MTUS FORMULARY P & T COMMITTEE
NSAID DRUG REVIEW

Several Non-Steroidal Anti-inflammatory Drugs (NSAIDs) are among the top 50 drugs by cost reimbursed under the workers compensation program. The Division of Workers Compensation (DWC) has decided the NSAIDs drug category would be an appropriate drug category for the MTUS P&T Committee's first categorical review. Discussion of the NSAIDs category will be the primary topic for discussion during the April 24, 2019 P&T Committee meeting. This review also includes drugs not normally thought of as NSAIDs such as aspirin and choline magnesium trisalicylate.

To assist Committee members to prepare for the meeting discussion, DWC has created or gathered reference material.

NSAIDs REVIEW

One of the most commonly used classes of drugs to treat pain and inflammation are Non-Steroidal Anti-Inflammatory Drugs (NSAIDs). One factor for such broad use is the over-the-counter availability of ibuprofen, naproxen, naproxen sodium and aspirin. NSAIDs exhibit analgesic, anti-inflammatory, and antipyretic effects by inhibiting the enzymatic action of cyclooxygenase (COX) which exists in two forms COX-1 and COX-2. COX-2 is the enzyme responsible for inflammation and fever, while COX-1 serves to protect the gastric mucosa and assists in making platelets stick together. The NSAID class consists of non-selective COX inhibitors (e.g. naproxen and ibuprofen), partially selective inhibitors that favor COX-2 over COX-1 (e.g. meloxicam and nabumetone) and the selective COX-2 inhibitor celecoxib (Celebrex).

Though DWC is confident that the P&T Committee members are fluent in the knowledge relating to NSAIDs and their use, the following NSAID category reviews can be used by members to refresh their knowledge on chemical composition, drug actions, safety concerns and use.

Members can click on the hyperlink of the document they wish to review. Each document is a PDF file that can be viewed using Adobe Acrobat Reader or other PDF viewer application.

- *Drug Class Review on Cyclo-oxygenase (COX)-2 Inhibitors and Non-steroidal Anti-inflammatory Drugs (NSAIDs)*; Oregon Health & Science University; 2006 https://www.ohsu.edu/sites/default/files/2019-01/NSAID_final_report_update-3_NOV_06.pdf
- *Drug Class Review Nonsteroidal Antiinflammatory Drugs (NSAIDs) Preliminary Scan Report #2*; Oregon Health & Science University; May 2014 http://www.orpdl.org/durm/meetings/meetingdocs/2014_11_20/archives/2014_11_20_NonsteroidalAntinflammatoryDrugsNSAIDsPrelimin.pdf
- *Therapeutic Class Overview Nonsteroidal Anti-Inflammatory Drugs (NSAIDs)*; University of Massachusetts Medical School; Nevada Medicaid; 2016 https://www.medicaid.nv.gov/Downloads/provider/Nonsteroidal%20Anti-Inflammatory%20Drugs%20(NSAIDs).pdf

DWC is not providing an opinion on the reviews so P&T members can make independent determinations on the utility of the various NSAIDs. However, in general the reviews conclude:

- All NSAID-containing agents are associated with a Black Box Warning regarding the increased risk of serious gastrointestinal adverse reactions.
- There are no significant short-term differences in oral NSAIDs for pain relief, though there may be response variability among individual patients.
- Celecoxib is not associated with higher risk of cardiovascular events and is gastroprotective (short term use) compared to other NSAIDs. Nabumetone is also more gastroprotective when compared to other NSAIDs.
- Non-selective NSAIDs have similar increased risk for GI events and all but naproxen have similar increased risk of serious cardiovascular events.
- Factors such as age, recent history of gastrointestinal bleeding, and concomitant use of antiulcer medication are important considerations for use of NSAIDs.

MDGUIDELINES FORMULARY RECOMMENDATIONS

The MDGuidelines Formulary Tool (at https://www.mdguidelines.com/tool/formulary) provides a significant amount of evidence-based recommendations for the use of NSAIDs for various work related medical conditions. P&T members are encouraged to review the details found within the online Formulary Tool.

