

# Common Terminology Criteria for Adverse Event v3.0 (CTCAE)

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## Quick Reference

The NCI Common Terminology Criteria for Adverse Events v3.0 is a descriptive terminology which can be utilized for Adverse Event (AE) reporting. A grading (severity) scale is provided for each AE term.

## Components and Organization

### CATEGORY

A CATEGORY is a broad classification of AEs based on anatomy and/or pathophysiology. Within each CATEGORY, AEs are listed accompanied by their descriptions of severity (Grade).

### Adverse Event Terms

An AE is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medical treatment or procedure that may or may *not* be considered related to the medical treatment or procedure. An AE is a term that is a unique representation of a specific event used for medical documentation and scientific analyses. Each AE term is mapped to a MedDRA term and code. AEs are listed alphabetically within CATEGORIES.

### Supra-ordinate Terms

A supra-ordinate term is located within a CATEGORY and is a grouping term based on disease process, signs, symptoms or diagnosis. A supra-ordinate term is followed by the word 'Select' and is accompanied by specific AEs that are all related to the supra-ordinate term. Supra-ordinate terms provide clustering and consistent representation of Grade for related AEs. Supra-ordinate terms are not AEs, are not mapped to a MedDRA term and code, cannot be graded and cannot be used for reporting.

### Remark

A 'REMARK' is a clarification of an AE.

### Also Consider

An 'ALSO CONSIDER' indicates additional AEs that are to be graded if they are clinically significant.

## Navigation Note

A 'NAVIGATION NOTE' indicates the location of an AE term within the CTCAE document. It lists signs/symptoms alphabetically and the CTCAE term will appear in the same CATEGORY unless the 'NAVIGATION NOTE' states differently.

### Grades

Grade refers to the severity of the AE. The CTCAE v3.0 displays Grades 1 through 5 with unique clinical descriptions of severity for each AE based on this general guideline:

- Grade 1 Mild AE
- Grade 2 Moderate AE
- Grade 3 Severe AE
- Grade 4 Life-threatening or disabling AE
- Grade 5 Death related to AE

A Semi-colon indicates 'or' within the description of the grade.

An 'Em dash' (—) indicates a grade not available.

Not all Grades are appropriate for all AEs. Therefore, some AEs are listed with fewer than five options for Grade selection.

### Grade 5

Grade 5 (Death) is not appropriate for some AEs and therefore is not an option.

The DEATH CATEGORY is new. Only one Supra-ordinate term is listed in this CATEGORY: 'Death not associated with CTCAE term – Select' with 4 AE options: Death NOS; Disease progression NOS; Multi-organ failure; Sudden death.

### Important:

- Grade 5 is the only appropriate Grade
- This AE is to be used in the situation where a death
  1. cannot be reported using a CTCAE v3.0 term associated with Grade 5, or
  2. cannot be reported within a CTCAE CATEGORY as 'Other (Specify)'

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## ALLERGY/IMMUNOLOGY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
1000	Allergic reaction/hypersensitivity (including drug fever)	Transient flushing or rash; drug fever <38 °C (<100.4 °F)	Rash; flushing; urticaria; dyspnea; drug fever ≥38 °C (≥100.4 °F)	Symptomatic bronchospasm, with or without urticaria; parenteral medication(s) indicated; allergy-related edema/angioedema; hypotension	Anaphylaxis	Death
REMARK: Urticaria with manifestations of allergic or hypersensitivity reaction is graded as Allergic reaction/hypersensitivity (including drug fever).						
ALSO CONSIDER: Cytokine release syndrome/acute infusion reaction.						
1001	Allergic rhinitis (including sneezing, nasal stuffiness, postnasal drip)	Mild, intervention not indicated	Moderate, intervention indicated	—	—	—
REMARK: Rhinitis associated with obstruction or stenosis is graded as Obstruction/stenosis of airway – <i>Select</i> in the PULMONARY/UPPER RESPIRATORY CATEGORY.						
1002	Autoimmune reaction	Asymptomatic and serologic or other evidence of autoimmune reaction, with normal organ function and intervention not indicated	Evidence of autoimmune reaction involving a non-essential organ or function (e.g., hypothyroidism)	Reversible autoimmune reaction involving function of a major organ or other adverse event (e.g., transient colitis or anemia)	Autoimmune reaction with life-threatening consequences	Death
ALSO CONSIDER: Colitis; Hemoglobin; Hemolysis (e.g., immune hemolytic anemia, drug-related hemolysis); Thyroid function, low (hypothyroidism)						
1003	Serum sickness	—	—	Present	—	Death
NAVIGATION NOTE: Splenic function is graded in the BLOOD/BONE MARROW CATEGORY.						
NAVIGATION NOTE: Urticaria as an isolated symptom is graded as Urticaria (hives, welts, wheals) in the DERMATOLOGY/SKIN CATEGORY.						
1004	Vasculitis	Mild, intervention not indicated	Symptomatic, non-steroidal medical intervention indicated	Steroids indicated	Ischemic changes; amputation indicated	Death
1249	Allergy/Immunology - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## AUDITORY/EAR

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
NAVIGATION NOTE: Earache (otalgia) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
1250	Hearing: patients with/without baseline audiogram and enrolled in a monitoring program <sup>1</sup>	Threshold shift or loss of 15 - 25 dB relative to baseline, averaged at 2 or more contiguous test frequencies in at least one ear; or subjective change in the absence of a Grade 1 threshold shift	Threshold shift or loss of >25 - 90 dB, averaged at 2 contiguous test frequencies in at least one ear.	Adult only: Threshold shift of >25 - 90 dB, averaged at 3 contiguous test frequencies in at least one ear  Pediatric: Hearing loss sufficient to indicate therapeutic intervention, including hearing aids (e.g., >=20 dB bilateral HL in the speech frequencies; >=30 dB unilateral HL; and requiring additional speech-language related services)	Adult only: Profound bilateral hearing loss (>90 dB)  Pediatric: Audiologic indication for cochlear implant and requiring additional speech-language related services	—
REMARK: Pediatric recommendations are identical to those for adults, unless specified. For children and adolescents (<=18 years of age) without a baseline test, pre-exposure/pre-treatment hearing should be considered to be <5 dB loss.						
1251	Hearing: patients without baseline audiogram and not enrolled in a monitoring program <sup>1</sup>	—	Hearing loss not requiring hearing aid or intervention (i.e., not interfering with ADL)	Hearing loss requiring hearing aid or intervention (i.e., interfering with ADL)	Profound bilateral hearing loss (>90 dB)	—
REMARK: Pediatric recommendations are identical to those for adults, unless specified. For children and adolescents (<=18 years of age) without a baseline test, pre-exposure/pre-treatment hearing should be considered to be <5 dB loss.						
1252	Otitis, external ear (non-infectious)	External otitis with erythema or dry desquamation	External otitis with moist desquamation, edema, enhanced cerumen or discharge; tympanic membrane perforation; tympanostomy	External otitis with mastoiditis; stenosis or osteomyelitis	Necrosis of soft tissue or bone	Death
ALSO CONSIDER: Hearing: patients with/without baseline audiogram and enrolled in a monitoring program <sup>1</sup> ; Hearing: patients without baseline audiogram and not enrolled in a monitoring program <sup>1</sup> .						
1253	Otitis, middle ear (non-infectious)	Serous otitis	Serous otitis, medical intervention indicated	Otitis with discharge; mastoiditis	Necrosis of the canal soft tissue or bone	Death

AUDITORY/EAR						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
1254	Tinnitus  ALSO CONSIDER: Hearing patients with/without baseline audiogram and enrolled in a monitoring program <sup>1</sup> ; Hearing patients without baseline audiogram and not enrolled in a monitoring program <sup>1</sup> .	—	Tinnitus not interfering with ADL	Tinnitus interfering with ADL	Disabling	—
1499	Auditory/Ear - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

<sup>1</sup> Drug-induced ototoxicity should be distinguished from age-related threshold decrements or unrelated cochlear insult. When considering whether an adverse event has occurred, it is first necessary to classify the patient into one of two groups. (1) The patient is under standard treatment/enrolled in a clinical trial <2.5 years, and has a 15 dB or greater threshold shift averaged across two contiguous frequencies; or (2) The patient is under standard treatment/enrolled in a clinical trial >2.5 years, and the difference between the expected age-related and the observed threshold shifts is 15 dB or greater averaged across two contiguous frequencies. Consult standard references for appropriate age- and gender-specific hearing norms, e.g., Morrell, et al. Age- and gender-specific reference ranges for hearing level and longitudinal changes in hearing level. Journal of the Acoustical Society of America 100:1949-1967, 1996; or Shotland, et al. Recommendations for cancer prevention trials using potentially ototoxic test agents. Journal of Clinical Oncology 19:1658-1663, 2001.

In the absence of a baseline prior to initial treatment, subsequent audiograms should be referenced to an appropriate database of normals. ANSI. (1996)

American National Standard: Determination of occupational noise exposure and estimation of noise-induced hearing impairment, ANSI S 3.44-1996. (Standard S 3.44). New York: American National Standards Institute. The recommended ANSI S3.44 database is Annex B.

## BLOOD/BONE MARROW

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
1500	Bone marrow cellularity	Mildly hypocellular or <=25% reduction from normal cellularity for age	Moderately hypocellular or >25 - <=50% reduction from normal cellularity for age	Severely hypocellular or >50 - <=75% reduction cellularity from normal for age	—	Death
1501	CD4 count	<LLN - 500/mm <sup>3</sup> <LLN - 0.5 x 10 <sup>9</sup> /L	<500 - 200/mm <sup>3</sup> <0.5 - 0.2 x 10 <sup>9</sup> /L	<200 - 50/mm <sup>3</sup> <0.2 x 0.05 - 10 <sup>9</sup> /L	<50/mm <sup>3</sup> <0.05 x 10 <sup>9</sup> /L	Death
1502	Haptoglobin	<LLN	—	Absent	—	Death
1503	Hemoglobin	<LLN - 10.0 g/dL <LLN - 6.2 mmol/L <LLN - 100 g/L	<10.0 - 8.0 g/dL <6.2 - 4.9 mmol/L <100 - 80g/L	<8.0 - 6.5 g/dL <4.9 - 4.0 mmol/L <80 - 65 g/L	<6.5 g/dL <4.0 mmol/L <65 g/L	Death
1504	Hemolysis (e.g., immune hemolytic anemia, drug-related hemolysis)	Laboratory evidence of hemolysis only (e.g., direct antiglobulin test [DAT, Coombs'] schistocytes)	Evidence of red cell destruction and >=2 gm decrease in hemoglobin, no transfusion	Transfusion or medical intervention (e.g., steroids) indicated	Catastrophic consequences of hemolysis (e.g., renal failure, hypotension, bronchospasm, emergency splenectomy)	Death
ALSO CONSIDER: Haptoglobin; Hemoglobin.						
1505	Iron overload	—	Asymptomatic iron overload, intervention not indicated	Iron overload, intervention indicated	Organ impairment (e.g., endocrinopathy, cardiopathy)	Death
1506	Leukocytes (total WBC)	<LLN - 3000/mm <sup>3</sup> <LLN - 3.0 x 10 <sup>9</sup> /L	<3000 - 2000/mm <sup>3</sup> <3.0 - 2.0 x 10 <sup>9</sup> /L	<2000 - 1000/mm <sup>3</sup> <2.0 - 1.0 x 10 <sup>9</sup> /L	<1000/mm <sup>3</sup> <1.0 x 10 <sup>9</sup> /L	Death
1507	Lymphopenia	<LLN - 800/mm <sup>3</sup> <LLN x 0.8 - 10 <sup>9</sup> /L	<800 - 500/mm <sup>3</sup> <0.8 - 0.5 x 10 <sup>9</sup> /L	<500 - 200 mm <sup>3</sup> <0.5 - 0.2 x 10 <sup>9</sup> /L	<200/mm <sup>3</sup> <0.2 x 10 <sup>9</sup> /L	Death
1508	Myelodysplasia	—	—	Abnormal marrow cytogenetics (marrow blasts <=5%)	RAEB or RAEB-T (marrow blasts >5%)	Death
1509	Neutrophils/granulocytes (ANC/AGC)	<LLN - 1500/mm <sup>3</sup> <LLN - 1.5 x 10 <sup>9</sup> /L	<1500 - 1000/mm <sup>3</sup> <1.5 - 1.0 x 10 <sup>9</sup> /L	<1000 - 500/mm <sup>3</sup> <1.0 - 0.5 x 10 <sup>9</sup> /L	<500/mm <sup>3</sup> <0.5 x 10 <sup>9</sup> /L	Death
1510	Platelets	<LLN - 75,000/mm <sup>3</sup> <LLN - 75.0 x 10 <sup>9</sup> /L	<75,000 - 50,000/mm <sup>3</sup> <75.0 - 50.0 x 10 <sup>9</sup> /L	<50,000 - 25,000/mm <sup>3</sup> <50.0 - 25.0 x 10 <sup>9</sup> /L	<25,000/mm <sup>3</sup> <25.0 x 10 <sup>9</sup> /L	Death
1511	Splenic function	Incidental findings (e.g., Howell-Jolly bodies)	Prophylactic antibiotics indicated	—	Life-threatening consequences	Death
1749	Blood/Bone Marrow - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## CARDIAC ARRHYTHMIA

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	Conduction abnormality/atrioventricular heart block  - <i>Select:</i>	Asymptomatic, intervention not indicated	Non-urgent medical intervention indicated	Incompletely controlled medically or controlled with device (e.g., pacemaker)	Life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock)	Death
1751	- Asystole					
1752	- AV Block-First degree					
1753	- AV Block-Second degree Mobitz Type I (Wenckebach)					
1754	- AV Block-Second degree Mobitz Type II					
1755	- AV Block-Third degree (Complete AV block)					
1756	- Conduction abnormality NOS					
1757	- Sick Sinus Syndrome					
1758	- Stokes-Adams Syndrome					
1759	- Wolff-Parkinson-White Syndrome					
1760	Palpitations  REMARK: Grade palpitations <u>only</u> in the absence of a documented arrhythmia.	Present	Present with associated symptoms (e.g., lightheadedness, shortness of breath)	---	---	---
1761	Prolonged QTc interval	QTc >0.45 - 0.47 second	QTc >0.47 - 0.50 second; >=0.06 second above baseline	QTc >0.50 second	QTc >0.50 second; life-threatening signs or symptoms (e.g., arrhythmia, CHF, hypotension, shock syncope); Torsade de pointes	Death
	Supraventricular and nodal arrhythmia  - <i>Select:</i>	Asymptomatic, intervention not indicated	Non-urgent medical intervention indicated	Symptomatic and incompletely controlled medically, or controlled with device (e.g., pacemaker)	Life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock)	Death
1763	- Atrial fibrillation					
1764	- Atrial flutter					
1765	- Atrial tachycardia/Paroxysmal Atrial Tachycardia					
1766	- Nodal/Junctional					
1767	- Sinus arrhythmia					
1768	- Sinus bradycardia					
1769	- Sinus tachycardia					
1770	- Supraventricular arrhythmia NOS					
1771	- Supraventricular extrasystoles (Premature Atrial Contractions; Premature Nodal/Junctional Contractions)					
1772	- Supraventricular tachycardia					
NAVIGATION NOTE: Syncope is graded as Syncope (fainting) in the NEUROLOGY CATEGORY						

## CARDIAC ARRHYTHMIA

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
1773	Vasovagal episode	—	Present without loss of consciousness	Present with loss of consciousness	Life-threatening consequences	Death
	Ventricular arrhythmia	Asymptomatic, no intervention indicated	Non-urgent medical intervention indicated	Symptomatic and incompletely controlled medically or controlled with device (e.g., defibrillator)	Life-threatening (e.g., arrhythmia associated with CHF, hypotension, syncope, shock)	Death
	-Select:					
1775	– Bigeminy					
1776	– Idioventricular rhythm					
1777	– PVCs					
1778	– Torsade de pointes					
1779	– Trigeminy					
1780	– Ventricular arrhythmia NOS					
1781	– Ventricular fibrillation					
1782	– Ventricular flutter					
1783	– Ventricular tachycardia					
1999	Cardiac Arrhythmia - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## CARDIAC GENERAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
NAVIGATION NOTE: Angina is graded as Cardiac ischemia/infarction in the CARDIAC GENERAL CATEGORY.						
2000	Cardiac ischemia/infarction	Asymptomatic arterial narrowing without ischemia	Asymptomatic and testing suggesting ischemia; stable angina	Symptomatic and testing consistent with ischemia; unstable angina; intervention indicated	Acute myocardial infarction	Death
2001	Cardiac troponin I (cTnI)	---	---	Levels consistent with unstable angina as defined by the manufacturer	Levels consistent with myocardial infarction as defined by the manufacturer	Death
2002	Cardiac troponin T (cTnT)	0.03 - <0.05 ng/mL	0.05 - <0.1 ng/mL	0.1 - <0.2 ng/mL	0.2 ng/mL	Death
2003	Cardiopulmonary arrest, cause unknown (non-fatal)	---	---	---	Life-threatening	---
REMARK: Grade 4 (non-fatal) is the only appropriate grade. CTCAE provides three alternatives for reporting Death: <ol style="list-style-type: none"> <li>1. A CTCAE term associated with Grade 5.</li> <li>2. A CTCAE 'Other (Specify, ___)' within any CATEGORY.</li> <li>3. Death not associated with CTCAE term – <i>Select</i> in the DEATH CATEGORY.</li> </ol>						
NAVIGATION NOTE: Chest pain (non-cardiac and non-pleuritic) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
NAVIGATION NOTE: CNS ischemia is graded as CNS cerebrovascular ischemia in the NEUROLOGY CATEGORY.						
2004	Hypertension	Asymptomatic, transient (<24 hrs) increase by >20 mmHg (diastolic) or to >150/100 if previously WNL; intervention not indicated  Pediatric: Asymptomatic, transient (<24 hrs) BP increase >ULN; intervention not indicated	Recurrent or persistent (>=24 hrs) or symptomatic increase by >20 mmHg (diastolic) or to >150/100 if previously WNL; monotherapy may be indicated  Pediatric: Recurrent or persistent (>=24 hrs) BP >ULN; monotherapy may be indicated	Requiring more than one drug or more intensive therapy than previously  Pediatric: Same as adult	Life-threatening consequences (e.g., hypertensive crisis)  Pediatric: Same as adult	Death
REMARK: Use age and gender-appropriate normal values >95 <sup>th</sup> percentile ULN for pediatric patients.						



