

COMMON TOXICITY CRITERIA (CTC)

| Adverse Event | Grade | | | | |
|---|--------|---|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| ALLERGY/IMMUNOLOGY | | | | | |
| Allergic reaction/ hypersensitivity (including drug fever) | none | transient rash, drug fever <38°C (<100.4°F) | urticaria, drug fever ≥38°C (≥100.4°F), and/or asymptomatic bronchospasm | symptomatic bronchospasm, requiring parenteral medication(s), with or without urticaria; allergy-related edema/angioedema | anaphylaxis |
| Note: Isolated urticaria, in the absence of other manifestations of an allergic or hypersensitivity reaction, is graded in the DERMATOLOGY/SKIN category. | | | | | |
| Allergic rhinitis (including sneezing, nasal stuffiness, postnasal drip) | none | mild, not requiring treatment | moderate, requiring treatment | - | - |
| Autoimmune reaction | none | serologic or other evidence of autoimmune reaction but patient is asymptomatic (e.g., vitiligo), all organ function is normal and no treatment is required | evidence of autoimmune reaction involving a non- essential organ or function (e.g., hypothyroidism), requiring treatment other than immunosuppressive drugs | reversible autoimmune reaction involving function of a major organ or other adverse event (e.g., transient colitis or anemia), requiring short-term immunosuppressive treatment | autoimmune reaction causing major grade 4 organ dysfunction; progressive and irreversible reaction; long-term administration of high- dose immuno- suppressive therapy required |
| Also consider Hypothyroidism, Colitis, Hemoglobin, Hemolysis. | | | | | |
| Serum sickness | none | - | - | present | - |
| Urticaria is graded in the DERMATOLOGY/SKIN category if it occurs as an isolated symptom. If it occurs with other manifestations of allergic or hypersensitivity reaction, grade as Allergic reaction/hypersensitivity above. | | | | | |
| Vasculitis | none | mild, not requiring treatment | symptomatic, requiring medication | requiring steroids | ischemic changes or requiring amputation |
| Allergy/Immunology - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| AUDITORY/HEARING | | | | | |
| Conductive hearing loss is graded as Middle ear/hearing in the AUDITORY/HEARING category. | | | | | |
| Earache is graded in the PAIN category. | | | | | |
| External auditory canal | normal | external otitis with erythema or dry desquamation | external otitis with moist desquamation | external otitis with discharge, mastoiditis | necrosis of the canal soft tissue or bone |
| Note: Changes associated with radiation to external ear (pinnae) are graded under Radiation dermatitis in the DERMATOLOGY/SKIN category. | | | | | |

| Adverse Event | Grade | | | | |
|--|------------------------------|--|---|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Inner ear/hearing | normal | hearing loss on audiometry only | tinnitus or hearing loss, not requiring hearing aid or treatment | tinnitus or hearing loss, correctable with hearing aid or treatment | severe unilateral or bilateral hearing loss (deafness), not correctable |
| Middle ear/hearing | normal | serous otitis without subjective decrease in hearing | serous otitis or infection requiring medical intervention; subjective decrease in hearing; rupture of tympanic membrane with discharge | otitis with discharge, mastoiditis or conductive hearing loss | necrosis of the canal soft tissue or bone |
| Auditory/Hearing - Other (Specify, _____) | normal | mild | moderate | severe | life-threatening or disabling |
| BLOOD/BONE MARROW | | | | | |
| Bone marrow cellularity | normal for age | mildly hypocellular or $\leq 25\%$ reduction from normal cellularity for age | moderately hypocellular or $>25 - \leq 50\%$ reduction from normal cellularity for age or >2 but <4 weeks to recovery of normal bone marrow cellularity | severely hypocellular or $>50 - \leq 75\%$ reduction in cellularity for age or 4 - 6 weeks to recovery of normal bone marrow cellularity | aplasia or >6 weeks to recovery of normal bone marrow cellularity |
| Normal ranges: | | | | | |
| children (≤ 18 years) | 90% cellularity average | | | | |
| younger adults (19-59) | 60 - 70% cellularity average | | | | |
| older adults (≥ 60 years) | 50% cellularity average | | | | |
| Note: Grade Bone marrow cellularity only for changes related to treatment not disease. | | | | | |
| CD4 count | WNL | $<LLN - 500/mm^3$ | 200 - $<500/mm^3$ | 50 - $<200/mm^3$ | $<50/mm^3$ |
| Haptoglobin | normal | decreased | - | absent | - |
| Hemoglobin (Hgb) | WNL | $<LLN - 10.0$ g/dL $<LLN - 100$ g/L $<LLN - 6.2$ mmol/L | 8.0 - <10.0 g/dL 80 - <100 g/L 4.9 - <6.2 mmol/L | 6.5 - <8.0 g/dL 65 - <80 g/L 4.0 - <4.9 mmol/L | <6.5 g/dL <65 g/L <4.0 mmol/L |
| For leukemia studies or bone marrow infiltrative/ myelophthisic processes, if specified in the protocol. | WNL | 10 - $<25\%$ decrease from pretreatment | 25 - $<50\%$ decrease from pretreatment | 50 - $<75\%$ decrease from pretreatment | $\geq 75\%$ decrease from pretreatment |
| Hemolysis (e.g., immune hemolytic anemia, drug-related hemolysis, other) | none | only laboratory evidence of hemolysis [e.g., direct antiglobulin test (DAT, Coombs') schistocytes] | evidence of red cell destruction and ≥ 2 gm decrease in hemoglobin, no transfusion | requiring transfusion and/or medical intervention (e.g., steroids) | catastrophic consequences of hemolysis (e.g., renal failure, hypotension, bronchospasm, emergency splenectomy) |
| Also consider Haptoglobin, Hemoglobin. | | | | | |

| Adverse Event | Grade | | | | |
|---|-------|--|--|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Leukocytes (total WBC) | WNL | <LLN - 3.0×10^9 /L <LLN - 3000/mm ³ | ≥ 2.0 - $<3.0 \times 10^9$ /L ≥ 2000 - <3000 /mm ³ | ≥ 1.0 - $<2.0 \times 10^9$ /L ≥ 1000 - <2000 /mm ³ | $<1.0 \times 10^9$ /L <1000/mm ³ |
| For BMT studies, if specified in the protocol. | WNL | ≥ 2.0 - $<3.0 \times 10^9$ /L ≥ 2000 - <3000 /mm ³ | ≥ 1.0 - $<2.0 \times 10^9$ /L ≥ 1000 - <2000 /mm ³ | ≥ 0.5 - $<1.0 \times 10^9$ /L ≥ 500 - <1000 /mm ³ | $<0.5 \times 10^9$ /L <500/mm ³ |
| <i>For pediatric BMT studies (using age, race and sex normal values), if specified in the protocol.</i> | | ≥ 75 - $<100\%$ LLN | ≥ 50 - $<75\%$ LLN | ≥ 25 - 50% LLN | $<25\%$ LLN |
| Lymphopenia | WNL | <LLN - 1.0×10^9 /L <LLN - 1000/mm ³ | ≥ 0.5 - $<1.0 \times 10^9$ /L ≥ 500 - <1000 /mm ³ | $<0.5 \times 10^9$ /L <500/mm ³ | - |
| <i>For pediatric BMT studies (using age, race and sex normal values), if specified in the protocol.</i> | | ≥ 75 - $<100\%$ LLN | ≥ 50 - $<75\%$ LLN | ≥ 25 - $<50\%$ LLN | $<25\%$ LLN |
| Neutrophils/granulocytes (ANC/AGC) | WNL | ≥ 1.5 - $<2.0 \times 10^9$ /L ≥ 1500 - <2000 /mm ³ | ≥ 1.0 - $<1.5 \times 10^9$ /L ≥ 1000 - <1500 /mm ³ | ≥ 0.5 - $<1.0 \times 10^9$ /L ≥ 500 - <1000 /mm ³ | $<0.5 \times 10^9$ /L <500/mm ³ |
| For BMT studies, if specified in the protocol. | WNL | ≥ 1.0 - $<1.5 \times 10^9$ /L ≥ 1000 - <1500 /mm ³ | ≥ 0.5 - $<1.0 \times 10^9$ /L ≥ 500 - <1000 /mm ³ | ≥ 0.1 - $<0.5 \times 10^9$ /L ≥ 100 - <500 /mm ³ | $<0.1 \times 10^9$ /L <100/mm ³ |
| For leukemia studies or bone marrow infiltrative/ myelophthitic process, if specified in the protocol. | WNL | 10 - $<25\%$ decrease from baseline | 25 - $<50\%$ decrease from baseline | 50 - $<75\%$ decrease from baseline | $\geq 75\%$ decrease from baseline |
| Platelets | WNL | <LLN - 75.0×10^9 /L <LLN - 75,000/mm ³ | ≥ 50.0 - $<75.0 \times 10^9$ /L $\geq 50,000$ - $<75,000$ /mm ³ | ≥ 10.0 - $<50.0 \times 10^9$ /L $\geq 10,000$ - $<50,000$ /mm ³ | $<10.0 \times 10^9$ /L <10,000/mm ³ |
| For BMT studies, if specified in the protocol. | WNL | ≥ 50.0 - $<75.0 \times 10^9$ /L $\geq 50,000$ - $<75,000$ /mm ³ | ≥ 20.0 - $<50.0 \times 10^9$ /L $\geq 20,000$ - $<50,000$ /mm ³ | ≥ 10.0 - $<20.0 \times 10^9$ /L $\geq 10,000$ - $<20,000$ /mm ³ | $<10.0 \times 10^9$ /L <10,000/mm ³ |
| For leukemia studies or bone marrow infiltrative/ myelophthitic process, if specified in the protocol. | WNL | 10 - $<25\%$ decrease from baseline | 25 - $<50\%$ decrease from baseline | 50 - $<75\%$ decrease from baseline | $\geq 75\%$ decrease from baseline |
| Transfusion: Platelets | none | - | - | yes | platelet transfusions and other measures required to improve platelet increment; platelet transfusion refractoriness associated with life-threatening bleeding. (e.g., HLA or cross matched platelet transfusions) |
| For BMT studies, if specified in the protocol. | none | 1 platelet transfusion in 24 hours | 2 platelet transfusions in 24 hours | ≥ 3 platelet transfusions in 24 hours | platelet transfusions and other measures required to improve platelet increment; platelet transfusion refractoriness associated with life-threatening bleeding. (e.g., HLA or cross matched platelet transfusions) |
| Also consider Platelets. | | | | | |

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|---|-------------|--|--|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| Transfusion: pRBCs | none | - | - | yes | - |
| For BMT studies, if specified in the protocol. | none | ≤2 u pRBC in 24 hours elective or planned | 3 u pRBC in 24 hours elective or planned | ≥4 u pRBC in 24 hours | hemorrhage or hemolysis associated with life-threatening anemia; medical intervention required to improve hemoglobin |
| <i>For pediatric BMT studies, if specified in the protocol.</i> | <i>none</i> | <i>≤15mL/kg in 24 hours elective or planned</i> | <i>>15 - ≤30mL/kg in 24 hours elective or planned</i> | <i>>30mL/kg in 24 hours</i> | <i>hemorrhage or hemolysis associated with life-threatening anemia; medical intervention required to improve hemoglobin</i> |
| Also consider Hemoglobin. | | | | | |
| Blood/Bone Marrow - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| CARDIOVASCULAR (ARRHYTHMIA) | | | | | |
| Conduction abnormality/ Atrioventricular heart block | none | asymptomatic, not requiring treatment (e.g., Mobitz type I second-degree AV block, Wenckebach) | symptomatic, but not requiring treatment | symptomatic and requiring treatment (e.g., Mobitz type II second-degree AV block, third-degree AV block) | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Nodal/junctional arrhythmia/dysrhythmia | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Palpitations | none | present | - | - | - |
| Note: Grade palpitations <u>only</u> in the absence of a documented arrhythmia. | | | | | |
| Prolonged QTc interval (QTc >0.48 seconds) | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Sinus bradycardia | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Sinus tachycardia | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment of underlying cause | - |
| Supraventricular arrhythmias (SVT/atrial fibrillation/flutter) | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Syncope (fainting) is graded in the NEUROLOGY category. | | | | | |
| Vasovagal episode | none | - | present without loss of consciousness | present with loss of consciousness | - |

