Executive Summary

Purpose: To promote safe, cost-effective use of both cyclooxygenase (COX)-2 inhibitors and non-selective nonsteroidal anti-inflammatory drugs (NSAIDs).

Why Issue was Selected: NSAIDs are one of the most commonly prescribed classes of drugs. They are more on the radar today in light of the opioid crisis and providers using non-opioid pain alternatives. Gastrointestinal (GI) problems are the most common side effects associated with NSAID use. NSAID-induced GI toxicities are a significant cause of morbidity and mortality in the U.S. and have a significant economic impact. NSAIDs have also been associated with increased cardiovascular risk. The Texas Medicaid Fee-For-Service Program spent $378,901 on NSAIDs this past year.

Program Specific Information:

<table>
<thead>
<tr>
<th>Performance Indicators</th>
<th>Exceptions</th>
<th>FFS (&lt;18 years)</th>
<th>MCO (&lt;18 years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increased risk of ADE: NSAIDs and GI toxicity</td>
<td>(1) 29</td>
<td>(224) 425</td>
<td></td>
</tr>
<tr>
<td>Use of a COX-2 inhibitor in the absence of risk factors for GI toxicity</td>
<td>(0) 12</td>
<td>(0) 380</td>
<td></td>
</tr>
<tr>
<td>Increased risk of ADE: NSAIDs and recent myocardial infarction</td>
<td>(0) 0</td>
<td>(0) 10</td>
<td></td>
</tr>
<tr>
<td>Increased risk of ADE: NSAID and bisphosphonate</td>
<td>(0) 0</td>
<td>(0) 1,245</td>
<td></td>
</tr>
<tr>
<td>Increased risk of ADE: NSAID-induced GI toxicity in patients with tobacco or alcohol use</td>
<td>(3) 89</td>
<td>(102) 5,226</td>
<td></td>
</tr>
<tr>
<td>Therapeutic Duplication: Concurrent use of &gt;1 NSAID</td>
<td>(0) 0</td>
<td>(7) 545</td>
<td></td>
</tr>
<tr>
<td>NSAID use in patients with cardiovascular risk</td>
<td>(0) 7</td>
<td>(31) 6,377</td>
<td></td>
</tr>
<tr>
<td>NSAID use in patients with congestive heart failure (CHF) and:</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>o Those with ER visits or hospitalizations;</td>
<td>(1) 18</td>
<td>(140) 4,406</td>
<td></td>
</tr>
<tr>
<td>o Those with hypertension;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>o Those with renal impairment</td>
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</tbody>
</table>

Setting & Population: Patients currently receiving COX-2 inhibitors or non-selective NSAIDs.

Types of Intervention: Cover letter and individual profiles
Main Outcome Measures:
Outcomes will be measured when 6 months of claims data is available. Improvements in compliance and days of therapy will be evaluated.

Anticipated Results:
Safe, cost-effective use of NSAIDs will be achieved by limiting duration of therapy when appropriate, reducing duplicate therapy, decreasing the risk of NSAID-induced GI adverse events, decreasing NSAID use in the presence of cardiovascular disease and following myocardial infarction, decreasing NSAID use in heart failure, and decreasing NSAID use in patients with history of alcohol or tobacco use. Physicians will be more aware of the costs of various NSAIDs, as well as the costs of preventive GI co-therapies and COX-2 inhibitors.

Performance Indicator #1: Increased Risk of Adverse Drug Events: NSAID-Induced GI Toxicity

Why has this indicator been selected?
NSAIDs are one of the most commonly prescribed classes of drugs. Gastrointestinal (GI) problems are common side effects associated with NSAID use. A boxed warning for all NSAIDs highlights GI risk with these agents (Appendix-Table 1).

The following are documented risk factors for NSAID-using patients and GI toxicity: age > 60, high dose NSAID, concurrent use of steroids, oral anticoagulants, or aspirin (>325mg/day), and prior history of a GI event.

NSAID discontinuation is the most effective method for reducing GI toxicity risk. Initiating prophylactic treatment in all patients requiring NSAIDs may be unnecessary and cost-prohibitive, but may be considered for high risk patients due to the substantial morbidity and mortality associated with NSAID-induced GI complications.