To assist P&T members, DWC developed two Excel workbooks in visualizing those recommendations. Members should use these spreadsheets to assist in identifying which drug/disease combination they wish to further explore using the Formulary Tool. For example, may note that naproxen has additional recommendations in the treatment of Acute Extensor Compartment Tenosyovitis and members can then review these recommendations using the Formulary Tool.

Each worksheet identifies a general category (e.g. Ankle and Foot Disorders) and lists all related conditions (e.g. Achilles Tendinopathy) under that general category. Each drug/condition combination is then color coded to identify the type of recommendation found in the guidelines. There are instances where multiple recommendations may exist; for these the drug/condition combination will be color coded and marked with the asterisk.

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Yes, Strong Evidence, "A" Level Evidence	**A**
Yes, Moderate Evidence, "B" Level Evidence	**B**
Yes, Limited Evidence, "C" Level Evidence	**C**
Yes, Insufficient Evidence (Consensus-based), "I" Level	**I**
No, Strong Evidence, "A" Level Evidence	**A**
No, Moderate Evidence, "B" Level Evidence	**B**
No, Limited Evidence, "C" Level Evidence	**C**
No, Insufficient Evidence (Consensus-based), "I" Level	**I**
No Recommendation	NR
No, Other = Not Recommended, Healthesystems recommendations based on leading sources as well as pharmacy and therapeutics (P&T) decisions (pharmacy and medical literature, safety, cost)	**NO**
Yes, Other = Recommended, Healthesystems recommendations based on leading sources as well as P&T decisions (pharmacy and medical literature, safety, cost)	**YES**
multiple recommendations apply (refer to MDGuidelines for detail)	*

DWC reminds members that these charts are not a substitute for the detail on the MDGuidelines website, only a visual guide to assist products they wish to review further using the Formulary Tool. The two workbooks provided are:

- NSAID conditions by alpha – this is an alphabetically listing of the drugs under review
- NSAID conditions by subclassifications – this is a listing or drugs under commonly used chemical classifications, grouping like drugs together

Diclofenac and naproxen sodium are highlighted yellow as not being included in the current MTUS Formulary as ingredients. Both diclofenac sodium and ketorolac tromethamine ophthalmic dosage forms are Exempt while the oral dosage forms are Non-Exempt.

DETAILED FORMULARY

The "*NSAID detail with UPI*" is an expanded MTUS Formulary listing. This expanded spreadsheet includes approved generic drug names, dosage forms, strengths and UPI numbers for each MTUS drug ingredient. Reference Brand Names are matched based on the listed generic name, dosage form and strength.

Two generic drug names to take note of are diclofenac and naproxen sodium. These are not listed on the MTUS formulary as ingredients and will be an aspect of the committee discussion on the identification of salt forms that have the same or similar utility to the drug ingredients listed.

Members can use this detailed list to identify drug/strength/dosage form combinations they wish to discuss further during the meeting.

COST DATA

Drug utilization and cost data was obtained for this review. This information is provided on four different spreadsheets. The drug pricing data used is from the new Medi-Cal data which uses the NADAC pricing. Each spreadsheet shows:

- Lowest Rate – which is the lowest rate Medi-Cal has on its file and reflects the maximum rate of reimbursement, except for "Do Not Substitute" (DNS) prescriptions.
- No-Sub Rate – is the rate that is used when DNS is indicated on the prescription
- FUL – is the federal upper limit for Medicaid; this value is provided to show that the new NADAC rate, in many cases, is lower than the FUL for generic drugs.

The spreadsheets provided are:

- Historical oral – This spreadsheet contains oral products showing the average prescription size found in the data. Products with blank values had no utilization shown in the data. Only the Lowest rate calculation was performed
- Daily dose – To provide a better comparison among product prices, a typical daily dose value was attached to each oral solid dosage form (liquids excluded) and then multiplied by both the Lowest Rate and the No-Sub Rate
- Ophthalmic Drugs – Lists of the ophthalmic drugs, with available package sizes; calculations based on rate times package size
- Topical Drugs – List of the topical drugs, with available package sizes; calculations based on rate times package size

NOTE: There was an inadvertent omission on data retrieval and celecoxib was left off, therefore there is a "blank" in the average prescription size. This information will be updated as soon as it is available.