

# Common Terminology Criteria for Adverse Events (CTCAE)

Version 4.0

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U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES

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**MYLAN PHARMS. INC. EXHIBIT 1093 PAGE 1**

# Common Terminology Criteria for Adverse Events v4.0 (CTCAE)

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## Reference

Common Terminology Criteria for Adverse Events is a descriptive terminology which is utilized for Adverse Event (AE) reporting. (severity) scale is provided for each AE

## Organizations and Organization

Organ Class, the highest level of the hierarchy, is identified by anatomical or clinical system, etiology, or purpose (e.g., investigations for laboratory test results). Terms are grouped by MedDRA Primary Class within each SOC, AEs are listed and defined by descriptions of severity (Grade).

## Terms

An Adverse Event (AE) is any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease or procedure that may or may not be related to the medical treatment or procedure. An AE is a term that is a unique identifier of a specific event used for documentation and scientific analyses. The AE v4.0 term is a MedDRA LLT (Lowest Level Term).

## Definitions

A brief definition is provided to clarify the meaning of each AE term.

## Grades

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

- Grade 1 Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- Grade 2 Moderate; minimal, local or noninvasive intervention indicated; limiting instrumental ADL\*.
- Grade 3 Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self care ADL\*\*.
- Grade 4 Life-threatening consequences; urgent intervention indicated.
- Grade 5 Death related to AE.

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

A single dash (-) indicates a grade is 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.

## Activities of Daily Living (ADL)

\*Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.

\*\*Self care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

## MYLAN PHARMS. INC. EXHIBIT 1093 PAGE 2

0 incorporates certain elements of the MedDRA terminology. For further details on MedDRA refer to the MedDRA MSSO Web site (<http://www.meddrasso.com>).

SOC	Page
Blood and lymphatic system disorders	3
Cardiac disorders	6
Congenital, familial and genetic disorders	15
Ear and labyrinth disorders	16
Endocrine disorders	19
Eye disorders	22
Gastrointestinal disorders	28
General disorders and administration site conditions	55
Hepatobiliary disorders	61
Immune system disorders	65
Infections and infestations	68
Injury, poisoning and procedural complications	87
Investigations	107
Metabolism and nutrition disorders	114
Musculoskeletal and connective tissue disorders	119
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	128
Nervous system disorders	129
Pregnancy, puerperium and perinatal conditions	141
Psychiatric disorders	142
Renal and urinary disorders	147
Reproductive system and breast disorders	153
Respiratory, thoracic and mediastinal disorders	164
Skin and subcutaneous tissue disorders	179
Social circumstances	188
Surgical and medical procedures	189
Vascular disorders	190

**Blood and lymphatic system disorders**

Adverse Event	Grade				
	1	2	3	4	5
<p>Disorder characterized by an reduction in the amount of hemoglobin in 100 ml of blood. Signs and symptoms of anemia may include pallor of the skin and weakness, shortness of breath, palpitations of the heart, soft systolic murmurs, lethargy, and fatigability.</p>	<p>Hemoglobin (Hgb) &lt;LLN - 10.0 g/dL; &lt;LLN - 6.2 mmol/L; &lt;LLN - 100 g/L</p>	<p>Hgb &lt;10.0 - 8.0 g/dL; &lt;6.2 - 4.9 mmol/L; &lt;100 - 80g/L</p>	<p>Hgb &lt;8.0 g/dL; &lt;4.9 mmol/L; &lt;80 g/L; transfusion indicated</p>	<p>Life-threatening consequences; urgent intervention indicated</p>	<p>Death</p>
<p>Disorder characterized by the inability of the bone marrow to produce hematopoietic elements.</p>	<p>Mildly hypocellular or &lt;=25% reduction from normal cellularity for age</p>	<p>Moderately hypocellular or &gt;25 - &lt;50% reduction from normal cellularity for age</p>	<p>Severely hypocellular or &gt;50 - &lt;=75% reduction cellularity from normal for age</p>	<p>Aplastic persistent for longer than 2 weeks</p>	<p>Death</p>
<p>Disorder characterized by systemic pathological activation of blood clotting mechanisms which results in clot formation throughout the body. There is an increased risk of hemorrhage as the body is depleted of platelets and coagulation factors.</p>	<p>-</p>	<p>Laboratory findings with no bleeding</p>	<p>Laboratory findings and bleeding</p>	<p>Life-threatening consequences; urgent intervention indicated</p>	<p>Death</p>
<p>Disorder characterized by an ANC &lt;1000/mm3 and a single temperature of &gt;38.3 degrees C (101 degrees F) or a sustained temperature of &gt;=38 degrees C (100.4 degrees F) for more than one hour.</p>	<p>-</p>	<p>-</p>	<p>ANC &lt;1000/mm3 with a single temperature of &gt;38.3 degrees C (101 degrees F) or a sustained temperature of &gt;=38 degrees C (100.4 degrees F) for more than one hour.</p>	<p>Life-threatening consequences; urgent intervention indicated</p>	<p>Death</p>

**MYLAN PHARMS. INC. EXHIBIT 1093 PAGE 4**

CTCAE 4.03 - June 14, 2010

Blood and lymphatic system disorders					
Case Event	Grade				
	1	2	3	4	5
	Laboratory evidence of hemolysis only (e.g., direct antiglobulin test; DAT; Coombs'; schistocytes; decreased haptoglobin)	Evidence of hemolysis and $\geq 2$ gm decrease in hemoglobin.	Transfusion or medical intervention indicated (e.g., steroids)	Life-threatening consequences; urgent intervention indicated	Death
order characterized by laboratory test results that indicate widespread erythrocyte cell membrane destruction.					
hemolytic syndrome	Evidence of RBC destruction (schistocytosis) without clinical consequences	-	Laboratory findings with clinical consequences (e.g., renal insufficiency, petechiae)	Life-threatening consequences, (e.g., CNS hemorrhage or thrombosis/embolism or renal failure)	Death
order characterized by a form of thrombotic microangiopathy with renal failure, hemolytic anemia, and severe thrombocytopenia.					
	-	-	$>100,000/mm^3$	Clinical manifestations of leucostasis; urgent intervention indicated	Death
order characterized by laboratory test results that indicate an increased number of white blood cells in the blood.					
joint pain	Mild pain	Moderate pain; limiting instrumental ADL	Severe pain; limiting self care ADL	-	-
order characterized by a sensation of marked discomfort in a lymph node.					
leukocytosis	Incidental findings (e.g., Howell-Jolly bodies); mild degree of thrombocytosis and leukocytosis	Prophylactic antibiotics indicated	-	Life-threatening consequences; urgent intervention indicated	Death

CTCAE 4.03 - June 14, 2010 : Blood and lymphatic system disorders

**MYLAN PHARMS. INC. EXHIBIT 1093 PAGE 5**

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