Candidates (denominator): Patients receiving a non-selective NSAID in the past 90 days for at least 35 days duration

Exception criteria (numerator):
Candidates with any of the following risk factors and with absence of therapy with a PPI or H₂ receptor antagonist:
- Concurrent warfarin use
- Concurrent corticosteroid use
- Concurrent aspirin use (≥81mg)
- High dose NSAID (>75% maximum recommended daily dose)
- History of GI event (peptic ulcer disease [PUD] or GI bleed diagnosis)
- Age > 60 years

Performance Indicator #2: Use of COX-2 Inhibitors in the Absence of Risk Factors for GI Toxicity

Why has this indicator been selected?
Non-selective NSAIDs and selective COX-2 inhibitors are reported to have equal analgesic efficacy. Use of selective COX-2 inhibitors in the absence of risk factors may not be cost-effective since COX-2 inhibitors are more expensive than generic non-selective NSAIDs.

Candidates (denominator): Patients receiving COX-2 inhibitors within the past 60 days.

Exception criteria (numerator):
Candidates without any of the risk factors listed in indicator #1, and without any of the following: inferred rheumatoid arthritis, osteoarthritis, ankylosing spondylitis, juvenile rheumatoid arthritis (JRA), juvenile idiopathic arthritis (JIA), pain relating to dysmenorrhea, and/or therapeutic failure of a non-selective NSAID product. Patients with at least 60 days of therapy with a PPI or H₂ receptor antagonist are excluded from this indicator.
### Performance Indicator #3: Increased Risk of Adverse Drug Events: NSAID Use and Recent Myocardial infarction

<table>
<thead>
<tr>
<th>Why has this indicator been selected?</th>
<th>According to guidelines from the American Heart Association, patients taking NSAIDs (selective and non-selective products) before a myocardial infarction (MI), should have those agents discontinued at the time of the presentation with MI because of the increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with their use.4,5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidates (denominator):</td>
<td>Patients with a myocardial infarction in the past 6 months who have pharmacy claims for an NSAID product in the past 45 days.</td>
</tr>
<tr>
<td>Exception criteria (numerator):</td>
<td>Candidates who have not been on more than 1 NSAID in the past year, who have at least 120 days of therapy with the NSAID in the past 180 days, and who have claims history for an NSAID product in the time period of 6 months to one year.</td>
</tr>
</tbody>
</table>

### Performance Indicator #4: Increased Risk of Adverse Drug Events: NSAID and Bisphosphonate

<table>
<thead>
<tr>
<th>Why has this indicator been selected?</th>
<th>Since NSAIDs and bisphosphonates are associated with gastrointestinal irritation, caution should be exercised in the concomitant use of NSAIDs with these agents.6,7 The bisphosphonates include risendronate (Actonel), alendronate (Fosamax), and ibandronate (Boniva).</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidates (denominator):</td>
<td>Patients receiving an NSAID or COX-2 inhibitor within the past 45 days.</td>
</tr>
<tr>
<td>Exception criteria (numerator):</td>
<td>Candidates receiving an interacting drug (bisphosphonate) concurrently, who are not already on a PPI or misoprostol.</td>
</tr>
</tbody>
</table>

### Performance Indicator #5: Increased Risk of Adverse Drug Events: NSAID-Induced GI Toxicity in patients with Tobacco or Alcohol Use

<table>
<thead>
<tr>
<th>Why has this indicator been selected?</th>
<th>NSAID discontinuation is the most effective method for reducing GI toxicity risk. Tobacco and alcohol use have been reported to increase the risk of NSAID-induced ulcers in some studies although the reported relationships between these factors are inconsistent.3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidates (denominator):</td>
<td>Patients receiving a NSAID or COX-2 inhibitor within the past 45 days.</td>
</tr>
<tr>
<td>Exception criteria (numerator):</td>
<td>Candidates with history of tobacco or alcohol abuse in the last 180 days either by medical diagnosis or inferred drug therapy with the following medications, and does not include any patients currently receiving PPIs: nicotine replacement therapy, bupropion (Zyban®), varenicline, acamprosate, disulfiram, or naltrexone.</td>
</tr>
</tbody>
</table>

