

Abstract 1461

DISPENSING ORAL TEMOZOLOMIDE IN CHILDREN: PRECISION AND STABILITY OF A NOVEL READY-TO-USE LIQUID FORMULATION IN COMPARISON WITH CAPSULE DERIVED MIXTURES

Type: Abstract Submission

Topic: AS05 SIOP Scientific programme / AS05.e Neuroblastoma

Authors: Caroline Lemarchand¹, Hugues Bienaymé¹, André Rieutord², Lionel Tortolano^{2,3}, Maxime Annereau², [Jeremy Bastid](#)¹;

¹ORPHELIA Pharma, ORPHELIA Pharma, Paris, France, ²Gustave Roussy, Clinical Pharmacy department, Villejuif, France,

³Université Paris-Saclay, EA 401 Matériaux et santé, UFR Pharmacie, Châtenay-Malabry, France

Background and Aims

Parents and caregivers often overcome the lack of commercially available pediatric formulations by mixing adult dosage forms with food. This study aimed at assessing the risks associated with handling of temozolomide (TMZ) capsules in comparison with a ready-to-use oral suspension specifically formulated for children (Ped-TMZ).

Methods

TMZ capsules were opened and their content (equivalent to 90 mg) mixed with food vehicles. Similar dose was sampled from Ped-TMZ. TMZ and its degradation product, amino-imidazole-carboxamide (AIC), were assayed using UV-HPLC at 0, 30 and 60 min. Statistical analysis was performed to evaluate TMZ recovery, AIC amount and impact of operator on accuracy. Acceptance criteria were pre-defined for TMZ (95.0-105.0%) and AIC (<1%) content.

Results

Mean TMZ recovery was $96.6 \pm 1.2\%$ for Ped-TMZ and $91.0 \pm 1.5\%$ and $91.6 \pm 1.4\%$ for the capsule-derived preparations with apple juice and applesauce, respectively. The recovery of TMZ in Ped-TMZ was systematically and significantly higher than that observed after handling of TMZ capsules ($p < 0.0001$) and within specifications. The recovery of TMZ from capsules in food never met acceptance criteria. In addition, the 4 tested food vehicles (applesauce, cream, milk, purée) had a significant effect on TMZ stability ($p = 0.0042$) and AIC significantly increased with time in 3 of the 4 vehicles ($p < 0.0001$). Only 1/72 preparations from capsules in food met the acceptance criteria, whereas Ped-TMZ showed no TMZ loss and AIC remained within specifications.

Conclusions

This study demonstrated a significant impact of handling TMZ capsules on dosing accuracy with a mean deliverable dose decreased by 9%, and possibly even greater in routine practice as complete food intake by the child is unlikely. Rapid degradation of TMZ was evidenced in certain food vehicles. When combined with the known effect of food on TMZ absorption, mixing capsule content with food may significantly reduce TMZ exposure, highlighting the need of age-appropriate TMZ formulations.

Print