## CARDIAC GENERAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
2005	Hypotension  ALSO CONSIDER: Syncope (fainting).	Changes, intervention not indicated	Brief (<24 hrs) fluid replacement or other therapy; no physiologic consequences	Sustained (≥24 hrs) therapy, resolves without persisting physiologic consequences	Shock (e.g., acidemia; impairment of vital organ function)	Death
2006	Left ventricular diastolic dysfunction	Asymptomatic diagnostic finding; intervention not indicated	Asymptomatic, intervention indicated	Symptomatic CHF responsive to intervention	Refractory CHF, poorly controlled; intervention such as ventricular assist device or heart transplant indicated	Death
2007	Left ventricular systolic dysfunction	Asymptomatic, resting ejection fraction (EF) <60 - 50%; shortening fraction (SF) <30 - 24%	Asymptomatic, resting EF <50 - 40%; SF <24 - 15%	Symptomatic CHF responsive to intervention; EF <40 - 20% SF <15%	Refractory CHF or poorly controlled; EF <20%; intervention such as ventricular assist device, ventricular reduction surgery, or heart transplant indicated	Death
NAVIGATION NOTE: Myocardial infarction is graded as Cardiac ischemia/infarction in the CARDIAC GENERAL CATEGORY.						
2008	Myocarditis	—	—	CHF responsive to intervention	Severe or refractory CHF	Death
2009	Pericardial effusion (non-malignant)	Asymptomatic effusion	—	Effusion with physiologic consequences	Life-threatening consequences (e.g., tamponade); emergency intervention indicated	Death
2010	Pericarditis	Asymptomatic, ECG or physical exam (rub) changes consistent with pericarditis	Symptomatic pericarditis (e.g., chest pain)	Pericarditis with physiologic consequences (e.g., pericardial constriction)	Life-threatening consequences; emergency intervention indicated	Death
NAVIGATION NOTE: Pleuritic pain is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
2011	Pulmonary hypertension	Asymptomatic without therapy	Asymptomatic, therapy indicated	Symptomatic hypertension, responsive to therapy	Symptomatic hypertension, poorly controlled	Death
2012	Restrictive cardiomyopathy	Asymptomatic, therapy not indicated	Asymptomatic, therapy indicated	Symptomatic CHF responsive to intervention	Refractory CHF, poorly controlled; intervention such as ventricular assist device, or heart transplant indicated	Death

## CARDIAC GENERAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
2013	Right ventricular dysfunction (cor pulmonale)	Asymptomatic without therapy	Asymptomatic, therapy indicated	Symptomatic cor pulmonale, responsive to intervention	Symptomatic cor pulmonale poorly controlled; intervention such as ventricular assist device, or heart transplant indicated	Death
2014	Valvular heart disease	Asymptomatic valvular thickening with or without mild valvular regurgitation or stenosis; treatment other than endocarditis prophylaxis not indicated	Asymptomatic; moderate regurgitation or stenosis by imaging	Symptomatic; severe regurgitation or stenosis; symptoms controlled with medical therapy	Life-threatening; disabling; intervention (e.g., valve replacement, valvuloplasty) indicated	Death
2249	Cardiac General - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## COAGULATION

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
2250	DIC (disseminated intravascular coagulation)  Remark: DIC (disseminated intravascular coagulation) must have increased fibrin split products or D-dimer Also Consider: Platelets.	—	Laboratory findings with <u>no</u> bleeding	Laboratory findings <u>and</u> bleeding	Laboratory findings, life-threatening or disabling consequences (e.g., CNS hemorrhage, organ damage, or hemodynamically significant blood loss)	Death
2251	Fibrinogen  REMARK: Use % decrease only when baseline is <LLN (local laboratory value).	<1.0 - 0.75 x LLN or <25% decrease from baseline	<0.75 - 0.5 x LLN or 25 - <50% decrease from baseline	<0.5 - 0.25 x LLN or 50 - <75% decrease from baseline	<0.25 x LLN or 75% decrease from baseline or absolute value <50 mg/dL	Death
2252	INR (International Normalized Ratio of prothrombin time)  ALSO CONSIDER: Hemorrhage, CNS; Hemorrhage, GI – <i>Select</i> ; Hemorrhage, GU – <i>Select</i> ; Hemorrhage, pulmonary/upper respiratory – <i>Select</i> .	>1 - 1.5 x ULN	>1.5 - 2 x ULN	>2 x ULN	—	—
2253	PTT (Partial Thromboplastin Time)  ALSO CONSIDER: Hemorrhage, CNS; Hemorrhage, GI – <i>Select</i> ; Hemorrhage, GU – <i>Select</i> ; Hemorrhage, pulmonary/upper respiratory – <i>Select</i> .	>1 - 1.5 x ULN	>1.5 - 2 x ULN	>2 x ULN	—	—
2254	Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura [TTP] or hemolytic uremic syndrome [HUS])  REMARK: Must have microangiopathic changes on blood smear (e.g., schistocytes, helmet cells, red cell fragments). ALSO CONSIDER: Creatinine; Hemoglobin; Platelets.	Evidence of RBC destruction (schistocytosis) without clinical consequences	—	Laboratory findings present with clinical consequences (e.g., renal insufficiency, petechiae)	Laboratory findings and life threatening or disabling consequences, (e.g., CNS hemorrhage/bleeding or thrombosis/embolism or renal failure)	Death
2499	Coagulation - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## CONSTITUTIONAL SYMPTOMS

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
2500	Fatigue (asthenia, lethargy, malaise)	Mild fatigue over baseline	Moderate or causing difficulty performing some ADL	Severe fatigue interfering with ADL	Disabling	—
2501	Fever (in the absence of neutropenia, where neutropenia is defined as ANC <1.0 x 10 <sup>9</sup> /L)	38.0 - 39.0 °C (100.4 - 102.2 °F)	>39.0 - 40.0 °C (102.3 - 104.0 °F)	>40.0 °C (>104.0 °F) for ≤24 hrs	>40.0 °C (>104.0 °F) for >24 hrs	Death
REMARK: The temperature measurements listed are oral or tympanic.						
ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever).						
Navigation Note: Hot Flashes are graded as Hot flashes/flushes in the ENDOCRINE CATEGORY						
2502	Hypothermia	—	35 - >32 °C 95 - >89.6 °F	32 - >28 °C 89.6 - >82.4 °F	≤28 °C 82.4 °F or life-threatening consequences (e.g., coma, hypotension, pulmonary edema, acidemia, ventricular fibrillation)	Death
2503	Insomnia	Occasional difficulty sleeping, not interfering with function	Difficulty sleeping, interfering with function but not interfering with ADL	Frequent difficulty sleeping, interfering with ADL	Disabling	—
REMARK: If pain or other symptoms interfere with sleep, do NOT grade as insomnia. Grade primary event(s) causing insomnia.						
2504	Obesity <sup>2</sup>	—	BMI 25 - 29.9 kg/m <sup>2</sup>	BMI 30 - 39.99 kg/m <sup>2</sup>	BMI ≥40 kg/m <sup>2</sup>	—
REMARK: BMI = (weight [kg]) / (height [m]) <sup>2</sup>						
2505	Odor (patient odor)	Mild odor	Pronounced odor	—	—	—
2506	Rigors/chills	Mild	Moderate, narcotics indicated	Severe or prolonged, not responsive to narcotics	—	—

<sup>2</sup> NHLBI Obesity Task Force. "Clinical Guidelines on the Identification, Evaluation, and Treatment of Overweight and Obesity in Adults," *The Evidence Report*, Obes Res 6:51S-209S, 1998

## CONSTITUTIONAL SYMPTOMS

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
2507	Sweating (diaphoresis)  ALSO CONSIDER: Hot flashes/flushes.	Mild and occasional	Frequent or drenching	—	—	—
2508	Weight gain  REMARK: Edema, depending on etiology, is graded in the CARDIAC GENERAL or LYMPHATICS CATEGORIES. ALSO CONSIDER: Ascites (non-malignant); Pleural effusion (non-malignant).	5 - <10% of baseline	10 - <20% of baseline	>=20% of baseline	—	—
2509	Weight loss	5 to <10% from baseline; intervention not indicated	10 - <20% from baseline; nutritional support indicated	>=20% from baseline; tube feeding or TPN indicated	—	—
2699	Constitutional Symptoms - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

DEATH						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Death not associated with CTCAE term	—	—	—	—	Death
	– <i>Select</i> :					
2751	– Death NOS					
2752	– Disease progression NOS					
2753	– Multi-organ failure					
2754	– Sudden death					
	REMARK: Grade 5 is the only appropriate grade. 'Death not associated with CTCAE term – <i>Select</i> ' is to be used where a death:					
	1. Cannot be attributed to a CTCAE term associated with Grade 5.					
	2. Cannot be reported within any CATEGORY using a CTCAE 'Other (Specify, __)'.					

## DERMATOLOGY/SKIN

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
3000	Atrophy, skin	Detectable	Marked	—	—	—
3001	Atrophy, subcutaneous fat	Detectable	Marked	—	—	—
ALSO CONSIDER: Induration/fibrosis (skin and subcutaneous tissue).						
3002	Bruising (in absence of Grade 3 or 4 thrombocytopenia)	Localized or in a dependent area	Generalized	—	—	—
3003	Burn	Minimal symptoms; intervention not indicated	Medical intervention; minimal debridement indicated	Moderate to major debridement or reconstruction indicated	Life-threatening consequences	Death
REMARK: Burn refers to all burns including radiation, chemical, etc.						
3004	Cheilitis	Asymptomatic	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL	—	—
3005	Dry skin	Asymptomatic	Symptomatic, not interfering with ADL	Interfering with ADL	—	—
3006	Flushing	Asymptomatic	Symptomatic	—	—	—
3007	Hair loss/alopecia (scalp or body)	Thinning or patchy	Complete	—	—	—
3008	Hyperpigmentation	Slight or localized	Marked or generalized	—	—	—
3009	Hypopigmentation	Slight or localized	Marked or generalized	—	—	—
3010	Induration/fibrosis (skin and subcutaneous tissue)	Increased density on palpation	Moderate impairment of function not interfering with ADL; marked increase in density and firmness on palpation with or without minimal retraction	Dysfunction interfering with ADL; very marked density, retraction or fixation	—	—
ALSO CONSIDER: Fibrosis-cosmesis; Fibrosis-deep connective tissue.						
3011	Injection site reaction/extravasation changes	Pain; itching; erythema	Pain or swelling, with inflammation or phlebitis	Ulceration or necrosis that is severe; operative intervention indicated	—	—
ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever); Ulceration.						

DERMATOLOGY/SKIN						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
3012	Nail changes	Discoloration; ridging (koilonychias); pitting	Partial or complete loss of nail(s); pain in nailbed(s)	Interfering with ADL	—	—
NAVIGATION NOTE: Petechiae is graded as Petechiae/purpura (hemorrhage/bleeding into skin or mucosa) in the HEMORRHAGE/BLEEDING CATEGORY.						
3013	Photosensitivity	Painless erythema	Painful erythema	Erythema with desquamation	Life-threatening; disabling	Death
3014	Pruritus/itching	Mild or localized	Intense or widespread	Intense or widespread and interfering with ADL	—	—
ALSO CONSIDER: Rash/desquamation.						
3015	Rash/desquamation	Macular or papular eruption or erythema without associated symptoms	Macular or papular eruption or erythema with pruritus or other associated symptoms; localized desquamation or other lesions covering <50% of body surface area (BSA)	Severe, generalized erythroderma or macular, papular or vesicular eruption; desquamation covering >=50% BSA	Generalized exfoliative, ulcerative, or bullous dermatitis	Death
REMARK: Rash/desquamation may be used for GVHD.						
3016	Rash: acne/acneiform	Intervention not indicated	Intervention indicated	Associated with pain, disfigurement, ulceration, or desquamation	—	Death
	Rash: dermatitis associated with radiation	Faint erythema or dry desquamation	Moderate to brisk erythema; patchy moist desquamation, mostly confined to skin folds and creases; moderate edema	Moist desquamation other than skin folds and creases; bleeding induced by minor trauma or abrasion	Skin necrosis or ulceration of full thickness dermis; spontaneous bleeding from involved site	Death
	– Select:					
3018	– Chemoradiation					
3019	– Radiation					
3020	Rash: erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis)	—	Scattered, but not generalized eruption	Severe (e.g., generalized rash or painful stomatitis); IV fluids, tube feedings, or TPN indicated	Life-threatening; disabling	Death
3021	Rash: hand-foot skin reaction	Minimal skin changes or dermatitis (e.g., erythema) without pain	Skin changes (e.g., peeling, blisters, bleeding, edema) or pain, not interfering with function	Ulcerative dermatitis or skin changes with pain interfering with function	—	—



## DERMATOLOGY/SKIN

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
3022	Skin breakdown/decubitus ulcer	—	Local wound care; medical intervention indicated	Operative debridement or other invasive intervention indicated (e.g., hyperbaric oxygen)	Life-threatening consequences; major invasive intervention indicated (e.g., tissue reconstruction, flap, or grafting)	Death
REMARK: Skin breakdown/decubitus ulcer is to be used for loss of skin integrity or decubitus ulcer from pressure or as the result of operative or medical intervention.						
3023	Striae	Mild	Cosmetically significant	—	—	—
3024	Telangiectasia	Few	Moderate number	Many and confluent	—	—
3025	Ulceration	—	Superficial ulceration <2 cm size; local wound care; medical intervention indicated	Ulceration >=2 cm size; operative debridement, primary closure or other invasive intervention indicated (e.g., hyperbaric oxygen)	Life-threatening consequences; major invasive intervention indicated (e.g., complete resection, tissue reconstruction, flap, or grafting)	Death
3026	Urticaria (hives, welts, wheals)	Intervention not indicated	Intervention indicated for <24 hrs	Intervention indicated for >=24 hrs	—	—
ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever).						
3027	Wound complication, non-infectious	Incisional separation of <=25% of wound, no deeper than superficial fascia	Incisional separation >25% of wound with local care; asymptomatic hernia	Symptomatic hernia without evidence of strangulation; fascial disruption/dehiscence without evisceration; primary wound closure or revision by operative intervention indicated; hospitalization or hyperbaric oxygen indicated	Symptomatic hernia with evidence of strangulation; fascial disruption with evisceration; major reconstruction flap, grafting, resection, or amputation indicated	Death
REMARK: Wound complication, non-infectious is to be used for separation of incision, hernia, dehiscence, evisceration, or second surgery for wound revision.						
3249	Dermatology/Skin - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## ENDOCRINE

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
3250	Adrenal insufficiency  REMARK: Adrenal insufficiency includes any of the following signs and symptoms: abdominal pain, anorexia, constipation, diarrhea, hypotension, pigmentation of mucous membranes, pigmentation of skin, salt craving, syncope (fainting), vitiligo, vomiting, weakness, weight loss. Adrenal insufficiency must be confirmed by laboratory studies (low cortisol frequently accompanied by low aldosterone).  ALSO CONSIDER: Potassium, serum-high (hyperkalemia); Thyroid function, low (hypothyroidism).	Asymptomatic, intervention not indicated	Symptomatic, intervention indicated	Hospitalization	Life-threatening; disabling	Death
3251	Cushingoid appearance (e.g., moon face, buffalo hump, centripetal obesity, cutaneous striae)  ALSO CONSIDER: Glucose, serum-high (hyperglycemia); Potassium, serum-low (hypokalemia).	—	Present	—	—	—
3252	Feminization of male	—	—	Present	—	—
NAVIGATION NOTE: Gynecomastia is graded in the SEXUAL/REPRODUCTIVE FUNCTION CATEGORY.						
3253	Hot flashes/flushes <sup>3</sup>	Mild	Moderate	Interfering with ADL	—	—
3254	Masculinization of female	—	—	Present	—	—
3255	Neuroendocrine: ACTH deficiency	Asymptomatic	Symptomatic, not interfering with ADL; intervention indicated	Symptoms interfering with ADL; hospitalization indicated	Life-threatening consequences (e.g., severe hypotension)	Death
3256	Neuroendocrine: ADH secretion abnormality (e.g., SIADH or low ADH)	Asymptomatic	Symptomatic, not interfering with ADL; intervention indicated	Symptoms interfering with ADL	Life-threatening consequences	Death
3257	Neuroendocrine: gonadotropin secretion abnormality	Asymptomatic	Symptomatic, not interfering with ADL; intervention indicated	Symptoms interfering with ADL; osteopenia; fracture; infertility	—	—
3258	Neuroendocrine: growth hormone secretion abnormality	Asymptomatic	Symptomatic, not interfering with ADL; intervention indicated	—	—	—
3259	Neuroendocrine: prolactin hormone secretion abnormality	Asymptomatic	Symptomatic, not interfering with ADL; intervention indicated	Symptoms interfering with ADL; amenorrhea; galactorrhea	—	Death

<sup>3</sup> Sloan JA, Loprinzi CL, Novotny PJ, Barton DL, Lavasseur BI, Windschitl HJ, "Methodologic Lessons Learned from Hot Flash Studies," *J Clin Oncol* 2001 Dec 1;19(23):4280-90

## ENDOCRINE

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
3260	Pancreatic endocrine: glucose intolerance	Asymptomatic, intervention not indicated	Symptomatic; dietary modification or oral agent indicated	Symptoms interfering with ADL; insulin indicated	Life-threatening consequences (e.g., ketoacidosis, hyperosmolar non-ketotic coma)	Death
3261	Parathyroid function, low (hypoparathyroidism)	Asymptomatic, intervention not indicated	Symptomatic; intervention indicated	---	---	---
3262	Thyroid function, high (hyperthyroidism, thyrotoxicosis)	Asymptomatic, intervention not indicated	Symptomatic, not interfering with ADL; thyroid suppression therapy indicated	Symptoms interfering with ADL; hospitalization indicated	Life-threatening consequences (e.g., thyroid storm)	Death
3263	Thyroid function, low (hypothyroidism)	Asymptomatic, intervention not indicated	Symptomatic, not interfering with ADL; thyroid replacement indicated	Symptoms interfering with ADL; hospitalization indicated	Life-threatening myxedema coma	Death
3499	Endocrine - Other (Specify, ___)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## GASTROINTESTINAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
NAVIGATION NOTE: Abdominal pain or cramping is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
3500	Anorexia	Loss of appetite without alteration in eating habits	Oral intake altered without significant weight loss or malnutrition; oral nutritional supplements indicated	Associated with significant weight loss or malnutrition (e.g., inadequate oral caloric and/or fluid intake); IV fluids, tube feedings or TPN indicated	Life-threatening consequences	Death
ALSO CONSIDER: Weight loss.						
3501	Ascites (non-malignant)	Asymptomatic	Symptomatic, medical intervention indicated	Symptomatic, invasive procedure indicated	Life-threatening consequences	Death
REMARK: Ascites (non-malignant) refers to documented non-malignant ascites or unknown etiology, but unlikely malignant, and includes chylous ascites.						
3502	Colitis	Asymptomatic, pathologic or radiographic findings only	Abdominal pain; mucus or blood in stool	Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs	Life-threatening consequences (e.g., perforation, bleeding, ischemia, necrosis, toxic megacolon)	Death
ALSO CONSIDER: Hemorrhage, GI – <i>Select</i> .						
3503	Constipation	Occasional or intermittent symptoms; occasional use of stool softeners, laxatives, dietary modification, or enema	Persistent symptoms with regular use of laxatives or enemas indicated	Symptoms interfering with ADL; obstipation with manual evacuation indicated	Life-threatening consequences (e.g., obstruction, toxic megacolon)	Death
ALSO CONSIDER: Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation); Obstruction, GI – <i>Select</i> .						
3504	Dehydration	Increased oral fluids indicated; dry mucous membranes; diminished skin turgor	IV fluids indicated <24 hrs	IV fluids indicated ≥24 hrs	Life-threatening consequences (e.g., hemodynamic collapse)	Death
ALSO CONSIDER: Diarrhea; Hypotension; Vomiting.						
3505	Dental: dentures or prosthesis	Minimal discomfort, no restriction in activities	Discomfort preventing use in some activities (e.g., eating), but not others (e.g., speaking)	Unable to use dentures or prosthesis at any time	—	—

## GASTROINTESTINAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
3506	Dental: periodontal disease	Gingival recession or gingivitis; limited bleeding on probing; mild local bone loss	Moderate gingival recession or gingivitis; multiple sites of bleeding on probing; moderate bone loss	Spontaneous bleeding; severe bone loss with or without tooth loss; osteonecrosis of maxilla or mandible	—	—
REMARK: Severe periodontal disease leading to osteonecrosis is graded as Osteonecrosis (avascular necrosis) in the MUSCULOSKELETAL CATEGORY.						
3507	Dental: teeth	Surface stains; dental caries; restorable, without extractions	Less than full mouth extractions; tooth fracture or crown amputation or repair indicated	Full mouth extractions indicated	—	—
3508	Dental: teeth development	Hypoplasia of tooth or enamel not interfering with function	Functional impairment correctable with oral surgery	Maldevelopment with functional impairment not surgically correctable	—	—
3509	Diarrhea	Increase of <4 stools per day over baseline; mild increase in ostomy output compared to baseline	Increase of 4 - 6 stools per day over baseline; IV fluids indicated <24hrs; moderate increase in ostomy output compared to baseline; not interfering with ADL	Increase of >=7 stools per day over baseline; incontinence; IV fluids >=24 hrs; hospitalization; severe increase in ostomy output compared to baseline; interfering with ADL	Life-threatening consequences (e.g., hemodynamic collapse)	Death
REMARK: Diarrhea includes diarrhea of small bowel or colonic origin, and/or ostomy diarrhea.						
ALSO CONSIDER: Dehydration; Hypotension.						
3510	Distension/bloating, abdominal	Asymptomatic	Symptomatic, but not interfering with GI function	Symptomatic, interfering with GI function	—	—
ALSO CONSIDER: Ascites (non-malignant); Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation); Obstruction, GI – <i>Select</i> .						

## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
3511	Dry mouth/salivary gland (xerostomia)	Symptomatic (dry or thick saliva) without significant dietary alteration; unstimulated saliva flow >0.2 ml/min	Symptomatic and significant oral intake alteration (e.g., copious water, other lubricants, diet limited to purees and/or soft, moist foods); unstimulated saliva 0.1 to 0.2 ml/min	Symptoms leading to inability to adequately aliment orally; IV fluids, tube feedings, or TPN indicated; unstimulated saliva <0.1 ml/min	---	---
<p>REMARK: Dry mouth/salivary gland (xerostomia) includes descriptions of grade using both subjective and objective assessment parameters. Record this event consistently throughout a patient's participation on study. If salivary flow measurements are used for initial assessment, subsequent assessments must use salivary flow.</p> <p>ALSO CONSIDER: Salivary gland changes/saliva.</p>						
3512	Dysphagia (difficulty swallowing)	Symptomatic, able to eat regular diet	Symptomatic and altered eating/swallowing (e.g., altered dietary habits, oral supplements); IV fluids indicated <24 hrs	Symptomatic and severely altered eating/swallowing (e.g., inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences (e.g., obstruction, perforation)	Death
<p>REMARK: Dysphagia (difficulty swallowing) is to be used for swallowing difficulty from oral, pharyngeal, esophageal, or neurologic origin. Dysphagia requiring dilation is graded as Stricture/stenosis (including anastomotic), GI – <i>Select</i>.</p> <p>ALSO CONSIDER: Dehydration; Esophagitis.</p>						
3513	Enteritis (inflammation of the small bowel)	Asymptomatic, pathologic or radiographic findings only	Abdominal pain; mucus or blood in stool	Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs	Life-threatening consequences (e.g., perforation, bleeding, ischemia, necrosis)	Death
<p>ALSO CONSIDER: Hemorrhage, GI – <i>Select</i>; Typhlitis (cecal inflammation).</p>						
3514	Esophagitis	Asymptomatic pathologic, radiographic, or endoscopic findings only	Symptomatic; altered eating/swallowing (e.g., altered dietary habits, oral supplements); IV fluids indicated <24 hrs	Symptomatic and severely altered eating/swallowing (e.g., inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences	Death
<p>REMARK: Esophagitis includes reflux esophagitis.</p> <p>ALSO CONSIDER: Dysphagia (difficulty swallowing).</p>						

## GASTROINTESTINAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	Fistula, GI	Asymptomatic, radiographic findings only	Symptomatic; altered GI function (e.g., altered dietary habits, diarrhea, or GI fluid loss); IV fluids indicated <24 hrs	Symptomatic and severely altered GI function (e.g., altered dietary habits, diarrhea, or GI fluid loss); IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences	Death
	– <i>Select</i> :					
3516	– Abdomen NOS					
3517	– Anus					
3518	– Biliary tree					
3519	– Colon/cecum/appendix					
3520	– Duodenum					
3521	– Esophagus					
3522	– Gallbladder					
3523	– Ileum					
3524	– Jejunum					
3525	– Oral cavity					
3526	– Pancreas					
3527	– Pharynx					
3528	– Rectum					
3529	– Salivary gland					
3530	– Small bowel NOS					
3531	– Stomach					
	REMARK: A fistula is defined as an abnormal communication between two body cavities, potential spaces, and/or the skin. The site indicated for a fistula should be the site from which the abnormal process is believed to have originated. For example, a tracheo-esophageal fistula arising in the context of a resected or irradiated esophageal cancer is graded as Fistula, GI – esophagus.					
3532	Flatulence	Mild	Moderate	—	—	—
3533	Gastritis (including bile reflux gastritis)	Asymptomatic radiographic or endoscopic findings only	Symptomatic; altered gastric function (e.g., inadequate oral caloric or fluid intake); IV fluids indicated <24 hrs	Symptomatic and severely altered gastric function (e.g., inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences; operative intervention requiring complete organ resection (e.g., gastrectomy)	Death
	ALSO CONSIDER: Hemorrhage, GI – <i>Select</i> ; Ulcer, GI – <i>Select</i> .					
	NAVIGATION NOTE: Head and neck soft tissue necrosis is graded as Soft tissue necrosis – <i>Select</i> in the MUSCULOSKELETAL/SOFT TISSUE CATEGORY.					
3534	Heartburn/dyspepsia	Mild	Moderate	Severe	—	—
3535	Hemorrhoids	Asymptomatic	Symptomatic; banding or medical intervention indicated	Interfering with ADL; interventional radiology, endoscopic, or operative intervention indicated	Life-threatening; consequences	Death

## GASTROINTESTINAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
3536	Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation)	Asymptomatic, radiographic findings only	Symptomatic; altered GI function (e.g., altered dietary habits); IV fluids indicated <24 hrs	Symptomatic and severely altered GI function; IV fluids, tube feeding, or TPN indicated >=24 hrs	Life-threatening consequences	Death
REMARK: Ileus, GI is to be used for altered upper or lower GI function (e.g., delayed gastric or colonic emptying).						
ALSO CONSIDER: Constipation; Nausea; Obstruction, GI – <i>Select</i> ; Vomiting.						
3537	Incontinence, anal	Occasional use of pads required	Daily use of pads required	Interfering with ADL; operative intervention indicated	Permanent bowel diversion indicated	Death
REMARK: Incontinence, anal is to be used for loss of sphincter control as sequelae of operative or therapeutic intervention.						
	Leak (including anastomotic), GI	Asymptomatic radiographic findings only	Symptomatic; medical intervention indicated	Symptomatic and interfering with GI function; invasive or endoscopic intervention indicated	Life-threatening consequences	Death
	– <i>Select</i> :					
3539	– Biliary tree					
3540	– Esophagus					
3541	– Large bowel					
3542	– Leak NOS					
3543	– Pancreas					
3544	– Pharynx					
3545	– Rectum					
3546	– Small bowel					
3547	– Stoma					
3548	– Stomach					
	REMARK: Leak (including anastomotic), GI – <i>Select</i> is to be used for clinical signs/symptoms or radiographic confirmation of anastomotic or conduit leak (e.g., biliary, esophageal, intestinal, pancreatic, pharyngeal, rectal), but without development of fistula.					
3549	Malabsorption	—	Altered diet; oral therapies indicated (e.g., enzymes, medications, dietary supplements)	Inability to aliment adequately via GI tract (i.e., TPN indicated)	Life-threatening consequences	Death



## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Mucositis/stomatitis (clinical exam)	Erythema of the mucosa	Patchy ulcerations or pseudomembranes	Confluent ulcerations or pseudomembranes; bleeding with minor trauma	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	Death
	– <i>Select:</i>					
3551	– Anus					
3552	– Esophagus					
3553	– Large bowel					
3554	– Larynx					
3555	– Oral cavity					
3556	– Pharynx					
3557	– Rectum					
3558	– Small bowel					
3559	– Stomach					
3560	– Trachea					
	REMARK: Mucositis/stomatitis (functional/symptomatic) may be used for mucositis of the upper aero-digestive tract caused by radiation, agents, or GVHD.					
	Mucositis/stomatitis (functional/symptomatic)	<u>Upper aerodigestive tract sites:</u> Minimal symptoms, normal diet; minimal respiratory symptoms but not interfering with function.	<u>Upper aerodigestive tract sites:</u> Symptomatic but can eat and swallow modified diet; respiratory symptoms interfering with function but not interfering with ADL.	<u>Upper aerodigestive tract sites:</u> Symptomatic and unable to adequately aliment or hydrate orally; respiratory symptoms interfering with ADL	Symptoms associated with life-threatening consequences	Death
	– <i>Select:</i>					
3562	– Anus					
3563	– Esophagus					
3564	– Large bowel					
3565	– Larynx					
3566	– Oral cavity					
3567	– Pharynx					
3568	– Rectum					
3569	– Small bowel					
3570	– Stomach					
3571	– Trachea					
3572	Nausea	Loss of appetite without alteration in eating habits	Oral intake decreased without significant weight loss, dehydration or malnutrition; IV fluids indicated <24 hrs	Inadequate oral caloric or fluid intake; IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences	Death
	ALSO CONSIDER: Anorexia; Vomiting.					

## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Necrosis, GI	---	---	Inability to aliment adequately by GI tract (e.g., requiring enteral or parenteral nutrition); interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences; operative intervention requiring complete organ resection (e.g., total colectomy)	Death
	- <i>Select</i> : - Anus - Colon/cecum/appendix - Duodenum - Esophagus - Gallbladder - Hepatic - Ileum - Jejunum - Oral - Pancreas - Peritoneal cavity - Pharynx - Rectum - Small bowel NOS - Stoma - Stomach					
3574						
3575						
3576						
3577						
3578						
3579						
3580						
3581						
3582						
3583						
3584						
3585						
3586						
3587						
3588						
3589						
	ALSO CONSIDER: Visceral arterial ischemia (non-myocardial).					
	Obstruction, GI	Asymptomatic radiographic findings only	Symptomatic; altered GI function (e.g., altered dietary habits, vomiting, diarrhea, or GI fluid loss); IV fluids indicated <24 hrs	Symptomatic and severely altered GI function (e.g., altered dietary habits, vomiting, diarrhea, or GI fluid loss); IV fluids, tube feedings, or TPN indicated ≥24 hrs; operative intervention indicated	Life-threatening consequences; operative intervention requiring complete organ resection (e.g., total colectomy)	Death
	- <i>Select</i> : - Cecum - Colon - Duodenum - Esophagus - Gallbladder - Ileum - Jejunum - Rectum - Small bowel NOS - Stoma - Stomach					
3591						
3592						
3593						
3594						
3595						
3596						
3597						
3598						
3599						
3600						
3601						
	NAVIGATION NOTE: Operative injury is graded as Intra-operative injury - <i>Select</i> Organ or Structure in the SURGERY/INTRA-OPERATIVE INJURY CATEGORY.					
	NAVIGATION NOTE: Pelvic pain is graded as Pain - <i>Select</i> in the PAIN CATEGORY.					

## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Perforation, GI  – <i>Select</i> : 3603 – Appendix 3604 – Biliary tree 3605 – Cecum 3606 – Colon 3607 – Duodenum 3608 – Esophagus 3609 – Gallbladder 3610 – Ileum 3611 – Jejunum 3612 – Rectum 3613 – Small bowel NOS 3614 – Stomach	Asymptomatic radiographic findings only	Medical intervention indicated; IV fluids indicated <24 hrs	IV fluids, tube feedings, or TPN indicated ≥24 hrs; operative intervention indicated	Life-threatening consequences	Death
3615	Proctitis	Rectal discomfort, intervention not indicated	Symptoms not interfering with ADL; medical intervention indicated	Stool incontinence or other symptoms interfering with ADL; operative intervention indicated	Life-threatening consequences (e.g., perforation)	Death
3616	Prolapse of stoma, GI  REMARK: Other stoma complications may be graded as Fistula, GI – <i>Select</i> ; Leak (including anastomotic), GI – <i>Select</i> ; Obstruction, GI – <i>Select</i> ; Perforation, GI – <i>Select</i> ; Stricture/stenosis (including anastomotic), GI – <i>Select</i> .	Asymptomatic	Extraordinary local care or maintenance; minor revision indicated	Dysfunctional stoma; major revision indicated	Life-threatening consequences	Death
NAVIGATION NOTE: Rectal or perirectal pain (proctalgia) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
3617	Salivary gland changes/saliva  ALSO CONSIDER: Dry mouth/salivary gland (xerostomia); Mucositis/stomatitis (clinical exam) – <i>Select</i> ; Mucositis/stomatitis (functional/symptomatic) – <i>Select</i> ; Taste alteration (dysgeusia).	Slightly thickened saliva; slightly altered taste (e.g., metallic)	Thick, ropy, sticky saliva; markedly altered taste; alteration in diet indicated; secretion-induced symptoms not interfering with ADL	Acute salivary gland necrosis; severe secretion-induced symptoms interfering with ADL	Disabling	—
NAVIGATION NOTE: Splenic function is graded in the BLOOD/BONE MARROW CATEGORY.						

## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Stricture/stenosis (including anastomotic), GI	Asymptomatic radiographic findings only	Symptomatic; altered GI function (e.g., altered dietary habits, vomiting, bleeding, diarrhea); IV fluids indicated <24 hrs	Symptomatic and severely altered GI function (e.g., altered dietary habits, diarrhea, or GI fluid loss); IV fluids, tube feedings, or TPN indicated >=24 hrs; operative intervention indicated	Life-threatening consequences; operative intervention requiring complete organ resection (e.g. total colectomy)	Death
	<i>– Select:</i>					
3619	– Anus					
3620	– Biliary tree					
3621	– Cecum					
3622	– Colon					
3623	– Duodenum					
3624	– Esophagus					
3625	– Ileum					
3626	– Jejunum					
3627	– Pancreas/pancreatic duct					
3628	– Pharynx					
3629	– Rectum					
3630	– Small bowel NOS					
3631	– Stoma					
3632	– Stomach					
3633	Taste alteration (dysgeusia)	Altered taste but no change in diet	Altered taste with change in diet (e.g., oral supplements); noxious or unpleasant taste; loss of taste	—	—	—
3634	Typhlitis (cecal inflammation)	Asymptomatic, pathologic or radiographic findings only	Abdominal pain; mucus or blood in stool	Abdominal pain, fever, change in bowel habits with ileus; peritoneal signs	Life-threatening consequences (e.g., perforation, bleeding, ischemia, necrosis); operative intervention indicated	Death
ALSO CONSIDER: Colitis; Hemorrhage, GI – <i>Select</i> ; Ileus, GI (functional obstruction of bowel, i.e., neuroconstipation).						

## GASTROINTESTINAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Ulcer, GI	Asymptomatic, radiographic or endoscopic findings only	Symptomatic; altered GI function (e.g., altered dietary habits, oral supplements); IV fluids indicated <24 hrs	Symptomatic and severely altered GI function (e.g., inadequate oral caloric or fluid intake); IV fluids, tube feedings, or TPN indicated >=24 hrs	Life-threatening consequences	Death
	– <i>Select:</i>					
3636	– Anus					
3637	– Cecum					
3638	– Colon					
3639	– Duodenum					
3640	– Esophagus					
3641	– Ileum					
3642	– Jejunum					
3643	– Rectum					
3644	– Small bowel NOS					
3645	– Stoma					
3646	– Stomach					
	ALSO CONSIDER: Hemorrhage, GI – <i>Select.</i>					
3647	Vomiting	1 episode in 24 hrs	2 - 5 episodes in 24 hrs; IV fluids indicated <24 hrs	>=6 episodes in 24 hrs; IV fluids, or TPN indicated >=24 hrs	Life-threatening consequences	Death
	ALSO CONSIDER: Dehydration.					
3999	Gastrointestinal – Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## GROWTH AND DEVELOPMENT

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
4000	Bone age (alteration in bone age)	—	±2 SD (standard deviation) from normal	—	—	—
4001	Bone growth: femoral head; slipped capital femoral epiphysis	Mild valgus/varus deformity	Moderate valgus/varus deformity, symptomatic, interfering with function but not interfering with ADL	Mild slipped capital femoral epiphysis; operative intervention (e.g., fixation) indicated; interfering with ADL	Disabling; severe slipped capital femoral epiphysis >60%; avascular necrosis	—
4002	Bone growth: limb length discrepancy	Mild length discrepancy <2 cm	Moderate length discrepancy 2 - 5 cm; shoe lift indicated	Severe length discrepancy >5 cm; operative intervention indicated; interfering with ADL	Disabling; epiphysiodesis	—
4003	Bone growth: spine kyphosis/lordosis	Mild radiographic changes	Moderate accentuation; interfering with function but not interfering with ADL	Severe accentuation; operative intervention indicated; interfering with ADL	Disabling (e.g., cannot lift head)	—
4004	Growth velocity (reduction in growth velocity)	10 - 29% reduction in growth from the baseline growth curve	30 - 49% reduction in growth from the baseline growth curve	>=50% reduction in growth from the baseline growth curve	—	—
4005	Puberty (delayed)	—	No breast development by age 13 yrs for females; no Tanner Stage 2 development by age 14.5 yrs for males	No sexual development by age 14 yrs for girls, age 16 yrs for boys; hormone replacement indicated	—	—
REMARK: Do not use testicular size for Tanner Stage in male cancer survivors.						
4006	Puberty (precocious)	—	Physical signs of puberty <7 years for females, <9 years for males	—	—	—
4007	Short stature	Beyond two standard deviations of age and gender mean height	Altered ADL	—	—	—
REMARK: Short stature is secondary to growth hormone deficiency.						
ALSO CONSIDER: Neuroendocrine: growth hormone secretion abnormality.						
4249	Growth and Development Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

HEMORRHAGE/BLEEDING						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
4250	Hematoma	Minimal symptoms, invasive intervention not indicated	Minimally invasive evacuation or aspiration indicated	Transfusion, interventional radiology, or operative intervention indicated	Life-threatening consequences; major urgent intervention indicated	Death
<p>REMARK: Hematoma refers to extravasation at wound or operative site or secondary to other intervention. Transfusion implies pRBC.</p> <p>ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).</p>						
4251	Hemorrhage/bleeding associated with surgery, intra-operative or postoperative	—	—	Requiring transfusion of 2 units non-autologous (10 cc/kg for pediatrics) pRBCs beyond protocol specification; postoperative interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences	Death
<p>REMARK: Postoperative period is defined as &lt;=72 hours after surgery. Verify protocol-specific acceptable guidelines regarding pRBC transfusion.</p> <p>ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).</p>						
4252	Hemorrhage, CNS	Asymptomatic, radiographic findings only	Medical intervention indicated	Ventriculostomy, ICP monitoring, intraventricular thrombolysis, or operative intervention indicated	Life-threatening consequences; neurologic deficit or disability	Death
<p>ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).</p>						

HEMORRHAGE/BLEEDING						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Hemorrhage, GI	Mild, intervention (other than iron supplements) not indicated	Symptomatic and medical intervention or minor cauterization indicated	Transfusion, interventional radiology, endoscopic, or operative intervention indicated; radiation therapy (i.e., hemostasis of bleeding site)	Life-threatening consequences; major urgent intervention indicated	Death
	– <i>Select:</i>					
4254	– Abdomen NOS					
4255	– Anus					
4256	– Biliary tree					
4257	– Cecum/appendix					
4258	– Colon					
4259	– Duodenum					
4260	– Esophagus					
4261	– Ileum					
4262	– Jejunum					
4263	– Liver					
4264	– Lower GI NOS					
4265	– Oral cavity					
4266	– Pancreas					
4267	– Peritoneal cavity					
4268	– Rectum					
4269	– Stoma					
4270	– Stomach					
4271	– Upper GI NOS					
4272	– Varices (esophageal)					
4273	– Varices (rectal)					
	REMARK: Transfusion implies pRBC.					
	ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).					



HEMORRHAGE/BLEEDING						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Hemorrhage, GU	Minimal or microscopic bleeding; intervention not indicated	Gross bleeding, medical intervention, or urinary tract irrigation indicated	Transfusion, interventional radiology, endoscopic, or operative intervention indicated; radiation therapy (i.e., hemostasis of bleeding site)	Life-threatening consequences; major urgent intervention indicated	Death
	– <i>Select:</i> 4275 – Bladder 4276 – Fallopian tube 4277 – Kidney 4278 – Ovary 4279 – Prostate 4280 – Retroperitoneum 4281 – Spermatic cord 4282 – Stoma 4283 – Testes 4284 – Ureter 4285 – Urethra 4286 – Urinary NOS 4287 – Uterus 4288 – Vagina 4289 – Vas deferens					
	REMARK: Transfusion implies pRBC. ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).					
	Hemorrhage, pulmonary/upper respiratory	Mild, intervention not indicated	Symptomatic and medical intervention indicated	Transfusion, interventional radiology, endoscopic, or operative intervention indicated; radiation therapy (i.e., hemostasis of bleeding site)	Life-threatening consequences; major urgent intervention indicated	Death
	– <i>Select:</i> 4291 – Bronchopulmonary NOS 4292 – Bronchus 4293 – Larynx 4294 – Lung 4295 – Mediastinum 4296 – Nose 4297 – Pharynx 4298 – Pleura 4299 – Respiratory tract NOS 4300 – Stoma 4301 – Trachea					
	REMARK: Transfusion implies pRBC. ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).					
4302	Petechiae/purpura (hemorrhage/bleeding into skin or mucosa)	Few petechiae	Moderate petechiae; purpura	Generalized petechiae or purpura	—	—
	ALSO CONSIDER: Fibrinogen; INR (International Normalized Ratio of prothrombin time); Platelets; PTT (Partial Thromboplastin Time).					

HEMORRHAGE/BLEEDING						
		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	NAVIGATION NOTE: Vitreous hemorrhage is graded in the OCULAR/VISUAL CATEGORY.					
4499	Hemorrhage/Bleeding - Other (Specify, _____)	Mild without transfusion	—	Transfusion indicated	Catastrophic bleeding, requiring major non- elective intervention	Death

## HEPATOBIILIARY/PANCREAS

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	NAVIGATION NOTE: Biliary tree damage is graded as Fistula, GI – <i>Select</i> ; Leak (including anastomotic), GI – <i>Select</i> ; Necrosis, GI – <i>Select</i> ; Obstruction, GI – <i>Select</i> ; Perforation, GI – <i>Select</i> ; Stricture/stenosis (including anastomotic), GI – <i>Select</i> in the GASTROINTESTINAL CATEGORY.					
4500	Cholecystitis	Asymptomatic, radiographic findings only	Symptomatic, medical intervention indicated	Interventional radiology, endoscopic, or operative intervention indicated	Life-threatening consequences (e.g., sepsis or perforation)	Death
	ALSO CONSIDER: Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils– <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils– <i>Select</i> ; Infection with unknown ANC – <i>Select</i> .					
4501	Liver dysfunction/failure (clinical)	—	Jaundice	Asterixis	Encephalopathy or coma	Death
	REMARK: Jaundice is not an AE, but occurs when the liver is not working properly or when a bile duct is blocked. It is graded as a result of liver dysfunction/failure or elevated bilirubin.					
	ALSO CONSIDER: Bilirubin (hyperbilirubinemia).					
4502	Pancreas, exocrine enzyme deficiency	—	Increase in stool frequency, bulk, or odor; steatorrhea	Sequelae of absorption deficiency (e.g., weight loss)	Life-threatening consequences	Death
	ALSO CONSIDER: Diarrhea.					
4503	Pancreatitis	Asymptomatic, enzyme elevation and/or radiographic findings	Symptomatic, medical intervention indicated	Interventional radiology or operative intervention indicated	Life-threatening consequences (e.g., circulatory failure, hemorrhage, sepsis)	Death
	ALSO CONSIDER: Amylase.					
	NAVIGATION NOTE: Stricture (biliary tree, hepatic or pancreatic) is graded as Stricture/stenosis (including anastomotic), GI – <i>Select</i> in the GASTROINTESTINAL CATEGORY.					
4749	Hepatobiliary/Pancreas - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

# INFECTION

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
4750	Colitis, infectious (e.g., Clostridium difficile)  ALSO CONSIDER: Hemorrhage, GI – Select; Typhlitis (cecal inflammation).	Asymptomatic, pathologic or radiographic findings only	Abdominal pain with mucus and/or blood in stool	IV antibiotics or TPN indicated	Life-threatening consequences (e.g., perforation, bleeding, ischemia, necrosis or toxic megacolon); operative resection or diversion indicated	Death
4751	Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection)(ANC <1.0 x 10 <sup>9</sup> /L, fever >=38.5 °C) ALSO CONSIDER: Neutrophils/granulocytes (ANC/AGC).	—	—	Present	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
	Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> AUDITORY/EAR – 4754 External ear (otitis externa) – 4755 Middle ear (otitis media) CARDIOVASCULAR – 4757 Artery – 4758 Heart (endocarditis) – 4759 Spleen – 4760 Vein DERMATOLOGY/SKIN – 4762 Lip/perioral – 4763 Peristomal – 4764 Skin (cellulitis) – 4765 Ungual (nails) GASTROINTESTINAL – 4767 Abdomen NOS – 4768 Anal/perianal – 4769 Appendix – 4770 Cecum – 4771 Colon – 4772 Dental-tooth – 4773 Duodenum – 4774 Esophagus – 4775 Ileum – 4776 Jejunum – 4777 Oral cavity-gums (gingivitis) – 4778 Peritoneal cavity – 4779 Rectum – 4780 Salivary gland – 4781 Small bowel NOS – 4782 Stomach  REMARK: Fever with Grade 3 or 4 neutrophils in the absence of documented infection is graded as Febrile neutropenia (fever of unknown origin without clinically or microbiologically documented infection). ALSO CONSIDER: Neutrophils/granulocytes (ANC/AGC).	—	Localized, local intervention indicated  GENERAL – 4784 Blood – 4785 Catheter-related – 4786 Foreign body (e.g., graft, implant, prosthesis, stent) – 4787 Wound HEPATOBIILIARY/PANCREAS – 4789 Biliary tree – 4790 Gallbladder (cholecystitis) – 4791 Liver – 4792 Pancreas LYMPHATIC – 4794 Lymphatic MUSCULOSKELETAL – 4796 Bone (osteomyelitis) – 4797 Joint – 4798 Muscle (infection myositis) – 4799 Soft tissue NOS NEUROLOGY – 4801 Brain (encephalitis, infectious) – 4802 Brain + Spinal cord (encephalomyelitis) – 4803 Meninges (meningitis) – 4804 Nerve-cranial – 4805 Nerve-peripheral – 4806 Spinal cord (myelitis) OCULAR – 4808 Conjunctiva – 4809 Cornea – 4810 Eye NOS – 4811 Lens	IV antibiotic, antifungal, or antiviral intervention indicated; interventional radiology or operative intervention indicated	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)  PULMONARY/UPPER RESPIRATORY – 4813 Bronchus – 4814 Larynx – 4815 Lung (pneumonia) – 4816 Mediastinum NOS – 4817 Mucosa – 4818 Neck NOS – 4819 Nose – 4820 Paranasal – 4821 Pharynx – 4822 Pleura (empyema) – 4823 Sinus – 4824 Trachea – 4825 Upper aerodigestive NOS – 4826 Upper airway NOS RENAL/GENITOURINARY – 4828 Bladder (urinary) – 4829 Kidney – 4830 Prostate – 4831 Ureter – 4832 Urethra – 4833 Urinary tract NOS SEXUAL/REPRODUCTIVE FUNCTION – 4835 Cervix – 4836 Fallopian tube – 4837 Pelvis NOS – 4838 Penis – 4839 Scrotum – 4840 Uterus – 4841 Vagina – 4842 Vulva	Death

# INFECTION

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Infection with normal ANC or Grade 1 or 2 neutrophils	—	Localized, local intervention indicated	IV antibiotic, antifungal, or antiviral intervention indicated; interventional radiology or operative intervention indicated	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
	<p>– <i>Select:</i></p> <p><b>AUDITORY/EAR</b></p> <ul style="list-style-type: none"> <li>– 4845 External ear (otitis externa)</li> <li>– 4846 Middle ear (otitis media)</li> </ul> <p><b>CARDIOVASCULAR</b></p> <ul style="list-style-type: none"> <li>– 4848 Artery</li> <li>– 4849 Heart (endocarditis)</li> <li>– 4850 Spleen</li> <li>– 4851 Vein</li> </ul> <p><b>DERMATOLOGY/SKIN</b></p> <ul style="list-style-type: none"> <li>– 4853 Lip/perioral</li> <li>– 4854 Peristomal</li> <li>– 4855 Skin (cellulitis)</li> <li>– 4856 Ungual (nails)</li> </ul> <p><b>GASTROINTESTINAL</b></p> <ul style="list-style-type: none"> <li>– 4858 Abdomen NOS</li> <li>– 4859 Anal/perianal</li> <li>– 4860 Appendix</li> <li>– 4861 Cecum</li> <li>– 4862 Colon</li> <li>– 4863 Dental-tooth</li> <li>– 4864 Duodenum</li> <li>– 4865 Esophagus</li> <li>– 4866 Ileum</li> <li>– 4867 Jejunum</li> <li>– 4868 Oral cavity-gums (gingivitis)</li> <li>– 4869 Peritoneal cavity</li> <li>– 4870 Rectum</li> <li>– 4871 Salivary gland</li> <li>– 4872 Small bowel NOS</li> <li>– 4873 Stomach</li> </ul>	<p><b>GENERAL</b></p> <ul style="list-style-type: none"> <li>– 4875 Blood</li> <li>– 4876 Catheter-related</li> <li>– 4877 Foreign body (e.g., graft, implant, prosthesis, stent)</li> <li>– 4878 Wound</li> </ul> <p><b>HEPATOBIILIARY/PANCREAS</b></p> <ul style="list-style-type: none"> <li>– 4880 Biliary tree</li> <li>– 4881 Gallbladder (cholecystitis)</li> <li>– 4882 Liver</li> <li>– 4883 Pancreas</li> </ul> <p><b>LYMPHATIC</b></p> <ul style="list-style-type: none"> <li>– 4885 Lymphatic</li> </ul> <p><b>MUSCULOSKELETAL</b></p> <ul style="list-style-type: none"> <li>– 4887 Bone (osteomyelitis)</li> <li>– 4888 Joint</li> <li>– 4889 Muscle (infection myositis)</li> <li>– 4890 Soft tissue NOS</li> </ul> <p><b>NEUROLOGY</b></p> <ul style="list-style-type: none"> <li>– 4892 Brain (encephalitis, infectious)</li> <li>– 4893 Brain + Spinal cord (encephalomyelitis)</li> <li>– 4894 Meninges (meningitis)</li> <li>– 4895 Nerve-cranial</li> <li>– 4896 Nerve-peripheral</li> <li>– 4897 Spinal cord (myelitis)</li> </ul> <p><b>OCULAR</b></p> <ul style="list-style-type: none"> <li>– 4899 Conjunctiva</li> <li>– 4900 Cornea</li> <li>– 4901 Eye NOS</li> <li>– 4902 Lens</li> </ul>	<p><b>PULMONARY/UPPER RESPIRATORY</b></p> <ul style="list-style-type: none"> <li>– 4904 Bronchus</li> <li>– 4905 Larynx</li> <li>– 4906 Lung (pneumonia)</li> <li>– 4907 Mediastinum NOS</li> <li>– 4908 Mucosa</li> <li>– 4909 Neck NOS</li> <li>– 4910 Nose</li> <li>– 4911 Paranasal</li> <li>– 4912 Pharynx</li> <li>– 4913 Pleura (empyema)</li> <li>– 4914 Sinus</li> <li>– 4915 Trachea</li> <li>– 4916 Upper aerodigestive NOS</li> <li>– 4917 Upper airway NOS</li> </ul> <p><b>RENAL/GENITOURINARY</b></p> <ul style="list-style-type: none"> <li>– 4919 Bladder (urinary)</li> <li>– 4920 Kidney</li> <li>– 4921 Prostate</li> <li>– 4922 Ureter</li> <li>– 4923 Urethra</li> <li>– 4924 Urinary tract NOS</li> </ul> <p><b>SEXUAL/REPRODUCTIVE FUNCTION</b></p> <ul style="list-style-type: none"> <li>– 4926 Cervix</li> <li>– 4927 Fallopian tube</li> <li>– 4928 Pelvis NOS</li> <li>– 4929 Penis</li> <li>– 4930 Scrotum</li> <li>– 4931 Uterus</li> <li>– 4932 Vagina</li> <li>– 4933 Vulva</li> </ul>			

# INFECTION

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	Infection with unknown ANC	—	Localized, local intervention indicated	IV antibiotic, antifungal, or antiviral intervention indicated; interventional radiology or operative intervention indicated	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
	<p>– <i>Select</i>:</p> <p><b>AUDITORY/EAR</b></p> <ul style="list-style-type: none"> <li>– 4936 External ear (otitis externa)</li> <li>– 4937 Middle ear (otitis media)</li> </ul> <p><b>CARDIOVASCULAR</b></p> <ul style="list-style-type: none"> <li>– 4939 Artery</li> <li>– 4940 Heart (endocarditis)</li> <li>– 4941 Spleen</li> <li>– 4942 Vein</li> </ul> <p><b>DERMATOLOGY/SKIN</b></p> <ul style="list-style-type: none"> <li>– 4944 Lip/perioral</li> <li>– 4945 Peristomal</li> <li>– 4946 Skin (cellulitis)</li> <li>– 4947 Ungual (nails)</li> </ul> <p><b>GASTROINTESTINAL</b></p> <ul style="list-style-type: none"> <li>– 4949 Abdomen NOS</li> <li>– 4950 Anal/perianal</li> <li>– 4951 Appendix</li> <li>– 4952 Cecum</li> <li>– 4953 Colon</li> <li>– 4954 Dental-tooth</li> <li>– 4955 Duodenum</li> <li>– 4956 Esophagus</li> <li>– 4957 Ileum</li> <li>– 4958 Jejunum</li> <li>– 4959 Oral cavity-gums (gingivitis)</li> <li>– 4960 Peritoneal cavity</li> <li>– 4961 Rectum</li> <li>– 4962 Salivary gland</li> <li>– 4963 Small bowel NOS</li> <li>– 4964 Stomach</li> </ul>		<p><b>GENERAL</b></p> <ul style="list-style-type: none"> <li>– 4966 Blood</li> <li>– 4967 Catheter-related</li> <li>– 4968 Foreign body (e.g., graft, implant, prosthesis, stent)</li> <li>– 4969 Wound</li> </ul> <p><b>HEPATOBIILIARY/PANCREAS</b></p> <ul style="list-style-type: none"> <li>– 4971 Biliary tree</li> <li>– 4972 Gallbladder (cholecystitis)</li> <li>– 4973 Liver</li> <li>– 4974 Pancreas</li> </ul> <p><b>LYMPHATIC</b></p> <ul style="list-style-type: none"> <li>– 4976 Lymphatic</li> </ul> <p><b>MUSCULOSKELETAL</b></p> <ul style="list-style-type: none"> <li>– 4978 Bone (osteomyelitis)</li> <li>– 4979 Joint</li> <li>– 4980 Muscle (infection myositis)</li> <li>– 4981 Soft tissue NOS</li> </ul> <p><b>NEUROLOGY</b></p> <ul style="list-style-type: none"> <li>– 4983 Brain (encephalitis, infectious)</li> <li>– 4984 Brain + Spinal cord (encephalomyelitis)</li> <li>– 4985 Meninges (meningitis)</li> <li>– 4986 Nerve-cranial</li> <li>– 4987 Nerve-peripheral</li> <li>– 4988 Spinal cord (myelitis)</li> </ul> <p><b>OCULAR</b></p> <ul style="list-style-type: none"> <li>– 4990 Conjunctiva</li> <li>– 4991 Cornea</li> <li>– 4992 Eye NOS</li> <li>– 4993 Lens</li> </ul>		<p><b>PULMONARY/UPPER RESPIRATORY</b></p> <ul style="list-style-type: none"> <li>– 4995 Bronchus</li> <li>– 4996 Larynx</li> <li>– 4997 Lung (pneumonia)</li> <li>– 4998 Mediastinum NOS</li> <li>– 4999 Mucosa</li> <li>– 5000 Neck NOS</li> <li>– 5001 Nose</li> <li>– 5002 Paranasal</li> <li>– 5003 Pharynx</li> <li>– 5004 Pleura (empyema)</li> <li>– 5005 Sinus</li> <li>– 5006 Trachea</li> <li>– 5007 Upper aerodigestive NOS</li> <li>– 5008 Upper airway NOS</li> </ul> <p><b>RENAL/GENITOURINARY</b></p> <ul style="list-style-type: none"> <li>– 5010 Bladder (urinary)</li> <li>– 5011 Kidney</li> <li>– 5012 Prostate</li> <li>– 5013 Ureter</li> <li>– 5014 Urethra</li> <li>– 5015 Urinary tract NOS</li> </ul> <p><b>SEXUAL/REPRODUCTIVE FUNCTION</b></p> <ul style="list-style-type: none"> <li>– 5017 Cervix</li> <li>– 5018 Fallopian tube</li> <li>– 5019 Pelvis NOS</li> <li>– 5020 Penis</li> <li>– 5021 Scrotum</li> <li>– 5022 Uterus</li> <li>– 5023 Vagina</li> <li>– 5024 Vulva</li> </ul>	
	<p>'Select' AEs appear at the end of the CATEGORY.</p> <p>REMARK: Infection with unknown ANC – <i>Select</i> is to be used in the rare case when ANC is unknown.</p>					