### Performance Indicator #6: Therapeutic Duplication: Concurrent Use of >1 NSAID

<table>
<thead>
<tr>
<th>Why has this indicator been selected?</th>
<th>Multiple NSAIDs should not be used concurrently due to increased risk of GI adverse effects and lack of evidence of increased efficacy.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candidates (denominator):</td>
<td>Patients receiving an NSAID product within the past 45 days.</td>
</tr>
</tbody>
</table>
Exception criteria (numerator): Candidates receiving > 1 NSAID product concurrently are identified.

Performance Indicator #7: NSAID use in Patients with Cardiovascular Risk

Why has this indicator been selected? A boxed warning for all NSAIDs highlights risks of serious cardiovascular thrombotic events, myocardial infarction, and stroke (Table 1).

Candidates (denominator): Patients receiving an NSAID or COX-2 inhibitor for > 90 days in the last 150 days.

Exception criteria (numerator): Candidates with a documented (i.e., diabetes, hyperlipidemia, artherosclerosis, post MI, peripheral vascular disease, cerebral atherosclerosis, angioplasty, stent placement, CABG, or artherectomy) or inferred (i.e., > 2 prescriptions for either nitroglycerin or pentoxifylline use in the last 180 days) history of cardiovascular disease.

Performance Indicator #8: NSAID use in Patients with Congestive Heart Failure

Why has this indicator been selected? According to the 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Diagnosis and Management of Chronic Heart Failure in the Adult, NSAIDs should be avoided in patients with CHF since their use can lead to an exacerbation of heart failure symptoms. Additionally, the use of NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended for the management of CHF.

Candidates (denominator): Patients receiving an NSAID or COX-2 inhibitor in the last 45 days.

Exception criteria (numerator): 1-Candidates with a history of congestive heart failure in the last 730 day, AND 2-Candidates with a history of congestive heart failure in the last 730 days and a hospitalization or emergency room visit with a primary diagnosis of congestive heart failure in the last 365 days, AND 3-Candidates with a history of both congestive heart failure and hypertension in the last 730 days, AND 4-Candidates with a history of both congestive heart failure in the last 730 days and renal impairment in the last 365 days.

Appendix

Table 1: NSAID Black Box Warning

<table>
<thead>
<tr>
<th>Boxed Warning for all NSAID Products</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cardiovascular Risk</strong></td>
</tr>
<tr>
<td>• NSAIDs may cause an increased risk of serious cardiovascular thrombotic events, myocardial infarction, and stroke, which can be fatal. All NSAIDs may have a similar risk. This risk may increase with duration of use. Patients with cardiovascular disease or risk factors for cardiovascular disease may be at greater risk.</td>
</tr>
<tr>
<td>• NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.</td>
</tr>
</tbody>
</table>

| **Gastrointestinal Risk** |
• NSAIDS cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.

References

RE: NSAID Drug Usage Evaluation (DUE)

Dear Dr. <<Name>>:

Thank you for providing quality care for Texas Fee-For-Service (FFS) Medicaid patients. The content of this letter has been approved by the Texas Drug Utilization Review (DUR) Board, whose function is to promote safe and cost-effective drug therapy and provide opportunities for continuous improvement of care.

This intervention was selected to assist providers in improving the safe use of non-steroidal anti-inflammatory drugs (NSAIDs). Amid efforts to reduce utilization of opioid analgesics to combat the opioid crisis, use of alternative treatments, such as NSAIDS, has grown. The Centers for Disease Control (CDC) and Prevention 2016 chronic pain guidance recommends non-pharmacologic therapy and non-opioid pharmacologic therapy as preferred treatments. Likewise, use of NSAIDS is recommended at the lowest dose and for the shortest period of time, due to risk of adverse events.

