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Bisphosphonate Step Therapy Criteria

Program may be implemented with the following options:

- 1) Option 1: generic before brand bisphosphonate OR
- 2) Option 2: generic before preferred brand before nonpreferred brand bisphosphonate

For BlueCross BlueShield of Illinois, BlueCross BlueShield of New Mexico, BlueCross BlueShield of Oklahoma and BlueCross BlueShield of Texas, Option 1 (1-step step therapy) will apply.

Boniva Injection will NOT be included in this step therapy program for BlueCross BlueShield of Illinois, BlueCross BlueShield of New Mexico, BlueCross BlueShield of Oklahoma and BlueCross BlueShield of Texas because these plans do not cover injectable bisphosphonates under the pharmacy benefit.

Brand	Generic	Dosage Form
Actonel [®]	risedronate	oral tablets
Actonel [®] with Calcium	risedronate/calcium carbonate	oral tablets
Boniva [®]	ibandronate	oral tablets, injection
Fosamax [®]	alendronate	oral tablets ^a , oral solution
Fosamax Plus D [™]	alendronate/cholecalciferol	oral tablets

^a generic available

FDA APPROVED INDICATIONS

The following information is taken from individual drug prescribing information and is provided here as background information only. Not all FDA-approved indications may be considered medically necessary. All criteria are found in the section "Prior Authorization Criteria for Approval."

Table 1: FDA Approved Indications¹⁻⁶

Available Products	FDA Indications ¹⁻⁶					
	Prevention of Osteoporosis in Post-menopausal women	Treatment of Osteoporosis Post-menopausal women	Treatment to Increase Bone Mass in Men with Osteoporosis	Treatment of Paget's Disease	Prevention of Glucocorticoid Induced Osteoporosis	Treatment of Glucocorticoid Induced Osteoporosis
Actonel (risedronate tablets)	✓	✓	✓	✓	✓	✓
Actonel w/ Calcium (risedronate tablets/calcium carbonate tablets)	✓	✓				
Boniva (ibandronate tablets)	✓	✓				
Boniva (ibandronate injection)		✓				
Fosamax (alendronate tablets, solution)	✓	✓	✓	✓		✓
Fosamax Plus D (alendronate/cholecalciferol tablets)		✓	✓			

IU=International Units, mg=milligrams, mL=milliliters

RATIONALE FOR STEP THERAPY

The intent of the step therapy option of the bisphosphonate program is to encourage the use of generic alendronate while accommodating for the use of brand bisphosphonate agents for the treatment of osteoporosis when generic alendronate cannot be used due to allergy, intolerance, or contraindication. The bisphosphonates included in the step edit are those agents approved for treatment or prevention of osteoporosis in men or women. Generic alendronate is available in all tablet strengths. Fosamax Plus D and Actonel with Calcium may be included as target agents in the step edit because both calcium and vitamin D are available over-the-counter.

The step therapy program for bisphosphonate agents has been developed with the opportunity to implement one of two options.

- (option 1): A one step edit that requires therapy with a generic bisphosphonate before therapy with brand agent.
- (option 2): A two step edit that requires therapy with a generic bisphosphonate before a preferred brand and both a generic and a preferred brand agent before use of a nonpreferred brand bisphosphonate agent.

Guidelines for the treatment of osteoporosis recommend a bisphosphonate agent as first-line treatment (see Formulary Chapter 4.9A /Calcium Regulators/Osteoporosis Agents).⁷ Alendronate and risedronate are both consistently mentioned as appropriate choices for initial treatment.⁷ None of the available guidelines include the newer bisphosphonate agent, ibandronate, which was approved for marketing after development of the guidelines.

Outcome studies evaluating the efficacy of alendronate and risedronate in post-menopausal women have been published.^{7,8} A summary of the outcomes for alendronate and risedronate are provided in Table 2. Data in this table was published before the approval of ibandronate.

Table 2. Fracture Outcomes ^{7,8}

Condition	Risedronate (Actonel)	Alendronate (Fosamax)
Primary Prevention of Vertebral Fractures	No	Yes (ARR 1.7%)
Secondary Prevention of Vertebral Fractures	Yes (ARR 5%-7.4%)	Yes (ARR 8.0%)
Primary Prevention of Hip Fractures	No	No
Secondary Prevention of Hip Fractures	Yes (ARR 1.4%)	Yes (ARR 1.1%)
Prevention of Glucocorticoid Induced Vertebral Fractures	Yes (ARR 11%)	Yes (ARR 6.1%)

