MEDICAL POLICY

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POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

Original Issue Date (Created):	**November 1, 2008**
Most Recent Review Date (Revised):	**September 24, 2013**
Effective Date:	**November 1, 2013**

I. POLICY

Preauthorization required.

Pamidronate (Aredia®) is approved by the U.S. Food and Drug Administration (FDA) for the following indications: Moderate to severe Paget's disease of the bone; moderate or severe hypercalcemia associated with malignancy, (with or without bone metastases); and in conjunction with standard antineoplastic therapy, for the treatment of osteolytic bone metastases of breast cancer and osteolytic lesions of multiple myeloma.

Pediatric Use: Safety and effectiveness of Aredia® in pediatric patients have not been established.

Pamidronate (Aredia®) may be considered **medically necessary** for the following conditions:

- Treatment of **moderate to severe Paget's disease of the bone** in patients when **ALL** of the following are met:
  - Single course* pamidronate (Aredia®)
  - The patient cannot tolerate or is unresponsive to oral agents (e.g. risedronate or alendronate); and
  - The patient's clinical condition meets ANY of the following:
    - Patient is symptomatic from active bone lesions
    - Patient is asymptomatic but has evidence of biochemically active disease (i.e. serum alkaline phosphatase at least three to four times the upper limit of normal)
    - Elective surgery planned for a Pagetic site (e.g., hip replacement)
    - Hypercalcemia from immobilization in a patient with active disease
    - Involvement at sites where prevention of disease progression may reduce further complications, e.g., skull, spine, weight-bearing long bones, and bone abutting a joint.

*** Note: Retreatment for Paget's disease of the Bone:**

A second course of therapy of pamidronate (Aredia®) may be considered **medically necessary** when there is increased serum alkaline phosphatase, failure to achieve normalization of serum alkaline phosphatase, or in those with symptoms.

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

The inability to swallow tablets is **not a medically necessary indication** for coverage of injectable bisphosphonates as alternative preparations of oral bisphosphonates are available (e.g. liquid alendronate).

- **Cancer-related indications**, for **ANY** of the following conditions:
  - Moderate or severe hypercalcemia associated with malignancy, with or without bone metastases.
  - Osteolytic bone metastases of breast cancer in conjunction with standard antineoplastic therapy.
  - Osteolytic lesions of multiple myeloma in conjunction with standard antineoplastic therapy.

The use of pamidronate (Aredia®) for non-FDA approved indications is considered **investigational**, as there is insufficient evidence to support a conclusion concerning the health outcomes or benefits associated with this procedure.

Cross-Reference:
MP-2.220 Bone Turnover Markers
MP-2.131 Ibandronate (Boniva®) Injection
MP-2.143 Zoledronic Acid (Reclast®, Zometa®)
MP-5.001 Bone Mineral Density Studies
MP-5.037 Whole Body Dual X-ray Absorptiometry (DEXA) to Determine Body Composition

II. PRODUCT VARIATIONS

[N] = No product variation, policy applies as stated
[Y] = Standard product coverage varies from application of this policy, see below

[N]Capital Cares 4 Kids
[N] PPO
[N] HMO
[Y] SeniorBlue HMO*
[Y] SeniorBlue PPO*
[N] Indemnity
[N] SpecialCare
[N] POS
[Y] FEP PPO**

*"FDA approved drugs used for indications other than what is indicated on the official label may be covered under Medicare if determined that the use is medically accepted, taking into consideration the major drug compendia, authoritative medical literature and/or accepted standards of medical practice." Refer to Medicare Benefit Policy Manual (100-2, Chapter 15, Section 50.4.2- Unlabeled Use of Drug)." *http://www.cms.gov/manuals/Downloads/bp102c15.pdf*

** The FEP program dictates that all drugs, devices or biological products approved by the U.S. Food and Drug Administration (FDA) may not be considered investigational. Therefore, FDA-approved drugs, devices or biological products may be assessed on the basis of medical necessity.

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

III. DESCRIPTION/BACKGROUND

Bisphosphonates

Bisphosphonates are used to treat osteoporosis and to prevent damaging changes to the bone caused by Paget's disease of the bone and bone metastases. Bisphosphonates suppress bone resorption and are the most widely used class of drugs to treat osteoporosis. Bisphosphonates may also be used for osteoporosis prevention.