The 2016 CDC Chronic Pain Guidelines are available at: https://www.cdc.gov/drugoverdose/prescribing/guideline.html

Claims data indicate that in the Texas Medicaid Fee-For-Service Program there were approximately 30,078 prescriptions filled last year for NSAIDs. This treatment resulted in a total cost of $378,901. The total Texas Medicaid Fee-For-Service performance indicators for all patients with opportunities for improving the safe use of NSAIDs are shown in the table below.

<table>
<thead>
<tr>
<th>NSAID DUE Management Indicator Summary</th>
<th>Number of Patients with Opportunities*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;18 Years</td>
</tr>
<tr>
<td>Identify patients at risk of adverse events, with factors that can increase GI toxicity:</td>
<td></td>
</tr>
<tr>
<td>• NSAIDs and GI toxicity</td>
<td>1</td>
</tr>
<tr>
<td>• NSAIDS with tobacco or alcohol use</td>
<td>3</td>
</tr>
<tr>
<td>• NSAID and bisphosphonate</td>
<td>0</td>
</tr>
<tr>
<td>Reserve use of a COX-2 inhibitor for patients with risk factors for GI toxicity</td>
<td>0</td>
</tr>
<tr>
<td>Reconsider NSAID therapy in patients who have had a recent myocardial infarction</td>
<td>0</td>
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</tbody>
</table>
• Recognize patients with concurrent use of >1 NSAID

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<td>0</td>
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</table>

• Evaluate NSAID use in patients with cardiovascular risk

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<tr>
<td>0</td>
<td>7</td>
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</table>

• Reconsider NSAID use in patients with congestive heart failure (CHF)

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<tbody>
<tr>
<td>1</td>
<td>18</td>
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</table>

*Based on data through February 2020.

The enclosed patient profiles reflect one or more of the above issues and are provided as a medical record reminder for when your patients return for their next appointments.

We acknowledge that there may be clinical variables influencing an individual patient’s management that are not apparent in claims data. However, we believe the issues identified may assist you in caring for your patient(s). It is possible that your license number may have been inadvertently assigned to the claim as an error at the pharmacy during the billing process. Also, some prescribed medications as well as some recommended laboratory monitoring or physical examinations may not appear on the patient's profile because they may have been privately purchased or were not billable to Medicaid Services. We thank you for reviewing this information and caring for Texas Medicaid patients, and we welcome the opportunity to discuss any comments or concerns you may have about our quality management program. Please feel free to call our office at 1-866-923-7208 with questions or concerns. Your current business address is now being used as your mailing address. If your business address is incorrect, it must be updated through your Texas licensing board.

Sincerely,

Medicaid Drug Use Review Board
Vendor Drug Program H-630
### NSAID DUE Indicator Summary

- **Identify patients at risk of adverse events, due to use of NSAIDs, with factors that can increase GI toxicity.** NSAID discontinuation is the most effective method for reducing GI toxicity in the presence of risk factors. The following are documented risk factors for NSAID-using patients and GI toxicity: age > 60, high dose NSAID, concurrent use of steroids, oral anticoagulants, or aspirin (>325mg/day), and prior history of a GI event. Tobacco and alcohol abuse cause additional stress to the GI system and may contribute to NSAID-induced ulcers. Likewise, bisphosphonates are associated with GI irritation; therefore, caution should be exercised in the concomitant use of these agents with NSAIDs. Patients are identified who are taking NSAIDS and have any of these risk factors.

- **Use COX-2 inhibitors for patients with risk factors for GI toxicity.** Non-selective NSAIDs and selective COX-2 inhibitors are reported to have equal analgesic efficacy, however, selective COX-2 inhibitors should be used alongside the presence of risk factors. Patients are identified who are receiving therapy with a COX-2 inhibitor and lack risk factors for GI toxicity. Risk factors include those previously listed, with the addition of rheumatoid arthritis (inferred from drug therapy). Failure of a non-selective product is considered justification for use.

- **Reconsider NSAID therapy in patients who have had a recent myocardial infarction.** According to guidelines from the American Heart Association, patients taking NSAIDs (selective and non-selective products) before a myocardial infarction (MI) should have those agents discontinued at the time of the presentation with MI, because of the increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture. We identified patients with an MI in the past 6 months on chronic NSAID therapy, who have claims history for an NSAID product 6 months to one year prior.