ARR=absolute risk reduction

Approval of ibandronate for the treatment of osteoporosis by the Food and Drug Administration (FDA) was based on a three-year phase III trial (BONE).⁹ Data from the BONE study demonstrated that daily ibandronate, relative to placebo, significantly reduced the 3-year risk for vertebral fracture from 9.6% to 4.7% (p=0.0001).⁹ Approval for the prevention of osteoporosis was based on a two-year trial.⁹ Data from the osteoporosis prevention study submitted to the FDA demonstrated ibandronate 2.5 mg relative to placebo, increased BMD of the lumbar spine and hip by 3.0% and 2.0% respectively.¹⁰ Data from the MOBILE study, submitted to the FDA for approval of once-monthly dosing, demonstrated that monthly ibandronate had at least an equal increase in BMD of the lumbar spine and hip compared to the daily administration of ibandronate.¹¹ Women treated with the 150 mg/month dose compared to Boniva 2.5 mg daily had the greatest increase in BMD.¹¹

ELECTRONIC EDITS

The bisphosphonate program may be implemented as one of two step therapy options:

- Option 1: a one step edit that requires therapy with a generic bisphosphonate agent within 90 days prior to a brand claim
- Option 2: a two step edit that requires prior use of a generic bisphosphonate agent within 90 days prior to payment for a preferred brand and use of both a generic and a preferred brand bisphosphonate agent within 180 days prior to a nonpreferred brand claim.

The overall process for a step therapy edit requires that another drug or drugs be tried within a specified time period prior to the claim drug. If the patient has met any of the requirements outlined below, the requested step therapy medication will be paid under the patient's current prescription benefit. If the patient does not meet the step therapy criteria, then the system will reject with the message indicating that prior authorization is necessary. The prior authorization (PA) criteria for approval would then be applied to requests submitted by the patient's practitioner for evaluation.

Option 1: Generic Before Brand Edit

The implementation of this option encourages the use of cost-effective generic bisphosphonate agent prior to use of any brand bisphosphonate. If the patient has a medication history including generic alendronate with a days supply beginning or ending within the 90 day look back parameter, the claim will automatically pay. Claims for brand bisphosphonates will also automatically pay if the patient's medication history contains evidence of the identical brand bisphosphonate within 90 days prior to the new claim. Approval of these agents if previous use is identified assures no disruption of therapy for those patients already stabilized on the medication. The 90-day search period was chosen to capture the most recent or current therapy for one preferred agent. The claims system is designed to identify and count any prerequisite drug claim with a days supply that begins or ends in the 90-day look-back parameter. If a generic bisphosphonate is not found, the Point of Sale message will be returned to the pharmacy stating the step is not met and PA is required. The *Prior Authorization Criteria for Approval* would then be applied to requests submitted by the patient's practitioner for evaluation.

Option 2: Generic before Preferred Brand before Nonpreferred Brand

The implementation of this option encourages the use of a cost-effective generic bisphosphonate prior to use of preferred brand agents, and the use of both a generic bisphosphonate and a preferred brand bisphosphonate prior to use of a nonpreferred brand bisphosphonate. This step edit option has been designed as two edits; one for preferred brand bisphosphonates and one for nonpreferred brand bisphosphonates. In order for a claim for a preferred brand bisphosphonate to pay automatically, the patient must have medication history of a previous claim for a generic bisphosphonate within 90 days prior to the current brand bisphosphonate claim. In order for a claim for nonpreferred brand bisphosphonate to pay automatically, the patient must have medication history of both a previous claim for a generic bisphosphonate and a claim for a preferred brand bisphosphonate within 180 days prior to the new claim for a nonpreferred brand bisphosphonate. Claims for either preferred or nonpreferred brand bisphosphonates will also automatically pay if the patient's medication history contains evidence of the identical brand bisphosphonate within 90 days prior to the new claim. Approval of these agents if previous use is identified assures no disruption of therapy for those patients already stabilized on the medication. The 90-day search period was chosen to capture the most recent or current therapy for one preferred agent; the 180-day search period is longer to review claims history for two preferred therapies. If the step therapy edit is not met, a Point of Sale message will be returned to the pharmacy stating the step is not met and prior authorization is required. The *Prior Authorization (PA) Criteria for Approval* would then be applied to requests submitted by the patient's practitioner for evaluation.

Table 3: Summary of Bisphosphonate Step Therapy

	OPTION 1 – BRAND OPTION 2 – PREFERRED BRAND	OPTION 2 – NONPREFERRED BRAND
Targeted Agent(s)	Brand bisphosphonate or Preferred brand bisphosphonate - Determined by client GPI 300420***** multisource code M,N, or O set up at drug or GPI 10 level	Nonpreferred brand bisphosphonate - Determined by client GPI 300420***** multisource code M,N, or O set up at drug or GPI 10 level
Is auto-grandfathering implemented? (lookback time frame)	Yes (90 days ^a)	Yes (90 days ^a)
Prerequisite Agent(s)	Generic bisphosphonate GPI 300420***** and MSC Y	Generic bisphosphonate GPI 300420***** and MSC Y AND Preferred brand bisphosphonate - Determined by client GPI 300420***** multisource code M,N, or O set up at drug or GPI 10 level
Number of prerequisites required	1	2
Prerequisite look-back time frame	90 days ^a	180 days ^b
Age-related edit?	No	No
Additional comments	The injectable (IV) dosage form of Boniva is not included in this step therapy program.	

a - The system searches for a claim with a days supply that begins or ends in the past 90 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 120 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

b - The system searches for two claims with a days supply that begins or ends in the past 180 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 210 days prior to the new claim. For claims that are dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 270 days prior to the new claim.