Oral bisphosphonates such as Alendronate (Fosamax®) and Risedronate (Actonel®) are available in daily or weekly dosages. Oral bisphosphonates can cause gastrointestinal disorders and patients must remain upright for thirty minutes (Alendronate and Risedronate). after swallowing the tablet whole with plain water on an empty stomach. Alendronate is also available as an oral liquid for individuals who have difficulty swallowing tablets. Injectable bisphosphonates provide an alternative for individuals who have difficulty with the dosing requirements of oral bisphosphonates.

Note: Emerging evidence has indicated a link between bisphosphonates and a rare but serious complication, osteonecrosis of the jaw. This may be more likely to occur after oral surgery.

Pamidronate (Aredia®)

Pamidronate (Aredia®) is a type of bisphosphonate used to treat and prevent damaging changes to the bone caused by Paget's disease of the bone and bone metastases. FDA approved indications for Aredia® include moderate to severe Paget's disease of the bone, hypercalcemia of malignancy and osteolytic bone metastases of breast cancer or multiple myeloma.

The recommended dose of pamidronate for Paget's disease of the bone is 30 mg daily administered as a 4-hour infusion on 3 consecutive days for a total dose of 90 mg. A limited number of patients with Paget's disease have received more than one treatment of pamidronate in clinical trials. When clinically indicated, patients should be retreated at the dose of initial therapy. Pamidronate dosing for oncology related indications varies by clinical condition.

In the absence of hypercalcemia, patients with predominantly lytic bone metastases or multiple myeloma, who are at risk of calcium or vitamin D deficiency, and patients with Paget's disease of the bone, should be given oral calcium and vitamin D supplementation in order to minimize the risk of hypocalcemia

Paget's Disease of the Bone

Paget's disease of the bone (osteitis deformans) is a chronic disease of the bone characterized by excessive osteoclastic bone resorption followed by excessive bone formation. Affected bones are thick but structurally weak and prone to fractures or deformity. Paget's disease occurs most

frequently in the spine, skull, pelvis and bones of the lower extremities. One or more bones may be affected. Paget's disease is rarely diagnosed in people less than 40 years of age. Oral agents for the treatment of Paget's disease of the bone include Alendronate (Fosamax®) and Risedronate (Actonel®).

Cancer-Related Bone Conditions

Bone metastasis can cause bone to wear away leaving small holes called osteolytic bone lesions, and can cause abnormal weak and unstable bone formation called osteoblastic bone lesions. Common areas of metastasis include the spine, pelvis, hip, femur, and skull. Affected bones are prone to fracture resulting in pain and decreased mobility. Vertebral fractures can cause spinal cord compression and subsequent paralysis. Hypercalcemia, a late complication of cancer, can cause nausea and vomiting, dehydration, coma, and death. Bisphosphonates can also reduce blood calcium levels by preventing release of calcium from the bones.

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IV. RATIONALE

Paget's Disease

Clinical Trials

In one double-blind clinical trial, 64 patients with moderate to severe Paget's disease of bone were enrolled to receive 5 mg, 15 mg, or 30 mg of Aredia as a single 4-hour infusion on 3 consecutive days, for total doses of 15 mg, 45 mg, and 90 mg of Aredia.

The mean baseline serum alkaline phosphatase levels were 1,409 U/L, 983 U/L, and 1,085 U/L, and the mean baseline urine hydroxyproline/creatinine ratios were 0.25, 0.19, and 0.19 for the 15-mg, 45-mg, and 90-mg groups, respectively.

The effects of Aredia on serum alkaline phosphatase (SAP) and urine hydroxyproline/creatinine ratios (UOHP/C) are summarized in the following table.

Percent of Patients With Significant % Decreases in SAP and UOHP/C

	SAP			UOHP/C		
% Decrease	15 mg	45 mg	90 mg	15 mg	45 mg	90 mg
≥50	26	33	60	15	47	72
≥30	40	65	83	35	57	85

The median maximum percent decreases from baseline in serum alkaline phosphatase and urinehydroxyproline/creatinine ratios were 25%, 41%, and 57%, and 25%, 47%, and 61% for the 15-mg, 45-mg, and 90-mg groups, respectively. The median time to response (≥50% decrease) for serum alkaline phosphatase was approximately 1 month for the 90-mg group, and the response duration ranged from 1 to 372 days.

