Toxicity criteria and severity descriptors for Crohn disease

ULN = upper limit of normal
ADL = activities of daily living
NIH = National Institute of Health

Prednisolone

Adverse event	Brief description of minimum grade	NIH common toxicity criteria grade
Gastro-intestinal		
Gastric irritation/ulcer	Requiring medical management	2 (or higher)
Nausea	Oral intake significantly reduced	2 (or higher)
Vomiting	Two or more episodes in 24 hours over pre-treatment	2 (or higher)
Weight gain	≥ 20% weight gain	3 (or higher)
Cardiovascular		
Hypertension	Requiring therapy or more intensive therapy than previously	3 (or higher)
Fluid retention	Symptomatic, limiting function, unresponsive to therapy or requiring drug discontinuation	3 (or higher)
Central nervous system[†]		
Insomnia	Frequent insomnia interfering with ADL	3 (or higher)
Mood alteration	Severe mood alteration interfering with ADL	3 (or higher)
Personality/behavioural	Disruptive to patient/family, requiring mental health intervention	3 (or higher)
Restlessness	Severe	3 (or higher)
Dermatological		
Acne/dermatological conditions	Severe	3 (or higher)
Purpura/bruising	Generalised or mucosal petechiae	3 (or higher)
Impaired healing	Requiring medical management	2 (or higher)
Laboratory		
Hyperglycaemia	Glucose 13.9 mmol / L or higher	3 (or higher)
Hypertriglyceridaemia	> 5 – 10 x ULN	3 (or higher)
Hypokalaemia	< 3.0 mmol / L	3 (or higher)
Endocrine		
Cushingoid appearance	Present	3 (or higher)
Disordered menstruation	Very irregular over pre-treatment	2 (or higher)
Ocular		
Cataracts	Symptomatic visual loss requiring treatment or interfering with function	3 (or higher)
Glaucoma	Increase in intraocular pressure with retinal changes	2 (or higher)
Musculo-skeletal		
Osteoporosis/fracture	Symptomatic, interfering with ADL	
Avascular necrosis	Symptomatic, interfering with function	2 (or higher)
Myopathy	Symptomatic, interfering with function	2 (or higher)
Miscellaneous		
Immuno-suppression	Severe, requiring treatment withdrawal	
Impaired healing	Symptomatic, interfering with ADL	
Growth retardation		

† Past psychiatric history **not** a contraindication

Azathioprine

Adverse event	Brief description of minimum grade	NIH common toxicity criteria grade
Haematological		
Leucocytes	< 2 x 10^9 / L	3 (or higher)
Haemoglobin	< 80g / L	3 (or higher)
Thrombocytes	< 50 x 10^9 / L	3 (or higher)
Neoplasms		
New malignancy	Serious malignancy present	4
Gastro-intestinal		
Nausea	Oral intake significantly reduced	2 (or higher)
Vomiting	Two or more episodes in 24 hours over pre-treatment	2 (or higher)
Diarrhoea	Increase of more than 4 stools per day over pre-treatment or incontinence	2 (or higher)
Stomatitis	Painful erythema, oedema or ulcers but can eat/swallow	2 (or higher)
Abdominal pain	Severe pain/analgesia interfering with ADL	3 (or higher)
Pancreatitis	Abdominal pain with pancreatic enzyme elevation	3 (or higher)
Hepatic		
Bilirubin	> 1.5 x ULN	2 (or higher)
Hepatic enzymes	> 2.5 x ULN	2(or higher)
Dermatological		
Rash	Rash with associated symptoms over less than 50% of body surface	2 (or higher)
Alopecia	Pronounced hair loss	3 (or higher)
Pulmonary		
Pneumonitis	X-Ray changes, requiring steroids and diuretics	2 (or higher)
Miscellaneous		
Hypersensitivity	Rash, drug fever > 38^{O}, aches etc.	2 (or higher)
Immuno-suppression/atypical infection	Severe/systemic infection requiring IV antibiotic/antifungal treatment or hospitalisation	3 (or higher)

