Cost Avoidance Utilizing a Batching Process for Isoproterenol

To the Editor:

Isoproterenol (Isuprel) is a potent nonselective beta-adrenergic agonist with low affinity for alpha receptors with cardiac and respiratory indications. The action of isoproterenol, first patented in the early 1940s, on cardiac rhythm function was described more than 60 years ago. The drug’s primary uses today are for cardiac rhythm support during pronounced bradycardia and cardiac arrest. It has gained wide use to aid in the induction of various forms of tachycardia during cardiac electrophysiology testing and catheter ablation procedures. Historically, the acceptably low cost of the drug had never impacted wide stocking of the drug on hospital pharmacy shelves. However, on February 10, 2015, shortly after Valeant Pharmaceuticals International Inc. purchased Isuprel from Marathon Pharmaceuticals LLC, the price of isoproterenol soared more than 500%. According to memos within Valeant, the price increases from the purchase of two Marathon medications represented approximately 80% of the growth for Valeant. Because the United States is the only country in the 34-member Organization for Economic Co-operation and Development that does not have any government regulation of prescription drug pricing, hospital pharmacies were unable to combat this dramatic increase. This increase, among others by the company, caught the eye of hospital pharmacy administration and members of Congress, including Democratic presidential candidate Bernie Sanders.

In April 2016, the outgoing chief executive of Valeant Pharmaceuticals appeared on Capitol Hill at the Senate Special Committee on Aging. The committee has been investigating companies that have been raising prices of older medications. The executive acknowledged that using price increases as a strategy was “a mistake” and that the company no longer planned to pursue this strategy and would offer discounts to hospitals using its medications. Valeant stock amid the public outcry has lost 90% of its value since last summer, and the company is facing $30 billion in debt. At the time of this writing, no discount has been offered.

At Morristown Medical Center, a 655-bed tertiary teaching hospital, the price increase was recognized quickly, because the price of a vial of isoproterenol rose from $12 to $1,695. This prompted an investigation into our use of the medication to ensure that it was judicious and appropriate. Two principal destinations for isoproterenol were documented in our institution: in cardiac resuscitation medication trays and in the cardiac electrophysiology (EP) laboratory. During cardiac resuscitation, isoproterenol remains a mainstay of treatment for symptomatic bradycardia. In the EP laboratory, typically more than 15 procedures weekly involve infusions of isoproterenol to aid in initiating supraventricular and ventricular tachycardia, to aid in assessing the results of electrode catheter ablation procedures, and during head-upright tilt-table testing to assess for potential neutrally mediated hypotension.

Recognizing the astounding cost increase that could occur, and following multiple interdisciplinary meetings, we removed vials of isoproterenol from the more than 100 cardiac resuscitation medication trays and allocated the drug sparingly in critical care areas for dissemination as might be needed. Our institution experienced a one-time cost savings of nearly $170,000. Subsequently, attention was directed to efforts for additional cost containment in the cardiac EP laboratories. Historically, one vial of isoproterenol (1 mg/5 mL) had been used per patient to make an infusion of isoproterenol 1 mg/250 mL 0.9% sodium chloride. During any one procedure, an average of only 10 mL to 20 mL of the infusion was used, resulting in a large amount of waste of a now very costly medication.

An isoproterenol ampule is a single-dose container; thus, once the vial is opened under an ISO 5 environment (intravenous [IV] room hood), it must be used within six hours as per U.S. Pharmacopeia compounding guidelines. After researching the stability of isoproterenol when compounded at a concentration of 200 mcg/250 mL 0.9% sodium chloride, it was found to be stable for 24 hours. After additional multidisciplinary meetings, physician approval for the concentration change was obtained, allowing us to make a drip with a concentration of isoproterenol 200 mcg/250 mL 0.9% sodium chloride and enabling multiple infusions from each vial.

A process of weekly communication between the cardiac EP laboratory and pharmacy was developed with nursing leadership. The cardiac EP staff communicated the patient schedule to pharmacy on a weekly basis, with additional cases added if needed. On a daily basis, pharmacy prepared the needed number of doses on the overnight shift and loaded the infusions into the automatic dispensing cabinet so they were available first thing in the morning. Education was completed for the nursing staff with the new administration process, and a drip chart reference was created to aid with the new concentration and infusion rate. The process enabled us to compound multiple doses (up to five) of isoproterenol infusions from one vial in a clean-room setting. We have been able to put a successful process of interdepartmental communication in place to provide timely, safe, and cost-efficient patient care. The process went into effect in early May 2015 and has to date, one year after implementation, resulted in a cost avoidance of more than $600,000. The batching process has allowed us to continue to treat this patient population while minimizing the budgetary impact. We intend to continue this process even as discounted pricing becomes available and expand this model to other costly agents.

Older generic medications are increasingly being purchased and marketed under expensive branded names. These medications will continue to have a large impact on pharmacy budgets, necessitating that we remain diligent in developing responsible processes to enable safe treatment of patients while limiting exorbitant costs. Stricter controls are needed to prevent prohibitive excessive price increases on critical medications, which may limit patient access to required therapies.

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