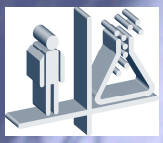

AMERICAN COUNCIL
ON SCIENCE AND HEALTH

# making sense of over-the-counter Pain relievers

# Making Sense of Over-the-Counter Pain Relievers

Prepared for
the American Council on Science and Health

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## *Introduction*

The last 100 years have been more comfortable for humankind as a result of the discovery and availability of over-the-counter pain relievers (or analgesics). This year marks the 100th anniversary of the introduction of aspirin by Bayer. It was not until 1955 that acetaminophen (Tylenol) became available over-the-counter (OTC) in the United States. Ibuprofen (Advil, Motrin, Nuprin) joined the over-the-counter arsenal 19 years later. And 1994 and 1995 brought U.S. Food and Drug Administration (FDA) approval of OTC naproxen sodium (Aleve) and ketoprofen (Actron**,** Orudis KT), respectively. Today, there are many choices of pain relievers and fever medications, but selecting one does not have to be a headache!

Each of these medications has been proved safe and effective, and in most cases, any one of them would be a reliable choice for pain relief and/or fever reduction. However, there are unique properties and differences that make specific products more desirable for certain conditions or individuals. This report will provide information that will help readers differentiate among and select appropriate OTC pain relievers. It will review the effectiveness and safety of the five pain medications currently approved for OTC use. In addition, it will alert readers to side effects, drug interactions, and conditions under which certain medications should not be used. Finally, relatively new and potential future uses will be discussed.

## *OTC Use of Common Pain Relievers*

The FDA recognizes two broad classes of drugs: OTC, or nonprescription, drugs, and Rx, or prescription, drugs. OTC agents are those that can be safely self-administered for short periods of time without a physician's prescription or guidance. Prescription drugs, on the other hand, require a prescription to be dispensed and are taken under the guidance of a health care professional.

The five pain relievers discussed in this manuscript are illustrated in **Table 1** (see insert).

## *The Discoveries*

Aspirin is the safe, modern form of a class of pain-relieving compounds called "salicylates," which have been used for millennia. Some 2400 years ago, Hippocrates provided the first written record recommending the consumption of willow bark extract (which was later discovered to contain salicylates) as treatment for the pain of childbirth. Since then, from ancient Greece to Europe in the Middle Ages, there have been many references that advise using willow leaves and bark for the treatment of a variety of conditions.

In the mid- to late 1800s, salicylate compounds were prepared in the laboratory, refined, and tested. In the 1890s, a chemist at Frederich Bayer and Company (present-day Bayer Corporation) tested a number of salicylate compounds and concluded that acetylsalicylic acid (aspirin) brought together the best combination of pain relief and safety. Bayer introduced aspirin in 1899. Shortly thereafter, other companies followed with the manufacture of their own brands of aspirin. Today aspirin ranks second only to alcohol as the most consumed drug in the world. In the United States alone it has been reported that annual aspirin consumption is in the neighborhood of 77,000 tons.

Acetaminophen belongs to a class of compounds that first had medical applications in the 1880s. Other members of the class were more popular at first but were later withdrawn from the U.S. market because they caused serious kidney problems. Acetaminophen has proved to be a safe form of this class of drugs and has been available as an OTC pain reliever in the United States since 1955.

The next major event in the development of OTC analgesics occurred in 1953, when researchers started searching for safer and more effective drugs for the treatment of rheumatoid arthritis. Eventually, a compound named ibuprofen was found to have a good safety profile in animal studies, as well as pain-relieving and fever-reducing properties, and also acted as an anti-inflammatory agent.

The first clinical trials demonstrating the efficacy and safety of ibuprofen in rheumatoid arthritis patients occurred in the 1960s. The drug, brand-named Motrin, was approved for prescription use in the United Staes in 1974, and was approved for OTC

use in 1984.

Because of their demonstrated safety and efficacy in clinical trials, naproxen (brand-named Naprosyn) and ketoprofen (Orudis) were granted prescription approval by the FDA in 1976 and 1986, respectively. Naproxen sodium (Aleve) was granted OTC approval in 1994, followed by the OTC approval of ketoprofen (Actron**,** Orudis KT) in 1995. Over time, confidence in their safety grew along with evidence of their effectiveness at higher prescription doses.