INFECTION						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
5025	Opportunistic infection associated with >=Grade 2 Lymphopenia  ALSO CONSIDER: Lymphopenia.	—	Localized, local intervention indicated	IV antibiotic, antifungal, or antiviral intervention indicated; interventional radiology or operative intervention indicated	Life-threatening consequences (e.g., septic shock, hypotension, acidosis, necrosis)	Death
5026	Viral hepatitis  REMARK: Non-viral hepatitis is graded as Infection – <i>Select</i> .  ALSO CONSIDER: Albumin, serum-low (hypoalbuminemia); ALT, SGPT (serum glutamic pyruvic transaminase); AST, SGOT (serum glutamic oxaloacetic transaminase); Bilirubin (hyperbilirubinemia); Encephalopathy.	Present; transaminases and liver function normal	Transaminases abnormal, liver function normal	Symptomatic liver dysfunction; fibrosis by biopsy; compensated cirrhosis	Decompensated liver function (e.g., ascites, coagulopathy, encephalopathy, coma)	Death
5249	Infection - Other (Specify, ___)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## LYMPHATICS

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
5250	Chyle or lymph leakage  ALSO CONSIDER: Chylothorax.	Asymptomatic, clinical or radiographic findings	Symptomatic, medical intervention indicated	Interventional radiology or operative intervention indicated	Life-threatening complications	Death
5251	Dermal change lymphedema, phlebolymphe <sup>d</sup> ema  REMARK: Dermal change lymphedema, phlebolymphe <sup>d</sup> ema refers to changes due to venous stasis.  ALSO CONSIDER: Ulceration.	Trace thickening or faint discoloration	Marked discoloration; leathery skin texture; papillary formation	---	---	---
5252	Edema: head and neck	Localized to dependent areas, no disability or functional impairment	Localized facial or neck edema with functional impairment	Generalized facial or neck edema with functional impairment (e.g., difficulty in turning neck or opening mouth compared to baseline)	Severe with ulceration or cerebral edema; tracheotomy or feeding tube indicated	Death
5253	Edema: limb	5 - 10% inter-limb discrepancy in volume or circumference at point of greatest visible difference; swelling or obscuration of anatomic architecture on close inspection; pitting edema	>10 - 30% inter-limb discrepancy in volume or circumference at point of greatest visible difference; readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour	>30% inter-limb discrepancy in volume; lymphorrhea; gross deviation from normal anatomic contour; interfering with ADL	Progression to malignancy (i.e., lymphangiosarcoma); amputation indicated; disabling	Death
5254	Edema: trunk/genital	Swelling or obscuration of anatomic architecture on close inspection; pitting edema	Readily apparent obscuration of anatomic architecture; obliteration of skin folds; readily apparent deviation from normal anatomic contour	Lymphorrhea; interfering with ADL; gross deviation from normal anatomic contour	Progression to malignancy (i.e., lymphangiosarcoma); disabling	Death
5255	Edema: viscera	Asymptomatic; clinical or radiographic findings only	Symptomatic; medical intervention indicated	Symptomatic and unable to aliment adequately orally; interventional radiology or operative intervention indicated	Life-threatening consequences	Death



## LYMPHATICS

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
5256	Lymphedema-related fibrosis	Minimal to moderate redundant soft tissue, unresponsive to elevation or compression, with moderately firm texture or spongy feel	Marked increase in density and firmness, with or without tethering	Very marked density and firmness with tethering affecting $\geq 40\%$ of the edematous area	—	—
5257	Lymphocele	Asymptomatic, clinical or radiographic findings only	Symptomatic; medical intervention indicated	Symptomatic and interventional radiology or operative intervention indicated	—	—
5258	Phlebolympathic cording	Asymptomatic, clinical findings only	Symptomatic; medical intervention indicated	Symptomatic and leading to contracture or reduced range of motion	—	—
5499	Lymphatics - Other (Specify, ___)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## METABOLIC/LABORATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
5500	Acidosis (metabolic or respiratory)	pH <normal, but $\geq 7.3$	—	pH <7.3	pH <7.3 with life-threatening consequences	Death
5501	Albumin, serum-low (hypoalbuminemia)	<LLN - 3 g/dL <LLN - 30 g/L	<3 - 2 g/dL <30 - 20 g/L	<2 g/dL <20 g/L	—	Death
5502	Alkaline phosphatase	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	—
5503	Alkalosis (metabolic or respiratory)	pH >normal, but $\leq 7.5$	—	pH >7.5	pH >7.5 with life-threatening consequences	Death
5504	ALT, SGPT (serum glutamic pyruvic transaminase)	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	—
5505	Amylase	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN	>2.0 - 5.0 x ULN	>5.0 x ULN	—
5506	AST, SGOT (serum glutamic oxaloacetic transaminase)	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	—
5507	Bicarbonate, serum-low	<LLN - 16 mmol/L	<16 - 11 mmol/L	<11 - 8 mmol/L	<8 mmol/L	Death
5508	Bilirubin (hyperbilirubinemia)	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 10.0 x ULN	>10.0 x ULN	—
	REMARK: Jaundice is not an AE, but may be a manifestation of liver dysfunction/failure or elevated bilirubin. If jaundice is associated with elevated bilirubin, grade bilirubin.					
5509	Calcium, serum-low (hypocalcemia)	<LLN - 8.0 mg/dL <LLN - 2.0 mmol/L  Ionized calcium: <LLN - 1.0 mmol/L	<8.0 - 7.0 mg/dL <2.0 - 1.75 mmol/L  Ionized calcium: <1.0 - 0.9 mmol/L	<7.0 - 6.0 mg/dL <1.75 - 1.5 mmol/L  Ionized calcium: <0.9 - 0.8 mmol/L	<6.0 mg/dL <1.5 mmol/L  Ionized calcium: <0.8 mmol/L	Death
	REMARK: Calcium can be falsely low if hypoalbuminemia is present. Serum albumin is <4.0 g/dL, hypocalcemia is reported after the following corrective calculation has been performed: Corrected Calcium (mg/dL) = Total Calcium (mg/dL) - 0.8 [Albumin (g/dL) - 4] <sup>4</sup> . Alternatively, direct measurement of ionized calcium is the definitive method to diagnose metabolically relevant alterations in serum calcium.					

<sup>4</sup>Crit Rev Clin Lab Sci 1984;21(1):51-97

## METABOLIC/LABORATORY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
5510	Calcium, serum-high (hypercalcemia)	>ULN - 11.5 mg/dL >ULN - 2.9 mmol/L  Ionized calcium >ULN - 1.5 mmol/L	>11.5 - 12.5 mg/dL >2.9 - 3.1 mmol/L  Ionized calcium >1.5 - 1.6 mmol/L	>12.5 - 13.5 mg/dL >3.1 - 3.4 mmol/L  Ionized calcium >1.6 - 1.8 mmol/L	>13.5 mg/dL >3.4 mmol/L  Ionized calcium >1.8 mmol/L	Death
5511	Cholesterol, serum-high (hypercholesteremia)	>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	Death
5512	CPK (creatine phosphokinase)	>ULN - 2.5 x ULN	>2.5 x ULN - 5 x ULN	>5 x ULN - 10 x ULN	>10 x ULN	Death
5513	Creatinine	>ULN - 1.5 x ULN	>1.5 - 3.0 x ULN	>3.0 - 6.0 x ULN	>6.0 x ULN	Death
REMARK: Adjust to age-appropriate levels for pediatric patients. ALSO CONSIDER: Glomerular filtration rate.						
5514	GGT (gamma-Glutamyl transpeptidase)	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 20.0 x ULN	>20.0 x ULN	—
5515	Glomerular filtration rate	<75 - 50% LLN	<50 - 25% LLN	<25% LLN, chronic dialysis not indicated	Chronic dialysis or renal transplant indicated	Death
ALSO CONSIDER: Creatinine.						
5516	Glucose, serum-high (hyperglycemia)	>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	Death
REMARK: Hyperglycemia, in general, is defined as fasting unless otherwise specified in protocol.						
5517	Glucose, serum-low (hypoglycemia)	<LLN - 55 mg/dL <LLN - 3.0 mmol/L	<55 - 40 mg/dL <3.0 - 2.2 mmol/L	<40 - 30 mg/dL <2.2 - 1.7 mmol/L	<30 mg/dL <1.7 mmol/L	Death
5518	Hemoglobinuria	Present	—	—	—	Death
5519	Lipase	>ULN - 1.5 x ULN	>1.5 - 2.0 x ULN	>2.0 - 5.0 x ULN	>5.0 x ULN	—
5520	Magnesium, serum-high (hypermagnesemia)	>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	Death
5521	Magnesium, serum-low (hypomagnesemia)	<LLN - 1.2 mg/dL <LLN - 0.5 mmol/L	<1.2 - 0.9 mg/dL <0.5 - 0.4 mmol/L	<0.9 - 0.7 mg/dL <0.4 - 0.3 mmol/L	<0.7 mg/dL <0.3 mmol/L	Death
5522	Phosphate, serum-low (hypophosphatemia)	<LLN - 2.5 mg/dl <LLN - 0.8 mmol/L	<2.5 - 2.0 mg/dL <0.8 - 0.6 mmol/L	<2.0 - 1.0 mg/dL <0.6 - 0.3 mmol/L	<1.0 mg/dL <0.3 mmol/L	Death
5523	Potassium, serum-high (hyperkalemia)	>ULN - 5.5 mmol/L	>5.5 - 6.0 mmol/L	>6.0 - 7.0 mmol/L	>7.0 mmol/L	Death

## METABOLIC/LABORATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
5524	Potassium, serum-low (hypokalemia)	<LLN - 3.0 mmol/L	—	<3.0 - 2.5 mmol/L	<2.5 mmol/L	Death
5525	Proteinuria	1+ or 0.15 - 1.0 g/24 hrs	2+ to 3+ or >1.0 - 3.5 g/24 hrs	4+ or >3.5 g/24 hrs	Nephrotic syndrome	Death
5526	Sodium, serum-high (hypernatremia)	>ULN - 150 mmol/L	>150 - 155 mmol/L	>155 - 160 mmol/L	>160 mmol/L	Death
5527	Sodium, serum-low (hyponatremia)	<LLN - 130 mmol/L	—	<130 - 120 mmol/L	<120 mmol/L	Death
5528	Triglyceride, serum-high (hypertriglyceridemia)	>ULN - 2.5 x ULN	>2.5 - 5.0 x ULN	>5.0 - 10 x ULN	>10 x ULN	Death
5529	Uric acid, serum-high (hyperuricemia)	>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	Death
ALSO CONSIDER: Creatinine; Potassium, serum-high (hyperkalemia); Renal failure; Tumor lysis syndrome.						
5749	Metabolic/Laboratory - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## MUSCULOSKELETAL/SOFT TISSUE

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
5750	Arthritis (non-septic)	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 ADL	Severe pain with inflammation, erythema, or joint swelling and interfering with ADL	Disabling	Death
REMARK: Report only when the diagnosis of arthritis (e.g., inflammation of a joint or a state characterized by inflammation of joints) is made. Arthralgia (sign or symptom of pain in a joint, especially non-inflammatory in character) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
5751	Bone: spine-scoliosis	<=20 degrees; clinically undetectable	>20 - 45 degrees; visible by forward flexion; interfering with function but not interfering with ADL	>45 degrees; scapular prominence in forward flexion; operative intervention indicated; interfering with ADL	Disabling (e.g., interfering with cardiopulmonary function)	Death
5752	Cervical spine-range of motion	Mild restriction of rotation or flexion between 60 - 70 degrees	Rotation <60 degrees to right or left; <60 degrees of flexion	Ankylosed/fused over multiple segments with no C-spine rotation	—	—
REMARK: 60 – 65 degrees of rotation is required for reversing a car; 60 – 65 degrees of flexion is required to tie shoes.						
5753	Exostosis	Asymptomatic	Involving multiple sites; pain or interfering with function	Excision indicated	Progression to malignancy (i.e., chondrosarcoma)	Death
5754	Extremity-lower (gait/walking)	Limp evident only to trained observer and able to walk >=1 kilometer; cane indicated for walking	Noticeable limp, or limitation of limb function, but able to walk >=0.1 kilometer (1 city block); quad cane indicated for walking	Severe limp with stride modified to maintain balance (widened base of support, marked reduction in step length); ambulation limited to walker; crutches indicated	Unable to walk	—
Also Consider: Ataxia (incoordination); Muscle weakness, generalized or specific area (not due to neuropathy) - <i>Select</i>						
5755	Extremity-upper (function)	Able to perform most household or work activities with affected limb	Able to perform most household or work activities with compensation from unaffected limb	Interfering with ADL	Disabling; no function of affected limb	—
5756	Fibrosis-cosmesis	Visible only on close examination	Readily apparent but not disfiguring	Significant disfigurement; operative intervention indicated if patient chooses	—	—

## MUSCULOSKELETAL/SOFT TISSUE

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
5757	Fibrosis-deep connective tissue  ALSO CONSIDER: Induration/fibrosis (skin and subcutaneous tissue); Muscle weakness, generalized or specific area (not due to neuropathy) – <i>Select</i> ; Neuropathy: motor; Neuropathy: sensory.	Increased density, "spongy" feel	Increased density with firmness or tethering	Increased density with fixation of tissue; operative intervention indicated; interfering with ADL	Life-threatening; disabling; loss of limb; interfering with vital organ function	Death
5758	Fracture	Asymptomatic, radiographic findings only (e.g., asymptomatic rib fracture on plain x-ray, pelvic insufficiency fracture on MRI, etc.)	Symptomatic but non-displaced; immobilization indicated	Symptomatic and displaced or open wound with bone exposure; operative intervention indicated	Disabling; amputation indicated	Death
5759	Joint-effusion  ALSO CONSIDER: Arthritis (non-septic).	Asymptomatic, clinical or radiographic findings only	Symptomatic; interfering with function but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	Death
5760	Joint-function <sup>5</sup>  ALSO CONSIDER: Arthritis (non-septic).	Stiffness interfering with athletic activity; <=25% loss of range of motion (ROM)	Stiffness interfering with function but not interfering with ADL; >25 - 50% decrease in ROM	Stiffness interfering with ADL; >50 - 75% decrease in ROM	Fixed or non-functional joint (arthrodesis); >75% decrease in ROM	—
5761	Local complication -device/prosthesis-related	Asymptomatic	Symptomatic, but not interfering with ADL; local wound care; medical intervention indicated	Symptomatic, interfering with ADL; operative intervention indicated (e.g., hardware/device replacement or removal, reconstruction)	Life-threatening; disabling; loss of limb or organ	Death
5762	Lumbar spine-range of motion	Stiffness and difficulty bending to the floor to pick up a very light object but able to do activity	Some lumbar spine flexion but requires a reaching aid to pick up a very light object from the floor	Ankylosed/fused over multiple segments with no L-spine flexion (i.e., unable to reach to floor to pick up a very light object)	—	—

<sup>5</sup>Adapted from the International *SFTR Method of Measuring and Recording Joint Motion, International Standard Orthopedic Measurements (ISOM)*, Jon J. Gerhardt and Otto A. Russee, Bern, Switzerland, Han Huber 9 Publisher), 1975.

