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BUMETANIDE (NASAL SPRAY) DRUG

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ABSTRACT OF BUMETANIDE

Bumetanide nasal spray is a novel intranasal formulation designed to offer a rapid, effective, and convenient alternative to traditional oral and intravenous (IV) bumetanide for the treatment of edema associated with heart failure, liver disease, and kidney disease, including nephrotic syndrome. This nasal spray bypasses gastrointestinal absorption, which can be problematic in patients with fluid overload who often develop diuretic resistance to oral medications. Clinical trials have demonstrated that the nasal spray provides bioequivalence to oral and IV forms, with similar pharmacokinetics, diuretic effects, and urine output, but with faster absorption and more consistent bioavailability. The nasal spray is well-tolerated, with minimal nasal irritation, and offers outpatient use benefits by enabling earlier intervention and potentially reducing hospital admissions. This new mode of delivery can improve patient adherence, provide a user- friendly self-administration option, and bridge treatment gaps in fluid overload episodes for patients at home or outpatient settings. It represents a meaningful advancement in edema management by combining efficacy with convenience and safety, thus improving quality of life and reducing healthcare costs related to hospitalization for edema management.

KEYWORDS: The nasal spray is well-tolerated, with minimal nasal irritation, and offers outpatient use benefits by enabling earlier intervention and potentially reducing hospital admissions.

The main keywords for bumetanide nasal spray drug are as follows.

Bumetanide, Loop diuretic, Nasal spray, Nasal administration, Edima, Heart failure, Congestive heart failure, Hepatic disease, Renal disease, Outpatient therapy, Diuretic resistance, Fluid overload, Decongestion, Sodium excretion, Bioavailability, Pharmacokinetics, Urine output, non-oral diuretic, Self-administration, FDA approved.

INTRODUCTION

Bumetanide is a potent loop diuretic used to manage edema associated with heart failure, renal, and liver diseases. It acts by inhibiting the sodium-potassium-chloride symporter in the loop of Henle, increasing urine output and reducing fluid accumulation. Traditionally administered orally or intravenously, its efficacy can be limited by variable gastrointestinal absorption, especially in heart failure patients with gut congestion. To overcome these challenges, **Bumetanide Nasal Spray (BNS)** has been developed as a novel intranasal formulation offering **rapid systemic absorption**, **high bioavailability**, and **greater absorption consistency**. Clinical studies, including those presented at AHA 2024, demonstrated that BNS (RSQ-777) provides **bioequivalent diuretic effects** to oral and IV forms, with **33% faster absorption** and **27% variability** compared to over 40% with oral administration.

This makes it suitable for patients who need quick diuretic action or cannot tolerate oral medications. Heart failure remains a significant global health concern, affecting over **6.5 million Americans** and costing approximately **$30.7 billion annually**. Fluid overload is a leading cause of hospitalization, with two-thirds of admissions due to the need for IV diuretics, costing

around **$17,000 per stay**. By offering a **self-administered outpatient therapy** that bypasses gastrointestinal limitations, Bumetanide Nasal Spray could reduce hospitalizations and improve treatment accessibility.

Development and Pharmacokinetics of Bumetanide Nasal Spray

Corstasis Therapeutics developed **bumetanide intranasal spray (RSQ-777)** to overcome limitations of oral diuretics, providing a **short-term outpatient treatment** for edema related to congestive heart failure, hepatic disease, and renal disease, including nephrotic syndrome.

Pharmacokinetic findings show that the nasal spray achieves **bioequivalence** to oral and intravenous forms, with a **33% faster absorption** than oral administration and an earlier onset of sodium excretion. Absorption variability is **27% for nasal and IV forms** versus over 40% for oral, indicating more **predictable and stable dosing**.

After 2 mg intranasal administration, **plasma concentrations peak within 1.02–1.50 hours**, comparable to 2 mg oral or 1 mg IV dosing, with steady levels between 1–2 hours post-dose.

Safety and Tolerability

Intranasal bumetanide is **generally safe and well-tolerated**, with no significant nasal irritation observed. Side effects are consistent with oral and IV formulations, but treatment-emergent adverse events are fewer than with oral dosing. Dose increases from 0.5 to 2 mg are **proportional**, and urine output is similar across nasal, oral, and IV routes, confirming **therapeutic equivalence**.

Classification

- **Drug Class:** Loop diuretic.
- **Primary Use:** Rapid reduction of fluid overload, including edema from heart failure, liver, or kidney disease.
- **Advantages of Nasal Spray:** Outpatient administration, bypasses gastrointestinal absorption, and enables rapid self-administration.

Mechanism of Action (MOA)

- Inhibits **sodium and chloride reabsorption** in the ascending loop of Henle.
- Promotes **excretion of sodium, chloride, and water**, reducing blood volume and relieving edema.
- Nasal administration provides **faster onset** due to rapid mucosal absorption, with urine output efficacy comparable to oral and IV forms.
- of edema in heart, liver, or kidney disease.

