Qnexa and the FDA: Why safe diet drugs are hard to come by

A panel of FDA doctors recently voted 20-2 in favor of approving a new weight loss drug Qnexa, manufactured by Vivus. This new drug is a combination of phentermine and topiramate. This drug had previously been rejected by the FDA over concerns of heart palpitations and causing birth defects if taken by a pregnant woman. The reasons for voting for approval now were not stated. It is the latest in a long line of drugs intended to produce weight loss. Doctors had previously attempted to use dinitrophenol, amphetamines, and fen-phen, a combination of phentermine and fenfluramine. The use of each of these were stopped because of serious adverse events. Currently, the only FDA approved drug for weight loss is orlistat. The FDA is expected to make a decision on Qnexa by mid-April.

Qnexa is a combination drug, containing phentermine, a sympathomimetic used to suppress appetite, and topiramate, an anticonvulsant with weight-loss side effects. In the CONQUER study, the use of phentermine 7.5mg/topiramate 46mg and 15mg/92mg showed statistically significant weight loss of 8.1kg and 10.2kg respectively compared to 1.4kg for placebo at 52 weeks. According to the FDA New Drug Application for Qnexa, the primary cardiac concern was with an increased number of arrhythmias (palpitations) seen during the OB-301 and OB-302 studies. Arrhythmias were seen in more than twice as many patients taking the high-dose combination than those taking placebo. This adverse event is due the phentermine component of the drug. The risk of teratogenicity from this medication is believed to be because of the topiramate component. According to the UK Epilepsy and Pregnancy Register, three out of 70 patient taking topiramate monotherapy had major malformations. According to the North American AED Pregnancy Register, the prevalence of major malformation with topiramate is 3.8%.

References

- Cohen, P.A. Phentermine plus topiramate in the treatment of obesity. The Lancet, Volume 378, Issue 9786, Page 126, 9 July 2011.
- Gadde, K.M., et al. Effects of low-dose, controlled-release, phentermine plus topiramate combination on weight and associated comorbidities in overweight and obese adults (CONQUER): a randomised, placebo-controlled, phase 3 trial. The Lancet, Volume 377, Issue 9774, Pages 1341 - 1352, 16 April 2011
- FDA New Drug Application for Qnexa (22580). July 15, 2010. Available at http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/Drugs/EndocrinologicandMetabolicDrugsAdvisoryCommittee/UCM227050.pdf

Prepared by: Bradley Hamilton, Doctor of Pharmacy Candidate