## MUSCULOSKELETAL/SOFT TISSUE

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Muscle weakness, generalized or specific area (not due to neuropathy)	Asymptomatic, weakness on physical exam	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	Life-threatening; disabling	Death
	– <i>Select</i> :					
5764	– Extraocular					
5765	– Extremity-lower					
5766	– Extremity-upper					
5767	– Facial					
5768	– Left-sided					
5769	– Ocular					
5770	– Pelvic					
5771	– Right-sided					
5772	– Trunk					
5773	– Whole body/generalized					
	ALSO CONSIDER: Fatigue (asthenia, lethargy, malaise).					
5774	Muscular/skeletal hypoplasia	Cosmetically and functionally insignificant hypoplasia	Deformity, hypoplasia, or asymmetry able to be remediated by prosthesis (e.g., shoe insert) or covered by clothing	Functionally significant deformity, hypoplasia, or asymmetry, unable to be remediated by prosthesis or covered by clothing	Disabling	—
5775	Myositis (inflammation/damage of muscle)	Mild pain, not interfering with function	Pain interfering with function, but not interfering with ADL	Pain interfering with ADL	Disabling	Death
	REMARK: Myositis implies muscle damage (i.e., elevated CPK). ALSO CONSIDER: CPK (creatine phosphokinase); Pain – <i>Select</i> .					
5776	Osteonecrosis (avascular necrosis)	Asymptomatic, radiographic findings only	Symptomatic and interfering with function, but not interfering with ADL; minimal bone removal indicated (i.e., minor sequestrectomy)	Symptomatic and interfering with ADL; operative intervention or hyperbaric oxygen indicated	Disabling	Death

MUSCULOSKELETAL/SOFT TISSUE						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
5777	Osteoporosis <sup>6</sup>	Radiographic evidence of osteoporosis or Bone Mineral Density (BMD) t-score -1 to -2.5 (osteopenia) and no loss of height or therapy indicated	BMD t-score < -2.5; loss of height <2 cm; anti-osteoporotic therapy indicated	Fractures; loss of height ≥2 cm	Disabling	Death
5778	Seroma	Asymptomatic	Symptomatic; medical intervention or simple aspiration indicated	Symptomatic, interventional radiology or operative intervention indicated	—	—
	Soft tissue necrosis	—	Local wound care; medical intervention indicated	Operative debridement or other invasive intervention indicated (e.g., hyperbaric oxygen)	Life-threatening consequences; major invasive intervention indicated (e.g., tissue reconstruction, flap, or grafting)	Death
	— <i>Select</i> :					
5780	— Abdomen					
5781	— Extremity-lower					
5782	— Extremity-upper					
5783	— Head					
5784	— Neck					
5785	— Pelvic					
5786	— Thorax					
5787	Trismus (difficulty, restriction or pain when opening mouth)	Decreased range of motion without impaired eating	Decreased range of motion requiring small bites, soft foods or purees	Decreased range of motion with inability to adequately aliment or hydrate orally	—	—
	NAVIGATION NOTE: Wound-infectious is graded as Infection – <i>Select</i> in the INFECTION CATEGORY.					
	NAVIGATION NOTE: Wound non-infectious is graded as Wound complication, non-infectious in the DERMATOLOGY/SKIN CATEGORY.					
5999	Musculoskeletal/Soft Tissue - Other (Specify, )	Mild	Moderate	Severe	Life-threatening; disabling	Death

<sup>6</sup>"Assessment of Fracture Risk and its Application to Screening for Postmenopausal Osteoporosis," Report of a *WHO Study Group Technical Report Series*, No. 843, 1994, v + 129 pages [C\*, E, F, R, S], ISBN 92 4 120843 0, Sw.fr. 22.-/US \$19.80; in developing countries: Sw.fr. 15.40, Order no. 1100843



## NEUROLOGY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
NAVIGATION NOTE: ADD (Attention Deficit Disorder) is graded as Cognitive disturbance.						
NAVIGATION NOTE: Aphasia, receptive and/or expressive, is graded as Speech impairment (e.g., dysphasia or aphasia).						
6000	Apnea	—	—	Present	Intubation indicated	Death
6001	Arachnoiditis/meningismus/radiculitis	Symptomatic, not interfering with function; medical intervention indicated	Symptomatic (e.g., photophobia, nausea) interfering with function but not interfering with ADL	Symptomatic, interfering with ADL	Life-threatening; disabling (e.g., paraplegia)	Death
ALSO CONSIDER: Fever (in the absence of neutropenia, where neutropenia is defined as ANC <1.0 x 10 <sup>9</sup> /L); Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – Select; Infection with normal ANC or Grade 1 or 2 neutrophils – Select; Infection with unknown ANC – Select; Pain – Select; Vomiting.						
6002	Ataxia (incoordination)	Asymptomatic	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL; mechanical assistance indicated	Disabling	Death
REMARK: Ataxia (incoordination) refers to the consequence of medical or operative intervention.						
6003	Brachial plexopathy	Asymptomatic	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL	Disabling	Death
6004	CNS cerebrovascular ischemia	—	Asymptomatic, radiographic findings only	Transient ischemic event or attack (TIA) <=24 hrs duration	Cerebral vascular accident (CVA, stroke), neurologic deficit >24 hrs	Death
NAVIGATION NOTE: CNS hemorrhage/bleeding is graded as Hemorrhage, CNS in the HEMORRHAGE/BLEEDING CATEGORY.						
6005	CNS necrosis/cystic progression	Asymptomatic, radiographic findings only	Symptomatic, not interfering with ADL; medical intervention indicated	Symptomatic and interfering with ADL; hyperbaric oxygen indicated	Life-threatening; disabling; operative intervention indicated to prevent or treat CNS necrosis/cystic progression	Death
6006	Cognitive disturbance	Mild cognitive disability; not interfering with work/school/life performance; specialized educational services/devices not indicated	Moderate cognitive disability; interfering with work/school/life performance but capable of independent living; specialized resources on part-time basis indicated	Severe cognitive disability; significant impairment of work/school/life performance	Unable to perform ADL; full-time specialized resources or institutionalization indicated	Death
REMARK: Cognitive disturbance may be used for Attention Deficit Disorder (ADD).						

## NEUROLOGY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
6007	Confusion	Transient confusion, disorientation, or attention deficit	Confusion, disorientation, or attention deficit interfering with function, but not interfering with ADL	Confusion or delirium interfering with ADL	Harmful to others or self; hospitalization indicated	Death
REMARK: Attention Deficit Disorder (ADD) is graded as Cognitive disturbance.						
NAVIGATION NOTE: Cranial neuropathy is graded as Neuropathy-cranial – <i>Select</i> .						
6008	Dizziness	With head movements or nystagmus only; not interfering with function	Interfering with function, but not interfering with ADL	Interfering with ADL	Disabling	—
REMARK: Dizziness includes disequilibrium, lightheadedness, and vertigo.						
ALSO CONSIDER: Neuropathy: cranial – <i>Select</i> ; Syncope (fainting).						
NAVIGATION NOTE: Dysphasia, receptive and/or expressive, is graded as Speech impairment (e.g., dysphasia or aphasia).						
6009	Encephalopathy		Mild signs or symptoms; not interfering with ADL	Signs or symptoms interfering with ADL; hospitalization indicated	Life-threatening; disabling	Death
ALSO CONSIDER: Cognitive disturbance; Confusion; Dizziness; Memory impairment; Mental status; Mood alteration – <i>Select</i> ; Psychosis (hallucinations/delusions); Somnolence/depressed level of consciousness.						
6010	Extrapyramidal/involuntary movement/restlessness	Mild involuntary movements not interfering with function	Moderate involuntary movements interfering with function, but not interfering with ADL	Severe involuntary movements or torticollis interfering with ADL	Disabling	Death
NAVIGATION NOTE: Headache/neuropathic pain (e.g., jaw pain, neurologic pain, phantom limb pain, post-infectious neuralgia, or painful neuropathies) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
6011	Hydrocephalus	Asymptomatic, radiographic findings only	Mild to moderate symptoms not interfering with ADL	Severe symptoms or neurological deficit interfering with ADL	Disabling	Death
6012	Irritability (children <3 years of age)	Mild; easily consolable	Moderate; requiring increased attention	Severe; inconsolable	—	—
6013	Laryngeal nerve dysfunction	Asymptomatic, weakness on clinical examination/testing only	Symptomatic, but not interfering with ADL; intervention not indicated	Symptomatic, interfering with ADL; intervention indicated (e.g., thyroplasty, vocal cord injection)	Life-threatening; tracheostomy indicated	Death

NEUROLOGY						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
6014	Leak, cerebrospinal fluid (CSF)	Transient headache; postural care indicated	Symptomatic, not interfering with ADL; blood patch indicated	Symptomatic, interfering with ADL; operative intervention indicated	Life-threatening; disabling	Death
	REMARK: Leak, cerebrospinal fluid (CSF) may be used for CSF leak associated with operation and persisting >72 hours.					
6015	Leukoencephalopathy (radiographic findings)	Mild increase in subarachnoid space (SAS); mild ventriculomegaly; small (+/- multiple) focal T2 hyperintensities, involving periventricular white matter or <1/3 of susceptible areas of cerebrum	Moderate increase in SAS; moderate ventriculomegaly; 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)	---	---
	REMARK: Leukoencephalopathy is a diffuse white matter process, specifically NOT associated with necrosis. Leukoencephalopathy (radiographic findings) does not include lacunas, which are areas that become void of neural tissue.					
6016	Memory impairment	Memory impairment not interfering with function	Memory impairment interfering with function, but not interfering with ADL	Memory impairment interfering with ADL	Amnesia	---
6017	Mental status <sup>7</sup>	---	1 - 3 point below age and educational norm in Folstein Mini-Mental Status Exam (MMSE)	>3 point below age and educational norm in Folstein MMSE	---	---
	Mood alteration	Mild mood alteration not interfering with function	Moderate mood alteration interfering with function, but not interfering with ADL; medication indicated	Severe mood alteration interfering with ADL	Suicidal ideation; danger to self or others	Death
	- Select:					
6019	- Agitation					
6020	- Anxiety					
6021	- Depression					
6022	- Euphoria					
6023	Myelitis	Asymptomatic, mild signs (e.g., Babinski's or Lhermitte's sign)	Weakness or sensory loss not interfering with ADL	Weakness or sensory loss interfering with ADL	Disabling	Death
NAVIGATION NOTE: Neuropathic pain is graded as Pain - Select in the PAIN CATEGORY.						

<sup>7</sup> Folstein MF, Folstein, SE and McHugh PR (1975) "Mini-Mental State: A Practical Method for Grading the State of Patients for the Clinician," *Journal of Psychiatric Research*, 12: 189-198

## NEUROLOGY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
6025 6026 6027 6028 6029 6030 6031 6032 6033 6034 6035 6036	Neuropathy: cranial  – <i>Select</i> : – CN I Smell – CN II Vision – CN III Pupil, upper eyelid, extra ocular movements – CN IV Downward, inward movement of eye – CN V Motor-jaw muscles; Sensory-facial – CN VI Lateral deviation of eye – CN VII Motor-face; Sensory-taste – CN VIII Hearing and balance – CN IX Motor-pharynx; Sensory-ear, pharynx, tongue – CN X Motor-palate; pharynx, larynx – CN XI Motor-sternomastoid and trapezius – CN XII Motor-tongue	Asymptomatic, detected on exam/testing only	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL	Life-threatening; disabling	Death
6037	Neuropathy: motor  REMARK: Cranial nerve <u>motor</u> neuropathy is graded as Neuropathy: cranial – <i>Select</i> . ALSO CONSIDER: Laryngeal nerve dysfunction; Phrenic nerve dysfunction.	Asymptomatic, weakness on exam/testing only	Symptomatic weakness interfering with function, but not interfering with ADL	Weakness interfering with ADL; bracing or assistance to walk (e.g., cane or walker) indicated	Life-threatening; disabling (e.g., paralysis)	Death
6038	Neuropathy: sensory  REMARK: Cranial nerve <u>sensory</u> neuropathy is graded as Neuropathy: cranial – <i>Select</i> .	Asymptomatic; loss of deep tendon reflexes or paresthesia (including tingling) but not interfering with function	Sensory alteration or paresthesia (including tingling), interfering with function, but not interfering with ADL	Sensory alteration or paresthesia interfering with ADL	Disabling	Death
6039	Personality/behavioral	Change, but not adversely affecting patient or family	Change, adversely affecting patient or family	Mental health intervention indicated	Change harmful to others or self; hospitalization indicated	Death
6040	Phrenic nerve dysfunction	Asymptomatic weakness on exam/testing only	Symptomatic but not interfering with ADL; intervention not indicated	Significant dysfunction; intervention indicated (e.g., diaphragmatic plication)	Life-threatening respiratory compromise; mechanical ventilation indicated	Death
6041	Psychosis (hallucinations/delusions)	—	Transient episode	Interfering with ADL; medication, supervision or restraints indicated	Harmful to others or self; life-threatening consequences	Death

## NEUROLOGY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6042	Pyramidal tract dysfunction (e.g., increased tone, hyperreflexia, positive Babinski, decreased fine motor coordination)	Asymptomatic, abnormality on exam or testing only	Symptomatic; interfering with function but not interfering with ADL	Interfering with ADL	Disabling; paralysis	Death
6043	Seizure	—	One brief generalized seizure; seizure(s) well controlled by anticonvulsants or infrequent focal motor seizures not interfering with ADL	Seizures in which consciousness is altered; poorly controlled seizure disorder, with breakthrough generalized seizures despite medical intervention	Seizures of any kind which are prolonged, repetitive, or difficult to control (e.g., status epilepticus, intractable epilepsy)	Death
6044	Somnolence/depressed level of consciousness	—	Somnolence or sedation interfering with function, but not interfering with ADL	Obtundation or stupor; difficult to arouse; interfering with ADL	Coma	Death
6045	Speech impairment (e.g., dysphasia or aphasia)	—	Awareness of receptive or expressive dysphasia, not impairing ability to communicate	Receptive or expressive dysphasia, impairing ability to communicate	Inability to communicate	—
REMARK: Speech impairment refers to a primary CNS process, not neuropathy or end organ dysfunction.						
ALSO CONSIDER: Laryngeal nerve dysfunction; Voice changes/dysarthria (e.g., hoarseness, loss, or alteration in voice, laryngitis).						
6046	Syncope (fainting)	—	—	Present	Life-threatening consequences	Death
ALSO CONSIDER: CNS cerebrovascular ischemia; Conduction abnormality/atrioventricular heart block – <i>Select</i> ; Dizziness; Supraventricular and nodal arrhythmia – <i>Select</i> ; Vasovagal episode; Ventricular arrhythmia – <i>Select</i> .						
NAVIGATION NOTE: Taste alteration (CN VII, IX) is graded as Taste alteration (dysgeusia) in the GASTROINTESTINAL CATEGORY.						
6047	Tremor	Mild and brief or intermittent but not interfering with function	Moderate tremor interfering with function, but not interfering with ADL	Severe tremor interfering with ADL	Disabling	—
6249	Neurology - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## OCULAR/VISUAL

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6250	Cataract	Asymptomatic, detected on exam only	Symptomatic, with moderate decrease in visual acuity (20/40 or better); decreased visual function correctable with glasses	Symptomatic with marked decrease in visual acuity (worse than 20/40); operative intervention indicated (e.g., cataract surgery)	—	—
6251	Dry eye syndrome	Mild, intervention not indicated	Symptomatic, interfering with function but not interfering with ADL; medical intervention indicated	Symptomatic or decrease in visual acuity interfering with ADL; operative intervention indicated	—	—
6252	Eyelid dysfunction	Asymptomatic	Symptomatic, interfering with function but not ADL; requiring topical agents or epilation	Symptomatic; interfering with ADL; surgical intervention indicated	—	—
REMARK: Eyelid dysfunction includes canalicular stenosis, ectropion, entropion, erythema, madarosis, symblepharon, telangiectasis, thickening, and trichiasis. ALSO CONSIDER: Neuropathy: cranial – <i>Select</i> .						
6253	Glaucoma	Elevated intraocular pressure (EIOP) with single topical agent for intervention; no visual field deficit	EIOP causing early visual field deficit (i.e., nasal step or arcuate deficit); multiple topical or oral agents indicated	EIOP causing marked visual field deficits (i.e., involving both superior and inferior visual fields); operative intervention indicated	EIOP resulting in blindness (20/200 or worse); enucleation indicated	—
6254	Keratitis (corneal inflammation/corneal ulceration)	Abnormal ophthalmologic changes only; intervention not indicated	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL; operative intervention indicated	Perforation or blindness (20/200 or worse)	—
NAVIGATION NOTE: Ocular muscle weakness is graded as Muscle weakness, generalized or specific area (not due to neuropathy) – <i>Select</i> in the MUSCULOSKELETAL/SOFT TISSUE CATEGORY.						
6255	Night blindness (nyctalopia)	Symptomatic, not interfering with function	Symptomatic and interfering with function but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	—

## OCULAR/VISUAL

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
6256	Nystagmus  ALSO CONSIDER: Neuropathy: cranial – <i>Select</i> ; Ophthalmoplegia/diplopia (double vision).	Asymptomatic	Symptomatic and interfering with function but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	—
6257	Ocular surface disease  REMARK: Ocular surface disease includes conjunctivitis, keratoconjunctivitis sicca, chemosis, keratinization, and palpebral conjunctival epithelial metaplasia.	Asymptomatic or minimally symptomatic but not interfering with function	Symptomatic, interfering with function but not interfering with ADL; topical antibiotics or other topical intervention indicated	Symptomatic, interfering with ADL; operative intervention indicated	—	—
6258	Ophthalmoplegia/diplopia (double vision)  ALSO CONSIDER: Neuropathy: cranial – <i>Select</i> .	Intermittently symptomatic, intervention not indicated	Symptomatic and interfering with function but not interfering with ADL	Symptomatic and interfering with ADL; surgical intervention indicated	Disabling	—
6259	Optic disc edema  ALSO CONSIDER: Neuropathy: cranial – <i>Select</i> .	Asymptomatic	Decreased visual acuity (20/40 or better); visual field defect present	Decreased visual acuity (worse than 20/40); marked visual field defect but sparing the central 20 degrees	Blindness (20/200 or worse)	—
6260	Proptosis/enophthalmos	Asymptomatic, intervention not indicated	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	—	—
6261	Retinal detachment	Exudative; no central vision loss; intervention not indicated	Exudative and visual acuity 20/40 or better but intervention not indicated	Rhegmatogenous or exudative detachment; operative intervention indicated	Blindness (20/200 or worse)	—
6262	Retinopathy	Asymptomatic	Symptomatic with moderate decrease in visual acuity (20/40 or better)	Symptomatic with marked decrease in visual acuity (worse than 20/40)	Blindness (20/200 or worse)	—

OCULAR/VISUAL						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
6263	Scleral necrosis/melt	Asymptomatic or symptomatic but not interfering with function	Symptomatic, interfering with function but not interfering with ADL; moderate decrease in visual acuity (20/40 or better); medical intervention indicated	Symptomatic, interfering with ADL; marked decrease in visual acuity (worse than 20/40); operative intervention indicated	Blindness (20/200 or worse); painful eye with enucleation indicated	---
6264	Uveitis	Asymptomatic	Anterior uveitis; medical intervention indicated	Posterior or pan-uveitis; operative intervention indicated	Blindness (20/200 or worse)	---
6265	Vision-blurred vision	Symptomatic not interfering with function	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	---
6266	Vision-flashing lights/floaters	Symptomatic not interfering with function	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	---
6267	Vision-photophobia	Symptomatic not interfering with function	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	Disabling	---
6268	Vitreous hemorrhage	Asymptomatic, clinical findings only	Symptomatic, interfering with function, but not interfering with ADL; intervention not indicated	Symptomatic, interfering with ADL; vitrectomy indicated	---	---
6269	Watery eye (epiphora, tearing)	Symptomatic, intervention not indicated	Symptomatic, interfering with function but not interfering with ADL	Symptomatic, interfering with ADL	---	---
6499	Ocular/Visual - Other (Specify, ___)	Symptomatic not interfering with function	Symptomatic and interfering with function, but not interfering with ADL	Symptomatic and interfering with ADL	Blindness (20/200 or worse)	Death