PRIOR AUTHORIZATION CRITERIA FOR APPROVAL

The intent of the *PA Criteria for Approval* for step therapy is to allow for approval of brand bisphosphonate agents under step therapy option 1 when the patient's medication history indicates prior generic alendronate tablets not identified by the electronic claims history edit. The PA criteria also allows for use of brand agents if the patient has allergies, intolerance, or contraindication to the use of generic alendronate. The PA Criteria for Approval for step therapy implementing option 2 allows approval of preferred brand agents when the patient's medication history indicates prior generic alendronate tablets not identified by the electronic claims history. The PA criteria also allows for use of preferred brand agents if the patient has allergies, intolerance, or contraindication to the use of generic alendronate. The PA Criteria for Approval for step therapy option 2 also allows approval of nonpreferred brand agents when there is claims history evidence or medical history evidence that both generic and preferred agents have been previously tried. The PA criteria also allows for use of nonpreferred brand agents if the patient has allergies, intolerance, or contraindication to the use of generic alendronate or brand preferred agents. The PA Criteria for Approval will also approve any brand bisphosphonate when the patient is currently receiving and stabilized on the brand agent. The PA length of approval has been set at twelve months to allow for changes in preferred and nonpreferred formulary status.

Step Therapy PA Criteria for Approval

Bisphosphonate Step Therapy Option 1

Initial and Renewal Evaluation

1. Has the Bisphosphonate Step Therapy criteria been implemented with a 1-step option (Option 1)?
If yes, continue to 2. If no, go to appropriate criteria question set.
2. Is the patient currently being treated with the requested brand bisphosphonate?
If yes, approve for 12 months. If no, continue to 3.
3. Does the patient's medication history indicate previous use of the generic bisphosphonate alendronate?
If yes, approve for 12 months. If no, continue to 4.
4. Does the patient have an allergy, contraindication, or intolerance to generic alendronate?
If yes, approve for 12 months. If no, deny.

Bisphosphonate Step Therapy Option 2

Initial and Renewal Evaluation

1. Has the Bisphosphonate Step Therapy criteria been implemented with a 2-step option (Option 2)?
If yes, continue to 2. If no, go to appropriate criteria question set.
2. Is the patient currently being treated with the requested brand bisphosphonate?
If yes, approve for 12 months. If no, continue to 3.
3. What drug is requested?
 - a. generic bisphosphonate
 - b. preferred brand bisphosphonate
 - c. nonpreferred brand bisphosphonateIf a, review is not applicable. Claim will adjudicate. If b, continue to 4. If c, continue to 6.
4. Has the patient tried and failed the generic bisphosphonate alendronate?
If yes, approve requested preferred brand for 12 months. If no, continue to 5.
5. Does the patient have an allergy, contraindication, or intolerance to the generic bisphosphonate alendronate?
If yes, approve requested preferred brand for 12 months. If no, deny.
6. Has the patient tried and failed the generic bisphosphonate alendronate?
If yes, continue to 8. If no, continue to 7.

7. Does the patient have an allergy, contraindication, or intolerance to the generic bisphosphonate alendronate?
If yes, continue to 8. If no, deny.
8. Has the patient tried and failed a preferred brand bisphosphonate?
If yes, approve requested nonpreferred brand agent for 12 months. If no, continue to 9.
9. Does the patient have an allergy, contraindication, or intolerance to a preferred brand bisphosphonate?
If yes, approve requested nonpreferred brand agent for 12 months. If no, deny.

SUMMARY

The intent of the step therapy edit for the Bisphosphonate Step Therapy Criteria is to encourage use of the generic bisphosphonate alendronate before brand products and to accommodate for the use of brand agents when generic alendronate cannot be used due to allergy, intolerance, or contraindication. The criteria have been designed with the option of implementing a one step edit requiring generic alendronate before brand agents or a two step edit requiring a generic before a preferred brand and both generic alendronate and preferred brand before a nonpreferred brand agent. The edit also allows automatic payment of claims for a brand bisphosphonate when a patient is already stabilized on the agent. The bisphosphonates included in the step edit are those agents approved for treatment or prevention of osteoporosis in men or women. Generic alendronate is available in all tablet strengths. Fosamax Plus D and Actonel with Calcium will be included as target agents in the step edit because both calcium and vitamin D are available over-the-counter.

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Document History

Criteria developed from PS_Fosamax_ST/QL_0208, PS_Bisphosphonate_QL_AR1107 approved by P & T UM Committee 08/2008
 Criteria changed to Bisphosphonate Step Therapy, approved by P & T: UM Committee 02/2009
 Initial Client Review, Client Specific Criteria, approved by HCSC Corporate Clinical Committee, 08/2009
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