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| Ventricular arrhythmia (PVCs/bigeminy/trigeminy/ventricular tachycardia) | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic and requiring treatment | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| Cardiovascular/ Arrhythmia - Other (Specify, _____) | none | asymptomatic, not requiring treatment | symptomatic, but not requiring treatment | symptomatic, and requiring treatment of underlying cause | life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock) |
| CARDIOVASCULAR (GENERAL) | | | | | |
| Acute vascular leak syndrome | absent | - | symptomatic, but not requiring fluid support | respiratory compromise or requiring fluids | life-threatening; requiring pressor support and/or ventilatory support |
| Cardiac-ischemia/infarction | none | non-specific T - wave flattening or changes | asymptomatic, ST - and T - wave changes suggesting ischemia | angina without evidence of infarction | acute myocardial infarction |
| Cardiac left ventricular function | normal | asymptomatic decline of resting ejection fraction of $\geq 10\%$ but $< 20\%$ of baseline value; shortening fraction $\geq 24\%$ but $< 30\%$ | asymptomatic but resting ejection fraction below LLN for laboratory or decline of resting ejection fraction $\geq 20\%$ of baseline value; $< 24\%$ shortening fraction | CHF responsive to treatment | severe or refractory CHF or requiring intubation |
| CNS cerebrovascular ischemia is graded in the NEUROLOGY category. | | | | | |
| Cardiac troponin I (cTnI) | normal | - | - | levels consistent with unstable angina as defined by the manufacturer | levels consistent with myocardial infarction as defined by the manufacturer |
| Cardiac troponin T (cTnT) | normal | ≥ 0.03 - < 0.05 ng/mL | ≥ 0.05 - < 0.1 ng/mL | ≥ 0.1 - < 0.2 ng/mL | ≥ 0.2 ng/mL |
| Edema | none | asymptomatic, not requiring therapy | symptomatic, requiring therapy | symptomatic edema limiting function and unresponsive to therapy or requiring drug discontinuation | anasarca (severe generalized edema) |
| Hypertension | none | asymptomatic, transient increase by > 20 mmHg (diastolic) or to $> 150/100^*$ if previously WNL; not requiring treatment | recurrent or persistent or symptomatic increase by > 20 mmHg (diastolic) or to $> 150/100^*$ if previously WNL; not requiring treatment | requiring therapy or more intensive therapy than previously | hypertensive crisis |
| *Note: For pediatric patients, use age and sex appropriate normal values $> 95^{\text{th}}$ percentile ULN. | | | | | |

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|--|-------|--|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Hypotension | none | changes, but not requiring therapy (including transient orthostatic hypotension) | requiring brief fluid replacement or other therapy but not hospitalization; no physiologic consequences | requiring therapy and sustained medical attention, but resolves without persisting physiologic consequences | shock (associated with acidemia and impairing vital organ function due to tissue hypoperfusion) |
| <p>Also consider Syncope (fainting).</p> <p>Notes: Angina or MI is graded as Cardiac-ischemia/infarction in the CARDIOVASCULAR (GENERAL) category.</p> <p><i>For pediatric patients, systolic BP 65 mmHg or less in infants up to 1 year old and 70 mmHg or less in children older than 1 year of age, use two successive or three measurements in 24 hours.</i></p> | | | | | |
| Myocarditis | none | - | - | CHF responsive to treatment | severe or refractory CHF |
| Operative injury of vein/artery | none | primary suture repair for injury, but not requiring transfusion | primary suture repair for injury, requiring transfusion | vascular occlusion requiring surgery or bypass for injury | myocardial infarction; resection of organ (e.g., bowel, limb) |
| Pericardial effusion/pericarditis | none | asymptomatic effusion, not requiring treatment | pericarditis (rub, ECG changes, and/or chest pain) | with physiologic consequences | tamponade (drainage or pericardial window required) |
| Peripheral arterial ischemia | none | - | brief episode of ischemia managed non-surgically and without permanent deficit | requiring surgical intervention | life-threatening or with permanent functional deficit (e.g., amputation) |
| Phlebitis (superficial) | none | - | present | - | - |
| <p>Notes: Injection site reaction is graded in the DERMATOLOGY/SKIN category.</p> <p>Thrombosis/embolism is graded in the CARDIOVASCULAR (GENERAL) category.</p> | | | | | |
| Syncope (fainting) is graded in the NEUROLOGY category. | | | | | |
| Thrombosis/embolism | none | - | deep vein thrombosis, not requiring anticoagulant | deep vein thrombosis, requiring anticoagulant therapy | embolic event including pulmonary embolism |
| Vein/artery operative injury is graded as Operative injury of vein/artery in the CARDIOVASCULAR (GENERAL) category. | | | | | |
| Visceral arterial ischemia (non-myocardial) | none | - | brief episode of ischemia managed non-surgically and without permanent deficit | requiring surgical intervention | life-threatening or with permanent functional deficit (e.g., resection of ileum) |
| Cardiovascular/General - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |

| Adverse Event | Grade | | | | |
|--|--------|--|---|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| COAGULATION | | | | | |
| Note: See the HEMORRHAGE category for grading the severity of bleeding events. | | | | | |
| DIC (disseminated intravascular coagulation) Also consider Platelets. Note: Must have increased fibrin split products or D-dimer in order to grade as DIC. | absent | - | - | laboratory findings present with <u>no</u> bleeding | laboratory findings <u>and</u> bleeding |
| Fibrinogen | WNL | ≥0.75 - <1.0 x LLN | ≥0.5 - <0.75 x LLN | ≥0.25 - <0.5 x LLN | <0.25 x LLN |
| For leukemia studies or bone marrow infiltrative/ myelophthitic process, if specified in the protocol. | WNL | <20% decrease from pretreatment value or LLN | ≥20 - <40% decrease from pretreatment value or LLN | ≥40 - <70% decrease from pretreatment value or LLN | <50 mg |
| Partial thromboplastin time (PTT) | WNL | >ULN - ≤1.5 x ULN | >1.5 - ≤2 x ULN | >2 x ULN | - |
| Phlebitis is graded in the CARDIOVASCULAR (GENERAL) category. | | | | | |
| Prothrombin time (PT) | WNL | >ULN - ≤1.5 x ULN | >1.5 - ≤2 x ULN | >2 x ULN | - |
| Thrombosis/embolism is graded in the CARDIOVASCULAR (GENERAL) category. | | | | | |
| Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/TTP or hemolytic uremic syndrome/HUS) For BMT studies, if specified in the protocol. | absent | - | - | laboratory findings present without clinical consequences | laboratory findings and clinical consequences, (e.g., CNS hemorrhage/ bleeding or thrombosis/ embolism or renal failure) requiring therapeutic intervention |
| | - | evidence of RBC destruction (schistocytosis) without clinical consequences | evidence of RBC destruction with elevated creatinine (≤3 x ULN) | evidence of RBC destruction with creatinine (>3 x ULN) not requiring dialysis | evidence of RBC destruction with renal failure requiring dialysis and/or encephalopathy |
| Also consider Hemoglobin, Platelets, Creatinine. Note: Must have microangiopathic changes on blood smear (e.g., schistocytes, helmet cells, red cell fragments). | | | | | |
| Coagulation - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| CONSTITUTIONAL SYMPTOMS | | | | | |
| Fatigue (lethargy, malaise, asthenia) | none | increased fatigue over baseline, but not altering normal activities | moderate (e.g., decrease in performance status by 1 ECOG level <u>or</u> 20% Karnofsky or <i>Lansky</i>) <u>or</u> causing difficulty performing some activities | severe (e.g., decrease in performance status by ≥2 ECOG levels <u>or</u> 40% Karnofsky or <i>Lansky</i>) <u>or</u> loss of ability to perform some activities | bedridden or disabling |
| Note: See Appendix III for performance status scales. | | | | | |

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|--|--------|--|--|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Fever (in the absence of neutropenia, where neutropenia is defined as AGC <1.0 x 10 ⁹ /L) Also consider Allergic reaction/hypersensitivity. Note: The temperature measurements listed above are oral or tympanic. | none | 38.0 - 39.0°C (100.4 - 102.2°F) | 39.1 - 40.0°C (102.3 - 104.0°F) | >40.0°C (>104.0°F) for <24hrs | >40.0°C (>104.0°F) for >24hrs |
| Hot flashes/flushes are graded in the ENDOCRINE category. | | | | | |
| Rigors, chills | none | mild, requiring symptomatic treatment (e.g., blanket) or non-narcotic medication | severe and/or prolonged, requiring narcotic medication | not responsive to narcotic medication | - |
| Sweating (diaphoresis) | normal | mild and occasional | frequent or drenching | - | - |
| Weight gain Also consider Ascites, Edema, Pleural effusion (non-malignant). | <5% | 5 - <10% | 10 - <20% | ≥20% | - |
| Weight gain associated with Veno-Occlusive Disease (VOD) for BMT studies, if specified in the protocol. Also consider Ascites, Edema, Pleural effusion (non-malignant). | <2% | ≥2 - <5% | ≥5 - <10% | ≥10% or as ascites | ≥10% or fluid retention resulting in pulmonary failure |
| Weight loss Also consider Vomiting, Dehydration, Diarrhea. | <5% | 5 - <10% | 10 - <20% | ≥20% | - |
| Constitutional Symptoms - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| DERMATOLOGY/SKIN | | | | | |
| Alopecia | normal | mild hair loss | pronounced hair loss | - | - |
| Bruising (in absence of grade 3 or 4 thrombocytopenia) Note: Bruising resulting from grade 3 or 4 thrombocytopenia is graded as Petechiae/purpura and Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia in the HEMORRHAGE category, <u>not</u> in the DERMATOLOGY/SKIN category. | none | localized or in dependent area | generalized | - | - |
| Dry skin | normal | controlled with emollients | not controlled with emollients | - | - |
| Erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis) | absent | - | scattered, but not generalized eruption | severe or requiring IV fluids (e.g., generalized rash or painful stomatitis) | life-threatening (e.g., exfoliative or ulcerating dermatitis or requiring enteral or parenteral nutritional support) |
| Flushing | absent | present | - | - | - |
| Hand-foot skin reaction | none | skin changes or dermatitis without pain (e.g., erythema, peeling) | skin changes with pain, not interfering with function | skin changes with pain, interfering with function | - |
| Injection site reaction | none | pain or itching or erythema | pain or swelling, with inflammation or phlebitis | ulceration or necrosis that is severe or prolonged, or requiring surgery | - |