No statistically significant differences between treatment groups, or statistically significant changes from baseline were observed for the bone pain response, mobility, and global evaluation in the 45-mg and 90-mg groups. Improvement in radiologic lesions occurred in some patients in the 90-mg group.

Twenty-five patients who had Paget's disease were retreated with 90 mg of Aredia. Of these, 44% had a ≥50% decrease in serum alkaline phosphatase from baseline after treatment, and 39% had a ≥50% decrease in urine hydroxyproline/creatinine ratio from baseline after treatment.

Hypercalcemia of Malignancy

Clinical Trials

In one double-blind clinical trial, 52 patients who had hypercalcemia of malignancy were enrolled to receive 30 mg, 60 mg, or 90 mg of Aredia as a single 24-hour intravenous infusion if their corrected serum calcium levels were ≥12.0 mg/dL after 48 hours of saline hydration.

The mean baseline-corrected serum calcium for the 30-mg, 60-mg, and 90-mg groups were 13.8 mg/dL, 13.8 mg/dL, and 13.3 mg/dL, respectively.

The majority of patients (64%) had decreases in albumin-corrected serum calcium levels by 24 hours after initiation of treatment. Mean-corrected serum calcium levels at days 2-7 after initiation of treatment with Aredia were significantly reduced from baseline in all three dosage groups. As a result, by 7 days after initiation of treatment with Aredia, 40%, 61%, and 100% of the patients receiving 30 mg, 60 mg, and 90 mg of Aredia, respectively, had normal-corrected serum calcium levels. Many patients (33%-53%) in the 60-mg and 90-mg dosage groups

continued to have normal-corrected serum calcium levels, or a partial response (≥15% decrease of corrected serum calcium from baseline), at Day 14.

In a second double-blind, controlled clinical trial, 65 cancer patients who had corrected serum calcium levels of ≥12.0 mg/dL after at least 24 hours of saline hydration were randomized to receive either 60 mg of Aredia as a single 24-hour intravenous infusion or 7.5 mg/kg of etidronate disodium as a 2-hour intravenous infusion daily for 3 days. Thirty patients were randomized to receive Aredia and 35 to receive etidronate disodium.

The mean baseline-corrected serum calcium for the Aredia 60-mg and etidronate disodium groups were 14.6 mg/dL and 13.8 mg/dL, respectively.

By Day 7, 70% of the patients in the Aredia group and 41% of the patients in the etidronate disodium group had normal-corrected serum calcium levels (P<0.05). When partial responders (≥15% decrease of serum calcium from baseline) were also included, the response rates were 97% for the Aredia group and 65% for the etidronate disodium group (P<0.01). Mean-corrected serum calcium for the Aredia and etidronate disodium groups decreased from baseline values to 10.4 and 11.2 mg/dL, respectively, on Day 7. At Day 14, 43% of patients in the Aredia group and 18% of patients in the etidronate disodium group still had normal-corrected serum calcium levels, or maintenance of a partial response. For responders in the Aredia and etidronate disodium groups, the median duration of response was similar (7 and 5 days, respectively). The time course of effect on corrected serum calcium is summarized in the following table.

Change in Corrected Serum Calcium by Time from Initiation of Treatment

Time (hr)	Mean Change from Baseline in Corrected Serum Calcium (mg/dL)		
	Aredia®	Etidronate Disodium	P-Value[1]
Baseline	14.6	13.8	
24	-0.3	-.05	
48	-1.5	-1.1	
72	-2.6	-2.0	
96	-3.5	-2.0	<0.01
168	-4.1	-2.5	<0.01

[1]Comparison between treatment groups

In a third multicenter, randomized, parallel double-blind trial, a group of 69 cancer patients with hypercalcemia was enrolled to receive 60 mg of Aredia as a 4- or 24-hour infusion, which was compared to a saline-treatment group. Patients who had a corrected serum calcium level of ≥12.0 mg/dL after 24 hours of saline hydration were eligible for this trial.

The mean baseline-corrected serum calcium levels for Aredia 60-mg 4-hour infusion, Aredia 60-mg 24-hour infusion, and saline infusion were 14.2 mg/dL, 13.7 mg/dL, and 13.7 mg/dL, respectively.

