Vimovo™ (naproxen/esomeprazole) Step Therapy Criteria with Medical Diagnoses Option

FDA APPROVED INDICATIONS AND DOSAGE

FDA Indication:
Carefully consider the potential benefits and risks of Vimovo and other treatment options before deciding to use Vimovo. Use the lowest effective dose for the shortest duration consistent with individual patient treatment goals.

Vimovo is indicated for the relief of signs and symptoms of osteoarthritis, rheumatoid arthritis, and ankylosing spondylitis and to decrease the risk of developing gastric ulcers in patients at risk of developing NSAID associated gastric ulcers. Vimovo is not recommended for initial treatment of acute pain because the absorption of naproxen is delayed compared to absorption from other naproxen-containing products. Controlled studies do not extend beyond 6 months.

Dosing: Dosage is one tablet twice daily of Vimovo 375 mg naproxen and 20 mg esomeprazole or 500 mg naproxen and 20 mg esomeprazole.

CLINICAL RATIONALE

Efficacy
The efficacy of Vimovo in treating the signs and symptoms of osteoarthritis was established in two 12-week randomized, double-blind, placebo-controlled trials in patients with osteoarthritis (OA) of the knee. Eligible patients were randomized to receive Vimovo 500 mg/20 mg BID, celecoxib 200 mg QD or placebo for 12 weeks. Patients had been on a stable dose of NSAIDs, COX-2 inhibitors, or other oral analgesic therapy for at least 6 weeks and were allowed to remain on low-dose aspirin for cardioprophylaxis. Patients receiving Vimovo had significantly better results compared to patients receiving placebo as measured by change from baseline of the WOMAC pain subscale and the WOMAC physical function subscale and a Patient Global Assessment Score. Further data regarding the celecoxib treatment arm are not yet publicly available.

Ulcer Prevention
Two randomized, multi-center, double blind trials (Study 1 and Study 2) compared the incidence of gastric ulcer formation in 428 patients taking Vimovo and 426 patients taking enteric-coated naproxen. Subjects were at least 18 years of age with a medical condition expected to require daily NSAID therapy for at least 6 months, and, if less than 50 years old, with a documented history of gastric or duodenal ulcer within the past 5 years. Approximately a quarter of patients were taking concurrent low dose aspirin (<325 mg daily). Vimovo given as 500 mg/20 mg twice daily statistically significantly reduced the 6 month cumulative incidence of gastric ulcers compared to enteric-coated naproxen 500 mg twice daily.
Safety
Vimovo has the same contraindications as celecoxib and NSAIDs such as hypersensitivity to other NSAIDs; asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAIDs; and treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery. The box warnings of cardiovascular and gastrointestinal risks are the same between Vimovo, celecoxib and NSAIDs. Precautions and warnings such as cardiovascular thrombotic events, hypertension, congestive heart failure and edema, and gastrointestinal effects are also the same for Vimovo, celecoxib and NSAIDs.1,6

The key clinical issue in prescribing celecoxib or Vimovo is whether the reduction in ulcer complications is great enough to warrant choosing one of these agents over a nonselective anti-inflammatory agent (NSAID) [i.e., diclofenac, diflunisal, fenoprofen, ibuprofen, flurbiprofen, indomethacin, ketoprofen, naproxen, piroxicam, salsalate].7

Strategies for gastroprotection include supplementation with a synthetic prostaglandin analog (misoprostol), gastric acid suppression (proton pump inhibitors), or the selective use of those NSAIDs least likely to inhibit gastric prostaglandins. This decision depends primarily on the individual patient’s risk for developing an NSAID-induced ulcer and their cardiovascular (CV) risk history.8-11 Risk factors for NSAID-related gastrointestinal (GI) complications are previous GI event, especially if complicated by age, concomitant use of anticoagulants, corticosteroids, other NSAIDs including low-dose aspirin, high-dose NSAID therapy, and chronic debilitating disorders, especially cardiovascular disease.12