| Adverse Event | Grade | | | | |
|---|--------|---|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Nail changes | normal | discoloration or ridging (koilonychia) or pitting | partial or complete loss of nail(s) or pain in nailbeds | - | - |
| Petechiae is graded in the HEMORRHAGE category. | | | | | |
| Photosensitivity | none | painless erythema | painful erythema | erythema with desquamation | - |
| Pigmentation changes (e.g., vitiligo) | none | localized pigmentation changes | generalized pigmentation changes | - | - |
| Pruritus | none | mild or localized, relieved spontaneously or by local measures | intense or widespread, relieved spontaneously or by systemic measures | intense or widespread and poorly controlled despite treatment | - |
| Purpura is graded in the HEMORRHAGE category. | | | | | |
| Radiation dermatitis | none | faint erythema or dry desquamation | moderate to brisk erythema or a patchy moist desquamation, mostly confined to skin folds and creases; moderate edema | confluent moist desquamation ≥ 1.5 cm diameter and not confined to skin folds; pitting edema | skin necrosis or ulceration of full thickness dermis; may include bleeding not induced by minor trauma or abrasion |
| Note: Pain associated with radiation dermatitis is graded separately in the PAIN category as Pain due to radiation. | | | | | |
| Radiation recall reaction (reaction following chemotherapy in the absence of additional radiation therapy that occurs in a previous radiation port) | none | faint erythema or dry desquamation | moderate to brisk erythema or a patchy moist desquamation, mostly confined to skin folds and creases; moderate edema | confluent moist desquamation ≥ 1.5 cm diameter and not confined to skin folds; pitting edema | skin necrosis or ulceration of full thickness dermis; may include bleeding not induced by minor trauma or abrasion |
| Rash/desquamation | none | macular or papular eruption or erythema without associated symptoms | macular or papular eruption or erythema with pruritus or other associated symptoms covering $<50\%$ of body surface or localized desquamation or other lesions covering $<50\%$ of body surface area | symptomatic generalized erythroderma or macular, papular or vesicular eruption or desquamation covering $\geq 50\%$ of body surface area | generalized exfoliative dermatitis or ulcerative dermatitis |
| Also consider Allergic reaction/hypersensitivity. | | | | | |
| Note: Stevens-Johnson syndrome is graded separately as Erythema multiforme in the DERMATOLOGY/SKIN category. | | | | | |
| Rash/dermatitis associated with high-dose chemotherapy or BMT studies. | none | faint erythema or dry desquamation | moderate to brisk erythema or a patchy moist desquamation, mostly confined to skin folds and creases; moderate edema | confluent moist desquamation ≥ 1.5 cm diameter and not confined to skin folds; pitting edema | skin necrosis or ulceration of full thickness dermis; may include spontaneous bleeding not induced by minor trauma or abrasion |
| Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol. | None | macular or papular eruption or erythema covering $<25\%$ of body surface area without associated symptoms | macular or papular eruption or erythema with pruritus or other associated symptoms covering $\geq 25 - <50\%$ of body surface or localized desquamation or other lesions covering $\geq 25 - <50\%$ of body surface area | symptomatic generalized erythroderma or symptomatic macular, papular or vesicular eruption, with bullous formation, or desquamation covering $\geq 50\%$ of body surface area | generalized exfoliative dermatitis or ulcerative dermatitis or bullous formation |
| Also consider Allergic reaction/hypersensitivity. | | | | | |
| Note: Stevens-Johnson syndrome is graded separately as Erythema multiforme in the DERMATOLOGY/SKIN category. | | | | | |

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|---|--------|--|--|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| Urticaria (hives, welts, wheals) | none | requiring no medication | requiring PO or topical treatment or IV medication or steroids for <24 hours | requiring IV medication or steroids for ≥24 hours | - |
| Wound-infectious | none | cellulitis | superficial infection | infection requiring IV antibiotics | necrotizing fasciitis |
| Wound-non-infectious | none | incisional separation | incisional hernia | fascial disruption without evisceration | fascial disruption with evisceration |
| Dermatology/Skin - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| ENDOCRINE | | | | | |
| Cushingoid appearance (e.g., moon face, buffalo hump, centripetal obesity, cutaneous striae) Also consider Hyperglycemia, Hypokalemia. | absent | - | present | - | - |
| Feminization of male | absent | - | - | present | - |
| Gynecomastia | none | mild | pronounced or painful | pronounced or painful and requiring surgery | - |
| Hot flashes/flushes | none | mild or no more than 1 per day | moderate and greater than 1 per day | - | - |
| Hypothyroidism | absent | asymptomatic, TSH elevated, no therapy given | symptomatic or thyroid replacement treatment given | patient hospitalized for manifestations of hypothyroidism | myxedema coma |
| Masculinization of female | absent | - | - | present | - |
| SIADH (syndrome of inappropriate antidiuretic hormone) | absent | - | - | present | - |
| Endocrine - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| GASTROINTESTINAL | | | | | |
| Amylase is graded in the METABOLIC/LABORATORY category. | | | | | |
| Anorexia | none | loss of appetite | oral intake significantly decreased | requiring IV fluids | requiring feeding tube or parenteral nutrition |
| Ascites (non-malignant) | none | asymptomatic | symptomatic, requiring diuretics | symptomatic, requiring therapeutic paracentesis | life-threatening physiologic consequences |
| Colitis | none | - | abdominal pain with mucus and/or blood in stool | abdominal pain, fever, change in bowel habits with ileus or peritoneal signs, and radiographic or biopsy documentation | perforation or requiring surgery or toxic megacolon |
| Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Melena/GI bleeding, Rectal bleeding/hematochezia, Hypotension. | | | | | |
| Constipation | none | requiring stool softener or dietary modification | requiring laxatives | obstipation requiring manual evacuation or enema | obstruction or toxic megacolon |

| Adverse Event | Grade | | | | |
|---|-------|--|--|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| Dehydration | none | dry mucous membranes and/or diminished skin turgor | requiring IV fluid replacement (brief) | requiring IV fluid replacement (sustained) | physiologic consequences requiring intensive care; hemodynamic collapse |
| Also consider Diarrhea, Vomiting, Stomatitis/pharyngitis (oral/pharyngeal mucositis), Hypotension. | | | | | |
| Diarrhea patients without colostomy: | none | increase of <4 stools/day over pre-treatment | increase of 4-6 stools/day, or nocturnal stools | increase of ≥7 stools/day or incontinence; or need for parenteral support for dehydration | physiologic consequences requiring intensive care; or hemodynamic collapse |
| patients with a colostomy: | none | mild increase in loose, watery colostomy output compared with pretreatment | moderate increase in loose, watery colostomy output compared with pretreatment, but not interfering with normal activity | severe increase in loose, watery colostomy output compared with pretreatment, interfering with normal activity | physiologic consequences, requiring intensive care; or hemodynamic collapse |
| Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol. | None | >500 - ≤1000mL of diarrhea/day | >1000 - ≤1500mL of diarrhea/day | >1500mL of diarrhea/day | severe abdominal pain with or without ileus |
| <i>For pediatric BMT studies, if specified in the protocol.</i> | | >5 - ≤10 mL/kg of diarrhea/day | >10 - ≤15 mL/kg of diarrhea/day | >15 mL/kg of diarrhea/day | - |
| Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Pain, Dehydration, Hypotension. | | | | | |
| Duodenal ulcer (requires radiographic or endoscopic documentation) | none | - | requiring medical management or non-surgical treatment | uncontrolled by outpatient medical management; requiring hospitalization | perforation or bleeding, requiring emergency surgery |
| Dyspepsia/heartburn | none | mild | moderate | severe | - |
| Dysphagia, esophagitis, odynophagia (painful swallowing) | none | mild dysphagia, but can eat regular diet | dysphagia, requiring predominantly pureed, soft, or liquid diet | dysphagia, requiring IV hydration | complete obstruction (cannot swallow saliva) requiring enteral or parenteral nutritional support, or perforation |
| Note: If the adverse event is radiation-related, grade <u>either</u> under Dysphagia-esophageal related to radiation <u>or</u> Dysphagia-pharyngeal related to radiation. | | | | | |
| Dysphagia- <u>esophageal</u> related to radiation | none | mild dysphagia, but can eat regular diet | dysphagia, requiring predominantly pureed, soft, or liquid diet | Dysphagia, requiring feeding tube, IV hydration or hyperalimentation | complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation |
| Also consider Pain due to radiation, Mucositis due to radiation. Note: Fistula is graded separately as Fistula-esophageal. | | | | | |
| Dysphagia- <u>pharyngeal</u> related to radiation | none | mild dysphagia, but can eat regular diet | dysphagia, requiring predominantly pureed, soft, or liquid diet | dysphagia, requiring feeding tube, IV hydration or hyperalimentation | complete obstruction (cannot swallow saliva); ulceration with bleeding not induced by minor trauma or abrasion or perforation |
| Also consider Pain due to radiation, Mucositis due to radiation. Note: Fistula is graded separately as Fistula-pharyngeal. | | | | | |
| Fistula-esophageal | none | - | - | present | requiring surgery |
| Fistula-intestinal | none | - | - | present | requiring surgery |

| Adverse Event | Grade | | | | |
|--|--------|------------------------|--|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| Fistula-pharyngeal | none | - | - | present | requiring surgery |
| Fistula-rectal/anal | none | - | - | present | requiring surgery |
| Flatulence | none | mild | moderate | - | - |
| Gastric ulcer (requires radiographic or endoscopic documentation) | none | - | requiring medical management or non- surgical treatment | bleeding without perforation, uncon- trolled by outpatient medical management; requiring hospitalization or surgery | perforation or bleeding, requiring emergency surgery |
| Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia. | | | | | |
| Gastritis | none | - | requiring medical management or non- surgical treatment | uncontrolled by out- patient medical management; requiring hospitalization or surgery | life-threatening bleeding, requiring emergency surgery |
| Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia. | | | | | |
| Hematemesis is graded in the HEMORRHAGE category. | | | | | |
| Hematochezia is graded in the HEMORRHAGE category as Rectal bleeding/hematochezia. | | | | | |
| Ileus (or neuroconstipation) | none | - | intermittent, not requiring intervention | requiring non-surgical intervention | requiring surgery |
| Mouth dryness | normal | mild | moderate | - | - |
| Mucositis Notes: Mucositis <u>not due to radiation</u> is graded in the GASTROINTESTINAL category for specific sites: Colitis, Esophagitis, Gastritis, Stomatitis/pharyngitis (oral/pharyngeal mucositis), and Typhlitis; or the RENAL/GENITOURINARY category for Vaginitis. Radiation-related mucositis is graded as Mucositis due to radiation. | | | | | |
| Mucositis due to radiation | none | erythema of the mucosa | patchy pseudomembra- nous reaction (patches generally ≤1.5 cm in diameter and non- contiguous) | confluent pseudomem- branous reaction (contiguous patches generally >1.5 cm in diameter) | necrosis or deep ulceration; may include bleeding not induced by minor trauma or abrasion |
| Also consider Pain due to radiation. | | | | | |
| Notes: Grade radiation mucositis of the larynx here. | | | | | |
| Dysphagia related to radiation is also graded as <u>either</u> Dysphagia-esophageal related to radiation <u>or</u> Dysphagia-pharyngeal related to radiation, depending on the site of treatment. | | | | | |
| Nausea | none | able to eat | oral intake significantly decreased | no significant intake, requiring IV fluids | - |
| Pancreatitis | none | - | - | abdominal pain with pancreatic enzyme elevation | complicated by shock (acute circulatory failure) |
| Also consider Hypotension. | | | | | |
| Note: Amylase is graded in the METABOLIC/LABORATORY category. | | | | | |
| Pharyngitis is graded in the GASTROINTESTINAL category as Stomatitis/pharyngitis (oral/pharyngeal mucositis). | | | | | |

