

One Year Post Exclusivity Adverse Event Review: Carboplatin

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Background Drug Information

- **Drug:** Paraplatin[®] (carboplatin aqueous solution) injection
- **Therapeutic Category:** Antineoplastic agent
- **Sponsor:** Bristol-Myers Squibb Company
- **Indication:** Initial and secondary treatment of advanced ovarian carcinoma. Safety and effectiveness in pediatric patients have not been established.
- **Original Market Approval:** March 3, 1989
- **Pediatric Exclusivity Granted:** April 30, 2004
- **Pediatric Information Added to the Label:** No new information added. Adverse events were similar to adults and were already labeled.

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- Use information difficult to obtain since the data resources available to the agency do not capture the use of carboplatin in the outpatient clinic setting, which represents approximately 60% of use.¹
- PremierTM database revealed pediatric use in 2.9% to 4% of discharges (total 168) in which carboplatin was billed between 1/04 and 12/04.²

¹IMS Health, IMS National Sales PerspectiveTM, Moving Annual Totals, May 2002-Apr 2005, Data Extracted June 2005

²Premier Rx Market Advisor, Jan 2004 – Dec 2004, Data extracted June 2005

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- 43 pediatric adverse event reports (36 unduplicated) identified during the 1 year post-exclusivity period:
 - Most events are currently labeled or would not be unexpected in association with the disease or the concomitant medications
 - There were 4 deaths, 9 life-threatening events, and 6 required hospitalization
 - 2 deaths were related to disease progression
 - 1 death in a patient who had an arrest during stem cell infusion (carboplatin used for bone marrow conditioning regimen)
 - 1 death due to acute myocarditis possibly related to ifosphamide or infection

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- 43 pediatric adverse event reports (36 unduplicated) identified during the 1 year post-exclusivity period:
 - Unlabeled events that warrant further analysis:
 - Portal vein thrombosis in 2 children on multiple additional chemotherapeutic agents
 - One case of blindness secondary to eye swelling and optic nerve atrophy in a patient with bilateral retinoblastoma who received subtenon carboplatin, cryotherapy and systemic chemotherapy
- Portal vein thrombosis has been associated with dactinomycin in the literature and with vincristine based on an ODS consult (July 2005)
- Off-patent Written Requests were issued in 2004 to evaluate the safety profiles of dactinomycin and vincristine, with particular focus on hepatic disease and hepatic veno-occlusive disease (study in progress through NCI and COG)

Summary:

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- Most adverse events, with the exception of hepatic veno-occlusive disease and blindness, reported in the 1 year post-exclusivity period are currently labeled or would not be unexpected in association with the disease or with the concomitant treatments received by the patients.
- This completes the one-year post-exclusivity AE reporting as mandated by BPCA.
- FDA recommends routine monitoring of AEs for carboplatin in all populations.
- Does the Advisory Committee concur?

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