Indications

- Short-term treatment of **edema (fluid retention)** in adults with:
- **Congestive heart failure (CHF)**
- **Liver disease**
- **Kidney disease**, including nephrotic syndrome

Uses and Advantages

- Provides an alternative for patients who have difficulty with **oral or IV diuretics**.
- Rapid, reliable diuretic effect with **self-administration** in outpatient or home settings.
- Bypasses gastrointestinal absorption issues and **diuretic resistance**.
- Single-use, once-daily nasal spray offering convenience and faster onset than oral formulations.
- Similar urine output and efficacy compared to oral and IV forms.

Common Side Effects: Dizziness, headache, nausea, muscle cramps, dehydration, dry mouth, increased urination.

Rare/Serious Side Effects: Severe skin reactions (Stevens-Johnson syndrome), low blood pressure, kidney impairment, hearing loss (ototoxicity), thrombocytopenia, severe allergic reactions (anaphylaxis), electrolyte imbalances.

Allergic Reactions: Rash, swelling of lips/face/throat, trouble breathing, hives, or severe skin reactions. Immediate medical attention is required.

- Nasal administration generally well-tolerated with **no significant nasal irritation** reported.

Clinical Notes

- FDA-approved brand: **Enbumyst**.
- Effective for **short-term outpatient management** of edema.
- Absorption is faster and more consistent than oral dosing, offering a **reliable alternative** for patients with variable oral absorption.
- Monitoring of **fluid and electrolyte balance** is essential, especially in chronic use or high-risk patients.

Contraindications

- **Anuria** (absence of urine)
- **Hepatic coma**
- **Hypersensitivity** to bumetanide or formulation components
- **Severe electrolyte depletion**
- Significant **nasal mucosal or structural abnormalities** (e.g., acute rhinitis, congestion)
- **Pregnancy and breastfeeding**: Use with caution due to unknown effects

Precautions

- Monitor **serum electrolytes** (sodium, potassium), **CO_2**, **BUN**, **creatinine**, **glucose**, and uric acid

- Monitor for **worsening renal function**, dehydration, and azotemia
- Avoid exceeding recommended doses to prevent **ototoxicity**
- Avoid use in patients with nasal structural/mucosal issues that could affect absorption
- Observe for common adverse effects: **hypovolemia, dizziness, headache, muscle cramps, hypotension, nausea, encephalopathy** (especially in liver disease)
- Use caution in patients with **diabetes, diarrhea**, or other fluid balance disorders.
- Inform healthcare providers about concurrent use of other **nasal sprays or interacting medications**

Drug Interactions

- **Lithium**: Risk of toxicity due to reduced renal clearance.
- **Probenecid**: Reduces bumetanide's diuretic effect.
- **Indomethacin**: Blunts urine volume and sodium excretion.
- **Aminoglycoside antibiotics** (e.g., gentamicin, amikacin): Increased risk of **ototoxicity.**
- **Nephrotoxic drugs**: Increased kidney damage risk.
- **Antihypertensives**: May potentiate effects, requiring dose adjustment.
- Other interactions: aspirin, digoxin, some anti-inflammatory medications.
- **Alcohol**: Interaction possible but not well-defined.

Clinical Trials and Efficacy

- Multiple phase 1 and comparative trials (e.g., RSQ-777-02) in healthy adults demonstrated:
- **Bioequivalence** to oral and IV bumetanide.
- **Faster absorption**: Tmax ~1 hour vs. 1.5 hours for oral tablets; IV remains fastest (~30 min).
- **Lower intrasubject absorption variability**: 27% for nasal/IV vs. >40% oral, ensuring more stable dosing.
- **Diuretic effect**: Urine output and sodium excretion comparable across all forms (~140 mmol/2h, ~300 mmol/24h).
- **Safety**: Well-tolerated; minor nasal dryness, fewer adverse events than oral administration.

Practical Advantages

- Rapid and consistent absorption; bypasses gastrointestinal limitations.
- Enables **self-administered outpatient therapy**, potentially reducing hospital admissions.
- Limitations: proper nasal technique required, effectiveness may be reduced by nasal congestion.

Patient Counselling and Usage

- Short-term therapy for edema; self-administered nasal spray.
- Follow instructions for single-use devices; alternate nostrils if multiple sprays needed.
- Avoid abrupt discontinuation; monitor fluid status, blood pressure, weight, and electrolytes.
- Avoid excess alcohol and nighttime dosing to reduce sleep disruption.
- Report all medications to healthcare providers to prevent drug interactions.
- Peak diuretic effect occurs ~1 hour post-dose; efficacy comparable to oral/IV formulations.

Future Development

- Bumetanide nasal spray (Enbumyst) offers a rapid, convenient outpatient alternative to oral and IV diuretics for edema in heart, liver, and kidney disease.