## *How They Work*

Aspirin, ibuprofen, naproxen sodium, and ketoprofen are all characterized as nonsteroidal anti-inflammatory drugs (NSAIDs) and act similarly. They work primarily at the site of injury or pain to lessen discomfort and prevent inflammation (the swelling, pain, and redness that result from an injury). They help to reduce fever by affecting an area in the brain. These properties of NSAIDs are believed to result from their ability block the production of certain compounds, called prostaglandins, that are produced by the body.

Prostaglandins are hormone-like substances that have a wide range of effects. Prostaglandins play a role in many bodily functions, including pain modulation, temperature control, and blood clotting. It is the blockage of prostaglandin production that underlies all of the beneficial—and adverse—effects of NSAIDs. Prostaglandins are important in the transmission of pain by sensitizing nerve endings, making it easier for them to send pain messages to the brain. Prostaglandins also are important in causing fever. By blocking the production of prostaglandins, aspirin and the other NSAIDs reduce the severity of pain related to inflammatory processes, and reduce fever.

Aspirin, more than the other NSAIDs, also reduces blood clotting by inhibiting platelets from sticking together, or aggregating. Aspirin irreversibly blocks the enzyme cyclooxygenase (COX), which allows platelets to clump or aggregate. This is why that low doses of aspirin are now recommended for some patients at risk for heart attack and for those at risk of stroke caused by blood clots in the brain.

Like NSAIDs, acetaminophen has pain-relieving and fever-reducing activity. Unlike NSAIDs, acetaminophen is believed to inhibit prostaglandin synthesis primarily in the central nervous system (the brain). It does not have anti-inflammatory benefits, nor does it reduce blood clotting. Therefore, it does not have any protective effect against heart attack in at-risk patients.

## *Comparing Effectiveness*

All the medications discussed in this report are obviously safe and effective enough to meet the FDA's criteria to be made available OTC to the public. They have been proved in clinical trials to work effectively and quickly without causing undue risk to patients.

Clinical trials involve the testing of medications under controlled conditions. The OTC medications discussed in this report have been tested under such conditions to determine whether they are effective in relieving pain that may result from sore throat or dental surgery, headache pain, menstrual pain, muscle soreness, and arthritis. They have also been tested for their ability to reduce fever in children and adults. Each of the OTC medications discussed here has been proved safe and effective for all these indications, except for certain conditions involving aspirin use in children (see **"Fever Reduction in Children,"** page 11).

As consumers, we seek the most effective medications for our pain and fever. What works well for one person may not work well for another. We seek the fastest-acting, longest-lasting treatments with few, if any, side effects. Perhaps the data from these clinical trials can help us select the appropriate drug. However, comparing the effectiveness of the various OTC agents is difficult. First, many of the published studies supporting the effectiveness of these medications were performed at doses above the approved OTC range. In reality, to claim that one OTC analgesic works better than another, each must have been studied at the OTC dose. Also, with regard to the new generation of NSAIDs, much of the data comparing these agents to one another and to older OTC drugs are not available to the general research community.

The following presentation is an attempt to explain and compare the available research on OTC pain medications. A summary of the data in the following section of the report can be found in **Table 2** (page 20).

## Pain Relief

For relief of pain, aspirin and acetaminophen are, in general, equally effective. With a 650-mg dose (two tablets) of either aspirin or acetaminophen, pain relief begins within one hour and lasts about four hours. Aspirin has demonstrated effectiveness against muscle soreness resulting from exercise or overexertion. Acetaminophen has not been shown to be as effective for this condition. Both have proved equally effective for headache and menstrual pain. For both medications, higher doses, up to the maximum approved OTC dose of 1000 mg, result in stronger pain relief.

Caffeine at doses equivalent to a strong cup of coffee has been shown to enhance the effectiveness of aspirin, acetaminophen, or their combination. Caffeine/pain reliever combinations have been marketed as Excedrin Extra Strength and Excedrin Migraine and are effective in reducing the pain, nausea, sensitivity to light and sound, and the functional disability associated with migraine headaches.

Classifying aspirin and acetaminophen as "mild analgesics," which is how they are often described in the medical literature, underestimates their effectiveness against pain. Actually, 500 mg or more of aspirin or acetaminophen consistently equals or surpasses the pain-relieving characteristics of marketed doses of oral narcotic agents, including 60 mg of codeine (the amount in two Tylenol #3 tablets) or 5 mg of oxycodone (the amount in one Percocet tablet).