The American Heart Association (AHA) issued a recommendation for the use of NSAIDs in patients with known CV disease or at risk of ischemic heart disease. They advise starting with acetaminophen or aspirin at the lowest efficacious dose, especially for short term needs. The AHA recommends a “stepped care approach” to management of musculoskeletal symptoms in the above patient group. The statement made in this guideline is, “If symptoms are not adequately controlled by nonselective NSAIDs, subsequent steps involve prescription drugs with increasing degrees of COX-2-inhibitory activity, ultimately concluding with COX-2-selective NSAIDs.”13

For additional clinical information see Prime Therapeutics Formulary Monograph Vimovo (naproxen/esomeprazole).

REFERENCES
3. Randomized, double-blind, parallel-group, placebo-controlled, multi-center study evaluating the efficacy of PN400 BID and celecoxib 200 mg QD in patients with osteoarthritis of the knee [clinical study report]. In House Data, AstraZeneca LP, PN-400-309.

**Document History**
Original Prime Standard ST QL criteria approved by P&T UM Committee 08/2010
Initial Client Specific Review Client Specific criteria approved by HCSC Corporate Clinical Committee 09/2010
Administrative addition of generic omeprazole/sodium bicarbonate as generic PPI 01/2011
**Vimovo™ Step Therapy**

**OBJECTIVE**
The intent of the Vimovo Step Therapy (ST) program is to accommodate the use of Vimovo in patients who are at high risk of developing an adverse gastrointestinal (GI) event when using a nonselective nonsteroidal anti-inflammatory drug (NSAID) based on Food and Drug Administration (FDA) approved prescribing information and/or clinical studies and/or treatment guidelines. Patients who are currently receiving Vimovo will be approved for continuation of that agent.

**TARGET DRUGS**
Vimovo™ (naproxen/esomeprazole)

**PRIOR AUTHORIZATION CRITERIA FOR APPROVAL**
Vimovo will be approved when ANY ONE of the following is met:

1. The patient is currently receiving Vimovo **OR**
2. The patient is 50 years of age or older **OR**
3. The patient has a history or current diagnosis of peptic ulcer (gastric or duodenal), gastrointestinal (GI) bleed, GI obstruction, GI perforation **OR**
4. The patient has a history or current diagnosis that may put the patient at increased risk for developing an adverse GI event **OR**
5. The patient is currently receiving a medication indicating risk for an adverse GI event

**Length of approval if criteria 2 or 3 are met:** indefinite
**Length of approval if criteria 1 or 4 or 5 are met:** 12 months
**Vimovo™ Step Therapy**

**ELECTRONIC EDIT**
For Vimovo step therapy edit, the 120-day search period was chosen to capture current or recent therapy with prerequisite agents; a 90-day search period for current or recent therapy with Vimovo.

**SUMMARY OF VIMOVO STEP THERAPY**

<table>
<thead>
<tr>
<th>Targeted Agent(s)</th>
<th>Vimovo</th>
</tr>
</thead>
<tbody>
<tr>
<td>Is auto-grandfathering implemented? (with look-back time frame)</td>
<td>Yes (90 days&lt;sup&gt;a&lt;/sup&gt;)</td>
</tr>
<tr>
<td>Prerequisite Agent(s)</td>
<td>systemic corticosteroid OR warfarin OR generic oral nonselective NSAID plus generic PPI OR generic oral nonselective NSAID plus generic misoprostol</td>
</tr>
<tr>
<td>Number of prerequisites required</td>
<td>1</td>
</tr>
<tr>
<td>Prerequisite look-back time frame</td>
<td>120 days&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Age-related edit?</td>
<td>Edit applied to patients &lt; 50 years of age</td>
</tr>
</tbody>
</table>

<sup>a</sup> - 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 dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

<sup>b</sup> - The system searches for a claim with a days supply that begins or ends in the past 120 days. For claims with a 30 day supply the system would be able to identify a claim processed between 1 and 180 days. For claims dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 210 days.

