



TITLE: Racemic Epinephrine for Acute Respiratory Distress: Review of Role and Guidelines for Use

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CONTEXT AND POLICY ISSUES:

Epinephrine is a drug with both α -adrenergic and β -adrenergic effects.¹ In acute respiratory disease it has had a role for almost 40 years as a liquid used in nebulizer therapy.² Its beneficial effect is thought to be due to vasoconstriction which then leads to decreased upper airway edema and decreased mucous production.^{2,3} The adverse effects associated with the drug in this situation are tachycardia, tremor, increase in blood pressure, and rebound episodes.⁴

Manufactured by Sanofi-Aventis, liquid racemic₁ epinephrine HCl 2.25% (Vaponefrin[®]) is administered via a medication nebulizer at a dose of 0.5 mL diluted with 2 to 4 mL of sterile water or normal saline over 10 to 15 minutes. The manufacturer's clinical indications include the "symptomatic relief of bronchial obstruction due to bronchial spasm and mucous secretions associated with bronchial asthma, hay fever, chronic bronchitis, pulmonary emphysema, and other pulmonary disease associated with bronchospasm."⁵ However, the majority of the literature identified was for the drug's use in the pediatric conditions of bronchiolitis and croup.

Bronchiolitis is the most common lower respiratory tract infection in infants. It is a common cause of attendance at emergency departments (EDs) and admission to hospital, particularly in winter. Reinfections are common. In 70% of cases the cause is the respiratory syncytial virus (RSV).⁶ Up to 3% of children under age one year are hospitalized with bronchiolitis and current treatment includes some mix of epinephrine and β 2-agonist bronchodilators such as salbutamol, corticosteroids, and ribavirin.⁷

¹ A racemic mixture has equal amounts of left- and right-handed forms of a molecule.

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Croup (laryngotracheitis) is also common, affecting 6% to 8% of children under age 5 years. Almost all cases are viral, generally caused by parainfluenza virus types 1 and 3. It occurs most often in boys and in late fall and winter. Most cases are mild with 2% to 4% requiring hospitalization. In addition to corticosteroids (oral, nebulizer, or injection), epinephrine by nebulizer has been one aspect of treatment.⁸

Vaponefrin[®], the only form of racemic epinephrine available in Canada, was voluntarily withdrawn from the market by the manufacturer in January 2007.⁹⁻¹¹ However, some EDs will likely stock the drug until it reaches the end of its shelf life. A policy issue has therefore arisen due to a potential for medical error. Racemic epinephrine 2.25% was distributed in 30 mL multi-dose bottles of clear liquid with a typical dose being 0.5 mL diluted in 2-4 mL of normal saline.⁵ The racemic drug concentration would be 22.5 mg/mL. An alternative drug is L-epinephrine 1:1000 (Adrenaline[®]) that also comes in 30 mL multi-dose bottles of clear liquid but the recommended comparable typical dose is 5 mL without the need for dilution; its drug concentration is only 1 mg/mL.⁹⁻¹¹ This difference may cause a medication error. Thus the evidence for the use of racemic epinephrine requires review.

RESEARCH QUESTIONS:

1. What is the role of racemic epinephrine in the treatment of patients in acute respiratory distress (specifically infants with croup and bronchiolitis)?
2. What are the guidelines for the treatment of pediatric patients with acute croup and bronchiolitis and is racemic epinephrine ever indicated?

METHODS:

HTIS reports are organized so that the higher quality evidence is presented first. Therefore, health technology assessment (HTA) reports, systematic reviews (SRs), and meta-analyses (MAs) are presented first. These are followed by randomized controlled trials (RCTs) and evidence-based guidelines.

Question #1: Role of racemic epinephrine

A limited literature search was conducted on key health technology assessment resources including PubMed, The Cochrane Library (Issue 4, 2008), Ovid Medline, EMBASE and CINAHL, University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, and international health technology agencies. A focused Internet search was conducted. Results include articles published between 2003 and October 2008, limited to English publications. No filters were applied to limit the retrieval by study type. Hand searching of the bibliographies of included references led to identification of relevant pre-2003 research.

Question #2: Guidelines for treatment of bronchiolitis and croup

A limited literature search was conducted on key health technology assessment resources, including PubMed, The Cochrane Library (Issue 4, 2008), University of York Centre for Reviews and Dissemination (CRD) databases, ECRI, EuroScan, international health technology agencies, and a focused Internet search. Results include articles published between 2006 and October 2008, and are limited to English publications only. Filters were applied to limit the retrieval to guidelines.