When comparing OTC doses of the newer NSAIDs with aspirin or acetaminophen, a trend emerges: a single dose of naproxen sodium (220 mg), ibuprofen (200 mg), or ketoprofen (12.5 mg) is roughly equivalent in strength to higher doses of aspirin or acetaminophen. Maximum OTC doses of these agents (440 mg of naproxen sodium**,** 400 mg of ibuprofen, or 25 mg of ketoprofen) appear more effective than either aspirin or acetaminophen. They work for a longer duration and effectively combat a

higher degree of pain.

Aspirin and acetaminophen, 650 to 1000 mg, generally begin to relieve pain within 60 minutes and relieve pain for 3 to 6 hours. Studies have shown that naproxen sodium, 220 to 440 mg, begins to relieve pain within 60 minutes and relieves pain for 8 to 12 hours—the longest duration of action among the OTC products. Ibuprofen, 200 to 400 mg, relieves pain within 60 minutes and lasts for 4 to 8 hours. Ketoprofen, 12.5 to 25 mg, has analgesic properties similar to those of ibuprofen, 200 to 400 mg (See **Table 1**, insert).

Naproxen sodium and ibuprofen have been especially effective for dental, throat, and headache pain, as well as muscle soreness. Few studies have been published evaluating OTC doses of the newer NSAIDs for menstrual pain (dysmenorrhea), but they do show some efficacy and are widely used for this condition.

## *Convenience Combinations*

Convenience combinations typically contain aspirin, acetaminophen, or ibuprofen plus at least one other entity, such as a nasal decongestant, antihistamine, cough suppressant, or antacid. These other entities simultaneously treat other symptoms that may accompany pain and fever. Examples of just a few of the marketed combinations are found in **Table 2** (page 20). These combinations can be worthwhile if in fact the patient has a variety of symptoms. However, they are often misused by the public, which leads to needless exposure to one or more of the constituents. For example, a patient complaining of nasal congestion without fever or headache is best treated with a nasal decongestant, not a combination that also contains aspirin, acetaminophen, or ibuprofen. Likewise, a patient experiencing only pain or fever should ingest a single-entity pain reliever such as naproxen sodium or ibuprofen. The additional constituents do not enhance pain relief; they only increase the risk of side effects.

## Safety Concerns

As with all drugs, unwanted effects are possible with OTC analgesics. All the OTC pain relievers, except acetaminophen, should be avoided during the third trimester (last three months) of pregnancy. If more than three alcohol-containing drinks per day are often consumed, that fact should be discussed with a physician before deciding on an OTC analgesic. Concomitant use of aspirin, naproxen sodium, ibuprofen, or ketoprofen and alcohol can increase the risks of gastrointestinal bleeding and ulcers. Concommitant acetaminophen and alcohol use can increase the risk of liver damage. Acetaminophen is known to damage the liver directly, although (except in chronic alcohol abusers) this occurs only in overdose. If there is a history or suspicion of excessive alcohol intake, acetaminophen should be avoided unless specifically recommended by a physician.

Fortunately, severe side effects from OTC analgesic use are rare, and their occurrence usually depends on the dose and duration of administration. Occasional OTC analgesic use that adheres to maximum dosage guidelines is generally considered safe. At prescription doses over longer periods of time, there are higher risks, which may increase with age, the use of other medications, or the presence of a complicating condition. As with any medication, intentional and unintentional overdose can cause serious consequences, including death.

## Fever Reduction in Children

In the pediatric population, the primary use of OTC medications is for the reduction of fever. However, there is considerable controversy concerning their routine use. Arguments against their use cite the ability of fever to enhance the immune response, the fact that even without medications fevers usually end quickly, and the ability of fever reducers to mask signs important for diagnosis, prognosis, or assessment of the response to antibiotics. Arguments supporting the routine use of fever-reducing medication include the prevention of seizures due to fever in young children and the enhancement of patient comfort. Even these seemingly rational arguments for the use of anti-fever agents are not convincingly support-

ed by scientific studies.

OTC analgesics are widely employed by the general public to relieve and comfort young children with fever, and more often than not, they are recommended by physicians to parents and patients for the control of fever. As of this date, OTC naproxen sodium and ketoprofen are not indicated for use in children under the ages of 12 and 16 years, respectively.