By Day 7 after initiation of treatment, 78%, 61%, and 22% of the patients had normal-corrected serum calcium levels for the 60-mg 4-hour infusion, 60-mg 24-hour infusion, and saline infusion, respectively. At Day 14, 39% of the patients in the Aredia 60-mg 4-hour infusion group and 26% of the patients in the Aredia 60-mg 24-hour infusion group had normal-corrected serum calcium levels or maintenance of a partial response.

For responders, the median duration of complete responses was 4 days and 6.5 days for Aredia 60-mg 4-hour infusion and Aredia 60-mg 24-hour infusion, respectively.

In all three trials, patients treated with Aredia had similar response rates in the presence or absence of bone metastases. Concomitant administration of furosemide did not affect response rates.

Thirty-two patients who had recurrent or refractory hypercalcemia of malignancy were given a second course of 60 mg of Aredia over a 4- or 24-hour period. Of these, 41% showed a complete response and 16% showed a partial response to the retreatment, and these responders had about a 3-mg/dL fall in meancorrected serum calcium levels 7 days after retreatment.

In a fourth multicenter, randomized, double-blind trial, 103 patients with cancer and hypercalcemia (corrected serum calcium ≥12.0 mg/dL) received 90 mg of Aredia as a 2-hour infusion. The mean baseline corrected serum calcium was 14.0 mg/dL. Patients were not required to receive IV hydration prior to drug administration, but all subjects did receive at least 500 mL of IV saline hydration concomitantly with the pamidronate infusion. By Day 10 after drug infusion, 70% of patients had normal corrected serum calcium levels (<10.8 mg/dL).

Osteolytic Bone Metastases of Breast Cancer and Osteolytic Lesions of Multiple Myeloma

Clinical Trials

In a double-blind, randomized, placebo-controlled trial, 392 patients with advanced multiple myeloma were enrolled to receive Aredia or placebo in addition to their underlying antimyeloma therapy to determine the effect of Aredia on the occurrence of skeletal-related events (SREs). SREs were defined as episodes of pathologic fractures, radiation therapy to bone, surgery to

bone, and spinal cord compression. Patients received either 90 mg of Aredia or placebo as a monthly 4-hour intravenous infusion for 9 months. Of the 392 patients, 377 were evaluable for efficacy (196 Aredia, 181 placebo). The proportion of patients developing any SRE was significantly smaller in the Aredia group (24% vs 41%, P<0.001), and the mean skeletal morbidity rate (#SRE/year) was significantly smaller for Aredia patients than for placebo patients (mean: 1.1 vs 2.1, P<.02). The times to the first SRE occurrence, pathologic fracture, and radiation to bone were significantly longer in the Aredia group (P=.001, .006, and .046, respectively). Moreover, fewer Aredia patients suffered any pathologic fracture (17% vs 30%, P=.004) or needed radiation to bone (14% vs 22%, P=.049).

In addition, decreases in pain scores from baseline occurred at the last measurement for those Aredia patients with pain at baseline (P=.026) but not in the placebo group. At the last measurement, a worsening from baseline was observed in the placebo group for the Spitzer quality of life variable (P<.001) and ECOG performance status (P<.011) while there was no significant deterioration from baseline in these parameters observed in Aredia-treated patients.*

After 21 months, the proportion of patients experiencing any skeletal event remained significantly smaller in the Aredia group than the placebo group (P=.015). In addition, the mean skeletal morbidity rate (#SRE/year) was 1.3 vs 2.2 for Aredia patients vs placebo patients (P=.008), and time to first SRE was significantly longer in the Aredia group compared to placebo (P=.016). Fewer Aredia patients suffered vertebral pathologic fractures (16% vs 27%, P=.005). Survival of all patients was not different between treatment groups.

Two double-blind, randomized, placebo-controlled trials compared the safety and efficacy of 90 mg of Aredia infused over 2 hours every 3 to 4 weeks for 24 months to that of placebo in preventing SREs in breast cancer patients with osteolytic bone metastases who had one or more predominantly lytic metastases of at least 1 cm in diameter: one in patients being treated with antineoplastic chemotherapy and the second in patients being treated with hormonal antineoplastic therapy at trial entry.