| Adverse Event | Grade | | | | |
|--|--------|---|---|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Proctitis | none | increased stool frequency, occasional blood-streaked stools or rectal discomfort (including hemorrhoids) not requiring medication | increased stool frequency, bleeding, mucus discharge, or rectal discomfort requiring medication; anal fissure | increased stool frequency/diarrhea requiring parenteral support; rectal bleeding requiring transfusion; or persistent mucus discharge, necessitating pads | perforation, bleeding or necrosis or other life-threatening complication requiring surgical intervention (e.g., colostomy) |
| <p>Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Pain due to radiation.</p> <p>Notes: Fistula is graded separately as Fistula-rectal/anal.</p> <p>Proctitis occurring more than 90 days after the start of radiation therapy is graded in the RTOG/EORTC Late Radiation Morbidity Scoring Scheme. (See Appendix IV)</p> | | | | | |
| Salivary gland changes | none | slightly thickened saliva; may have slightly altered taste (e.g., metallic); additional fluids may be required | thick, ropy, sticky saliva; markedly altered taste; alteration in diet required | - | acute salivary gland necrosis |
| Sense of smell | normal | slightly altered | markedly altered | - | - |
| Stomatitis/pharyngitis (oral/pharyngeal mucositis) | none | painless ulcers, erythema, or mild soreness in the absence of lesions | painful erythema, edema, or ulcers, but can eat or swallow | painful erythema, edema, or ulcers requiring IV hydration | severe ulceration or requires parenteral or enteral nutritional support or prophylactic intubation |
| For BMT studies, if specified in the protocol. | none | painless ulcers, erythema, or mild soreness in the absence of lesions | painful erythema, edema or ulcers but can swallow | painful erythema, edema, or ulcers preventing swallowing or requiring hydration or parenteral (or enteral) nutritional support | severe ulceration requiring prophylactic intubation or resulting in documented aspiration pneumonia |
| <p>Note: Radiation-related mucositis is graded as Mucositis due to radiation.</p> | | | | | |
| Taste disturbance (dysgeusia) | normal | slightly altered | markedly altered | - | - |
| Typhlitis (inflammation of the cecum) | none | - | - | abdominal pain, diarrhea, fever, and radiographic or biopsy documentation | perforation, bleeding or necrosis or other life-threatening complication requiring surgical intervention (e.g., colostomy) |
| <p>Also consider Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Hypotension, Febrile neutropenia.</p> | | | | | |
| Vomiting | none | 1 episode in 24 hours over pretreatment | 2-5 episodes in 24 hours over pretreatment | ≥6 episodes in 24 hours over pretreatment; or need for IV fluids | requiring parenteral nutrition; or physiologic consequences requiring intensive care; hemodynamic collapse |
| <p>Also consider Dehydration.</p> | | | | | |
| <p>Weight gain is graded in the CONSTITUTIONAL SYMPTOMS category.</p> | | | | | |
| <p>Weight loss is graded in the CONSTITUTIONAL SYMPTOMS category.</p> | | | | | |
| Gastrointestinal - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |

| Adverse Event | Grade | | | | |
|---|-------|--------------------------|---------------------------------------|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| HEMORRHAGE | | | | | |
| <p>Notes: Transfusion in this section refers to pRBC infusion.</p> <p>For <u>any</u> bleeding with grade 3 or 4 platelets (<50,000), <u>always</u> grade Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia. Also consider Platelets, Transfusion: pRBCs, and Transfusion: platelets in addition to grading severity by grading the site or type of bleeding.</p> <p>If the site or type of Hemorrhage/bleeding is listed, also use the grading that incorporates the site of bleeding: CNS Hemorrhage/bleeding, Hematuria, Hematemesis, Hemoptysis, Hemorrhage/bleeding with surgery, Melena/lower GI bleeding, Petechiae/purpura (Hemorrhage/bleeding into skin), Rectal bleeding/hematochezia, Vaginal bleeding.</p> <p>If the platelet count is ≥50,000 and the site or type of bleeding is listed, grade the specific site. If the site or type is <u>not</u> listed and the platelet count is ≥50,000, grade Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia and specify the site or type in the OTHER category.</p> | | | | | |
| Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia | none | mild without transfusion | | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| <p>Also consider Platelets, Hemoglobin, Transfusion: platelets, Transfusion: pRBCs, site or type of bleeding. If the site is not listed, grade as Hemorrhage-Other (Specify site, _____).</p> <p>Note: This adverse event must be graded for any bleeding with grade 3 or 4 thrombocytopenia.</p> | | | | | |
| Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia | none | mild without transfusion | | requiring transfusion | catastrophic bleeding requiring major non-elective intervention |
| <p>Also consider Platelets, Hemoglobin, Transfusion: platelets, Transfusion: pRBCs, Hemorrhage - Other (Specify site, _____).</p> <p>Note: Bleeding in the absence of grade 3 or 4 thrombocytopenia is graded here only if the specific site or type of bleeding is not listed elsewhere in the HEMORRHAGE category. Also grade as Other in the HEMORRHAGE category.</p> | | | | | |
| CNS hemorrhage/bleeding | none | - | - | bleeding noted on CT or other scan with no clinical consequences | hemorrhagic stroke or hemorrhagic vascular event (CVA) with neurologic signs and symptoms |
| Epistaxis | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| Hematemesis | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| Hematuria (in the absence of vaginal bleeding) | none | microscopic only | intermittent gross bleeding, no clots | persistent gross bleeding or clots; may require catheterization or instrumentation, or transfusion | open surgery or necrosis or deep bladder ulceration |
| Hemoptysis | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| Hemorrhage/bleeding associated with surgery | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| <p>Note: Expected blood loss at the time of surgery is not graded as an adverse event.</p> | | | | | |
| Melena/GI bleeding | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |

| Adverse Event | Grade | | | | |
|--|--------|--|--|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Petechiae/purpura (hemorrhage/bleeding into skin or mucosa) | none | rare petechiae of skin | petechiae or purpura in dependent areas of skin | generalized petechiae or purpura of skin or petechiae of any mucosal site | - |
| Rectal bleeding/hematochezia | none | mild without transfusion or medication | persistent, requiring medication (e.g., steroid suppositories) and/or break from radiation treatment | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| Vaginal bleeding | none | spotting, requiring <2 pads per day | requiring ≥2 pads per day, but not requiring transfusion | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| Hemorrhage - Other (Specify site, _____) | none | mild without transfusion | - | requiring transfusion | catastrophic bleeding, requiring major non-elective intervention |
| HEPATIC | | | | | |
| Alkaline phosphatase | WNL | >ULN - 2.5 x ULN | >2.5 - 5.0 x ULN | >5.0 - 20.0 x ULN | >20.0 x ULN |
| Bilirubin | WNL | >ULN - 1.5 x ULN | >1.5 - 3.0 x ULN | >3.0 - 10.0 x ULN | >10.0 x ULN |
| Bilirubin associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol. | normal | ≥2 - <3 mg/100 mL | ≥3 - <6 mg/100 mL | ≥6 - <15 mg/100 mL | ≥15 mg/100 mL |
| GGT (γ - Glutamyl transpeptidase) | WNL | >ULN - 2.5 x ULN | >2.5 - 5.0 x ULN | >5.0 - 20.0 x ULN | >20.0 x ULN |
| Hepatic enlargement | absent | - | - | present | - |
| Note: Grade Hepatic enlargement only for treatment related adverse event including Venous Occlusive Disease. | | | | | |
| Hypoalbuminemia | WNL | <LLN - 3 g/dL | ≥2 - <3 g/dL | <2 g/dL | - |
| Liver dysfunction/ failure (clinical) | normal | - | - | asterixis | encephalopathy or coma |
| Portal vein flow | normal | - | decreased portal vein flow | reversal/retrograde portal vein flow | - |
| SGOT (AST) (serum glutamic oxaloacetic transaminase) | WNL | >ULN - 2.5 x ULN | >2.5 - 5.0 x ULN | >5.0 - 20.0 x ULN | >20.0 x ULN |
| SGPT (ALT) (serum glutamic pyruvic transaminase) | WNL | >ULN - 2.5 x ULN | >2.5 - 5.0 x ULN | >5.0 - 20.0 x ULN | >20.0 x ULN |
| Hepatic - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| INFECTION/FEBRILE NEUTROPENIA | | | | | |
| Catheter-related infection | none | mild, no active treatment | moderate, localized infection, requiring local or oral treatment | severe, systemic infection, requiring IV antibiotic or antifungal treatment or hospitalization | life-threatening sepsis (e.g., septic shock) |

| Adverse Event | Grade | | | | |
|--|--------|------------------------------|--|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection) (ANC <1.0 x 10 ⁹ /L, fever ≥38.5°C) Also consider Neutrophils. Note: Hypothermia instead of fever may be associated with neutropenia and is graded here. | none | - | - | Present | Life-threatening sepsis (e.g., septic shock) |
| Infection (documented clinically or microbiologically) with grade 3 or 4 neutropenia (ANC <1.0 x 10 ⁹ /L) Also consider Neutrophils. Notes: Hypothermia instead of fever may be associated with neutropenia and is graded here. In the absence of documented infection grade 3 or 4 neutropenia with fever is graded as Febrile neutropenia. | none | - | - | present | life-threatening sepsis (e.g., septic shock) |
| Infection with unknown ANC Note: This adverse event criterion is used in the rare case when ANC is unknown. | none | - | - | present | life-threatening sepsis (e.g., septic shock) |
| Infection without neutropenia Also consider Neutrophils. | none | mild, no active treatment | moderate, localized infection, requiring local or oral treatment | severe, systemic infection, requiring IV antibiotic or antifungal treatment, or hospitalization | life-threatening sepsis (e.g., septic shock) |
| Wound-infectious is graded in the DERMATOLOGY/SKIN category. | | | | | |
| Infection/Febrile Neutropenia - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| LYMPHATICS | | | | | |
| Lymphatics | normal | mild lymphedema | moderate lymphedema requiring compression; lymphocyst | severe lymphedema limiting function; lymphocyst requiring surgery | severe lymphedema limiting function with ulceration |
| Lymphatics - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| METABOLIC/LABORATORY | | | | | |
| Acidosis (metabolic or respiratory) | normal | pH <normal, but ≥7.3 | - | pH <7.3 | pH <7.3 with life- threatening physiologic consequences |
| Alkalosis (metabolic or respiratory) | normal | pH >normal, but ≤7.5 | - | pH >7.5 | pH >7.5 with life- threatening physiologic consequences |
| Amylase | WNL | >ULN - 1.5 x ULN | >1.5 - 2.0 x ULN | >2.0 - 5.0 x ULN | >5.0 x ULN |
| Bicarbonate | WNL | <LLN - 16 mEq/dL | 11 - 15 mEq/dL | 8 - 10 mEq/dL | <8 mEq/dL |