SUMMARY OF FINDINGS

Question #1: Role of racemic epinephrine

The evidence below is confined to the use of racemic epinephrine in the management of the acute pediatric respiratory conditions bronchiolitis and croup as the bulk of the relevant literature was limited to these indications. Brief mention is also made of its use in the only other clinical indications mentioned in the literature: post-extubation of newborns, asthma, and transient tachypnea of the newborn (TTN).

Bronchiolitis

Systematic Reviews and Meta-analyses

Two relevant SRs were located, a Cochrane Collaboration review specific to use of epinephrine in bronchiolitis¹² and an SR examining drug treatment of bronchiolitis⁷

The Cochrane review was produced by researchers in Canada (Edmonton, Calgary and Montreal) and was last updated in 2003.¹² Its objective was to compare epinephrine to placebo and to other bronchodilators in infants under age 2 years with bronchiolitis. Studies were eligible for review if they (1) were RCTs comparing epinephrine to placebo or other bronchodilators, (2) involved infants under age 2 years with bronchiolitis, and (3) presented at least one quantitative outcome measure.

The literature search ended in May 2003. Included were 14 RCTs, half on inpatients and half on outpatients. Six studies used racemic epinephrine, seven used L-epinephrine, and drug type was not reported in one. The data were not examined according to type of epinephrine. Analysis of epinephrine versus placebo and versus the bronchodilator salbutamol was carried out, as was analysis of inpatient versus outpatient response (Table 1):

Table 1: Findings of Cochrane review of bronchiolitis treatment¹²

| Comparison | Setting | # Studies | Significant outcomes |
|---|------------|-----------|--|
| Epinephrine (racemic or L-epinephrine) versus placebo | Inpatient | 5 | One significant outcome favoured epinephrine, i.e., change in clinical score 60 minutes post-treatment. |
| | Outpatient | 3 | Four significant outcomes favoured epinephrine, i.e., change in clinical score 60 minutes post-treatment, change in oxygen saturation at 30 minutes, respiratory rate at 30 minutes, and subjective improvement. Heart rate at 60 minutes favoured placebo. Subsequent admission rates did not differ significantly. |
| Epinephrine (racemic or L-epinephrine) versus salbutamol | Inpatient | 4 | One significant outcome favoured epinephrine, i.e., respiratory rate at 30 minutes. |
| | Outpatient | 4 | Four significant outcomes favoured epinephrine, i.e., change in oxygen saturation at 60 minutes, respiratory rate at 60 minutes, heart rate at 90 minutes, and "improvement". Pallor at 30 minutes favoured salbutamol. Admission rates did not differ significantly. |

The Cochrane authors concluded that there is some evidence to support the use of epinephrine (versus placebo or salbutamol) among outpatients, although this finding is based on a small number of studies of varying internal validity, but there is insufficient evidence to support its use

among inpatients. They commented on the need to conduct large, multi-centered RCTs as well as the need to develop a validated, reliable scoring system sensitive to important clinical changes in patients with bronchiolitis.

The objective of the second SR, produced by researchers from North Carolina, was to assess the effectiveness of commonly used treatments for bronchiolitis in infants and children.⁷ Studies were eligible for review if they were RCTs assessing various drug treatments (eight types of treatment were mentioned) for children up to age 5, with outcome measures including morbidity, mortality, adverse effects, or harms.

The literature search ended in 2003. Included were 44 RCTs with the drug therapies being epinephrine (n=8 studies), β_2 -agonist bronchodilators (n=13), corticosteroids (n=13), and ribavirin (n=10). The eight epinephrine studies (n=660 patients) were all included in the Cochrane review described in the bullet above. Four studied racemic and four studied L-epinephrine and the results were not assessed by the form of the drug.

