

APPENDIX I

Intravenous Methotrexate Dose Modifications for Toxicity

Absolute neutrophil count (ANC) < 1,000/ μ L and/or platelet count < 100,000/ μ L

Methotrexate should be omitted for ANC less than 1,000/ μ L and/or platelet count less than 100,000/ μ L. Once ANC recovers to equal or above 1,000/ μ L, and platelet count equal to or above 100,000/ μ L, methotrexate should be administered on first due date following held dose; dosage should be 20% less than last administered dose. If the latter dose is tolerated, escalation should continue by 50 mg/m² increments.

Liver Dysfunction

Withhold dose if direct (conjugated) bilirubin is > 1 mg/dL and/or AST/ALT is > 1,000 U/L and/or PT/INR is prolonged (unrelated to Vitamin K deficiency) on two determinations at least one week apart. Exclude viral hepatitis. Restart at full dose when AST/ALT is < 400 U/L and direct (conjugated) bilirubin is < 1 mg/dL and PT/INR is normal.

Mucositis

For Grade 2 (CTCAE vs 2) stomatitis of > 3 days duration: decrease dose by 20%. For Grade 3-4 stomatitis, withhold intravenous methotrexate until resolved; resume at 50% dose and subsequently escalate to 75% to 100% dose at 10-day intervals if Grade 3-4 toxicity does not recur. Consider culturing lesions for herpes simplex if mucositis persists or recurs.

Kidney Dysfunction Grades 2-4 (CTCAE vs 2)

Omit IV MTX until Grade 0 toxicity (resolved). Resume at 100% dose

CCG-1991 Participating Institution

Princess Margaret Hospital for Children
Children's Healthcare of Atlanta - Egleston
Primary Children's Hospital
University of Wisconsin Hospital and Clinics
Nationwide Children's Hospital
Connecticut Children's Medical Center
Children's Hospitals and Clinics of Minnesota - Minneapolis
Children's Hospital of The King's Daughters
Valley Children's Hospital
New York Medical College
Methodist Children's Hospital of South Texas
Seattle Children's Hospital
Norton Children's Hospital
Children's Hospital of Philadelphia
Children's Hospital and Clinic-Saint Paul
Miller Children's and Women's Hospital Long Beach
Presbyterian - Saint Lukes Medical Center - Health One
Children's Hospital of Orange County
Children's Hospital of Los Angeles
Saint Joseph's Regional Medical Center
Children's Specialty Center of Nevada II
Kaiser Permanente-Oakland
Mary Bridge Children's Hospital and Health Center
Phoenix Children's Hospital
Allan Blair Cancer Centre
Beaumont Children's Hospital-Royal Oak
Columbia University/Herbert Irving Cancer Center
Covenant Children's Hospital

Michigan State University Clinical Center
Cincinnati Children's Hospital Medical Center
Alfred I duPont Hospital for Children
Children's National Medical Center
North Shore University Hospital
Riley Hospital for Children
Dayton Children's Hospital
Montefiore Medical Center - Moses Campus
University of Iowa/Holden Comprehensive Cancer Center
Saint Vincent Hospital Cancer Center Green Bay
Group Health Cooperative of Puget Sound Oncology Consortium
UCSF Medical Center-Mission Bay
Dell Children's Medical Center of Central Texas
Kaiser Permanente Downey Medical Center
Advocate Children's Hospital-Park Ridge
C S Mott Children's Hospital
Loma Linda University Medical Center
University of Kentucky/Markey Cancer Center
Loyola University Medical Center
Vanderbilt University/Ingram Cancer Center
CancerCare Manitoba
Albany Medical Center
Children's Mercy Hospitals and Clinics
Sanford Broadway Medical Center
IWK Health Centre
British Columbia Children's Hospital
Rainbow Babies and Childrens Hospital
Henry Ford Hospital
Children's Hospital Colorado

Helen DeVos Children's Hospital at Spectrum Health
Blank Children's Hospital
Newark Beth Israel Medical Center
Baystate Medical Center
Morristown Medical Center
Bronson Methodist Hospital
Deaconess Medical Center
University of Illinois - Rockford
University of Minnesota/Masonic Cancer Center
Marshfield Clinic
Brooklyn Hospital Center
The Steven and Alexandra Cohen Children's Medical Center of New York
Texas Tech University Health Sciences Center-Amarillo
Maimonides Medical Center
Penn State Children's Hospital
Saint Luke's Mountain States Tumor Institute
Geisinger Medical Center
Laura and Isaac Perlmutter Cancer Center at NYU Langone
Janeway Child Health Centre
Children's Hospital of Pittsburgh of UPMC
Children's Hospital and Medical Center of Omaha
Mattel Children's Hospital UCLA
University of Nebraska Medical Center
Palmetto Health Richland
Children's Hospital and Research Center at Oakland
Southern Illinois University School of Medicine
Medical Center of Central Georgia
Memorial Health University Medical Center
Children's Hospital Medical Center of Akron

Bellin Memorial Hospital
Saint Barnabas Medical Center
Santa Barbara Cottage Hospital
Sinai Hospital of Baltimore
Augusta University Medical Center
Memorial Sloan Kettering Cancer Center
East Tennessee Children's Hospital
UNC Lineberger Comprehensive Cancer Center
Cedars-Sinai Medical Center
Cleveland Clinic Foundation
Children's Hospital
University of Chicago Comprehensive Cancer Center
NYU Winthrop Hospital
Mercy Children's Hospital
Brookdale Hospital Medical Center
Weill Medical College of Cornell University
M D Anderson Cancer Center
Mayo Clinic
University of Illinois
Saskatoon Cancer Centre
Tod Children's Hospital - Forum Health
Saint Vincent Hospital and Health Care Center
The Toledo Hospital/Toledo Children's Hospital
Starship Children's Hospital
Gundersen Lutheran Health System/CCOP
City of Hope Comprehensive Cancer Center
MedStar Georgetown University Hospital
Sanford USD Medical Center - Sioux Falls
Oregon Health and Science University

Saint Peter's University Hospital

Dakota Midwest Cancer Institute

Mount Sinai Hospital

Providence Sacred Heart Medical Center and Children's Hospital

UC Irvine Medical Center/Chao Family Comprehensive Cancer Center

Royal Children's Hospital

State University of New York Downstate Medical Center

T C Thompson Children's Hospital

Cabell Huntington Hospital