**DETAILS OF VIMOVO STEP THERAPY**

<table>
<thead>
<tr>
<th>Targeted Agents</th>
<th>GPIs (multisource code)</th>
<th>Prior Agents</th>
<th>GPIs (multisource code)</th>
<th>Look-back Time frames</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vimovo</td>
<td>6610990244**** (M, N, O)</td>
<td><strong>For Prerequisites, ANY ONE of:</strong></td>
<td>2210************ (M, N, O, Y) 83200030******** (M, N, O, Y) 661000******** plus 4927************ or 499960******** (Y) 661000******** plus 49250030******* (Y)</td>
<td><strong>Prerequisite look-back time frame:</strong> 120 days&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td></td>
<td></td>
<td>systemic corticosteroid OR warfarin OR generic oral nonselective NSAID plus generic PPI OR generic oral nonselective NSAID plus generic misoprostol</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>For auto-grandfathering, ANY ONE of:</strong> Vimovo</td>
<td>6610990244**** (M, N, or O) set up at a drug or GPI 10 level</td>
<td><strong>Auto-grandfathering look-back time frame:</strong> 90 days&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> - The system searches for a claim with a days supply that begins or ends in the past 120 days. For claims with a 30 day supply the system would be able to identify a claim processed for payment between 1 and 150 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 210 days.
b - 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 dispensed as an extended days supply (90 days), the system would identify a claim processed between 1 and 180 days.

PRIOR AUTHORIZATION CRITERIA QUESTION SET
Initial and Renewal Evaluation
1. Is the patient currently being treated with Vimovo?
   If yes, approve for 12 months. If no, continue to 2.

2. Is the patient 50 years of age or older?
   If yes, approve indefinitely. If no, continue to 3.

3. Please indicate if the patient has a history or current diagnosis of one of the following?
   a. Peptic ulcer (includes duodenal and stomach)
   b. Gastrointestinal (GI) bleed
   c. GI obstruction
   d. GI perforation
   e. None
   If a, b, c, or d, approve indefinitely. If e, continue to 4.

4. Is the patient currently taking an oral anticoagulant [e.g., Coumadin (warfarin)]?
   If yes, approve for 12 months. If no, continue to 5.

5. Is the patient currently taking systemic corticosteroids on a regular basis (i.e., long-term daily or pulse-therapy)?
   If yes, approve for 12 months. If no, continue to 6.

6. Is the patient currently taking a generic oral nonselective NSAID with generic misoprostol or a generic oral nonselective NSAID with a generic PPI?
   If yes, approve for 12 months. If no, continue to 7.

7. Does the patient have a current diagnosis or medical history that may put the patient at increased risk for developing a GI adverse event?
   If yes, approve for 12 months. If no, deny.
Vimovo Step Therapy – Medical Diagnoses Option

OBJECTIVE
The intent of the identification of patients with certain medical diagnoses is to allow coverage of Vimovo therapy in members at high risk for adverse events from nonselective NSAID therapy. Selected medical diagnoses are used to identify patients for pre-approval of Vimovo therapy through the implementation process. Medical claims data will be used to identify plan members with the listed ICD-9 codes found in the primary field in the past 24 months.

<table>
<thead>
<tr>
<th>EVENT</th>
<th>ICD-9CM Code*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ulcer and/or bleed, Duodenal</td>
<td>532, 532.X, 532.XX</td>
</tr>
<tr>
<td>Ulcer and/or bleed, Peptic</td>
<td>533, 533.X, 533.XX</td>
</tr>
<tr>
<td>Ulcer and/or bleed, Gastric</td>
<td>531, 531.X, 531.XX</td>
</tr>
</tbody>
</table>

*The Medical Diagnoses Criteria will approve ICD-9 codes of three or more digits as applicable to ensure that patients who have been assigned incomplete codes will be included.

These patients would be exempt from the step therapy process for Vimovo. Medical claims data must be supplied to Prime in order to implement this option.