| Adverse Event | Grade | | | | |
|--|-------|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| CPK (creatine phosphokinase) | WNL | >ULN - 2.5 x ULN | >2.5 - 5 x ULN | >5 - 10 x ULN | >10 x ULN |
| Hypercalcemia | WNL | >ULN - 11.5 mg/dL >ULN - 2.9 mmol/L | >11.5 - 12.5 mg/dL >2.9 - 3.1 mmol/L | >12.5 - 13.5 mg/dL >3.1 - 3.4 mmol/L | >13.5 mg/dL >3.4 mmol/L |
| Hypercholesterolemia | WNL | >ULN - 300 mg/dL >ULN - 7.75 mmol/L | >300 - 400 mg/dL >7.75 - 10.34 mmol/L | >400 - 500 mg/dL >10.34 - 12.92 mmol/L | >500 mg/dL >12.92 mmol/L |
| Hyperglycemia | WNL | >ULN - 160 mg/dL >ULN - 8.9 mmol/L | >160 - 250 mg/dL >8.9 - 13.9 mmol/L | >250 - 500 mg/dL >13.9 - 27.8 mmol/L | >500 mg/dL >27.8 mmol/L or acidosis |
| Hyperkalemia | WNL | >ULN - 5.5 mmol/L | >5.5 - 6.0 mmol/L | >6.0 - 7.0 mmol/L | >7.0 mmol/L |
| Hypermagnesemia | WNL | >ULN - 3.0 mg/dL >ULN - 1.23 mmol/L | - | >3.0 - 8.0 mg/dL >1.23 - 3.30 mmol/L | >8.0 mg/dL >3.30 mmol/L |
| Hypernatremia | WNL | >ULN - 150 mmol/L | >150 - 155 mmol/L | >155 - 160 mmol/L | >160 mmol/L |
| Hypertriglyceridemia | WNL | >ULN - 2.5 x ULN | >2.5 - 5.0 x ULN | >5.0 - 10 x ULN | >10 x ULN |
| Hyperuricemia | WNL | >ULN - ≤10 mg/dL ≤0.59 mmol/L without physiologic consequences | - | >ULN - ≤10 mg/dL ≤0.59 mmol/L with physiologic consequences | >10 mg/dL >0.59 mmol/L |
| Also consider Tumor lysis syndrome, Renal failure, Creatinine, Hyperkalemia. | | | | | |
| Hypocalcemia | WNL | <LLN - 8.0 mg/dL <LLN - 2.0 mmol/L | 7.0 - <8.0 mg/dL 1.75 - <2.0 mmol/L | 6.0 - <7.0 mg/dL 1.5 - <1.75 mmol/L | <6.0 mg/dL <1.5 mmol/L |
| Hypoglycemia | WNL | <LLN - 55 mg/dL <LLN - 3.0 mmol/L | 40 - <55 mg/dL 2.2 - <3.0 mmol/L | 30 - <40 mg/dL 1.7 - <2.2 mmol/L | <30 mg/dL <1.7 mmol/L |
| Hypokalemia | WNL | <LLN - 3.0 mmol/L | - | 2.5 - <3.0 mmol/L | <2.5 mmol/L |
| Hypomagnesemia | WNL | <LLN - 1.2 mg/dL <LLN - 0.5 mmol/L | 0.9 - <1.2 mg/dL 0.4 - <0.5 mmol/L | 0.7 - <0.9 mg/dL 0.3 - <0.4 mmol/L | <0.7 mg/dL <0.3 mmol/L |
| Hyponatremia | WNL | <LLN - 130 mmol/L | - | 120 - <130 mmol/L | <120 mmol/L |
| Hypophosphatemia | WNL | <LLN - 2.5 mg/dL <LLN - 0.8 mmol/L | ≥2.0 - <2.5 mg/dL ≥0.6 - <0.8 mmol/L | ≥1.0 - <2.0 mg/dL ≥0.3 - <0.6 mmol/L | <1.0 mg/dL <0.3 mmol/L |
| Hypothyroidism is graded in the ENDOCRINE category. | | | | | |
| Lipase | WNL | >ULN - 1.5 x ULN | >1.5 - 2.0 x ULN | >2.0 - 5.0 x ULN | >5.0 x ULN |
| Metabolic/Laboratory - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| MUSCULOSKELETAL | | | | | |
| Arthralgia is graded in the PAIN category. | | | | | |
| Arthritis | none | mild pain with inflammation, erythema or joint swelling but not interfering with function | moderate pain with inflammation, erythema, or joint swelling interfering with function, but not interfering with activities of daily living | severe pain with inflammation, erythema, or joint swelling and interfering with activities of daily living | disabling |

| Adverse Event | Grade | | | | |
|--|-------------|---|---|---|---|
| | 0 | 1 | 2 | 3 | 4 |
| Muscle weakness (not due to neuropathy) | normal | asymptomatic with weakness on physical exam | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | bedridden or disabling |
| Myalgia [tenderness or pain in muscles] is graded in the PAIN category. | | | | | |
| Myositis (inflammation/damage of muscle) | none | mild pain, not interfering with function | pain interfering with function, but not interfering with activities of daily living | pain interfering with function and interfering with activities of daily living | bedridden or disabling |
| Also consider CPK. Note: Myositis implies muscle damage (i.e., elevated CPK). | | | | | |
| Osteonecrosis (avascular necrosis) | none | asymptomatic and detected by imaging only | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | symptomatic; or disabling |
| Musculoskeletal - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| NEUROLOGY | | | | | |
| Aphasia, receptive and/or expressive, is graded under Speech impairment in the NEUROLOGY category. | | | | | |
| Arachnoiditis/meningismus/radiculitis | absent | mild pain not interfering with function | moderate pain interfering with function, but not interfering with activities of daily living | severe pain interfering with activities of daily living | unable to function or perform activities of daily living; bedridden; paraplegia |
| Also consider Headache, Vomiting, Fever. | | | | | |
| Ataxia (incoordination) | normal | asymptomatic but abnormal on physical exam, and not interfering with function | mild symptoms interfering with function, but not interfering with activities of daily living | moderate symptoms interfering with activities of daily living | bedridden or disabling |
| CNS cerebrovascular ischemia | none | - | - | transient ischemic event or attack (TIA) | permanent event (e.g., cerebral vascular accident) |
| CNS hemorrhage/bleeding is graded in the HEMORRHAGE category. | | | | | |
| <i>Cognitive disturbance/learning problems</i> | <i>none</i> | <i>cognitive disability; not interfering with work/school performance; preservation of intelligence</i> | <i>cognitive disability; interfering with work/school performance; decline of 1 SD (Standard Deviation) or loss of developmental milestones</i> | <i>cognitive disability; resulting in significant impairment of work/school performance; cognitive decline >2 SD</i> | <i>inability to work/frank mental retardation</i> |

| Adverse Event | Grade | | | | |
|--|---------------|--|---|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| Confusion | normal | confusion or disorientation or attention deficit of brief duration; resolves spontaneously with no sequelae | confusion or disorientation or attention deficit interfering with function, but not interfering with activities of daily living | confusion or delirium interfering with activities of daily living | harmful to others or self; requiring hospitalization |
| Cranial neuropathy is graded in the NEUROLOGY category as Neuropathy-cranial. | | | | | |
| Delusions | normal | - | - | present | toxic psychosis |
| Depressed level of consciousness | normal | somnolence or sedation not interfering with function | somnolence or sedation interfering with function, but not interfering with activities of daily living | obtundation or stupor; difficult to arouse; interfering with activities of daily living | coma |
| Note: Syncope (fainting) is graded in the NEUROLOGY category. | | | | | |
| Dizziness/lightheadedness | none | not interfering with function | interfering with function, but not interfering with activities of daily living | interfering with activities of daily living | bedridden or disabling |
| Dysphasia, receptive and/or expressive, is graded under Speech impairment in the NEUROLOGY category. | | | | | |
| Extrapyramidal/ involuntary movement/ restlessness | none | mild involuntary movements not interfering with function | moderate involuntary movements interfering with function, but not interfering with activities of daily living | severe involuntary movements or torticollis interfering with activities of daily living | bedridden or disabling |
| Hallucinations | normal | - | - | present | toxic psychosis |
| Headache is graded in the PAIN category. | | | | | |
| Insomnia | normal | occasional difficulty sleeping not interfering with function | difficulty sleeping interfering with function, but not interfering with activities of daily living | frequent difficulty sleeping, interfering with activities of daily living | - |
| Note: This adverse event is graded when insomnia is related to treatment. If pain or other symptoms interfere with sleep do NOT grade as insomnia. | | | | | |
| <i>Irritability (children <3 years of age)</i> | <i>normal</i> | <i>mild; easily consolable</i> | <i>moderate; requiring increased attention</i> | <i>severe; inconsolable</i> | <i>-</i> |
| Leukoencephalopathy associated radiological findings | none | mild increase in SAS (subarachnoid space) and/or mild ventriculomegaly; and/or small (+/- multiple) focal T2 hyperintensities, involving periventricular white matter or <1/3 of susceptible areas of cerebrum | moderate increase in SAS; and/or moderate ventriculomegaly; and/or focal T2 hyperintensities extending into centrum ovale; or involving 1/3 to 2/3 of susceptible areas of cerebrum | severe increase in SAS; severe ventriculomegaly; near total white matter T2 hyperintensities or diffuse low attenuation (CT); focal white matter necrosis (cystic) | severe increase in SAS; severe ventriculomegaly; diffuse low attenuation with calcification (CT); diffuse white matter necrosis (MRI) |
| Memory loss | normal | memory loss not interfering with function | memory loss interfering with function, but not interfering with activities of daily living | memory loss interfering with activities of daily living | amnesia |

| Adverse Event | Grade | | | | |
|---|--------|--|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Mood alteration-anxiety, agitation | normal | mild mood alteration not interfering with function | moderate mood alteration interfering with function, but not interfering with activities of daily living | severe mood alteration interfering with activities of daily living | suicidal ideation or danger to self |
| Mood alteration-depression | normal | mild mood alteration not interfering with function | moderate mood alteration interfering with function, but not interfering with activities of daily living | severe mood alteration interfering with activities of daily living | suicidal ideation or danger to self |
| Mood alteration-euphoria | normal | mild mood alteration not interfering with function | moderate mood alteration interfering with function, but not interfering with activities of daily living | severe mood alteration interfering with activities of daily living | danger to self |
| Neuropathic pain is graded in the PAIN category. | | | | | |
| Neuropathy-cranial | absent | - | present, not interfering with activities of daily living | present, interfering with activities of daily living | life-threatening, disabling |
| Neuropathy-motor | normal | subjective weakness but no objective findings | mild objective weakness interfering with function, but not interfering with activities of daily living | objective weakness interfering with activities of daily living | paralysis |
| Neuropathy-sensory | normal | loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function | objective sensory loss or paresthesia (including tingling), interfering with function, but not interfering with activities of daily living | sensory loss or paresthesia interfering with activities of daily living | permanent sensory loss that interferes with function |
| Nystagmus | absent | present | - | - | - |
| Also consider Vision-double vision. | | | | | |
| Personality/behavioral | normal | change, but not disruptive to patient or family | disruptive to patient or family | disruptive to patient and family; requiring mental health intervention | harmful to others or self; requiring hospitalization |
| Pyramidal tract dysfunction (e.g., ↑ tone, hyperreflexia, positive Babinski, ↓ fine motor coordination) | normal | asymptomatic with abnormality on physical examination | symptomatic or interfering with function but not interfering with activities of daily living | interfering with activities of daily living | bedridden or disabling; paralysis |
| Seizure(s) | none | - | seizure(s) self-limited and consciousness is preserved | seizure(s) in which consciousness is altered | seizures of any type which are prolonged, repetitive, or difficult to control (e.g., status epilepticus, intractable epilepsy) |
| Speech impairment (e.g., dysphasia or aphasia) | normal | - | awareness of receptive or expressive dysphasia, not impairing ability to communicate | receptive or expressive dysphasia, impairing ability to communicate | inability to communicate |
| Syncope (fainting) | absent | - | - | present | - |
| Also consider CARDIOVASCULAR (ARRHYTHMIA), Vasovagal episode, CNS cerebrovascular ischemia. | | | | | |