- **Future research aims to**
- Expand patient access and integration into outpatient care.
- Refine formulations to improve mucosal absorption and reduce variability.
- Conduct clinical trials in specific patient populations to optimize dosing and long-term safety.
- Enable self-administered therapy to reduce hospital admissions and improve quality of life.

Safety Profile

- Generally **well-tolerated**, comparable to oral and IV bumetanide.
- **Common adverse effects**: hypovolemia (~4.8%), headache (~3%), occasional nasal dryness.
- **Serious adverse effects**: muscle cramps, hypotension, severe skin reactions, hearing loss, and allergic reactions—similar to oral forms.
- No significant nasal irritation or pain reported in trials.
- Demonstrates consistent and faster absorption with stable diuretic effect.

Advantages

- **Convenient self-administration** for outpatient or home use.
- **Bypasses gastrointestinal absorption** and first-pass metabolism.
- **Rapid and predictable absorption**, with faster onset than oral tablets.
- **Comparable efficacy** to oral and IV forms in inducing diuresis and sodium excretion.
- **Stable and less variable absorption** than oral formulations.
- **Potential to reduce hospitalizations** by providing a rescue or short-term outpatient therapy.

Limitations

- **Effectiveness depends on correct nasal spray technique.**
- **Nasal congestion or mucosal issues** may reduce absorption and therapeutic effect.
- **Limited clinical data** in patients with heart failure, liver, or kidney disease—most studies were in healthy volunteers.
- **Long-term safety and real-world effectiveness**

remain under investigation.

Dosage Forms and Strength

- Available as a **unit-dose nasal spray**, delivering **0.5 mg per 0.1 mL.**
- Recommended dose: **0.5–2 mg once daily**, adjustable based on patient response.
- Multiple sprays may be used to achieve the prescribed dose (1 spray = 0.5 mg; 4 sprays = 2 mg).
- **Single-use devices**; not reusable or primed.
- Intended for **short-term outpatient use**, transitioning to oral diuretics when feasible.

Regulatory Status

- **FDA approved in September 2025** under the brand name **Enbumyst**.
- Indicated for **edema associated with heart failure, liver disease, and kidney disease**.
- Approval supported by pharmacokinetic and pharmacodynamic studies demonstrating **comparable efficacy, faster absorption, and more consistent dosing** versus oral formulations.

Clinical Studies (RSQ-777-02 and others)

- Conducted in **68 healthy adults** comparing **nasal, oral, and IV bumetanide**.

- **Key Findings**
- **Similar urine output and sodium excretion** across all routes.
- Nasal spray **absorbed 33% faster** than oral tablets (Tmax ~1 hr vs. 1.5 hr).
- **Lower absorption variability** (27%) for nasal vs. oral (>40%).
- **Fewer adverse events** with nasal spray (16.2%) compared to oral (23.9%).
- Onset of sodium excretion was fastest with nasal spray, advantageous for rapid relief of fluid overload.
- Studies were **limited to healthy adults aged 18–55**, predominantly male (66%) and mostly White (60%), with other racial and ethnic representation included.
- Patient population studies (heart failure, edema) are **pending** to confirm real-world efficacy.

Clinical Implications

- Nasal spray offers a **rapid, reliable, outpatient alternative** to oral or IV diuretics.
- Particularly useful for **patients with compromised oral absorption or needing fast diuresis**.
- Proper administration technique and nasal health are important for effectiveness.

Primary Clinical Applications

- **Treatment of edema associated with.**
- Congestive heart failure (CHF).
- Hepatic (liver) disease.
- Renal (kidney) disease, including nephrotic syndrome.
- Offers a **novel outpatient option** for diuretic therapy, enabling **self-administration at home**, faster relief, and potentially fewer hospital admissions.
- Particularly beneficial for patients with **gastrointestinal absorption issues or diuretic resistance**.

Clinical Use and Advantages

- **Efficacy:** Comparable urine output and sodium excretion to oral and IV bumetanide.
- **Absorption:** 33% faster than oral tablets; more consistent (27% variability vs. >40% oral).
- **Safety:** Well-tolerated; minimal nasal irritation reported.
- Enables **early intervention** in ambulatory patients, reducing the need for hospitalization.

Additional Notes

- Bumetanide remains effective in **cases resistant to other loop diuretics** like furosemide.
- Nasal spray adds flexibility for **outpatient or inpatient use** alongside oral and IV dosing.

CONCLUSION

Bumetanide is a well-established, versatile diuretic with proven efficacy for classic indications (edema), a favorable safety profile, and ongoing investigation for off-label and repurposed uses, especially in neurology. New delivery routes (such as nasal spray) continue to enhance its clinical utility, expanding therapeutic options and patient convenience in 2025. Bumetanide is a loop diuretic that is primarily used for treating edema associated with heart, liver, and kidney diseases, and it continues to be highly effective, with new nasal-spray formulations gaining FDA approval in 2025 for outpatient therapy. Recent clinical and translational research also supports its repurposing potential for neurological conditions, although the evidence is still emerging and not uniformly positive.

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