These authors noted limitations in the data, commenting on the fact that studies were small and therefore likely underpowered and the outcomes were short-term and generally not clinically meaningful, although two of five studies reporting on admissions/ hospitalization found a benefit in the epinephrine group. The authors stated, "Aside from some transient improvements in clinical scores and related measures, we found little evidence to suggest that epinephrine is an effective treatment for bronchiolitis...the weight of evidence does not support the use of nebulized epinephrine".⁷

Randomized Controlled Trials

Four relevant RCTs have been published since the reviews described above:

A 2005 publication described an RCT of racemic epinephrine versus salbutamol carried out in Canada's Maritime provinces.¹³ Patients were aged 2 years or younger (mean age 6.4 months; n=62) and hospitalized for bronchiolitis. Those receiving epinephrine had less wheezing and greater symptom improvement throughout their stay but there was no significant difference in hospital length of stay, despite a trend favouring the epinephrine group (2.6 versus 3.4 days). Adverse events were not significantly different in the two study arms.

A 3-arm RCT in New Mexico compared use of racemic epinephrine to nebulized albuterol or placebo for outpatient treatment of children aged 2 years or younger (n=65; mean age 7.6 months).¹⁴ In their introduction, the study authors noted the conclusions of both the SRs described above but questioned whether suitable doses of the drugs had been chosen, particularly whether adequate doses of β_2 -agonist bronchodilators had been employed. They therefore adjusted drug dosages, hoping to find a benefit. However, their results showed no difference among the three groups with respect to all outcome measures employed: clinical scores, oxygen saturation levels, need for hospitalization, or need for home oxygen therapy. The authors suggested that their small sample size and the need to enroll patients over five winters may have hidden any beneficial effects of the drugs but admitted that neither racemic epinephrine nor nebulized albuterol may be indicated for children who are ill with bronchiolitis.

The most recent RCT was much larger, enrolling 703 children.¹⁵ Its objective was to compare the effect of nebulized racemic epinephrine to nebulized racemic albuterol with the primary outcome measure being successful discharge from the ED. Conducted at two sites, the study included children up to age 18 months who had bronchiolitis severe enough to warrant

treatment but not intubation. Crude results showed no difference between study arms although when the results were adjusted for severity of illness, the patients who received albuterol had significantly better outcomes than did the epinephrine patients, i.e., they were more likely to be discharged home than admitted to hospital (adjusted risk ratio 1.18; 95% confidence interval 1.02 to 1.36).

A recently published comparative RCT examined the responses to three different nebulized bronchodilators (racemic epinephrine, levalbuterol, and racemic albuterol) and saline as a placebo.¹⁶ The drug was administered in a blinded fashion every 6 hours to 22 infants (mean age 6 months) in respiratory failure with RSV bronchiolitis. It took more than 5 years to recruit the study population. The authors had postulated that racemic epinephrine would be more effective than the alternatives with respect to bronchodilation but results showed an equal benefit from all three active therapies. However, the authors noted that overall the response to therapy was small and probably clinically insignificant whereas adverse effects such as tachycardia were observed and could be clinically significant. They concluded that use of the drugs is of questionable value and difficult to justify.

Limitations

A major limitation of the evidence is the lack of distinction between racemic and L-epinephrine in the two SRs, thus conclusions specific to racemic epinephrine from these SRs are not possible. With respect to the RCTs, the majority of the studies were very small and in some cases patients had to be enrolled over a number of years to capture adequate patient numbers.

Croup

Systematic Reviews and Meta-analyses

There are no published SRs reporting specifically on use of epinephrine for croup, although a Cochrane Collaboration protocol² is available and was last updated in May 2007.² The researchers are from the Cochrane Acute Respiratory Infections Group based in Alberta. The objective of the SR is to assess the efficacy and safety of nebulized epinephrine when used for children with croup in an emergency department or hospital. A secondary objective is to examine the effectiveness and adverse effects of racemic versus L-epinephrine. Only RCTs and quasi-RCTs will be available for inclusion once this review is conducted.

In addition, a Cochrane Collaboration review on glucocorticoids in croup has been published by the same Alberta-based Cochrane Acute Respiratory Infections Group.¹⁷ Among the 31 RCTs included in their review were three trials of inhaled steroids versus epinephrine (n=205 patients). Results among these trials did not show significantly different benefits accruing from steroid (dexamethasone or budesonide) versus epinephrine use at 6, 12 and 24 hours. Only one of the included RCTs tracked return visits and/or readmissions and none were reported.

² A Cochrane protocol sets out the intent to undertake a review and contains the following sections: background, objectives, criteria for included studies, search strategy, and proposed methods.