## PAIN

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	Pain  – <i>Select:</i> AUDITORY/EAR – 6502 External ear – 6503 Middle ear CARDIOVASCULAR – 6505 Cardiac/heart – 6506 Pericardium DERMATOLOGY/SKIN – 6508 Face – 6509 Lip – 6510 Oral-gums – 6511 Scalp – 6512 Skin GASTROINTESTINAL – 6514 Abdomen NOS – 6515 Anus – 6516 Dental/teeth/peridontal – 6517 Esophagus – 6518 Oral cavity – 6519 Peritoneum – 6520 Rectum – 6521 Stomach GENERAL – 6523 Pain NOS – 6524 Tumor pain	Mild pain not interfering with function	Moderate pain; pain or analgesics interfering with function, but not interfering with ADL  HEPATOBIILIARY/PANCREAS – 6526 Gallbladder – 6527 Liver LYMPHATIC – 6529 Lymph node MUSCULOSKELETAL – 6531 Back – 6532 Bone – 6533 Buttock – 6534 Extremity-limb – 6535 Intestine – 6536 Joint – 6537 Muscle – 6538 Neck – 6539 Phantom (pain associated with missing limb) NEUROLOGY – 6541 Head/headache – 6542 Neuralgia/peripheral nerve OCULAR – 6544 Eye PULMONARY/UPPER RESPIRATORY – 6546 Chest wall – 6547 Chest/thorax NOS	Severe pain; pain or analgesics severely interfering with ADL	Disabling	—
					PULMONARY/UPPER RESPIRATORY (continued) – 6548 Larynx – 6549 Pleura – 6550 Sinus – 6551 Throat/pharynx/larynx RENAL/GENITOURINARY – 6553 Bladder – 6554 Kidney SEXUAL/REPRODUCTIVE FUNCTION – 6556 Breast – 6557 Ovulatory – 6558 Pelvis – 6559 Penis – 6560 Perineum – 6561 Prostate – 6562 Scrotum – 6563 Testicle – 6564 Urethra – 6565 Uterus – 6566 Vagina	—
6749	Pain - Other (Specify, ___)	Mild pain not interfering with function	Moderate pain; pain or analgesics interfering with function, but not interfering with ADL	Severe pain; pain or analgesics severely interfering with ADL	Disabling	—

## PULMONARY/UPPER RESPIRATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6750	Adult Respiratory Distress Syndrome (ARDS)  ALSO CONSIDER: Dyspnea (shortness of breath); Hypoxia; Pneumonitis/pulmonary infiltrates.	—	—	Present, intubation not indicated	Present, intubation indicated	Death
6751	Aspiration  ALSO CONSIDER: Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> ; Laryngeal nerve dysfunction; Neuropathy: cranial – <i>Select</i> ; Pneumonitis/pulmonary infiltrates.	Asymptomatic (silent aspiration); endoscopy or radiographic (e.g. barium swallow) findings	Symptomatic (e.g., altered eating habits, coughing or choking episodes consistent with aspiration); medical intervention indicated (e.g., antibiotics, suction or oxygen)	Clinical or radiographic signs of pneumonia or pneumonitis; unable to aliment orally	Life-threatening (e.g., aspiration pneumonia or pneumonitis)	Death
6752	Atelectasis  ALSO CONSIDER: Adult Respiratory Distress Syndrome (ARDS); Cough; Dyspnea (shortness of breath); Hypoxia; Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> ; Obstruction/stenosis of airway – <i>Select</i> ; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes).	Asymptomatic	Symptomatic (e.g., dyspnea, cough), medical intervention indicated (e.g., bronchoscopic suctioning, chest physiotherapy, suctioning)	Operative (e.g., stent, laser) intervention indicated	Life-threatening respiratory compromise	Death
6753	Bronchospasm, wheezing  ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever); Dyspnea (shortness of breath).	Asymptomatic	Symptomatic not interfering with function	Symptomatic interfering with function	Life-threatening	Death
6754	Carbon monoxide diffusion capacity (DL <sub>CO</sub> )  ALSO CONSIDER: Hypoxia; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes).	90 - 75% of predicted value	<75 - 50% of predicted value	<50 - 25% of predicted value	<25% of predicted value	Death
6755	Chylothorax	Asymptomatic	Symptomatic; thoracentesis or tube drainage indicated	Operative intervention indicated	Life-threatening (e.g., hemodynamic instability or ventilatory support indicated)	Death
6756	Cough	Symptomatic, non-narcotic medication only indicated	Symptomatic and narcotic medication indicated	Symptomatic and significantly interfering with sleep or ADL	—	—

## PULMONARY/UPPER RESPIRATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6757	Dyspnea (shortness of breath)	Dyspnea on exertion, but can walk 1 flight of stairs without stopping	Dyspnea on exertion but unable to walk 1 flight of stairs or 1 city block (0.1km) without stopping	Dyspnea with ADL	Dyspnea at rest; intubation/ventilator indicated	Death
ALSO CONSIDER: Hypoxia; Neuropathy: motor; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes).						
6758	Edema, larynx	Asymptomatic edema by exam only	Symptomatic edema, no respiratory distress	Stridor; respiratory distress; interfering with ADL	Life-threatening airway compromise; tracheotomy, intubation, or laryngectomy indicated	Death
ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever)						
6759	FEV <sub>1</sub>	90 - 75% of predicted value	<75 - 50% of predicted value	<50 - 25% of predicted value	<25% of predicted	Death
	Fistula, pulmonary/upper respiratory	Asymptomatic, radiographic findings only	Symptomatic, tube thoracostomy or medical management indicated; associated with altered respiratory function but not interfering with ADL	Symptomatic and associated with altered respiratory function interfering with ADL; or endoscopic (e.g., stent) or primary closure by operative intervention indicated	Life-threatening consequences; operative intervention with thoracoplasty, chronic open drainage or multiple thoracotomies indicated	Death
	- <i>Select</i> :					
6761	- Bronchus					
6762	- Larynx					
6763	- Lung					
6764	- Oral cavity					
6765	- Pharynx					
6766	- Pleura					
6767	- Trachea					
REMARK: A fistula is defined as an abnormal communication between two body cavities, potential spaces, and/or the skin. The site indicated for a fistula should be the site from which the abnormal process is believed to have arisen. For example, a tracheo-esophageal fistula arising in the context of a resected or irradiated esophageal cancer should be graded as Fistula, GI – esophagus in the GASTROINTESTINAL CATEGORY.						
NAVIGATION NOTE: Hemoptysis is graded as Hemorrhage, pulmonary/upper respiratory – <i>Select</i> in the HEMORRHAGE/BLEEDING CATEGORY.						
6768	Hiccoughs (hiccups, singultus)	Symptomatic, intervention not indicated	Symptomatic, intervention indicated	Symptomatic, significantly interfering with sleep or ADL	—	—
6769	Hypoxia	—	Decreased O <sub>2</sub> saturation with exercise (e.g., pulse oximeter <88%); intermittent supplemental oxygen	Decreased O <sub>2</sub> saturation at rest; continuous oxygen indicated	Life-threatening; intubation or ventilation indicated	Death

## PULMONARY/UPPER RESPIRATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6770	Nasal cavity/paranasal sinus reactions  ALSO CONSIDER: Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils <i>Select</i> ; Infection with unknown ANC – <i>Select</i> .	Asymptomatic mucosal crusting, blood-tinged secretions	Symptomatic stenosis or edema/narrowing interfering with airflow	Stenosis with significant nasal obstruction; interfering with ADL	Necrosis of soft tissue or bone	Death
6772	Obstruction/stenosis of airway or stenosis on exam, endoscopy, or radiograph  – <i>Select</i> : – Bronchus – Larynx – Pharynx – Trachea	Asymptomatic obstruction or stenosis on exam, endoscopy, or radiograph	Symptomatic (e.g., noisy airway breathing), but causing no respiratory distress; medical management indicated (e.g., steroids)	Interfering with ADL; stridor or endoscopic intervention indicated (e.g., stent, laser)	Life-threatening airway compromise; tracheotomy or intubation indicated	Death
6773						
6774						
6775						
6776						
ALSO CONSIDER: Atelectasis; Cough; Dyspnea (shortness of breath); Hypoxia; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes). NAVIGATION NOTE: Pleuritic pain is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
6777	Pneumonitis/pulmonary infiltrates	Asymptomatic, radiographic findings only	Symptomatic, not interfering with ADL	Symptomatic, interfering with ADL; O <sub>2</sub> indicated	Life-threatening; ventilatory support indicated	Death
ALSO CONSIDER: Adult Respiratory Distress Syndrome (ARDS); Cough; Dyspnea (shortness of breath); Hypoxia; Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> ; Pneumonitis/pulmonary infiltrates; Pulmonary fibrosis (radiographic changes).						
6778	Pneumothorax	Asymptomatic, radiographic findings only	Symptomatic; intervention indicated (e.g., hospitalization for observation, tube placement without sclerosis)	Sclerosis and/or operative intervention indicated	Life-threatening, causing hemodynamic instability (e.g., tension pneumothorax); ventilatory support indicated	Death
6779	Prolonged chest tube drainage or air leak after pulmonary resection	—	Sclerosis or additional tube thoracostomy indicated	Operative intervention indicated (e.g., thoracotomy with stapling or sealant application)	Life-threatening; debilitating; organ resection indicated	Death

## PULMONARY/UPPER RESPIRATORY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
6780	Prolonged intubation after pulmonary resection (>24 hrs after surgery)	—	Extubated within 24 - 72 hrs postoperatively	Extubated >72 hrs postoperatively, but before tracheostomy indicated	Tracheostomy indicated	Death
NAVIGATION NOTE: Pulmonary embolism is graded as Grade 4 either as Thrombosis/embolism (vascular access-related) or Thrombosis/thrombus/embolism in the VASCULAR CATEGORY.						
6781	Pulmonary fibrosis (radiographic changes)	Minimal radiographic findings (or patchy or bi-basilar changes) with estimated radiographic proportion of total lung volume that is fibrotic of <25%	Patchy or bi-basilar changes with estimated radiographic proportion of total lung volume that is fibrotic of 25 - <50%	Dense or widespread infiltrates/consolidation with estimated radiographic proportion of total lung volume that is fibrotic of 50 - <75%	Estimated radiographic proportion of total lung volume that is fibrotic is >=75%; honeycombing	Death
REMARK: Fibrosis is usually a "late effect" seen >3 months after radiation or combined modality therapy (including surgery). It is thought to represent scar/fibrotic lung tissue. It may be difficult to distinguish from pneumonitis that is generally seen within 3 months of radiation or combined modality therapy.  ALSO CONSIDER: Adult Respiratory Distress Syndrome (ARDS); Cough; Dyspnea (shortness of breath); Hypoxia; Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>3</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> .						
NAVIGATION NOTE: Recurrent laryngeal nerve dysfunction is graded as Laryngeal nerve dysfunction in the NEUROLOGY CATEGORY.						
6782	Vital capacity	90 - 75% of predicted value	<75 - 50% of predicted value	<50 - 25% of predicted value	<25% of predicted value	Death
6783	Voice changes/dysarthria (e.g., hoarseness, loss or alteration in voice, laryngitis)	Mild or intermittent hoarseness or voice change, but fully understandable	Moderate or persistent voice changes, may require occasional repetition but understandable on telephone	Severe voice changes including predominantly whispered speech; may require frequent repetition or face-to-face contact for understandability; requires voice aid (e.g., electrolarynx) for <=50% of communication	Disabling; non-understandable voice or aphonic; requires voice aid (e.g., electrolarynx) for >50% of communication or requires >50% written communication	Death
ALSO CONSIDER: Laryngeal nerve dysfunction; Speech impairment (e.g., dysphasia or aphasia).						
6999	Pulmonary/Upper Respiratory - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death

RENAL/GENITOURINARY						
CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
7000	Bladder spasms	Symptomatic, intervention not indicated	Symptomatic, antispasmodics indicated	Narcotics indicated	Major surgical intervention indicated (e.g., cystectomy)	—
7001	Cystitis	Asymptomatic	Frequency with dysuria; macroscopic hematuria	Transfusion; IV pain medications; bladder irrigation indicated	Catastrophic bleeding; major non-elective intervention indicated	Death
	ALSO CONSIDER: Infection (documented clinically or microbiologically) with Grade 3 or 4 neutrophils (ANC <1.0 x 10 <sup>9</sup> /L) – <i>Select</i> ; Infection with normal ANC or Grade 1 or 2 neutrophils – <i>Select</i> ; Infection with unknown ANC – <i>Select</i> ; Pain – <i>Select</i> .					
	Fistula, GU	Asymptomatic, radiographic findings only	Symptomatic; noninvasive intervention indicated	Symptomatic interfering with ADL; invasive intervention indicated	Life-threatening consequences; operative intervention requiring partial or full organ resection; permanent urinary diversion	Death
	– <i>Select</i> :					
7003	– Bladder					
7004	– Genital tract-female					
7005	– Kidney					
7006	– Ureter					
7007	– Urethra					
7008	– Uterus					
7009	– Vagina					
	REMARK: A fistula is defined as an abnormal communication between two body cavities, potential spaces, and/or the skin. The site indicated for a fistula should be the site from which the abnormal process is believed to have originated.					
7010	Incontinence, urinary	Occasional (e.g., with coughing, sneezing, etc.), pads not indicated	Spontaneous, pads indicated	Interfering with ADL; intervention indicated (e.g., clamp, collagen injections)	Operative intervention indicated (e.g., cystectomy or permanent urinary diversion)	—
	Leak (including anastomotic), GU	Asymptomatic, radiographic findings only	Symptomatic; medical intervention indicated	Symptomatic, interfering with GU function; invasive or endoscopic intervention indicated	Life-threatening	Death
	– <i>Select</i> :					
7012	– Bladder					
7013	– Fallopian tube					
7014	– Kidney					
7015	– Spermatic cord					
7016	– Stoma					
7017	– Ureter					
7018	– Urethra					
7019	– Uterus					
7020	– Vagina					
7021	– Vas deferens					
	REMARK: Leak (including anastomotic), GU – <i>Select</i> refers to clinical signs and symptoms or radiographic confirmation of anastomotic leak but without development of fistula.					

## RENAL/GENITOURINARY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	Obstruction, GU	Asymptomatic, radiographic or endoscopic findings only	Symptomatic but no hydronephrosis, sepsis or renal dysfunction; dilation or endoscopic repair or stent placement indicated	Symptomatic and altered organ function (e.g., sepsis or hydronephrosis, or renal dysfunction); operative intervention indicated	Life-threatening consequences; organ failure or operative intervention requiring complete organ resection indicated	Death
	– <i>Select</i> : – Bladder – Falloopian tube – Prostate – Spermatic cord – Stoma – Testes – Ureter – Urethra – Uterus – Vagina – Vas deferens					
7023						
7024						
7025						
7026						
7027						
7028						
7029						
7030						
7031						
7032						
7033						
NAVIGATION NOTE: Operative injury is graded as Intra-operative injury – <i>Select Organ or Structure</i> in the SURGERY/INTRA-OPERATIVE INJURY CATEGORY.						
	Perforation, GU	Asymptomatic radiographic findings only	Symptomatic, associated with altered renal/GU function	Symptomatic, operative intervention indicated	Life-threatening consequences or organ failure; operative intervention requiring organ resection indicated	Death
	– <i>Select</i> : – Bladder – Falloopian tube – Kidney – Ovary – Prostate – Spermatic cord – Stoma – Testes – Ureter – Urethra – Uterus – Vagina – Vas deferens					
7035						
7036						
7037						
7038						
7039						
7040						
7041						
7042						
7043						
7044						
7045						
7046						
7047						
7048	Prolapse of stoma, GU  REMARK: Other stoma complications may be graded as Fistula, GU – <i>Select</i> ; Leak (including anastomotic), GU – <i>Select</i> ; Obstruction, GU – <i>Select</i> ; Perforation, GU – <i>Select</i> ; Stricture/stenosis (including anastomotic), GU – <i>Select</i> .	Asymptomatic; special intervention, extraordinary care not indicated	Extraordinary local care or maintenance; minor revision under local anesthesia indicated	Dysfunctional stoma; operative intervention or major stomal revision indicated	Life-threatening consequences	Death
7049	Renal failure ALSO CONSIDER: Glomerular filtration rate.	—	—	Chronic dialysis not indicated	Chronic dialysis or renal transplant indicated	Death

## RENAL/GENITOURINARY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
	Stricture/stenosis (including anastomotic), GU  – <i>Select</i> : 7051 – Bladder 7052 – Fallopian tube 7053 – Prostate 7054 – Spermatic cord 7055 – Stoma 7056 – Testes 7057 – Ureter 7058 – Urethra 7059 – Uterus 7060 – Vagina 7061 – Vas deferens	Asymptomatic, radiographic or endoscopic findings only	Symptomatic but no hydronephrosis, sepsis or renal dysfunction; dilation or endoscopic repair or stent placement indicated	Symptomatic and altered organ function (e.g., sepsis or hydronephrosis, or renal dysfunction); operative intervention indicated	Life-threatening consequences; organ failure or operative intervention requiring organ resection indicated	Death
	ALSO CONSIDER: Obstruction, GU – <i>Select</i> .					
7062	Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) ALSO CONSIDER: Acidosis (metabolic or respiratory); Bicarbonate, serum-low; Calcium, serum-low (hypocalcemia); Phosphate, serum-low (hypophosphatemia).	Asymptomatic, intervention not indicated	Mild, reversible and manageable with replacement	Irreversible, requiring continued replacement	—	—
7063	Urinary frequency/urgency	Increase in frequency or nocturia up to 2 x normal; enuresis	Increase >2 x normal but <hourly	>= 1 x/hr; urgency; catheter indicated	—	—
7064	Urinary retention (including neurogenic bladder)  REMARK: The etiology of retention (if known) is graded as Obstruction, GU – <i>Select</i> ; Stricture/stenosis (including anastomotic), GU – <i>Select</i> . ALSO CONSIDER: Obstruction, GU – <i>Select</i> ; Stricture/stenosis (including anastomotic), GU – <i>Select</i> .	Hesitancy or dribbling, no significant residual urine; retention occurring during the immediate postoperative period	Hesitancy requiring medication; or operative bladder atony requiring indwelling catheter beyond immediate postoperative period but for <6 weeks	More than daily catheterization indicated; urological intervention indicated (e.g., TURP, suprapubic tube, urethrotomy)	Life-threatening consequences; organ failure (e.g., bladder rupture); operative intervention requiring organ resection indicated	Death
7065	Urine color change REMARK: Urine color refers to change that is not related to other dietary or physiologic cause (e.g., bilirubin, concentrated urine, and hematuria).	Present	—	—	—	—
7249	Renal/Genitourinary - Other (Specify, _____)	Mild	Moderate	Severe	Life-threatening; disabling	Death



## SECONDARY MALIGNANCY

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
7250	Secondary Malignancy - possibly related to cancer treatment (Specify, _____)	—	—	Non-life-threatening basal or squamous cell carcinoma of the skin	Solid tumor, leukemia or lymphoma	Death
<p>Remark: Secondary malignancy excludes metastasis from initial primary. Any malignancy possibly related to cancer treatment (including AML/MDS) should be reported via the routine reporting mechanisms outlined in each protocol. Important: Secondary Malignancy is an exception to NCI Expedited Adverse Event Reporting Guidelines. Secondary Malignancy is "Grade 4, present" but NCI does not require AdEERS Expedited Reporting for any (related or unrelated to treatment) Secondary Malignancy. A diagnosis of AML/MDS following treatment with an NCI-sponsored investigational agent is to be reported using the form available from the CTEP Web Site at <a href="http://ctep.cancer.gov">http://ctep.cancer.gov</a>. Cancers not suspected of being treatment-related are <u>not</u> to be reported here.</p>						