382 patients receiving chemotherapy were randomized, 185 to Aredia and 197 to placebo. 372 patients receiving hormonal therapy were randomized, 182 to Aredia and 190 to placebo. All but three patients were evaluable for efficacy. Patients were followed for 24 months of therapy or until they went off study. Median duration of follow-up was 13 months in patients receiving chemotherapy and 17 months in patients receiving hormone therapy. Twenty-five percent of the patients in the chemotherapy study and 37% of the patients in the hormone therapy study received Aredia for 24 months. The efficacy results are shown in the table below:

Breast Cancer Patients Receiving Chemotherapy			Breast Cancer Patients Receiving Hormonal Therapy		
Any SRE	Radiation	Fractures	Any SRE	Radiation	Fractures

	A	P	A	P	A	P	A	P	A	P	A	P
N	185	195	185	195	185	195	182	189	182	189	182	189
Skeletal Morbidity Rate (#SRE/year) Mean	2.5	3.7	0.8	1.3	1.6	2.2	2.4	3.6	0.6	1.2	1.6	2.2
P-Value	<.001		<.001†		<.018†		.021		.013†		.040†	
Proportion of patients having an SRE	46%	65%	28%	45%	36%	49%	55%	63%	31%	40%	45%	55%
P-Value	<.001		<.001†		<.014†		.094		.058†		.054†	
Median Time to SRE (months)	13.9	7.0	NR**	14.2	25.8	13.3	10.9	7.4	NR**	23.4	20.6	12.8
P-Value	<.001		<.001†		<.009†		.118		.016†		.113†	

†Fractures and radiation to bone were two of several secondary endpoints. The statistical significance of these analyses may be overestimated since numerous analyses were performed.

**NR = Not Reached.

Bone lesion response was radiographically assessed at baseline and at 3, 6, and 12 months. The complete partial response rate was 33% in Aredia patients and 18% in placebo patients treated with chemotherapy (P=.001). No difference was seen between Aredia and placebo in hormonally-treated patients.

Pain and analgesic scores, ECOG performance status and Spitzer quality of life index were measured at baseline and periodically during the trials. The changes from baseline to the last measurement carried forward are shown in the following table:

Mean Change (Δ) from Baseline at Last Measurement

	Breast Cancer Patients Receiving Chemotherapy					Breast Cancer Patients Receiving Hormonal Therapy				
	Aredia®		Placebo		A vs P P-Value*	Aredia®		Placebo		A vs P
	N	Mean Δ	N	Mean Δ		N	Mean Δ	N	Mean Δ	P-Value*
Pain Score	175	+0.93	183	+1.69	.050	173	+0.50	179	+1.60	.007
Analgesic Score	175	+0.74	183	+1.55	.009	173	+0.90	179	+2.28	<.001
ECOG PS	178	+0.81	186	+1.19	.002	175	+0.95	182	+0.90	.773
Spitzer QOL	177	-1.76	185	-2.21	.103	173	-1.86	181	-2.05	.409

Decreases in pain, analgesic scores and ECOG PS, and increases in Spitzer QOL indicate an improvement from

baseline.
*The statistical significance of analyses of these secondary endpoints of pain, quality of life, and performance status in all three trials may be overestimated since numerous analyses were performed.

V. DEFINITIONS

ALKALINE PHOSPHATASE is an enzyme present in all tissues and in high concentration in bone, kidneys, intestines, biliary ducts, plasma, and teeth. It may be elevated in serum in some diseases of the bone and liver and some other illnesses. The normal adult value is 20 to 140 IU/L (international units per liter).

ANTINEOPLASTIC AGENTS are substances that inhibit or prevent the growth of neoplasms.

BONE RESORPTION is bone loss due to osteoclastic activity.

FRACTURE is a traumatic injury to a bone in which the continuity of the bone tissue is broken.

MORPHOMETRIC FRACTURE is a fracture identified by a change in the shape of a bone, rather than from pain or other symptoms.

MYELOMA is a malignant tumor composed of plasma cells of the type normally found in the bone marrow.

OFF-LABEL USE is the use of a prescription drug or medical device in the treatment of an illness or injury for which it has not been specifically approved by the FDA.

OSTEOCLASTIC refers to osteoclasts, especially with reference to their activity in the absorption and removal of osseous (bone) tissue.

OSTEOCLASTS are large multinucleated cells formed from differentiated macrophages that are responsible for the breakdown of bone.

OSTEONECROSIS is the death of a segment of bone usually caused by insufficient blood flow to a region of the skeleton.