- **Recognize patients with concurrent use of >1 NSAID.** Multiple NSAIDs should not be used concurrently due to increased risk of GI adverse effects and lack of evidence of increased efficacy. Patients on duplicate NSAIDs are identified.

- **Evaluate NSAID use in patients with cardiovascular risk.** Both non-selective and selective NSAIDs have a boxed warning in product labeling for increased cardiovascular risk, including risk of thrombotic events, myocardial infarction, and stroke. The risk may increase with duration of use and in patients with cardiovascular disease or risk factors for cardiovascular disease. The American Heart Association recommends a step-care approach with NSAIDS in patients with known cardiac disease or risk factors for cardiac disease. Initial pharmacotherapy should include acetaminophen, aspirin, tramadol, followed by nonacetylated salicylates, non COX-2 selective NSAIDs, NSAIDs with some COX-2 activity, and lastly, COX-2 selective NSAIDS. In general, the lowest NSAID dose should be used that will control symptoms. We identified patients receiving chronic NSAID therapy who had documented cardiovascular disease, or where cardiovascular disease was inferred from drug therapy claims.

- **Reconsider NSAID use in patients with congestive heart failure (CHF).** According to the 2013 American College of Cardiology Foundation/American Heart Association Guideline for the Diagnosis and Management of Chronic Heart Failure in the Adult, NSAIDs should be avoided in patients with CHF since their use can lead to an exacerbation of heart failure symptoms. Additionally the use of NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended in the management of CHF. Patients were identified who had recent NSAID claims and a diagnosis of CHF, a recent ER visit or CHF related hospitalization, CHF with hypertension, or CHF with renal impairment.
- **NSAID use in patients with severe hepatic disease.** NSAIDs (e.g. sulindac, etodolac, diclofenac, others) should be used with caution in patients with severe hepatic disease. Hepatic reactions have occurred with patients taking NSAIDs and those with hepatic impairment are at increased risk for developing these complications. Elevations in liver function tests (LFTs) can also occur. Patients with impaired liver function should be monitored closely while receiving NSAIDS, especially when used chronically, as dosing reductions may be needed. While we have not specifically targeted this clinical indicator in this intervention, we are providing this information as a reminder around the use of NSAIDs in your patients.

### Table 1: NSAID Black Box Warning

<table>
<thead>
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</tr>
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<td>- NSAIDs are contraindicated for the treatment of peri-operative pain in the setting of coronary artery bypass graft (CABG) surgery.</td>
</tr>
<tr>
<td><strong>Gastrointestinal Risk</strong></td>
</tr>
<tr>
<td>- NSAIDS cause an increased risk of serious gastrointestinal adverse events including bleeding, ulceration, and perforation of the stomach or intestines, which can be fatal. These events can occur at any time during use and without warning symptoms. Elderly patients are at greater risk for serious gastrointestinal events.</td>
</tr>
</tbody>
</table>

### References:

Incr ADE: NSAID with history of PUD diagnosis
Increased risk of adverse event - NSAID use with history of GI Event: According to claims data, this patient has a history of peptic ulcer disease or a GI bleed. For patients at high risk for NSAID-induced GI events (including prior GI events, advanced age, high dose NSAIDs, and concurrent use of anticoagulants or steroids), consider GI protective co-therapy with misoprostol or a proton pump inhibitor, or possibly switching to a COX-2 inhibitor. Prescribers should carefully weigh the risk-vs-benefit ratio of non-selective NSAID or selective COX-2 inhibitor therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs. NSAIDs should be discontinued, if possible, in patients with active ulcer disease. Proton pump inhibitor co-therapy is recommended if NSAIDs must be continued in the presence of active ulcer disease.

Incr ADE: High Dosage NSAID
Increased risk of adverse event - High dose NSAID use: Higher dose NSAID use (defined here as >75% of the maximum recommended daily dose) may place patients at increased risk for adverse GI events. Use of the lowest effective NSAID dose is recommended. For high risk patients (risk factors include prior GI events, advanced age, high dose NSAIDs, and concurrent use of anticoagulants or steroids), consider GI protective co-therapy with misoprostol or a proton pump inhibitor. Prescribers should carefully weigh the risk-vs-benefit ratio of non-selective NSAID or selective COX-2 inhibitor therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs.