Mercaptopurine

Adverse event	Brief description of minimum grade	NIH common toxicity criteria grade
Haematological		
Leucocytes	< 2 x 10^9 / L	3 (or higher)
Haemoglobin	< 80g / L	3 (or higher)
Thrombocytes	< 50 x 10^9 / L	3 (or higher)
Gastro-intestinal		
Nausea	Oral intake significantly reduced	2 (or higher)
Vomiting	Two or more episodes in 24 hours over pre-treatment	2 (or higher)
Anorexia	Oral intake significantly reduced	2 (or higher)
Stomatitis (oral ulcers etc)	Painful erythema, oedema or ulcers but can eat/swallow	2 (or higher)
Pancreatitis	Abdominal pain with pancreatic enzyme elevation	3 (or higher)
Hepatic		
Bilirubin	> 1.5 x ULN	2 (or higher)
Hepatic enzymes	> 2.5 x ULN	2 (or higher)
Dermatological		
Rash	Rash with associated symptoms over less than 50% of body surface	2 (or higher)
Alopecia	Pronounced hair loss	3 (or higher)
Neoplasia		
Secondary malignancy (e.g. leukaemia)	Present	4
Miscellaneous		
Hypersensitivity	Rash, drug fever > 38^O, arthralgia etc.	2 (or higher)
Joint pain	Moderate pain/analgesics, significantly interferes with function	2 (or higher)

Methotrexate

Adverse event	Brief description of minimum grade	NIH common toxicity criteria grade
Alimentary tract		
Diarrhoea	Increase of more than 4 stools per day over pre-treatment or incontinence	2 (or higher)
Nausea	Oral intake significantly decreased and symptoms that do not respond to at least two of the following: • reduction of the methotrexate dose • folinic acid/folic acid supplementation • switching from oral dosing to intramuscular dosing • splitting the methotrexate dose over 12 hours A minimum of three doses of methotrexate should have been trialled	2 (or higher)
Stomatitis	Painful erythema, oedema or ulcers but able to eat/swallow	2 (or higher)
Vomiting	Two or more episodes in 24 hours over pre-treatment	2 (or higher)
Blood		
Haemoglobin	< 80 g/L	3 (or higher)
Clinical haemorrhage	Requiring transfusion	3 (or higher)
Leukocytes	$< 2 \times 10^9$ /L	3 (or higher)
Phlebitis	Present	2 (or higher)
Thrombocytes	$< 50 \times 10^9$ /L	3 (or higher)
Cardiovascular		
Arrhythmia	Symptomatic and requiring therapy	3 (or higher)
Cardiac function	Congestive heart failure responsive to treatment	3 (or higher)
Pericardial effusion/pericarditis	Pericarditis (pericardial rub, ECG changes or chest pain)	2 (or higher)
Central nervous system		
Ataxia	Mild symptoms interfering with function but not interfering with ADL	2 (or higher)
Hearing	Tinnitus or hearing loss not requiring treatment	2 (or higher)
Incoordination	Mild symptoms interfering with function but not interfering with ADL	2 (or higher)
Mood alteration	Moderate mood alteration interfering with function but not interfering with ADL	2 (or higher)
Vision	Symptomatic and interfering with function but not interfering with ADL	3 (or higher)
Dermatological		
Alopecia	Pronounced hair loss	2 (or higher)
Rash	Rash with associated symptoms over less than 50 % of body surface	2 (or higher)
Hepatic		
Bilirubin	> 1.5 x ULN	2 (or higher)
Elevated transaminases	• ALT and/or AST > 2.5 x ULN **or** • ALT and/or AST > 1.5 x ULN	2 (or higher)

	on three occasions over a three month period	
Elevated serum alkaline phosphatase	2.5 x ULN	2 (or higher)
Respiratory		
Pneumonitis/pulmonary infiltrates	Radiographic changes and requiring steroids/diuretics	2 (or higher)
Pulmonary fibrosis	Requiring steroids/diuretics	2 (or higher)
Cough (severe)	Severe cough/coughing spasm that is poorly controlled or unresponsive to treatment. Evidence of reversal on treatment withdrawal	3 (or higher)
Renal		
Renal impairment	Creatinine clearance < 30ml / min	3 (or higher)
Other		
Allergic reaction	Urticaria, drug fever > 38^0C or bronchospasm	2 (or higher)
Infection	Severe, systemic infection, requiring IV antimicrobial treatment or hospitalisation	3 (or higher)
Headaches (severe)	Severe pain (requiring compound analgesics) where pain/analgesics severely interfere with ADL	3 (or higher)
Nodulosis (following introduction of methotrexate therapy)	Development of multiple new nodules causing significant local pressure symptoms and distress to patient	