Randomized Controlled Trials

Four RCTs examined the use of racemic epinephrine for croup versus either placebo or no treatment. Unfortunately, none of these are recent: three are from the 1970's¹⁸⁻²⁰ and one is from 1994.¹ In addition, an RCT published in 1992 compared racemic and L-epinephrine²¹ and a 2001 trial compared racemic epinephrine to an inhaled helium-oxygen mixture (Heliox).²²

The earliest placebo-controlled double blind RCT, published in 1973, was performed in response to several earlier positive case series of the therapy.¹⁸ The researchers performed a 2-year retrospective review of their experience with 234 children admitted with croup-type illnesses, a prospective uncontrolled study of the therapy (n=35), and a small RCT (n=20). For the RCT, 20 children (aged 5 to 60 months) with moderately severe croup were randomized to nebulized racemic epinephrine or saline. Of the 10 children receiving active treatment, five (50%) had a clinically significant response. However, the same proportion in the control group showed a clinically significant response. The researchers concluded that the benefit to nebulization treatment was perhaps administration of humidified air rather than the drug. Their retrospective review showed no benefit from the drug with respect to length of hospitalization nor need for tracheotomy.

Two very small placebo-controlled RCTs from the 1970's studied the use of nebulized racemic epinephrine delivered by an intermittent positive pressure breathing device (IPPB). The first, published in 1975 by researchers from Montreal, included 14 children randomized to receive either racemic epinephrine in a weight-adjusted dose via IPPB or saline as a placebo.¹⁹ Results showed a benefit at 20 minutes but no difference between groups at 24 to 36 hours after admission, suggesting no effect on the natural course of the illness. The researchers commented that the lack of lasting effect suggested the drug was useful acutely but a patient treated in the ED should not be promptly discharged, due to risk of relapse of acute symptoms. The second RCT, published in 1978 by researchers in Colorado, enrolled 20 children with moderate-to-severe croup and found that those receiving epinephrine had significantly improved croup scores at 10 and 30 minutes but the benefit was no longer seen at 2 hours.²⁰ The authors concluded that racemic epinephrine by nebulizer is effective for the acute signs of croup.

The most recent placebo-controlled RCT is almost 15 years old, having been published by Swedish researchers in 1994.¹ Of interest were the effects of racemic epinephrine for acute management of croup and also evaluation of a clinical scoring system for assessing treatment effects. Enrolled were 54 children (aged 4 months to 11 years) with mild-to-moderate croup. Those in the active treatment (racemic epinephrine) arm benefited with respect to some outcomes (total clinical score, inspiratory stridor, chest retractions, and air entry) although not all (oxygen saturation and clinical scores pre- and post-treatment).

In a 1992 trial, inhaled racemic epinephrine and L-epinephrine were compared by researchers in Washington, D.C.²¹ The double-blind RCT enrolled 31 children (aged 6 to 72 months) with moderate-to-severe croup. There was no control group. Children in both treatment arms improved with respect to all outcomes (croup score, heart rate, blood pressure, respiratory rate at 5, 15, 30, 60, 90, and 120 minutes post-treatment). The authors noted that racemic epinephrine was in common use for acute treatment of croup but L-epinephrine had not been employed despite the fact that it is less expensive and more readily available worldwide as it is stocked as a resuscitation medication.

A racemic epinephrine versus Heliox RCT was conducted at a Level 1 Trauma Centre in Michigan and the results published in 2001.²² Enrolled were 33 randomly assigned consecutive children (mean age 24 months) with moderate-to-severe croup who also received intramuscular dexamethasone; data for 29 were available for the final analysis. The authors did not include a saline/placebo arm as all enrolled children were ill enough to receive aggressive treatment. Outcomes as measured by croup scores, oxygen saturation, respiratory rate, and heart rate were the same for both groups of children.

Limitations

The evidence base for use of racemic epinephrine in croup is surprisingly small – very few studies and very small studies – and somewhat dated. A pending Cochrane review will be a welcome addition to the literature. An expert from the University of Washington performed a narrative review of the RCTs described above and commented that it will not be possible to combine the trial results in a meta-analysis as they differed in measurement of effectiveness (both in time and scoring systems) and co-interventions.²³ A limitation of the comparative RCTs described above is the lack of a placebo arm, making it difficult to directly attribute improvement to treatment.