Incr ADE: NSAID & H2RA/Sucralfate Use
Increased risk of adverse event - NSAID & H2RA/sucralfate: It appears that your patient has received an NSAID and histamine-2 receptor antagonist (H2RA) or sucralfate concurrently. Routine use of H2RAs or sucralfate in asymptomatic patients receiving NSAIDs is not recommended. Use of these agents may mask symptoms of GI mucosal injury without preventing serious GI complications. Please review the need for this combination of medications. For high risk patients, consider the use of GI protective co-therapy with misoprostol or a proton pump inhibitor. Prescribers should carefully weigh the risk-vs-benefit ratio of non-selective NSAID or selective COX-2 inhibitor therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs.

Incr ADE: NSAID-Steroid use
Increased risk of adverse event - Concurrent NSAID and steroid use: Patients receiving corticosteroids and NSAIDs concurrently may be at increased risk of adverse GI events. For high risk patients (risk factors include prior GI events, advanced age, high dose NSAIDs, and concurrent use of anticoagulants or steroids), consider GI protective co-therapy with misoprostol or a proton pump inhibitor. Consideration may also be given to switching to a COX-2 inhibitor, which may be less GI toxic than traditional non-selective NSAIDs. Prescribers should carefully weigh the risk-vs-benefit ratio of non-selective NSAID or selective COX-2 inhibitor therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs.

Incr ADE: NSAIDs & Oral Anticoagulants
Increased risk of adverse event - Concurrent NSAIDs and Oral Anticoagulants: NSAIDs may increase the risk of bleeding in patients receiving anticoagulants due to effects on GI mucosa and platelet function. If
used concomitantly, monitor for signs and symptoms of bleeding. For patients at high risk for NSAID-induced GI events, consider GI protective co-therapy with misoprostol, a proton pump inhibitor, or possibly switching to a COX-2 inhibitor. Prescribers should carefully weigh the risk-vs-benefit ratio of non-selective NSAID or selective COX-2 inhibitor therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs.

**4189**
**Duplicate Therapy: Nonselective NSAIDs**
Potential therapeutic duplication: Concurrent use of more than one nonselective NSAID. Please review the need for this combination of medications and, if you have not already done so, verify that your patient has discontinued the appropriate agent(s).

**4190**
**Duplicate Therapy: Nonselective NSAID + COX-2 Inhibitor**
Potential therapeutic duplication: Concurrent use of a nonselective NSAID and COX-2 inhibitor. Please review the need for this combination of medications.

**4236**
**COX-2 use w/o non-dx GI risk factors & trial of other NSAIDs**
COX-2 use w/o GI Risk Factors & trial of other NSAIDs: According to submitted pharmacy claims data, none of the following recognized risk factors for NSAID-induced GI toxicity were identified for this patient: Advanced age, high-dose NSAID use, or concurrent use of anticoagulants or corticosteroids. A prior history of peptic ulcer disease or GI bleeding is a significant risk factor for developing future GI complications. A potential history of GI event was inferred from GI drug use. There may be other factors involved in choosing this therapy that are not identifiable by claims data. Recognizing these limitations, please consider patient-specific factors and re-evaluate the need for this therapy versus the use of a generic, non-selective NSAID.

**10480**
**INCR ADE: NSAIDS CHF exacerbation**
Increased risk of adverse event - NSAIDS and CHF exacerbation: According to submitted pharmacy and medical claims, your patient is currently taking an NSAID and has a history of an ER visit or hospitalization related to congestive heart failure (CHF) in the past year. According to the American College of Cardiology/American Heart Association Guideline 2017 Update for the Diagnosis and Management of Chronic Heart Failure in the Adult, NSAIDs should be avoided in patients with CHF since their use can lead to an exacerbation of heart failure symptoms. Additionally the use of NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended in the management of CHF. Please consider an alternative for your patient, however if NSAID use is necessary please monitor for symptoms of worsening heart failure.

