
Novartis Pharmaceuticals Corporation

59 Route 10

East Hanover, NJ 07936

Appendix: 1
Risk Factors/Conditions for Osteonecrosis

Zometa[®] (zoledronic acid) Injection

and

Aredia[®] (pamidronate disodium) Injection

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Oncologic Drugs Advisory Committee Meeting

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1 Conditions leading to or associated with osteonecrosis

(From: [\[Assouline-Dayan, et al \(2002\)\]](#) Pathogenesis and natural history of osteonecrosis. Sem Arthr & Rheum 32: 94-124)

Trauma	Disorders
Burns	Systemic Lupus Erythematosus
Fractures	Polymyositis
Dislocations	Polymyalgia Rheumatica
Vascular Trauma	Raynaud's Disease
Kienböck Disease	Rheumatoid Arthritis
Non-Traumatic Conditions	Ankylosing Spondylitis
Hematologic	Sjögren's Syndrome
Hemoglobinopathies	Giant Cell Arteritis
Sickle-Cell Anemia	Thrombophlebitis
Thalasseмии	Lipid Emboli
Disseminated Intravascular Coagulation	Ehler-Danlos Syndrome
Polycythemia	Orthopedic Problems
Hemophilia	Slipped Capital Femoral Epiphysis
Metabolic/Endocrinologic	Congenital Hip Dislocation
Hypercholesterolemia	Hereditary Dysostosis
Gout	Legg-Calvé-Perthes' Disease
Hyperparathyroidism	Extrinsic Dietary or Environmental Factors
Hyperlipidemia	Dysbaric Conditions (Caisson Disease)
Pregnancy	Alcohol Consumption
Cushing's Disease	Cigarette Smoking
Chronic Renal Failure	Iatrogenic
Gaucher's Disease	Corticosteroids
Diabetes (in association with obesity)	Radiation Exposure
Fabry's Disease	Hemodialysis
Gastrointestinal	Organ Transplantation
Pancreatitis	Laser Surgery
Inflammatory Bowel Disease	Idiopathic
Neoplastic	
Marrow Infiltrative Disorders	
Infectious	
Osteomyelitis	
Human Immunodeficiency Virus	
Meningococcemia	
Vascular/Rheumatologic/Connective Tissue	

2 Localized and systemic diseases and pathophysiologic processes associated with ischemic osteonecrosis

(from [Bouquot and McMahon (2000)] Neuropathic pain in maxillofacial osteonecrosis. J Oral Maxillofac Surg 58: 1003-1020)

DISEASE OR ETIOLOGIC FACTOR	SUBCATEGORIES	DISEASE OR ETIOLOGIC FACTOR	SUBCATEGORIES
Alcohol abuse	Cirrhosis	Hypercoagulable state, systemic	Antiphospholipid antibody syndrome Factor V ^{Leiden} gene mutation Hyperhomocystinemia Homozygosity for MTHFR or CBS Protein C deficiency Protein S deficiency
Arthritis	Pancreatitis Subchondral cyst Subchondral marrow edema		
Atmospheric pressure variations	Caisson's disease Deep sea diving		
Blood dyscrasias	Disseminated intravascular coagulation Leukemia Sickle cell anemia Chemotherapy for cancer	Hyperdipidemia and embolic fat	Diabetes mellitus Dysbaric phenomena Fracture of bone Hemoglobinopathies Osteomyelitis, acute
Cancer	Cancer-induced hyperocoagulation Lymphoma Metastatic intraosseous carcinoma Radiation therapy for cancer	Hypersensitivity reactions	Allograft organ rejection Anaphylactic shock Immune globulin therapy Shwartzman reaction to endotoxin Transfusion reactions
Chronic inactivity	Bedridden Full body cast Paraplegic Hypercortisolism Inflammatory bowel disease		
Corticosteroids	Lupus erythematosus Transplants Birth control pills Estrogen replacement therapy Fertility drugs Pregnancy Prostate chemotherapy	Hypertension Hypothyroidism Inflammation, intraosseous	Infection, bacterial and viral Trauma (mild or severe) Autoimmunity/hypersensitivity With corticosteroid therapy Without corticosteroid therapy Brain injury/surgery Regional or generalized Anorexia nervosa Gaucher's disease Tobacco smoking
Estrogen	Transient ischemic osteoporosis	Lupus erythematosus	
Gaucher's disease	Acute infection/inflammation	Neurodamage Osteoporosis Starvation Storage diseases Tobacco use	
Hemodialysis	Chronic infection/inflammation	Vascular occlusive disease	Atherosclerosis
Hypercoagulable state, local	Chronic infection/inflammation Increased intrame-dullary pressures	Vasculitis Vasoconstriction	Local anesthetic use Raynaud phenomenon