiously because preload reduction can cause reduced cardiac output with hypotension and renal impairment.⁹ • Start with a low dose, and increase to achieve target weight (e.g., a 0.5 to 1 kg weight loss daily to goal) and symptoms.^{2,10} Titrate to eliminate clinical signs/symptoms of fluid overload without causing hypotension or renal insufficiency, or limiting the up-titration of disease-modifying agents (e.g., ACEIs, ARBs, potassium-sparing diuretics).^{1,2} • Not all patients will need a daily scheduled dose.² Consider transitioning to as-needed use once patients are stable and receiving optimized guideline-directed medical therapy (i.e., beta-blockers and inhibitors of the renin-angiotensin system), without signs of fluid retention [Evidence level B-1].¹ <ul style="list-style-type: none"> • Patients can self-titrate dose based on daily weights.² Customize our patient education handout, <i>Heart Failure Meds and More</i>, with your patient’s diuretic dose and instructions. • Giving furosemide or bumetanide twice daily might improve efficacy.² But first, try increasing the once-daily dose to the maximum single dose (or where there’s no further diuresis); diuresis depends on how high the loop concentration gets in the urine.¹¹ • If furosemide or bumetanide is given twice daily, give the second dose in the afternoon to minimize nocturia.² • Check renal function and electrolytes at baseline and one to two weeks after initiation or dosage increase.¹⁰ <p>Dosing of loops for chronic heart failure:</p> <ul style="list-style-type: none"> • Furosemide: initial 20 to 40 mg once or twice daily; max total daily dose 240 mg (600 mg in renal impairment).^{2,10,11} • Bumetanide: initial 0.5 to 1 mg once or twice daily; max total daily dose 10 mg.^{2,11} • Torsemide: initial 10 to 20 mg once daily; max total daily dose 200 mg.^{2,11}
<p>What are some considerations when switching loop diuretics?</p> <p><i>Continued...</i></p>	<p>General considerations</p> <ul style="list-style-type: none"> • Furosemide is the most commonly used loop diuretic.² A switch to bumetanide or torsemide could be considered for patients: <ul style="list-style-type: none"> • who require hospitalization for acute heart failure despite furosemide use.⁸ • who are not achieving good symptomatic control despite optimization of guideline-directed medical therapy and furosemide.⁷ • who may have impaired furosemide absorption due to splanchnic congestion.⁸

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Clinical Question	Pertinent Information or Resources
<p>Considerations when switching loop diuretics, continued</p>	<ul style="list-style-type: none"> • Consider switching to torsemide rather than bumetanide; torsemide has a longer duration of action and more evidence in heart failure.^{2,6,7} <p>Dosing considerations:</p> <ul style="list-style-type: none"> • Bumetanide 0.5 to 1 mg orally = furosemide 40 mg orally⁵ • Torsemide 10 to 20 mg orally = furosemide 40 mg orally⁵ • Oral furosemide bioavailability is only about 50%.⁴ • Ethacrynic acid 50 mg orally ~ furosemide 40 mg orally¹⁴
<p>Can other diuretics be combined with loops to improve response?</p>	<ul style="list-style-type: none"> • Switching from furosemide to bumetanide or torsemide may be preferable to adding a thiazide to improve response, as combining diuretics increases the risk of electrolyte disturbances.^{2,8} • Consider adding spironolactone or eplerenone before trying a thiazide; spironolactone and eplerenone provide some diuresis, offset potassium loss, and improve outcomes, particularly in heart failure with reduced ejection fraction.^{2,11} • If a thiazide is added, it is not necessary to time the thiazide so that it is given prior to the loop.¹² (For example, there is no proof that giving the thiazide 30 minutes before the loop provides better diuresis.) • Contrary to popular belief, thiazides can be effective if CrCl is <30 mL/min.⁸ Metolazone may be most effective.¹³

a. U.S. cost is wholesale average cost. U.S. medication pricing by Elsevier, accessed January 2020. Canadian cost is wholesale.

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Levels of Evidence

In accordance with our goal of providing Evidence-Based information, we are citing the **LEVEL OF EVIDENCE** for the clinical recommendations we publish.

Level	Definition	Study Quality
A	Good-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. High-quality RCT 2. SR/Meta-analysis of RCTs with consistent findings 3. All-or-none study
B	Inconsistent or limited-quality patient-oriented evidence.*	<ol style="list-style-type: none"> 1. Lower-quality RCT 2. SR/Meta-analysis with low-quality clinical trials or of studies with inconsistent findings 3. Cohort study 4. Case control study
C	Consensus; usual practice; expert opinion; disease-oriented evidence (e.g., physiologic or surrogate endpoints); case series for studies of diagnosis, treatment, prevention, or screening.	

***Outcomes that matter to patients** (e.g., morbidity, mortality, symptom improvement, quality of life).

RCT = randomized controlled trial; **SR** = systematic review

[Adapted from Ebell MH, Siwek J, Weiss BD, et al. Strength of Recommendation Taxonomy (SORT): a patient-centered approach to grading evidence in the medical literature. *Am Fam Physician* 2004;69:548-56. <http://www.aafp.org/afp/2004/0201/p548.pdf>]

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