**10481**
**INCR ADE: NSAID W/CHF and HTN**
Increased risk of adverse event - NSAID w/ CHF and HTN: According to submitted pharmacy and medical claims, your patient is currently taking an NSAID and has a history of congestive heart failure (CHF) and hypertension (HTN). As a result of their inhibitory effect on prostaglandin synthesis, NSAIDs can cause both sodium and water retention leading to an increase in blood pressure. Additionally, NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended in management of CHF. Clinical treatment guidelines for the management of CHF
recommend avoiding the use of NSAIDs in these patients since their use can lead to exacerbation of heart failure symptoms. Please consider an alternative therapy for your patient, however if NSAID use is necessary please monitor blood pressure and symptoms of worsening heart failure.

10483
INCR ADE: NSAIDS W/CHF and Renal Imp
Inc ADE: NSAIDS / CHF & renal impairment: According to submitted pharmacy and medical claims, your patient is currently taking an NSAID and has a history of congestive heart failure (CHF) and renal impairment. As a result of their inhibitory effect on prostaglandin synthesis, NSAIDs can decrease renal blood flow and increase the risk of renal toxicity. Additionally the use of NSAIDS can enhance the renal toxicity of diuretics and ACE-inhibitors, both of which are recommended in the management of CHF.
Clinical treatment guidelines for the management of CHF recommend avoiding the use of NSAIDs since these patients are at an increased risk for NSAID-associated renal toxicity as well as their use can lead to an exacerbation of heart failure symptoms. Please consider an alternative therapy for your patient, however if NSAID use is necessary please monitor renal function and for symptoms of worsening heart failure.

10484
INCR ADE: NSAID Use and CHF
Increased risk of adverse event - NSAID use and CHF: According to submitted pharmacy and medical claims, your patient is currently taking an NSAID and has a history of congestive heart failure (CHF).
According to the American College of Cardiology/American Heart Association Guideline 2005 Update for the Diagnosis and Management of Chronic Heart Failure in the Adult, NSAIDs should be avoided in patients with CHF since their use can lead to an exacerbation of heart failure symptoms. Additionally the use of NSAIDs can attenuate the efficacy and enhance the toxicity of diuretics and ACE-inhibitors, both of which are recommended in the management of CHF. Please consider an alternative therapy for your patient, however if NSAID use is necessary please monitor for symptoms of worsening heart failure.

10486
INCR ADE: NSAIDS and Smoking
Increased risk of adverse event - NSAIDS and smoking: According to submitted pharmacy and medical claims, your patient is currently taking an NSAID and has a history of smoking or is receiving smoking cessation therapy. The combination of NSAID use and cigarette smoking may increase the risk for the development of NSAID-induced ulcers. Please review this information with your patient and determine if any changes are appropriate.

10487
INCR ADE: NSAIDS and Alcohol Use
Increased risk of adverse event - NSAIDS and alcohol use: According to submitted pharmacy and medical claims data, your patient is currently taking an NSAID and has a history of alcohol use or is receiving drug therapy for alcohol dependence. The combination of NSAID use and alcohol consumption may increase the risk for the development of NSAID-induced ulcers. Please review this information with your patient and determine if any changes are appropriate.

10703
Incr ADE: NSAIDs and Antiplatelet Agents
Increased Risk of ADE - NSAID and Antiplatelet Agent: It appears your patient has received a non-steroidal anti-inflammatory drug and antiplatelet agent concurrently. Concomitant use of these agents is
not recommended due to increased risk of gastrointestinal (GI) ulceration. Please review the need for this combination of medications, consider the use of appropriate alternatives, or regularly monitor for signs and symptoms of GI toxicity.

**10705**

**INCR ADE: NSAID Use with Advanced Age (> 60)**

Increased risk of adverse event - NSAID use with advanced age (> 60): Elderly patients may be at increased risk for NSAID-associated adverse events including GI toxicity, compromise of existing renal function, and possibly cognitive dysfunction. If appropriate, consider the use of acetaminophen as an alternative to NSAIDs. For patients at high risk of NSAID-induced GI toxicity, consider protective co-therapy with misoprostol or a proton pump inhibitor. Prescribers should carefully weigh the risk-vs-benefit ratio of NSAID therapy for each patient due to concerns of increased risk for cardiovascular events with use of these drugs.