VI. BENEFIT VARIATIONS

The existence of this medical policy does not mean that this service is a covered benefit under the member's contract. Benefit determinations should be based in all cases on the applicable contract language. Medical policies do not constitute a description of benefits. A member's individual or group customer benefits govern which services are covered, which are excluded, and which are subject to benefit limits and which require preauthorization. Members and

providers should consult the member's benefit information or contact Capital for benefit information.

VII. DISCLAIMER

Capital's medical policies are developed to assist in administering a member's benefits, do not constitute medical advice and are subject to change. Treating providers are solely responsible for medical advice and treatment of members. Members should discuss any medical policy related to their coverage or condition with their provider and consult their benefit information to determine if the service is covered. If there is a discrepancy between this medical policy and a member's benefit information, the benefit information will govern. Capital considers the information contained in this medical policy to be proprietary and it may only be disseminated as permitted by law.

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IX. CODING INFORMATION

Note: This list of codes may not be all-inclusive, and codes are subject to change at any time. The identification of a code in this section does not denote coverage as coverage is determined by the terms of member benefit information. In addition, not all covered services are eligible for separate reimbursement.

Covered when medically necessary:

HCPCS Code	Description
J2430	INJECTION, PAMIDRONATE DISODIUM, PER 30 MG

ICD-9-CM Diagnosis Code*	Description
170.0-170.8	MALIGNANT NEOPLASM OF BONE AND ARTICULAR CARTILAGE
174.0-174.9	MALIGNANT NEOPLASM OF FEMALE BREAST
175.0-175.9	MALIGNANT NEOPLASM OF MALE BREAST
198.5	SECONDARY MALIGNANT NEOPLASM BONE AND BONE MARROW
203.00	MULTIPLE MYELOMA, WITHOUT MENTION OF HAVING ACHIEVED REMISSION
203.01	MULTIPLE MYELOMA IN REMISSION
275.42	HYPERCALCEMIA
731.0 – 731.1	OSTEITIS DEFORMANS WITHOUT MENTION OF BONE TUMOR

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

The following ICD-10 diagnosis codes will be effective October 1, 2013

ICD-10-CM Diagnosis Code*	Description
C50.011	Malignant neoplasm of nipple and areola, right female breast
C50.012	Malignant neoplasm of nipple and areola, left female breast
C50.019	Malignant neoplasm of nipple and areola, unspecified female breast

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

ICD-10-CM Diagnosis Code*	Description
C50.111	Malignant neoplasm of central portion of right female breast
C50.112	Malignant neoplasm of central portion of left female breast
C50.119	Malignant neoplasm of central portion of unspecified female breast
C50.211	Malignant neoplasm of upper-inner quadrant of right female breast
C50.212	Malignant neoplasm of upper-inner quadrant of left female breast
C50.219	Malignant neoplasm of upper-inner quadrant of unspecified female breast
C50.311	Malignant neoplasm of lower-inner quadrant of right female breast
C50.312	Malignant neoplasm of lower-inner quadrant of left female breast
C50.319	Malignant neoplasm of lower-inner quadrant of unspecified female breast
C50.411	Malignant neoplasm of upper-outer quadrant of right female breast
C50.412	Malignant neoplasm of upper-outer quadrant of left female breast
C50.419	Malignant neoplasm of upper-outer quadrant of unspecified female breast
C50.511	Malignant neoplasm of lower-outer quadrant of right female breast
C50.512	Malignant neoplasm of lower-outer quadrant of left female breast
C50.519	Malignant neoplasm of lower-outer quadrant of unspecified female breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.611	Malignant neoplasm of axillary tail of right female breast
C50.612	Malignant neoplasm of axillary tail of left female breast
C50.619	Malignant neoplasm of axillary tail of unspecified female breast
C50.811	Malignant neoplasm of overlapping sites of right female breast
C50.812	Malignant neoplasm of overlapping sites of left female breast
C50.819	Malignant neoplasm of overlapping sites of unspecified female breast
C50.911	Malignant neoplasm of unspecified site of right female breast
C50.912	Malignant neoplasm of unspecified site of left female breast
C50.919	Malignant neoplasm of unspecified site of unspecified female breast
C50.021	Malignant neoplasm of nipple and areola, right male breast
C50.022	Malignant neoplasm of nipple and areola, left male breast
C50.029	Malignant neoplasm of nipple and areola, unspecified male breast
C50.121	Malignant neoplasm of central portion of right male breast
C50.122	Malignant neoplasm of central portion of left male breast
C50.129	Malignant neoplasm of central portion of unspecified male breast
C50.221	Malignant neoplasm of upper-inner quadrant of right male breast
C50.222	Malignant neoplasm of upper-inner quadrant of left male breast