| Adverse Event | Grade | | | | |
|--|--------|--|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Tremor | none | mild and brief or intermittent but not interfering with function | moderate tremor interfering with function, but not interfering with activities of daily living | severe tremor interfering with activities of daily living | - |
| Vertigo | none | not interfering with function | interfering with function, but not interfering with activities of daily living | interfering with activities of daily living | bedridden or disabling |
| Neurology - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| OCULAR/VISUAL | | | | | |
| Cataract | none | asymptomatic | symptomatic, partial visual loss | symptomatic, visual loss requiring treatment or interfering with function | - |
| Conjunctivitis | none | abnormal ophthalmologic changes, but asymptomatic or symptomatic without visual impairment (i.e., pain and irritation) | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |
| Dry eye | normal | mild, not requiring treatment | moderate or requiring artificial tears | - | - |
| Glaucoma | none | increase in intraocular pressure but no visual loss | increase in intraocular pressure with retinal changes | visual impairment | unilateral or bilateral loss of vision (blindness) |
| Keratitis (corneal inflammation/ corneal ulceration) | none | abnormal ophthalmologic changes but asymptomatic or symptomatic without visual impairment (i.e., pain and irritation) | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | unilateral or bilateral loss of vision (blindness) |
| Tearing (watery eyes) | none | mild: not interfering with function | moderate: interfering with function, but not interfering with activities of daily living | interfering with activities of daily living | - |
| Vision-blurred vision | normal | - | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |
| Vision-double vision (diplopia) | normal | - | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |
| Vision-flashing lights/floaters | normal | mild, not interfering with function | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |

| Adverse Event | Grade | | | | |
|---|--------|--|--|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Vision-night blindness (nyctalopia) | normal | abnormal electro-retinography but asymptomatic | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |
| Vision-photophobia | normal | - | symptomatic and interfering with function, but not interfering with activities of daily living | symptomatic and interfering with activities of daily living | - |
| Ocular/Visual - Other (Specify, _____) | normal | mild | moderate | severe | unilateral or bilateral loss of vision (blindness) |
| PAIN | | | | | |
| Abdominal pain or cramping | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Arthralgia (joint pain) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Arthritis (joint pain with clinical signs of inflammation) is graded in the MUSCULOSKELETAL category. | | | | | |
| Bone pain | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Chest pain (non-cardiac and non-pleuritic) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Dysmenorrhea | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Dyspareunia | none | mild pain not interfering with function | moderate pain interfering with sexual activity | severe pain preventing sexual activity | - |
| Dysuria is graded in the RENAL/GENITOURINARY category. | | | | | |
| Earache (otalgia) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Headache | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |

| Adverse Event | Grade | | | | |
|---|--------|---|--|--|----------------------|
| | 0 | 1 | 2 | 3 | 4 |
| Hepatic pain | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Myalgia (muscle pain) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Neuropathic pain (e.g., jaw pain, neurologic pain, phantom limb pain, post-infectious neuralgia, or painful neuropathies) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Pain due to radiation | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Pelvic pain | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Pleuritic pain | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Rectal or perirectal pain (proctalgia) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Tumor pain (onset or exacerbation of tumor pain due to treatment) | none | mild pain not interfering with function | moderate pain: pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain: pain or analgesics severely interfering with activities of daily living | disabling |
| Tumor flare is graded in the SYNDROME category. | | | | | |
| Pain - Other (Specify, _____) | none | mild | moderate | severe | disabling |
| PULMONARY | | | | | |
| Adult Respiratory Distress Syndrome (ARDS) | absent | - | - | - | present |
| Apnea | none | - | - | present | requiring intubation |

| Adverse Event | Grade | | | | |
|---|--------------------------------------|---|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Carbon monoxide diffusion capacity (DL _{CO}) | ≥90% of pretreatment or normal value | ≥75 - <90% of pretreatment or normal value | ≥50 - <75% of pretreatment or normal value | ≥25 - <50% of pretreatment or normal value | <25% of pretreatment or normal value |
| Cough | absent | mild, relieved by non-prescription medication | requiring narcotic antitussive | severe cough or coughing spasms, poorly controlled or unresponsive to treatment | - |
| Dyspnea (shortness of breath) | normal | - | dyspnea on exertion | dyspnea at normal level of activity | dyspnea at rest or requiring ventilator support |
| FEV ₁ | ≥90% of pretreatment or normal value | ≥75 - <90% of pretreatment or normal value | ≥50 - <75% of pretreatment or normal value | ≥25 - <50% of pretreatment or normal value | <25% of pretreatment or normal value |
| Hiccoughs (hiccups, singultus) | none | mild, not requiring treatment | moderate, requiring treatment | severe, prolonged, and refractory to treatment | - |
| Hypoxia | normal | - | decreased O ₂ saturation with exercise | decreased O ₂ saturation at rest, requiring supplemental oxygen | decreased O ₂ saturation, requiring pressure support (CPAP) or assisted ventilation |
| Pleural effusion (non-malignant) | none | asymptomatic and not requiring treatment | symptomatic, requiring diuretics | symptomatic, requiring O ₂ or therapeutic thoracentesis | life-threatening (e.g., requiring intubation) |
| Pleuritic pain is graded in the PAIN category. | | | | | |
| Pneumonitis/pulmonary infiltrates | none | radiographic changes but asymptomatic or symptoms not requiring steroids | radiographic changes and requiring steroids or diuretics | radiographic changes and requiring oxygen | radiographic changes and requiring assisted ventilation |
| Pneumothorax | none | no intervention required | chest tube required | sclerosis or surgery required | life-threatening |
| Pulmonary embolism is graded as Thrombosis/embolism in the CARDIOVASCULAR (GENERAL) category. | | | | | |
| Pulmonary fibrosis | none | radiographic changes, but asymptomatic or symptoms not requiring steroids | requiring steroids or diuretics | requiring oxygen | requiring assisted ventilation |
| Note: Radiation-related pulmonary fibrosis is graded in the RTOG/EORTC Late Radiation Morbidity Scoring Scheme-Lung. (See Appendix IV) | | | | | |
| Voice changes/stridor/larynx (e.g., hoarseness, loss of voice, laryngitis) | normal | mild or intermittent hoarseness | persistent hoarseness, but able to vocalize; may have mild to moderate edema | whispered speech, not able to vocalize; may have marked edema | marked dyspnea/stridor requiring tracheostomy or intubation |
| Notes: Cough from radiation is graded as cough in the PULMONARY category. Radiation-related hemoptysis from larynx/pharynx is graded as Grade 4 Mucositis due to radiation in the GASTROINTESTINAL category. Radiation-related hemoptysis from the thoracic cavity is graded as Grade 4 Hemoptysis in the HEMORRHAGE category. | | | | | |
| Pulmonary - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |

| Adverse Event | Grade | | | | |
|---|----------------------------|--|--|--|---|
| | 0 | 1 | 2 | 3 | 4 |
| RENAL/GENITOURINARY | | | | | |
| Bladder spasms | absent | mild symptoms, not requiring intervention | symptoms requiring antispasmodic | severe symptoms requiring narcotic | - |
| Creatinine | WNL | >ULN - 1.5 x ULN | >1.5 - 3.0 x ULN | >3.0 - 6.0 x ULN | >6.0 x ULN |
| <i>Note: Adjust to age-appropriate levels for pediatric patients.</i> | | | | | |
| Dysuria (painful urination) | none | mild symptoms requiring no intervention | symptoms relieved with therapy | symptoms not relieved despite therapy | - |
| Fistula or GU fistula (e.g., vaginal, vesicovaginal) | none | - | - | requiring intervention | requiring surgery |
| Hemoglobinuria | - | present | - | - | - |
| Hematuria (in the absence of vaginal bleeding) is graded in the HEMORRHAGE category. | | | | | |
| Incontinence | none | with coughing, sneezing, etc. | spontaneous, some control | no control (in the absence of fistula) | - |
| Operative injury to bladder and/or ureter | none | - | injury of bladder with primary repair | sepsis, fistula, or obstruction requiring secondary surgery; loss of one kidney; injury requiring anastomosis or re-implantation | septic obstruction of both kidneys or vesicovaginal fistula requiring diversion |
| Proteinuria | normal or <0.15 g/24 hours | 1+ or 0.15 - 1.0 g/24 hours | 2+ to 3+ or 1.0 - 3.5 g/24 hours | 4+ or >3.5 g/24 hours | nephrotic syndrome |
| <i>Note: If there is an inconsistency between absolute value and dip stick reading, use the absolute value for grading.</i> | | | | | |
| Renal failure | none | - | - | requiring dialysis, but reversible | requiring dialysis and irreversible |
| Ureteral obstruction | none | unilateral, not requiring surgery | - | bilateral, not requiring surgery | stent, nephrostomy tube, or surgery |
| Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) | none | asymptomatic, not requiring treatment | mild, reversible and manageable with oral replacement | reversible but requiring IV replacement | irreversible, requiring continued replacement |
| Also consider Acidosis, Bicarbonate, Hypocalcemia, Hypophosphatemia. | | | | | |
| Urinary frequency/urgency | normal | increase in frequency or nocturia up to 2 x normal | increase >2 x normal but <hourly | hourly or more with urgency, or requiring catheter | - |
| Urinary retention | normal | hesitancy or dribbling, but no significant residual urine; retention occurring during the immediate postoperative period | hesitancy requiring medication or occasional in/out catheterization (<4 x per week), or operative bladder atony requiring indwelling catheter beyond immediate postoperative period but for <6 weeks | requiring frequent in/out catheterization (≥4 x per week) or urological intervention (e.g., TURP, suprapubic tube, urethrotomy) | bladder rupture |

| Adverse Event | Grade | | | | |
|---|--------|--|--|--|-------------------------------|
| | 0 | 1 | 2 | 3 | 4 |
| Urine color change (not related to other dietary or physiologic cause e.g., bilirubin, concentrated urine, hematuria) | normal | asymptomatic, change in urine color | - | - | - |
| Vaginal bleeding is graded in the HEMORRHAGE category. | | | | | |
| Vaginitis (not due to infection) | none | mild, not requiring treatment | moderate, relieved with treatment | severe, not relieved with treatment, or ulceration not requiring surgery | ulceration requiring surgery |
| Renal/Genitourinary - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |
| SECONDARY MALIGNANCY | | | | | |
| Secondary Malignancy - Other (Specify type, _____) excludes metastasis from initial primary | none | - | - | - | present |
| SEXUAL/REPRODUCTIVE FUNCTION | | | | | |
| Dyspareunia is graded in the PAIN category. | | | | | |
| Dysmenorrhea is graded in the PAIN category. | | | | | |
| Erectile impotence | normal | mild (erections impaired but satisfactory) | moderate (erections impaired, unsatisfactory for intercourse) | no erections | - |
| Female sterility | normal | - | - | sterile | - |
| Feminization of male is graded in the ENDOCRINE category. | | | | | |
| Irregular menses (change from baseline) | normal | occasionally irregular or lengthened interval, but continuing menstrual cycles | very irregular, but continuing menstrual cycles | persistent amenorrhea | - |
| Libido | normal | decrease in interest | severe loss of interest | - | - |
| Male infertility | - | - | oligospermia (low sperm count) | azoospermia (no sperm) | - |
| Masculinization of female is graded in the ENDOCRINE category. | | | | | |
| Vaginal dryness | normal | mild | requiring treatment and/or interfering with sexual function, dyspareunia | - | - |
| Sexual/Reproductive Function - Other (Specify, _____) | none | mild | moderate | severe | disabling |
| SYNDROMES (not included in previous categories) | | | | | |
| Acute vascular leak syndrome is graded in the CARDIOVASCULAR (GENERAL) category. | | | | | |
| ARDS (Adult Respiratory Distress Syndrome) is graded in the PULMONARY category. | | | | | |

