National Comprehensive Cancer Network®

NCCN Chemotherapy Order Templates (NCCN Templates®)
Appendix B

Carboplatin Dosing in Adults

Calvert Equation[1]

- Carboplatin Dose (mg) = Target area under the curve (AUC mg/mL/min) x (GFR* + 25)

*GFR estimated by calculated creatinine clearance using Cockcroft-Gault Equation (see below).

Cockcroft-Gault Equation[2]

$$\text{CrCl (male; mL/min)} = \frac{(140 - \text{age}) \times (\text{weight in kg})}{72 \times \text{serum creatinine (mg/dL)}}$$

CrCl (female; mL/min) = 0.85 x CrCl (male)

Maximum Carboplatin Dose Calculation[3]

The FDA has recommended that physicians consider capping the dose of carboplatin for desired exposure (AUC) to avoid potential toxicity due to overdosing. The maximum dose is based on a GFR estimate that is capped at 125 mL/min for patients with normal renal function.

Based on the Calvert formula described in the carboplatin label, the maximum doses can be calculated as:

Maximum Carboplatin Dose (mg) = Target AUC (mg/mL/min) x (125 mL/min + 25)

For a target AUC = 6, the maximum dose is 6 x 150 = 900 mg
For a target AUC = 5, the maximum dose is 5 x 150 = 750 mg
For a target AUC = 4, the maximum dose is 4 x 150 = 600 mg

Additional Considerations[4]

- Overweight or obese patients (BMI ≥ 25 kg/m^2): Consider using an adjusted body weight.

Adjusted body weight (kg) = ideal body weight (IBW) + 0.4 x (total body weight [TBW] – IBW)

- Patients with abnormally low serum creatinine (Cr), including elderly or cachectic patients: Consider using a minimum Cr of 0.7 mg/dL to avoid overestimation of CrCl.

- Measured CrCl: Consider using ethylene diamine tetraacetic acid (EDTA) or a 24-hour urine to measure CrCl (not a serum creatinine-based mathematical equation) when dosing at an AUC greater than 6 or when using an un-capped CrCl

- An increasing number of studies suggest that estimated Glomerular Filtration Rate (eGFR) calculated using the Chronic Kidney Disease Epidemiology (CKD-EPI) is more accurate for estimation of creatinine clearance. While some institutions utilize CKD-EPI, Cockroft-Gault is still the standard of practice

Carboplatin Dosing in Pediatrics

- Several investigators have characterized carboplatin pharmacokinetics and pharmacodynamics in children, which led to the development of a variety of dosing formulas.

Modified Pediatric Calvert Equations

- Marina et al[5]
  Carboplatin Dose (mg/m^2)* = Target area under the curve (AUC mg/mL/min) x [(0.93 x GFR*[$mL/min/m^2$]) + 15]

- Newell et al[6]
  Carboplatin Dose (mg)* = Target area under the curve (AUC mg/mL/min) x (GFR*[mL/min] + [0.36 x weight in kg])

- Pinkerton et al[7]
  Carboplatin Dose (mg)* = Target area under the curve (AUC mg/mL/min) x ([GFR*[mL/min] x 1.2] + 20)

- Mann et al[8]
  Carboplatin Dose (mg)* = Target area under the curve (AUC mg/mL/min] x [GFR*[mL/min] + (15 x BSA [m^2])]

*Note appropriate units for carboplatin dose (i.e. mg/m^2 or mg) and confirm units of measure for GFR (i.e. $mL/min/m^2$ or mL/min) when performing calculations for the equations above.

Additional Considerations

- GFR Estimation: Use of Tc-99m labeled DTPA clearance, a 24-hour urine collection, or other validated methods to measure creatinine clearance are preferred for determining a carboplatin dose to achieve a desired AUC in children. If use of the aforementioned methods is not feasible, estimation by use of a serum creatinine-based mathematical equation may be considered, such as the Bedside Schwartz equation[9] (GFR [$mL/min/1.73m^2$] = 0.413 x [(height in cm) ÷ serum creatinine (mg/dL)]) or another pediatric GFR equation as appropriate.

- Carboplatin dosing: Dose and frequency of carboplatin in pediatric patients varies. Carboplatin is not always dosed on AUC and is commonly regimen-specific in regards to dosing by AUC, mg/m^2, or mg/kg. Refer to the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for standard dosing recommendations based on regimen.

REFERENCES

1. Calvert AH, Newell DR, Gumbrell LA, et al. Carboplatin dosage: prospective evaluation of a simple formula based on renal function. *J Clin Oncol*.1989;7:1748–1756.
2. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron*. 1976;16:31–41.
3. US Food & Drug Administration. Carboplatin dosing. Available at: https://wayback.archive-it.org/7993/20170113081146/http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDER/ucm228974.htm. Revised November 27, 2015. Accessed October 16, 2017.
4. Updated FAQ's for dosing of carboplatin [newsletter]. Philadelphia, PA: Gynecologic Oncology Group Newsletter; Spring 2011. Available at: https://www.gog.org. Accessed October 26, 2017.
5. Marina NM, Rodman J, Shema SJ, et al. Phase I study of escalating targeted doses of carboplatin combined with ifosfamide and etoposide in children with relapsed solid tumors. *J Clin Oncol*. 1993;11:554–560.
6. Newell DR, Pearson AD, Balmanno K, et al. Carboplatin pharmacokinetics in children: the development of a pediatric dosing formula. *J Clin Oncol*. 1993;11(12):2314–2323.
7. Pinkerton CR, Broadbent V, Horwich A, et al. 'JEB' – a carboplatin based regimen for malignant germ cell tumours in children. *Br J Cancer*. 1990;62(2):257-262.
8. Mann JR, Raafat F, Robinson K, et al. UKCCSG's germ cell tumor (GCT) studies: improving outcome for children with malignant extracranial non-gonadal tumours – carboplatin, etoposide and bleomycin are effective and less toxic than previous regimens. *Med Pediatr Oncol*. 1998;20(4):217-227.
9. Schwartz GJ, Muñoz A, Schneider MF, et al. New equations to estimate GFR in children with CKD. *J Am Soc Nephrol*. 2009 Mar;20(3):629-637.