## SEXUAL/REPRODUCTIVE FUNCTION

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
7500	Breast function/lactation	Mammary abnormality, not functionally significant	Mammary abnormality, functionally significant	—	—	—
7501	Breast nipple/areolar deformity	Limited areolar asymmetry with no change in nipple/areolar projection	Asymmetry of nipple areolar complex with slight deviation in nipple projection	Marked deviation of nipple projection	—	—
7502	Breast volume/hypoplasia	Minimal asymmetry; minimal hypoplasia	Asymmetry exists, $\leq 1/3$ of the breast volume; moderate hypoplasia	Asymmetry exists, $>1/3$ of the breast volume; severe hypoplasia	—	—
REMARK: Breast volume is referenced with both arms straight overhead.						
NAVIGATION NOTE: Dysmenorrhea is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
NAVIGATION NOTE: Dyspareunia is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
NAVIGATION NOTE: Dysuria (painful urination) is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
7503	Erectile dysfunction	Decrease in erectile function (frequency/rigidity of erections) but erectile aids not indicated	Decrease in erectile function (frequency/rigidity of erections), erectile aids indicated	Decrease in erectile function (frequency/rigidity of erections) but erectile aids not helpful; penile prosthesis indicated	—	—
7504	Ejaculatory dysfunction	Diminished ejaculation	Anejaculation or retrograde ejaculation	—	—	—
NAVIGATION NOTE: Feminization of male is graded in the ENDOCRINE CATEGORY.						
7505	Gynecomastia	—	Asymptomatic breast enlargement	Symptomatic breast enlargement; intervention indicated	—	—
ALSO CONSIDER: Pain – <i>Select</i> .						
7506	Infertility/sterility	—	Male: oligospermia/low sperm count Female: diminished fertility/ovulation	Male: sterile/azoospermia Female: infertile/anovulatory	—	—
7507	Irregular menses (change from baseline)	1 - 3 months without menses	$>3$ - 6 months without menses but continuing menstrual cycles	Persistent amenorrhea for $>6$ months	—	—

## SEXUAL/REPRODUCTIVE FUNCTION

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
7508	Libido	Decrease in interest but not affecting relationship; intervention not indicated	Decrease in interest and adversely affecting relationship; intervention indicated	—	—	—
NAVIGATION NOTE: Masculinization of female is graded in the ENDOCRINE CATEGORY.						
7509	Orgasmic dysfunction	Transient decrease	Decrease in orgasmic response requiring intervention	Complete inability of orgasmic response; not responding to intervention	—	—
NAVIGATION NOTE: Pelvic pain is graded as Pain – <i>Select</i> in the PAIN CATEGORY.						
NAVIGATION NOTE: Ulcers of the labia or perineum are graded as Ulceration in DERMATOLOGY/SKIN CATEGORY.						
7510	Vaginal discharge (non-infectious)	Mild	Moderate to heavy; pad use indicated	—	—	—
7511	Vaginal dryness	Mild	Interfering with sexual function; dyspareunia; intervention indicated	—	—	—
ALSO CONSIDER: Pain – <i>Select</i> .						
7512	Vaginal mucositis	Erythema of the mucosa; minimal symptoms	Patchy ulcerations; moderate symptoms or dyspareunia	Confluent ulcerations; bleeding with trauma; unable to tolerate vaginal exam, sexual intercourse or tampon placement	Tissue necrosis; significant spontaneous bleeding; life-threatening consequences	—
7513	Vaginal stenosis/length	Vaginal narrowing and/or shortening not interfering with function	Vaginal narrowing and/or shortening interfering with function	Complete obliteration; not surgically correctable	—	—
7514	Vaginitis (not due to infection)	Mild, intervention not indicated	Moderate, intervention indicated	Severe, not relieved with treatment; ulceration, but operative intervention not indicated	Ulceration and operative intervention indicated	—
7749	Sexual/Reproductive Function - Other (Specify, )	Mild	Moderate	Severe	Disabling	Death

## SURGERY/INTRA-OPERATIVE INJURY

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
	NAVIGATION NOTE: Intra-operative hemorrhage is graded as Hemorrhage/bleeding associated with surgery, intra-operative or postoperative in the HEMORRHAGE/BLEEDING CATEGORY.					
	Intra-operative injury - Select Organ or Structure -Select: REMARK: The 'Select' AEs are defined as significant, unanticipated injuries that are recognized at the time of surgery. These AEs do not refer to additional surgical procedures that must be performed because of a change in the operative plan based on intra-operative findings. Any sequelae resulting from the intra-operative injury that result in an adverse outcome for the patient must also be recorded and graded under the relevant CTCAE Term.	Primary repair of injured organ/structure indicated	Partial resection of injured organ/structure indicated	Complete resection or reconstruction of injured organ/structure indicated	Life threatening consequences; disabling	_____
	AUDITORY/EAR - 7752 Inner ear - 7753 Middle ear - 7754 Outer ear NOS - 7755 Outer ear-Pinna CARDIOVASCULAR - 7757 Artery-aorta - 7758 Artery-carotid - 7759 Artery-cerebral - 7760 Artery-extremity (lower) - 7761 Artery-extremity (upper) - 7762 Artery-hepatic - 7763 Artery-major visceral artery - 7764 Artery-pulmonary - 7765 Artery NOS - 7766 Heart - 7767 Spleen - 7768 Vein-extremity (lower) - 7769 Vein-extremity (upper) - 7770 Vein-hepatic - 7771 Vein-inferior vena cava - 7772 Vein-jugular - 7773 Vein-major visceral vein - 7774 Vein-portal vein - 7775 Vein-pulmonary - 7776 Vein-superior vena cava - 7777 Vein NOS DERMATOLOGY/SKIN - 7779 Breast - 7780 Nails - 7781 Skin ENDOCRINE - 7783 Adrenal gland - 7784 Parathyroid - 7785 Pituitary	ENDOCRINE (continued) - 7786 Thyroid HEAD AND NECK - 7788 Gingiva - 7789 Larynx - 7790 Lip/perioral area - 7791 Face NOS - 7792 Nasal cavity - 7793 Nasopharynx - 7794 Neck NOS - 7795 Nose - 7796 Oral cavity NOS - 7797 Parotid gland - 7798 Pharynx - 7799 Salivary duct - 7800 Salivary gland - 7801 Sinus - 7802 Teeth - 7803 Tongue - 7804 Upper aerodigestive NOS GASTROINTESTINAL - 7806 Abdomen NOS - 7807 Anal sphincter - 7808 Anus - 7809 Appendix - 7810 Cecum - 7811 Colon - 7812 Duodenum - 7813 Esophagus - 7814 Ileum - 7815 Jejunum - 7816 Oral - 7817 Peritoneal cavity - 7818 Rectum - 7819 Small bowel NOS	GASTROINTESTINAL (continued) - 7820 Stoma (GI) - 7821 Stomach HEPATOBILIARY/ PANCREAS - 7823 Biliary tree-common bile duct - 7824 Biliary tree-common hepatic duct - 7825 Biliary tree-left hepatic duct - 7826 Biliary tree-right hepatic duct - 7827 Biliary tree NOS - 7828 Gallbladder - 7829 Liver - 7830 Pancreas - 7831 Pancreatic duct MUSCULOSKELETAL - 7833 Bone - 7834 Cartilage - 7835 Extremity-lower - 7836 Extremity-upper - 7837 Joint - 7838 Ligament - 7839 Muscle - 7840 Soft tissue NOS - 7841 Tendon NEUROLOGY - 7843 Brain - 7844 Meninges - 7845 Spinal cord NERVES - 7847 Brachial plexus - 7848 CN I (olfactory) - 7849 CN II (optic) - 7850 CN III (oculomotor) - 7851 CN IV (trochlear)	NEUROLOGY (continued) NERVES: - 7852 CN V (trigeminal) motor - 7853 CN V (trigeminal) sensory - 7854 CN VI (abducens) - 7855 CN VII (facial) motor face - 7856 CN VII (facial) sensory taste - 7857 CN VIII (vestibulocochlear) - 7858 CN IX (glossopharyngeal) motor pharynx - 7859 CN IX (glossopharyngeal) sensory ear-pharynx-tongue - 7860 CN X (vagus) - 7861 CN XI (spinal accessory) - 7862 CN XII (hypoglossal) - 7863 Cranial nerve or branch NOS - 7864 Lingual - 7865 Lung thoracic - 7866 Peripheral motor NOS - 7867 Peripheral sensory NOS - 7868 Recurrent laryngeal - 7869 Sacral plexus - 7870 Sciatic - 7871 Thoracodorsal OCULAR - 7873 Conjunctiva - 7874 Cornea - 7875 Eye NOS - 7876 Lens - 7877 Retina	PULMONARY/UPPER RESPIRATORY - 7879 Bronchus - 7880 Lung - 7881 Mediastinum - 7882 Pleura - 7883 Thoracic duct - 7884 Trachea - 7885 Upper airway NOS RENAL/GENITOURINARY - 7887 Bladder - 7888 Cervix - 7889 Fallopian tube - 7890 Kidney - 7891 Ovary - 7892 Pelvis NOS - 7893 Penis - 7894 Prostate - 7895 Scrotum - 7896 Testis - 7897 Ureter - 7898 Urethra - 7899 Urinary conduit - 7900 Urinary tract NOS - 7901 Uterus - 7902 Vagina - 7903 Vulva	
7999	Intra-operative Injury - Other (Specify, ___) REMARK: Intra-operative Injury – Other (Specify, ___) is to be used only to report an organ/structure not included in the 'Select' AEs found at the end of the CATEGORY. Any sequelae resulting from the intra-operative injury that result in an adverse outcome for the patient must also be recorded and graded under the relevant CTCAE Term.	Primary repair of injured organ/structure indicated	Partial resection of injured organ/structure indicated	Complete resection or reconstruction of injured organ/structure indicated	Life threatening consequences; disabling	_____

## SYNDROMES

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
NAVIGATION NOTE: Acute vascular leak syndrome is graded in the VASCULAR CATEGORY.						
NAVIGATION NOTE: Adrenal insufficiency is graded in the ENDOCRINE CATEGORY.						
NAVIGATION NOTE: Adult Respiratory Distress Syndrome (ARDS) is graded in the PULMONARY/UPPER RESPIRATORY CATEGORY.						
8000	Alcohol intolerance syndrome (antabuse-like syndrome) REMARK: An antabuse-like syndrome occurs with some new anti-androgens (e.g., nilutamide) when patient also consumes alcohol.	—	—	Present	—	Death
NAVIGATION NOTE: Autoimmune reaction is graded as Autoimmune reaction/hypersensitivity (including drug fever) in the ALLERGY/IMMUNOLOGY CATEGORY.						
8001	Cytokine release syndrome/acute infusion reaction  REMARK: Cytokine release syndromes/acute infusion reactions are different from Allergic/hypersensitive reactions, although some of the manifestations are common to both AEs. An acute infusion reaction may occur with an agent that causes cytokine release (e.g., monoclonal antibodies or other biological agents). Signs and symptoms usually develop during or shortly after drug infusion and generally resolve completely within 24 hrs of completion of infusion. Signs/symptoms may include: Allergic reaction/hypersensitivity (including drug fever); Arthralgia (joint pain); Bronchospasm; Cough; Dizziness; Dyspnea (shortness of breath); Fatigue (asthenia, lethargy, malaise); Headache; Hypertension; Hypotension; Myalgia (muscle pain); Nausea; Pruritis/itching; Rash/desquamation; Rigors/chills; Sweating (diaphoresis); Tachycardia; Tumor pain (onset or exacerbation of tumor pain due to treatment); Urticaria (hives, welts, wheals); Vomiting.  ALSO CONSIDER: Allergic reaction/hypersensitivity (including drug fever); Bronchospasm, wheezing; Dyspnea (shortness of breath); Hypertension; Hypotension; Hypoxia; Prolonged QTc interval; Supraventricular and nodal arrhythmia – <i>Select</i> ; Ventricular arrhythmia – <i>Select</i> .	Mild reaction; infusion interruption not indicated; intervention not indicated	Requires therapy or infusion interruption but responds promptly to symptomatic treatment (e.g., antihistamines, NSAIDS, narcotics, IV fluids); prophylactic medications indicated for <=24 hrs	Prolonged (i.e., not rapidly responsive to symptomatic medication and/or brief interruption of infusion); recurrence of symptoms following initial improvement; hospitalization indicated for other clinical sequelae (e.g., renal impairment, pulmonary infiltrates)	Life-threatening; pressor or ventilatory support indicated	Death
NAVIGATION NOTE: Disseminated intravascular coagulation (DIC) is graded in the COAGULATION CATEGORY.						
NAVIGATION NOTE: Fanconi's syndrome is graded as Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) in the RENAL/GENITOURINARY CATEGORY.						
8002	Flu-like syndrome  REMARK: Flu-like syndrome represents a constellation of symptoms which may include cough with catarrhal symptoms, fever, headache, malaise, myalgia, prostration, and is to be used when the symptoms occur in a cluster consistent with one single pathophysiological process.	Symptoms present but not interfering with function	Moderate or causing difficulty performing some ADL	Severe symptoms interfering with ADL	Disabling	Death
NAVIGATION NOTE: Renal tubular acidosis is graded as Urinary electrolyte wasting (e.g., Fanconi's syndrome, renal tubular acidosis) in the RENAL/GENITOURINARY CATEGORY.						

## SYNDROMES

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
8003	"Retinoic acid syndrome"	Fluid retention; less than 3 kg of weight gain; intervention with fluid restriction and/or diuretics indicated	Mild to moderate signs/symptoms; steroids indicated	Severe signs/symptoms; hospitalization indicated	Life-threatening; ventilatory support indicated	Death
<p>REMARK: Patients with acute promyelocytic leukemia may experience a syndrome similar to "retinoic acid syndrome" in association with other agents such as arsenic trioxide. The syndrome is usually manifested by otherwise unexplained fever, weight gain, respiratory distress, pulmonary infiltrates and/or pleural effusion, with or without leukocytosis.</p> <p>ALSO CONSIDER: Acute vascular leak syndrome; Pleural effusion (non-malignant); Pneumonitis/pulmonary infiltrates.</p>						
<p>NAVIGATION NOTE: SIADH is graded as Neuroendocrine: ADH secretion abnormality (e.g., SIADH or low ADH) in the ENDOCRINE CATEGORY.</p>						
<p>NAVIGATION NOTE: Stevens-Johnson syndrome is graded as Rash: erythema multiforme (e.g., Stevens-Johnson syndrome, toxic epidermal necrolysis) in the DERMATOLOGY/SKIN CATEGORY.</p>						
<p>NAVIGATION NOTE: Thrombotic microangiopathy is graded as Thrombotic microangiopathy (e.g., thrombotic thrombocytopenic purpura [TTP] or hemolytic uremic syndrome [HUS]) in the COAGULATION CATEGORY.</p>						
8004	Tumor flare	Mild pain not interfering with function	Moderate pain; pain or analgesics interfering with function, but not interfering with ADL	Severe pain; pain or analgesics interfering with function and interfering with ADL	Disabling	Death
<p>REMARK: Tumor flare is characterized by a constellation of signs and symptoms 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.</p> <p>ALSO CONSIDER: Calcium, serum-high (hypercalcemia).</p>						
8005	Tumor lysis syndrome	—	—	Present	—	Death
<p>ALSO CONSIDER: Creatinine; Potassium, serum-high (hyperkalemia).</p>						
8249	Syndromes - Other (Specify, ___)	Mild	Moderate	Severe	Life-threatening; disabling	Death

## VASCULAR

		Grade				
CTCAE Code	Adverse Event	1	2	3	4	5
8250	Acute vascular leak syndrome	—	Symptomatic, fluid support not indicated	Respiratory compromise or fluids indicated	Life-threatening; pressor support or ventilatory support indicated	Death
8251	Peripheral arterial ischemia	—	Brief (<24 hrs) episode of ischemia managed non-surgically and without permanent deficit	Recurring or prolonged (>=24 hrs) and/or invasive intervention indicated	Life-threatening, disabling and/or associated with end organ damage (e.g., limb loss)	Death
8252	Phlebitis (including superficial thrombosis) ALSO CONSIDER: Injection site reaction/extravasation changes.	—	Present	—	—	—
8253	Portal vein flow	—	Decreased portal vein flow	Reversal/retrograde portal vein flow	—	—
8254	Thrombosis/embolism (vascular access-related)	—	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) not indicated	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) indicated	Embolic event including pulmonary embolism or life-threatening thrombus	Death
8255	Thrombosis/thrombus/embolism	—	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) not indicated	Deep vein thrombosis or cardiac thrombosis; intervention (e.g., anticoagulation, lysis, filter, invasive procedure) indicated	Embolic event including pulmonary embolism or life-threatening thrombus	Death
	Vessel injury-artery	Asymptomatic diagnostic finding; intervention not indicated	Symptomatic (e.g., claudication); not interfering with ADL; repair or revision not indicated	Symptomatic interfering with ADL; repair or revision indicated	Life-threatening; disabling; evidence of end organ damage (e.g., stroke, MI, organ or limb loss)	Death
	– <i>Select:</i>					
8257	– Aorta					
8258	– Carotid					
8259	– Extremity-lower					
8260	– Extremity-upper					
8261	– Other NOS					
8262	– Visceral					
	NAVIGATION NOTE: Vessel injury to an artery intra-operatively is graded as Intra-operative injury – <i>Select Organ or Structure</i> in the SURGERY/INTRA-OPERATIVE INJURY CATEGORY.					

## VASCULAR

CTCAE Code	Adverse Event	Grade				
		1	2	3	4	5
8264 8265 8266 8267 8268 8269 8270	Vessel injury-vein  – <i>Select</i> : – Extremity-lower – Extremity-upper – IVC – Jugular – Other NOS – SVC – Viscera	Asymptomatic diagnostic finding; intervention not indicated	Symptomatic (e.g., claudication); not interfering with ADL; repair or revision not indicated	Symptomatic interfering with ADL; repair or revision indicated	Life-threatening; disabling; evidence of end organ damage	Death
NAVIGATION NOTE: Vessel injury to a vein intra-operatively is graded as Intra-operative injury – <i>Select Organ or Structure</i> in the SURGERY/INTRA-OPERATIVE INJURY CATEGORY.						
8271	Visceral arterial ischemia (non-myocardial)  ALSO CONSIDER: CNS cerebrovascular ischemia.	—	Brief (<24 hrs) episode of ischemia managed medically and without permanent deficit	Prolonged (>=24 hrs) or recurring symptoms and/or invasive intervention indicated	Life-threatening; disabling; evidence of end organ damage	Death
8499	Vascular - Other (Specify, ___)	Mild	Moderate	Severe	Life-threatening; disabling	Death