| Adverse Event | Grade | | | | |
|--|--------|---|--|---|-------------------------------|
| | 0 | 1 | 2 | 3 | 4 |
| Autoimmune reactions are graded in the ALLERGY/IMMUNOLOGY category. | | | | | |
| DIC (disseminated intravascular coagulation) is graded in the COAGULATION category. | | | | | |
| Fanconi's syndrome is graded as Urinary electrolyte wasting in the RENAL/GENITOURINARY category. | | | | | |
| Renal tubular acidosis is graded as Urinary electrolyte wasting in the RENAL/GENITOURINARY category. | | | | | |
| Stevens-Johnson syndrome (erythema multiforme) is graded in the DERMATOLOGY/SKIN category. | | | | | |
| SIADH (syndrome of inappropriate antidiuretic hormone) is graded in the ENDOCRINE category. | | | | | |
| Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/TTP or hemolytic uremic syndrome/HUS) is graded in the COAGULATION category. | | | | | |
| Tumor flare | none | mild pain not interfering with function | moderate pain; pain or analgesics interfering with function, but not interfering with activities of daily living | severe pain; pain or analgesics interfering with function and interfering with activities of daily living | Disabling |
| Also consider Hypercalcemia. | | | | | |
| Note: Tumor flare is characterized by a constellation of symptoms and signs in direct relation to initiation of therapy (e.g., anti-estrogens/androgens or additional hormones). The symptoms/signs include tumor pain, inflammation of visible tumor, hypercalcemia, diffuse bone pain, and other electrolyte disturbances. | | | | | |
| Tumor lysis syndrome | absent | - | - | present | - |
| Also consider Hyperkalemia, Creatinine. | | | | | |
| Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) is graded in the RENAL/GENITOURINARY category. | | | | | |
| Syndromes - Other (Specify, _____) | none | mild | moderate | severe | life-threatening or disabling |

Appendix I

Adverse Event Module

To be implemented at the request of the study sponsor or principal investigator in the protocol or by protocol amendment when more detailed information is considered pertinent.

| | | |
|--|--------------------|-----------------|
| Adverse Event: | Date of Treatment: | Course Number: |
| Date of onset: | | Grade at onset: |
| Date of first change in grade: | | Grade: |
| Date of next change in grade: | | Grade: |
| Date of next change in grade: | | Grade: |
| Date of next change in grade: | | Grade: |
| Date of next change in grade: | | Grade: |
| Did adverse event resolve? Yes _____ No _____ | | |
| If so, date of resolution of adverse event: | | |
| Date of last observation (if prior to recovery): | | |
| Reason(s) observations stopped (if prior to recovery): | | |
| Was patient retreated? Yes _____ No _____ | | |
| If yes, was treatment delayed for recovery? Yes _____ No _____ | | |
| Date of next treatment? | | |
| Dose reduced for next treatment? Yes _____ No _____ | | |

Additional Comments:

If module is being activated for new adverse event not currently in CTC, please provide definitions for adverse event grading:

Grade 0 = _____

Grade 1 = _____

Grade 2 = _____

Grade 3 = _____

Grade 4 = _____

Appendix II Infection Module

To be implemented at the request of the study sponsor or principal investigator in the protocol or by protocol amendment when more detailed information is considered pertinent.

1. Use the Common Toxicity Criteria definitions to grade the severity of the infection.
2. Specify type of infection from the following (CHOOSE ONE):
BACTERIAL FUNGAL PROTOZOAL VIRAL UNKNOWN

3. Specify site of infection from the following (CHOOSE ALL THAT APPLY):

BLOOD CULTURE POSITIVE
BONE INFECTION
CATHETER (intravenous)
CATHETER (intravenous), tunnel infection
CENTRAL NERVOUS SYSTEM INFECTION
EAR INFECTION
EYE INFECTION
GASTROINTESTINAL INFECTION
ORAL INFECTION
PNEUMONIA
SKIN INFECTION
UPPER RESPIRATORY INFECTION
URINARY TRACT INFECTION
VAGINAL INFECTION
INFECTION, not otherwise specified (Specify site, _____)

4. Specify organism, if known: _____.
5. Prophylactic antibiotic, antifungal, or antiviral therapy administration

Yes _____ No _____

If prophylaxis was given prior to infection, please specify below:

Antibiotic prophylaxis _____

Antifungal prophylaxis _____

Antiviral prophylaxis _____

Other prophylaxis _____

Appendix III Performance Status Scales/Scores

| PERFORMANCE STATUS CRITERIA | | | | | |
|--|---|------------------|--|----------------|--|
| <i>Karnofsky and Lansky performance scores are intended to be multiples of 10.</i> | | | | | |
| ECOG (Zubrod) | | Karnofsky | | Lansky* | |
| Score | Description | Score | Description | Score | Description |
| 0 | Fully active, able to carry on all pre-disease performance without restriction. | 100 | Normal, no complaints, no evidence of disease. | 100 | Fully active, normal. |
| | | 90 | Able to carry on normal activity; minor signs or symptoms of disease. | 90 | Minor restrictions in physically strenuous activity. |
| 1 | Restricted in physically strenuous activity but ambulatory and able to carry out work of a light or sedentary nature, e.g., light housework, office work. | 80 | Normal activity with effort; some signs or symptoms of disease. | 80 | Active, but tires more quickly |
| | | 70 | Cares for self, unable to carry on normal activity or do active work. | 70 | Both greater restriction of and less time spent in play activity. |
| 2 | Ambulatory and capable of all selfcare but unable to carry out any work activities. Up and about more than 50% of waking hours. | 60 | Requires occasional assistance, but is able to care for most of his/her needs. | 60 | Up and around, but minimal active play; keeps busy with quieter activities. |
| | | 50 | Requires considerable assistance and frequent medical care. | 50 | Gets dressed, but lies around much of the day; no active play; able to participate in all quiet play and activities. |
| 3 | Capable of only limited selfcare, confined to bed or chair more than 50% of waking hours. | 40 | Disabled, requires special care and assistance. | 40 | Mostly in bed; participates in quiet activities. |
| | | 30 | Severely disabled, hospitalization indicated. Death not imminent. | 30 | In bed; needs assistance even for quiet play. |
| 4 | Completely disabled. Cannot carry on any selfcare. Totally confined to bed or chair. | 20 | Very sick, hospitalization indicated. Death not imminent. | 20 | Often sleeping; play entirely limited to very passive activities. |
| | | 10 | Moribund, fatal processes progressing rapidly. | 10 | No play; does not get out of bed. |

*The conversion of the Lansky to ECOG scales is intended for NCI reporting purposes only.

Appendix IV

RTOG/EORTC Late Radiation Morbidity Scoring Scheme

Use for adverse event occurring greater than 90 days after radiation therapy.

| Adverse Event | Grade | | | | |
|---|-------------------------|--|--|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Bladder- Late RT Morbidity Scoring | No change from baseline | Slight epithelial atrophy/minor telangiectasia (microscopic hematuria) | Moderate frequency/generalized telangiectasia/intermittent macroscopic hematuria | Severe frequency and dysuria/severe generalized telangiectasia (often with petechiae); frequent hematuria; reduction in bladder capacity (<150 mL) | Necrosis/contracted bladder (capacity <100 mL)/severe hemorrhagic cystitis |
| Bone- Late RT Morbidity Scoring | No change from baseline | Asymptomatic; no growth retardation; reduced bone density | Moderate pain or tenderness; growth retardation; irregular bone sclerosis | Severe pain or tenderness; complete arrest of bone growth; dense bone sclerosis | Necrosis/spontaneous fracture |
| Brain- Late RT Morbidity Scoring | No change from baseline | Mild headache; slight lethargy | Moderate headache; great lethargy | Severe headaches; severe CNS dysfunction (partial loss of power or dyskinesia) | Seizures or paralysis; coma |
| Esophagus- Late RT Morbidity Scoring | No change from baseline | Mild fibrosis; slight difficulty in swallowing solids; no pain on swallowing | Unable to take solid food normally; swallowing semi-solid food; dilation may be indicated | Severe fibrosis; able to swallow only liquids; may have pain on swallowing; dilation required | Necrosis/perforation; fistula |
| Eye- Late RT Morbidity Scoring | No change from baseline | Asymptomatic cataract; minor corneal ulceration or keratitis | Symptomatic cataract; moderate corneal ulceration; minor retinopathy or glaucoma | Severe keratitis; severe retinopathy or detachment; severe glaucoma | Panophthalmitis; blindness |
| Heart- Late RT Morbidity Scoring | No change from baseline | Asymptomatic or mild symptoms; transient T wave inversion and ST changes; sinus tachycardia >110 (at rest) | Moderate angina on effort; mild pericarditis; normal heart size; persistent abnormal T wave and ST changes; low QRS | Severe angina; pericardial effusion; constrictive pericarditis; moderate heart failure; cardiac enlargement; EKG abnormalities | Tamponade/severe heart failure/severe constrictive pericarditis |
| Joint- Late RT Morbidity Scoring | No change from baseline | Mild joint stiffness; slight limitation of movement | Moderate stiffness; intermittent or moderate joint pain; moderate limitation of movement | Severe joint stiffness; pain with severe limitation of movement | Necrosis/complete fixation |
| Kidney- Late RT Morbidity Scoring | No change from baseline | Transient albuminuria; no hypertension; mild impairment of renal function; urea 25 - 35 mg%; creatinine 1.5 - 2.0 mg%; creatinine clearance >75% | Persistent moderate albuminuria (2+); mild hypertension; no related anemia; moderate impairment of renal function; urea >36 - 60 mg%; creatinine clearance >50 - 74% | Severe albuminuria; severe hypertension; persistent anemia (<10 g%); severe renal failure; urea >60 mg%; creatinine >4 mg%; creatinine clearance <50% | Malignant hypertension; uremic coma/urea >100% |
| Larynx- Late RT Morbidity Scoring | No change from baseline | Hoarseness; slight arytenoid edema | Moderate arytenoid edema; chondritis | Severe edema; severe chondritis | Necrosis |

Appendix IV (continued)

RTOG/EORTC Late Radiation Morbidity Scoring Scheme

Use for adverse event occurring greater than 90 days after radiation therapy.

