Differences in Product Labeling for Medications that Prolong QTc Interval

Kukin, Alina; Pradel, Francoise

Background

When faced with a medication that prolongs the QTc interval, clinicians are often challenged with determining the clinical significance of this effect and process for monitoring. In 2005, the Food and Drug Administration (FDA) set forth guidance for manufacturers to assess the risk of QT/QTc interval prolongation and proarrhythmias for non-antiarrhythmic medication. This document provides recommendations for including the results of these evaluations in product labeling. The purpose of this project was to compare and contrast the differences and the utility of the information provided regarding QTc and proarrhythmic risk between medications approved for use before 2005 and after 2006.

Methods

Thirty product labels of medications known to prolong the QTc interval were randomly selected; 15 before 2005 and 15 after 2006. The product labeling for the branded version of the medication, if still available, were selected. If multiple routes of administration were available, the oral formulation labeling was selected for evaluation. Each label was reviewed to assess if the information provided included: msec change in QTc interval, clinical significance of the QTc interval change, dose dependent change in QTc interval, restriction for use based on baseline QTc, risk of torsades de pointe (TdP), recommendation for QTc monitoring, risk factors associated with QTc prolongation, and populations to avoid/use caution with therapy based on QTc risk.

Results

The product labels for medications prior to 2005 were less likely to include information regarding risk of QTc prolongation. The labels for the majority of medications before and after the 2005 guidelines documented the msec change in QTc interval (6/15 for medications before 2005 and 10/15 for medications after 2006). There were a similar amount of product labels before and after 2005 that included information regarding dose dependence, cutoff for initiating therapy, guidance for management of QTc interval prolongation, and potential associated risk factors. However, slightly more product labels provided guidance on the clinical significance of an increase in the QTc interval for drugs published before the 2005 guidelines (11/15 for medications before 2005 and 9/15 for medications after 2006). For the other medications, no information is provided regarding association of QTc interval prolongation with increased risk of TdP.

Conclusion

After the guidelines were published, reporting of the potential change in the QTc interval in msec and recommendations for routine monitoring increased. Recommendations did not include frequency of monitoring, and this was left to clinical judgment. The frequency of recommendations on actions to be taken in the event of QTc interval prolongation did not increase. Despite the recommendations from the 2005 FDA guidelines, newer product labels were less likely to discuss the association of QTc prolongation with increased risk of TdP. More

information regarding clinical significance of QTc interval prolongation should be included to help clinicians to determine best monitoring practices.