Other conditions: post-extubation of newborns, asthma, and TTN

Systematic Reviews and Meta-analyses: post-extubation of newborns

A 2002 Cochrane review reported on the use of nebulized racemic epinephrine to accompany extubation of newborn infants following a period of mechanical ventilation.²⁴ After extubation, respiratory insufficiency can result due to an increase in upper airway resistance. Use of racemic epinephrine for this purpose has been routine in some neonatal units. The primary objective of the review was to assess whether nebulized epinephrine administered immediately after extubation decreases the need for subsequent additional respiratory support. The literature search ended in 2001 and only RCTs were eligible for inclusion – however, none were located. The authors concluded that there is no evidence to either support or refute the use of inhaled nebulized racemic epinephrine post-extubation in neonates.

RCT: Asthma

Due to its accepted use in bronchiolitis, researchers in Ottawa tested the use of racemic epinephrine versus nebulized salbutamol for children (aged 1 to 17 years) with acute asthma presenting to the ED.²⁵ The double-blind RCT randomized 120 patients to either racemic epinephrine or salbutamol at 0, 20, and 40 minutes; all received oral steroids as well. Outcomes showed no differences between groups in pulmonary score, length of stay, admission to hospital, or relapse rate but the epinephrine-treated group had significantly more minor adverse effects. The authors concluded that in this group of children there is no significant clinical benefit of nebulized epinephrine over salbutamol and the latter remains the treatment of choice.

RCT: TTN

The literature linked only one other acute respiratory disorder to racemic epinephrine – TTN – a condition caused by delayed clearance of fetal lung fluid at birth affecting 0.5 % to 2.8% of newborns. An RCT from Harvard in Boston randomized 20 affected newborns to three doses of inhaled racemic epinephrine with normal saline (n=15) or normal saline alone as a placebo (n=5). Results showed no difference in rate of resolution of tachypnea or adverse effects.²⁶

Question #2: Guidelines for treatment of bronchiolitis and croup**Bronchiolitis**

Two sets of clinical practice guidelines (CPGs) for management of bronchiolitis were located, both published in 2006:

The American Academy of Pediatrics (AAP) developed guidelines for diagnosis and management of bronchiolitis, publishing these in the AAP's official journal "Pediatrics".²⁷ The CPG expert subcommittee employed an evidence base developed by the Agency for Healthcare Quality and Research (AHRQ), with the comprehensive literature search extending to July 2004. The guideline awarded a quality grade to the evidence base underlying each recommendation (grades A to D plus X). AAP guidelines are reviewed every 5 years.

In the AAP CPG, epinephrine was discussed under the use of bronchodilators. The following recommendations were made, each being assigned a grade B with respect to evidence (RCTs with limitations; preponderance of harm of use over benefit):

- Bronchodilators should not be used routinely.
- A carefully monitored trial of α -adrenergic medication (e.g., epinephrine) or β -adrenergic medication (e.g., salbutamol) is an option but only if there is documented positive clinical response using an objective means of evaluation.

The guideline admits that use of bronchodilators is controversial and that RCTs have failed to demonstrate consistent benefits from either α or β -adrenergic agents. The guideline cites a Cochrane meta-analysis indicating that, at most, one child in four may have a transient improvement of unknown clinical significance due to use of bronchodilators, and that overall the benefits may not outweigh the risks and costs of therapy. They could find no evidence of long-term benefit. In the guideline, there is an evidence section devoted to epinephrine. Many of the RCTs presented above are reviewed but a distinction is not made between the forms of epinephrine and no comments are included specific to racemic epinephrine.

With respect to the AAP's overall recommended acute management of bronchiolitis, details can be found in the 22-page guideline. In brief, routine use of inhaled bronchodilators and corticosteroids is not recommended, although there are situations when these therapies may be carefully employed (details are set out in the guideline). There are seldom situations in which antivirals or antibiotics would be indicated and chest physiotherapy is not recommended. Therapy primarily focuses on adequate hydration and supplemental oxygen as needed.

The Scottish Intercollegiate Guidelines Network (SIGN), part of NHS Quality Scotland, is a collaboration between clinicians and patients. SIGN guidelines are developed by multidisciplinary groups of experts using standard methodology based on SRs of the evidence, including systematic literature reviews. In November 2007, SIGN published a national guideline devoted to the diagnosis and management of bronchiolitis.²⁸ The literature search spanned the years 2000 to 2005. With respect to nebulized epinephrine (drug form not stated), SIGN specifically recommended against its use, i.e., "nebulized epinephrine is not recommended for the treatment of acute bronchiolitis in infants,"²⁸ as a Grade A recommendation₃.