**10707**

**INC ADE: Use of NSAIDs w/ hx of CVD**

Inc ADE: NSAID & history of CVD: According to submitted claims data, this patient has a medical claim for cardiovascular disease (CVD) or diabetes, and is receiving chronic prescription NSAID therapy. The selective COX-2 inhibitors and other nonselective NSAIDs have been associated with increased cardiovascular risk. The risk appears to be amplified in patients with established CVD. According to guidance from The American Heart Association, the risk of cardiovascular events is proportional to COX-2 selectivity and the underlying risk in the patient. A stepped-care approach is recommended, starting with acetaminophen, aspirin, tramadol, short-term narcotic analgesics, and nonacetylated salicylates, followed by non-selective NSAIDs, NSAIDs with some COX-2 activity, and lastly, the COX-2 selective NSAIDs. Please review the risk vs. benefit of continued NSAID use in this patient and determine if another analgesic is appropriate.

**10708**

**INC ADE: NSAIDs**

Increased risk of adverse event - NSAID & CVD: According to pharmacy claims data, this patient has cardiovascular disease (inferred from drug therapy) and is receiving prescription NSAID therapy. The selective COX-2 inhibitors and other nonselective NSAIDs have been associated with increased cardiovascular risk. The risk appears to be amplified in patients with established CVD. According to guidance from The American Heart Association, the risk of cardiovascular events is proportional to COX-2 selectivity and the underlying risk in the patient. A stepped-care approach is recommended, starting with acetaminophen, aspirin, tramadol, short-term narcotic analgesics, and nonacetylated salicylates, followed by non-selective NSAIDs, NSAIDs with some COX-2 activity, and lastly, the COX-2 selective NSAIDs. Please review the risk vs. benefit of continued NSAID use in this patient and determine if another analgesic is appropriate.

**10732**

**Incr ADE: Bisphosphonates and NSAID**

Increased risk of adverse event - NSAID & bisphosphonate: According to submitted pharmacy claims, it appears your patient has received a bisphosphonate (alendronate, risedronate, or ibandronate) and a non-steroidal anti-inflammatory drug (NSAID) concurrently. Since NSAIDs and bisphosphonates are associated with gastrointestinal irritation, caution should be exercised in the concomitant use of NSAIDs with these agents. Please review the need for this combination of medications, consider the use of appropriate alternatives, or regularly monitor for signs and symptoms of GI toxicity.
Incr ADE: NSAID Use and Myocardial Infarction
Increased risk of adverse event - NSAID & myocardial infarction: According to submitted pharmacy and medical claims data, your patient has had a recent myocardial infarction and continues to receive a non-steroidal anti-inflammatory drug (NSAID). American Heart Association treatment guidelines for the management of patients with myocardial infarction recommends patients routinely taking NSAIDs prior to the cardiac event discontinue the agent at the time of the event because of increased risk of mortality, reinfarction, hypertension, heart failure, and myocardial rupture associated with NSAID use. NSAID products, including the selective COX-2 inhibitors and other nonselective NSAIDs, have been associated with increased cardiovascular risk. The risk appears to be amplified in patients with established CVD. Please review the risk vs. benefit of continued NSAID use in this patient and determine if another analgesic is appropriate.

Duplicate Therapy: NSAID/H2 Antagonist + COX-2 Inhibitor
Duplicate Therapy - Nonselective NSAID and COX-2 Inhibitor: Based on pharmacy claims data, it appears you patient is receiving concurrent therapy with a nonselective NSAID and a COX-2 Inhibitor. If your patient has been placed on a COX-2 inhibitor due to the presence of risk factors for GI toxicity, use of a nonselective NSAID may negate the potential benefit of the selective COX-2 agent and may increase the risk for adverse events. Please review the risks with your patient and determine the best medication for them to use.