Background

Anaphylaxis is a severe, life-threatening, multisystem allergic reaction occurring in about 2% of the United States population. Intramuscular epinephrine administered through auto-injectors is the preferred and most effective lifesaving immediate treatment for anaphylaxis emergences. The current US prescription drug market carries a variety of high-priced formulations of intramuscular epinephrine injections, which were recently plagued by drug shortages, increased costs, prompting a call for action. Evidence shows that the rising costs of auto-injectors is outweighed by increased effectiveness and reduced cost of anaphylaxis among healthcare professionals. With an estimated direct annual cost of $1.2 billion for anaphylaxis, only 15 million are for direct epinephrine cost expenditures. It is imperative that the burden of anaphylaxis be reduced. One potential solution to consider a potential regulatory status change for epinephrine by allowing over-the-counter (OTC) access to consumers.

Objective

To investigate the feasibility of switching the Federal Drug Administration’s (FDA) regulatory status of epinephrine auto-injectors from prescription (Rx) to over-the-counter (OTC).

Method

Multiple literature searches were conducted to determine the possibility of switching epinephrine auto-injectors from prescription to over-the-counter status. Eligible studies identified through searches in electronic databases utilizing PubMed, Google Scholar, and Medline, focusing on articles available from 1987 to September 2018. Searches included only English language and full text studies. The search terms used included “anaphylaxis epidemiology,” “anaphylaxis economic burden,” “intramuscular epinephrine injection cost,” “epinephrine injection manufacturing cost,” “epinephrine injection auto-injector cost,” “epinephrine abuse,” “epinephrine overdose,” “epinephrine auto-injector.” The comprehensive review was performed by a team of pharmacists and a pharmacy student in accordance with the Consumer Healthcare Products Association’s (CHPA) “Briefing Information of the Reo-OTC Switch Process.” A sample drug facts label (DFL) was drafted for potential future use in the testing and development of a switch program. The drug facts label acts as an abbreviated patient-friendly prescribing information leaflet.

Results

Upon review of the prescribing (PI) and product information leaflets (PIL) of currently available epinephrine auto-injectors, the key messages needed for safe and effective use of epinephrine were extracted and drafted into a proposed drug facts label (DFL) (Table 1). The language used in the DFL is a simplified version of the PI targeting a 6th grade reading level. The key messages included:

- Indications – translated into “uses”
- Warnings – split between the “do not use” and “ask a doctor before use if you” sections. In the presence of any relevant comorbidities, patients are encouraged to consult a healthcare provider before use to avoid complications through self-care.
- Drug interactions – the interacting medications were grouped and labeled by disease state in order to accommodate for prescribing issues on the label.
- Pregnancy – due to lack of data, and a “category C” rating, it is preferred that patients consult a healthcare provider to weigh the risks versus benefits prior to use.
- Directions – the proposed label is intended for the 0.3mg dose which is indicated for patients weighing over 30 kilograms. The instructions provided were brief due to several auto-injector devices available with varying methods of operation.

These critical warnings were strategically placed in bold print within the directions section of the DFL. These warnings carry a critical level of risk of complication. Patient understanding of these messages is crucial to ensuring the safety of OTC epinephrine use.

Discussion

The DFL is the consumer’s guide to self-selection of medicinal therapy in lieu of the healthcare professional’s preferred medical advice. It is intended to go through numerous revisions until the consumer can safely and effectively use the medication. In order to determine this, the label and medication must undergo label comprehension, self-selection, and actual use studies that will identify comprehensive issues that consumers may experience with the labeling. Potential comprehension issues with the current DFL in Table 1, could revolve around the “directions” section with patients or bystanders having trouble understanding proper administration technique, as well as the role of epinephrine not being meant to replace proper medical care. The directions provided in Table 1 do not include information on using the auto-injector device; these instructions vary among brands and manufacturers. A decision would need to be made whether this information would be placed on the DFL itself, or in the self-adjudged consumer information leaflet. In turn, a human factors study may be required in order to demonstrate consumer understanding of the auto-injector device itself. These hurdles would need to be properly resolved through intensive testing label.

Furthermore, switching epinephrine carries issues that are difficult to overcome by releasing the drug entering the market, such as patients either abusing (supported by past epinephrine inhaler abuse) or incorrectly using the medication in the absence of actual anaphylaxis. These issues would create a large barrier in the path to approval, as conventional labeling testing would be unlikely to provide a solution.

Conclusions

Creating a switch program for epinephrine auto-injectors could increase availability and decrease costs, potentially resulting in reduced deaths due to anaphylaxis thereby reducing burden on the health system. On the other hand, OTC availability of epinephrine may possibly lead to increased improper usage. By assessing all of these results, it is difficult to take a stance on whether or not to switch this medication until creative solutions to the barriers are presented. Any sponsoring organization attempting to switch epinephrine to OTC status would have to carefully weigh the risks and benefits of the switch.

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References available upon request.