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

ICD-10-CM Diagnosis Code*	Description
C50.229	Malignant neoplasm of upper-inner quadrant of unspecified male breast
C50.321	Malignant neoplasm of lower-inner quadrant of right male breast
C50.322	Malignant neoplasm of lower-inner quadrant of left male breast
C50.329	Malignant neoplasm of lower-inner quadrant of unspecified male breast
C50.421	Malignant neoplasm of upper-outer quadrant of right male breast
C50.422	Malignant neoplasm of upper-outer quadrant of left male breast
C50.429	Malignant neoplasm of upper-outer quadrant of unspecified male breast
C50.521	Malignant neoplasm of lower-outer quadrant of right male breast
C50.522	Malignant neoplasm of lower-outer quadrant of left male breast
C50.529	Malignant neoplasm of lower-outer quadrant of unspecified male breast
C50.621	Malignant neoplasm of axillary tail of right male breast
C50.622	Malignant neoplasm of axillary tail of left male breast
C50.629	Malignant neoplasm of axillary tail of unspecified male breast
C50.821	Malignant neoplasm of overlapping sites of right male breast
C50.822	Malignant neoplasm of overlapping sites of left male breast
C50.829	Malignant neoplasm of overlapping sites of unspecified male breast
C50.921	Malignant neoplasm of unspecified site of right male breast
C50.922	Malignant neoplasm of unspecified site of left male breast
C50.929	Malignant neoplasm of unspecified site of unspecified male breast
C90.00	Multiple myeloma not having achieved remission
C90.01	Multiple myeloma in remission
E83.52	Hypercalcemia
M88.0	Osteitis deformans of skull
M88.1	Osteitis deformans of vertebrae
M88.811	Osteitis deformans of right shoulder
M88.812	Osteitis deformans of left shoulder
M88.819	Osteitis deformans of unspecified shoulder
M88.821	Osteitis deformans of right upper arm
M88.822	Osteitis deformans of left upper arm
M88.829	Osteitis deformans of unspecified upper arm
M88.831	Osteitis deformans of right forearm
M88.832	Osteitis deformans of left forearm
M88.839	Osteitis deformans of unspecified forearm
M88.841	Osteitis deformans of right hand
M88.842	Osteitis deformans of left hand

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

ICD-10-CM Diagnosis Code*	Description
M88.849	Osteitis deformans of unspecified hand
M88.851	Osteitis deformans of right thigh
M88.852	Osteitis deformans of left thigh
M88.859	Osteitis deformans of unspecified thigh
M88.861	Osteitis deformans of right lower leg
M88.862	Osteitis deformans of left lower leg
M88.869	Osteitis deformans of unspecified lower leg
M88.871	Osteitis deformans of right ankle and foot
M88.872	Osteitis deformans of left ankle and foot
M88.879	Osteitis deformans of unspecified ankle and foot
M88.88	Osteitis deformans of other bones
M88.89	Osteitis deformans of multiple sites
M88.9	Osteitis deformans of unspecified bone

*If applicable, please see Medicare LCD or NCD for additional covered diagnoses.

POLICY TITLE	PAMIDRONATE (AREDIA®)
POLICY NUMBER	MP-2.142

X. POLICY HISTORY

MP- 2.142	**CAC 1/26/10** Created a separate policy for Pamidronate (Aredia®) from the previous Injectable Bisphosphonate policy.
	CAC 1/25/11 Removed specific clinical conditions from policy criteria regarding symptomatic active bone lesions. Removed not medically necessary indication regarding pamidronate substitution for oral bisphosphonates for convenience purposes. Removed the preauthorization requirement.
	CAC 4/24/12 Consensus
	7/24/13 Admin coding review complete--rsb
	9/24/13 Consensus. No change to policy statements. References updated.

[Note: Final page is signature page and is kept on file, but not issued with Policy.]