| Adverse Event | Grade | | | | |
|---|-------------------------|---|---|---|--|
| | 0 | 1 | 2 | 3 | 4 |
| Liver- Late RT Morbidity Scoring | No change from baseline | Mild lassitude; nausea; dyspepsia; slightly abnormal liver function | Moderate symptoms; some abnormal liver function tests; serum albumin normal | Disabling hepatic insufficiency; liver function tests grossly abnormal; low albumin; edema or ascites | Necrosis/hepatic coma or encephalopathy |
| Lung- Late RT Morbidity Scoring | No change from baseline | Asymptomatic or mild symptoms (dry cough); slight radiographic appearances | Moderate symptomatic fibrosis or pneumonitis (severe cough); low grade fever; patchy radiographic appearances | Severe symptomatic fibrosis or pneumonitis; dense radiographic changes | Severe respiratory insufficiency/continuous O ₂ /assisted ventilation |
| Mucous membrane- Late RT Morbidity Scoring | No change from baseline | Slight atrophy and dryness | Moderate atrophy and telangiectasia; little mucus | Marked atrophy with complete dryness; severe telangiectasia | Ulceration |
| Salivary glands- Late RT Morbidity Scoring | No change from baseline | Slight dryness of mouth; good response on stimulation | Moderate dryness of mouth; poor response on stimulation | Complete dryness of mouth; no response on stimulation | Fibrosis |
| Skin- Late RT Morbidity Scoring | No change from baseline | Slight atrophy; pigmentation change; some hair loss | Patchy atrophy; moderate telangiectasia; total hair loss | Marked atrophy; gross telangiectasia | Ulceration |
| Small/Large intestine- Late RT Morbidity Scoring | No change from baseline | Mild diarrhea; mild cramping; bowel movement 5 x daily; slight rectal discharge or bleeding | Moderate diarrhea and colic; bowel movement >5 x daily; excessive rectal mucus or intermittent bleeding | Obstruction or bleeding, requiring surgery | Necrosis/perforation fistula |
| Spinal cord- Late RT Morbidity Scoring | No change from baseline | Mild Lhermitte's syndrome | Severe Lhermitte's syndrome | Objective neurological findings at or below cord level treatment | Mono-, para-, quadriplegia |
| Subcutaneous tissue- Late RT Morbidity Scoring | No change from baseline | Slight induration (fibrosis) and loss of subcutaneous fat | Moderate fibrosis but asymptomatic; slight field contracture; <10% linear reduction | Severe induration and loss of subcutaneous tissue; field contracture >10% linear measurement | Necrosis |
| Radiation - Other (Specify, _____) | None | Mild | Moderate | Severe | Life-threatening or disabling |

Appendix V

BMT-Specific Adverse Events

Summary of BMT-Specific Adverse Events that may be used **if specified by the protocol**. These differ from the standard CTC and may be more relevant to the transplant setting. They are listed here for the convenience of investigators writing transplant protocols. They are also included in the CTC document.

| Adverse Event | Grade | | | | |
|--|-----------------|--|--|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Bilirubin associated with graft versus host disease for BMT studies . | normal | ≥2 - <3 mg/100 mL | ≥3 - <6 mg/100 mL | ≥6 - <15 mg/100 mL | ≥15 mg/100 mL |
| Diarrhea associated with graft versus host disease (GVHD) for BMT studies. | none | >500 - ≤1000mL of diarrhea/day | >1000 - ≤1500mL of diarrhea/day | >1500mL of diarrhea/day | severe abdominal pain with or without ileus |
| <i>Diarrhea for pediatric BMT studies.</i> | | <i>>5 - ≤10 mL/kg of diarrhea/day</i> | <i>>10 - ≤15 mL/kg of diarrhea/day</i> | <i>>15 mL/kg of diarrhea/day</i> | - |
| Hepatic enlargement | absent | - | - | present | - |
| Leukocytes (total WBC) for BMT studies. | WNL | ≥2.0 - <3.0 X 10 ⁹ /L ≥2000 - <3000/mm ³ | ≥1.0 - <2.0 x 10 ⁹ /L ≥1000 - <2000/mm ³ | ≥0.5 - <1.0 x 10 ⁹ /L ≥500 - <1000/mm ³ | <0.5 x 10 ⁹ /L <500/mm ³ |
| <i>Leukocytes (total WBC) for pediatric BMT studies (using age, race and sex normal values).</i> | | <i>≥75 - <100% LLN</i> | <i>≥50 - <75% LLN</i> | <i>≥25 - 50% LLN</i> | <i><25% LLN</i> |
| <i>Lymphopenia for pediatric BMT studies (using age, race and sex normal values).</i> | mm ³ | <i>≥75-<100%LLN</i> | <i>≥50-<75%LLN</i> | <i>≥25-<50%LLN</i> | <i><25%LLN</i> |
| Neutrophils/granulocytes (ANC/AGC) for BMT studies. | WNL | ≥1.0 - <1.5 x 10 ⁹ /L ≥1000 - <1500/mm ³ | ≥0.5 - <1.0 x 10 ⁹ /L ≥500 - <1000/mm ³ | ≥0.1 - <0.5 x 10 ⁹ /L ≥100 - <500/mm ³ | <0.1 x 10 ⁹ /L <100/mm ³ |
| Platelets for BMT studies. | WNL | ≥50.0 - <75.0 x 10 ⁹ /L ≥50,000 - <75,000/mm ³ | ≥20.0 - <50.0 x 10 ⁹ /L ≥20,000 - <50,000/mm ³ | ≥10.0 - <20.0 x 10 ⁹ /L ≥10,000 - <20,000/mm ³ | <10.0 x 10 ⁹ /L <10,000/mm ³ |
| Rash/dermatitis associated with high-dose chemotherapy or BMT studies. | none | faint erythema or dry desquamation | moderate to brisk erythema or a patchy moist desquamation, mostly confined to skin folds and creases; moderate edema | confluent moist desquamation, ≥1.5 cm diameter, not confined to skin folds; pitting edema | skin necrosis or ulceration of full thickness dermis; may include spontaneous bleeding not induced by minor trauma or abrasion |
| Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies. | none | macular or papular eruption or erythema covering <25% of body surface area without associated symptoms | macular or papular eruption or erythema with pruritus or other associated symptoms covering ≥25 - <50% of body surface or localized desquamation or other lesions covering ≥25 - <50% of body surface area | symptomatic generalized erythroderma or symptomatic macular, papular or vesicular eruption, with bullous formation, or desquamation covering ≥50% of body surface area | generalized exfoliative dermatitis or ulcerative dermatitis or bullous formation |

Appendix V (Continued)

BMT-Specific Adverse Events

Summary of BMT-Specific Adverse Events that may be used **if specified by the protocol**. These differ from the standard CTC and may be more relevant to the transplant setting. They are listed here for the convenience of investigators writing transplant protocols. They are also included in the CTC document.

| Adverse Event | Grade | | | | |
|--|-------------|--|---|--|--|
| | 0 | 1 | 2 | 3 | 4 |
| Stomatitis/pharyngitis (oral/pharyngeal mucositis) for BMT studies. | none | painless ulcers, erythema, or mild soreness in the absence of lesions | painful erythema, edema or ulcers but can swallow | painful erythema, edema, or ulcers preventing swallowing or requiring hydration or parenteral (or enteral) nutritional support | severe ulceration requiring prophylactic intubation or resulting in documented aspiration pneumonia |
| Transfusion: Platelets for BMT studies. | none | 1 platelet transfusion in 24 hours | 2 platelet transfusions in 24 hours | ≥3 platelet transfusions in 24 hours | platelet transfusions and other measures required to improve platelet increment; platelet transfusion refractoriness associated with life-threatening bleeding. (e.g., HLA or cross matched platelet transfusions) |
| Transfusion: pRBCs for BMT studies. | none | ≤2 u pRBC in 24 hours elective or planned | 3 u pRBC in 24 hours elective or planned | ≥4 u pRBC in 24 hours | hemorrhage or hemolysis associated with life-threatening anemia; medical intervention required to improve hemoglobin |
| <i>Transfusion: pRBCs for pediatric BMT studies.</i> | <i>none</i> | <i>≤15mL/kg in 24 hours elective or planned</i> | <i>>15 - ≤30mL/kg in 24 hours elective or planned</i> | <i>>30mL/kg in 24 hours</i> | <i>hemorrhage or hemolysis associated with life-threatening anemia; medical intervention required to improve hemoglobin</i> |
| Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura/TTP or hemolytic uremic syndrome/HUS) for BMT studies. | - | evidence of RBC destruction (schistocytosis) without clinical consequences | evidence of RBC destruction with elevated creatinine (≤3 x ULN) | evidence of RBC destruction with creatinine (>3 x ULN) not requiring dialysis | evidence of RBC destruction with renal failure requiring dialysis and/or encephalopathy |
| Weight gain associated with Venous-Occlusive Disease (VOD) for BMT studies. | <2% | ≥2 - <5% | ≥5 - <10% | ≥10% or as ascites | ≥10% or fluid retention resulting in pulmonary failure |

Appendix VI

BMT Complex/Multicomponent Events

| Adverse Event | Grade | | | | |
|---|--------|------|----------|--------|------------------|
| | 0 | 1 | 2 | 3 | 4 |
| Note: The grading of Complex/Multicomponent Events in bone marrow transplant will be defined in the protocol. The grading scale must use the CTC criteria for grading the specific component events (adverse events). | | | | | |
| Failure to engraft | absent | mild | moderate | severe | life-threatening |
| Also consider Hemoglobin, Neutrophils/granulocytes (ANC/AGC), Neutrophils/granulocytes (ANC/AGC) for BMT studies, if specified in the protocol, Platelets, Platelets for BMT studies, if specified in the protocol | | | | | |
| Graft versus host disease | absent | mild | moderate | severe | life-threatening |
| Also consider Fatigue, Rash/desquamation, Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, Diarrhea for patients without colostomy, Diarrhea for patients with colostomy, Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, Diarrhea for pediatric BMT studies, if specified in the protocol, Bilirubin, Bilirubin associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol | | | | | |
| Stem cell infusion complications | absent | mild | moderate | severe | life-threatening |
| Also consider Allergic reaction/hypersensitivity, Conduction abnormality/Atrioventricular heart block, Nodal/junctional arrhythmia/dysrhythmia, Prolonged QTc interval (QTc >0.48 seconds), Sinus bradycardia, Sinus tachycardia, Supraventricular arrhythmias (SVT/atrial fibrillation/flutter), Vasovagal episode, Ventricular arrhythmia (PVCs/bigeminy/trigeminy/ventricular tachycardia), Cardiovascular/Arrhythmia - Other (Specify, _____), Hypertension, Hypotension, Fever (in the absence of neutropenia, where neutropenia is defined as AGC <1.0 x 10 ⁹ /L), Rigors/chills, Sweating (diaphoresis), Rash/desquamation, Rash/desquamation associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, Urticaria (hives, welts, wheals), Diarrhea for patients without colostomy, Diarrhea for patients with colostomy, Diarrhea associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, Diarrhea for pediatric BMT studies, if specified in the protocol, Nausea, Vomiting, Hemorrhage/bleeding with grade 3 or 4 thrombocytopenia, Hemorrhage/bleeding without grade 3 or 4 thrombocytopenia, Hemoptysis, Alkaline phosphatase, Bilirubin, Bilirubin associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, GGT, SGOT (AST), SGPT (ALT), Infection (documented clinically or microbiologically) with grade 3 or 4 neutropenia (ANC <1.0 x 10 ⁹ /L), Infection without neutropenia, Hyperkalemia, Hypermnatremia, Hypokalemia, Depressed level of consciousness, Seizures, Abdominal pain, Headache, Creatinine, Hemoglobinuria | | | | | |
| Veno-Occlusive Disease (VOD) | absent | mild | moderate | severe | life-threatening |
| Also consider Weight gain associated with Veno-Occlusive Disease (VOD) for BMT studies, if specified in the protocol, Bilirubin, Bilirubin associated with graft versus host disease (GVHD) for BMT studies, if specified in the protocol, Depressed level of consciousness, Hepatic pain, Renal failure, Hepatic enlargement | | | | | |