₃ A Grade A recommendation by SIGN is based on at least one high quality SR or RCT.

With respect to recommended acute management of bronchiolitis, details can be found in the 46-page guideline. In brief, the SIGN experts recommended use of supplemental oxygen by mask and nasogastric feeding as necessary as well as nasal suction. Otherwise, based on the evidence reviewed, they recommended against all drug therapies examined including antivirals, antibiotics, inhaled β -2 agonists, inhaled and oral corticosteroids, and anticholinergics. Chest physiotherapy was also not recommended.

Croup

Only one guideline was located for the management of croup, this being produced by the Alberta Clinical Practice Guidelines Working Group as part of the TOPS (Toward Optimized Practice) Program.²⁹ The guideline was updated in 2008. Although the specific methodology for this guideline is not included in the publication, the TOPS website includes a description of the methods underlying their CPG development processes, including checklists for assessment of the rigor and quality of underlying studies.³⁰

Epinephrine is discussed under emergency department care. The advice provided by TOPS is supported by citation of three RCTs ranging in publication dates from 1978 to 1995:

Epinephrine is indicated in patients with severe respiratory distress (as indicated by marked sternal wall indrawing and agitation):

- Improvement occurs within minutes and begins to wear off after one hour.
- Treatment does not alter disease symptoms beyond two hours.
- L-epinephrine 1:1000 is as effective as racemic epinephrine and institutional preference may guide management.
- Nebulized epinephrine therapy does not mandate admission to hospital.^{4(p3)}²⁹

With respect to recommended acute management of croup, details can be found in the 13-page guideline but in brief, for management in the ED, TOPS recommends oxygen, oral dexamethasone, and epinephrine as outlined above. Not recommended for routine use are nebulized steroids (budesonide), antibiotics, oral decongestants, and sedation.

Asthma

Guidelines for asthma were also accessed to determine whether epinephrine was ever mentioned as a form of management. Only one guideline mentioned the drug, this being a 2008 document produced by the United States National Heart, Lung and Blood Institute (NHLBI) where passing mention of epinephrine 1:1000 (L-epinephrine) by injection was included in a drug dosage table.³¹ The NHLBI guideline was developed by an expert panel based on SRs of the evidence. The SRs involved comprehensive literature searches, development of evidence tables, and ranking of the strength of the evidence. The literature search for the NHLBI asthma CPG ended in December 2006.

Otherwise, evidence-based guidelines from the British Thoracic Society³² and consensus-based (and industry supported) guidelines from the international PRACTALL group³³ do not mention the drug at all.

⁴ The TOPS guideline specifies that as the drug's duration of effect does not exceed 2 hours, a child should not be discharged from care for at least 2 hours post-treatment.

CONCLUSIONS AND IMPLICATIONS FOR DECISION OR POLICY MAKING:

For several decades, racemic epinephrine by nebulizer has been included in the armamentarium of drugs used for infants and children who present with acute respiratory distress due to bronchiolitis or croup. Small RCTs performed years ago suggested a benefit but large or recent trials have not been performed and indeed the SRs and CPGs located for this review did not routinely advocate use of the drug, particularly for bronchiolitis. With respect to croup, the Alberta guideline cited above²⁹ suggested that epinephrine can be employed in severe cases but suggested use of L-epinephrine as an alternative to the racemic form as the former has been shown to be as effective and safe as the latter.

The L- versus racemic epinephrine clinical equivalency has been noted by several other experts who comment on the practicality of preferentially employing L-epinephrine (Adrenaline[®]) rather than the racemic form.^{4,23} Reasons given are that L-epinephrine is routinely stocked as a resuscitation drug and it is as efficacious and well tolerated as the racemic form, as well as being less costly.

The switch from racemic to L-epinephrine is illustrated by three recent Canadian physician/pharmacist/nursing newsletters (from Alberta, British Columbia, and the Northwest Territories/Nunavut) that have informed providers about the withdrawal of racemic epinephrine and provided equivalency information for the L-epinephrine 1:1000 product.⁹⁻¹¹

The foregoing information may be useful for decision-makers in hospital pharmacies and urgent care clinics when considering whether to continue to stock racemic epinephrine.

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