Acetaminophen has proved to be an effective fever reducer in children. In one study, it caused fever to decline within 30 minutes. Peak effectiveness was reached in about three hours, and effectiveness ebbed by the sixth hour. Sponging the child with tepid water has been shown to be as effective as using anti-fever medication, and the two used in combination were more effective than either treatment alone. The fever reducing effects of ibuprofen have also been well studied in children. Ibuprofen begins to reduce fever within 30 minutes, with a duration of action of six to eight hours.

**Aspirin should not be used to reduce fever in children, because of the threat of a condition called "Reye's syndrome."** First described in 1963, **Reye's syndrome** is an acute childhood illness that produces brain inflammation and liver disease. Infants and children may develop Reye**'**s syndrome after a viral infection such as influenza or chickenpox. Symptoms—including tiredness, agitation, delirium, and seizures—appear suddenly. Without aggressive treatment, the disease progresses to deep coma, brain dysfunction, and, in 80% to 90% of cases, death. In the 1970s and 1980s, studies suggested a strong association between aspirin therapy and Reye's syndrome. Expert panels of pediatricians recommend that **children not be treated with aspirin for flu-like symptoms, fever, or chickenpox**. Parents have taken this advice, and the incidence of Reye's syndrome has decreased.Acetaminophen, naproxen, and ibuprofen have not been implicated in the induction of Reye's syndrome.

### Long-term Use

In many ways, we are dealing with two different drugs when we compare a medication taken within the guidelines of the OTC labeling with the same

medication taken at higher doses and over longer durations. These higher-dose and longer-duration uses are best referred to as prescription conditions. Under these conditions, there is a greater expectation of efficacy, but there is also a greater likelihood of adverse drug reactions than with standard OTC usage, when medications are taken at lower doses for shorter periods of time. However, when such dosage is used under a health professional's guidance, the benefit is usually thought to outweigh the potential risk. For example, a patient with a sprained ankle who consumes a maximum OTC dose of 660 mg of naproxen sodium for 10 days is less likely to suffer adverse effects than an arthritis patient who consumes a prescription anti-inflammatory dose of 1000 to 1500 mg of naproxen per day for many months.

The most serious side effects associated with long-term, high-dose (prescription) use of NSAIDs are gastrointestinal (GI) problems and kidney abnormalities. These problems are believed to result from the NSAIDs' ability to inhibit prostaglandin production. In the GI tract, especially the stomach and duodenum, prostaglandins decrease acid secretion and increase the production of protective mucus and bicarbonate, which protect the stomach from injury. In the kidneys, prostaglandins help maintain blood flow, especially in people with preexisting kidney disease.

Taking excessive doses of acetaminophen, or taking it in conjunction with alcohol, has caused serious liver problems. This is discussed at some length in "Precautions, Contraindications, and Drug Interactions" (page 15).

### Overdose

The potential for accidental or intentional overdose with any medication is an important public health concern. According to the American Association of Poison Control Centers, there were 128 deaths attributed to aspirin overdose and 124 deaths attributed to acetaminophen overdose between 1988 and 1993. During this reporting period, only one death was attributed to ibuprofen overdose, and no deaths were attributed to naproxen/naproxen sodium

overdose. These low numbers may reflect not only the relative safety of these products, but also the fact that they were used less commonly.

Aspirin overdose remains a relatively common means of attempting suicide in young adults. It was (before Reye's Syndrome warnings) also a major culprit in accidental overdoses in children younger than five years of age. Serious effects of aspirin overdose typically occur at doses in excess of 15 to 25 tablets in adults. In children, toxicity was often the result of a therapeutic overdose; that is, the parent administered two to four times the recommended dose for a period of several days. Fatalities in children and adults can result without proper medical care. The early signs of overdose usually appear within the first three to four hours after ingestion and include nausea, vomiting, ringing in the ears, fever, and hyperventilation. Visual disturbances, hallucinations, delirium, and seizures can also occur. The treatment of aspirin overdose is primarily supportive. It may involve pumping of the stomach and administration of substances to prevent absorption, promote excretion, and combat chemical imbalances and dehydration.

Acetaminophen, like the NSAIDs, is a safe agent when used as recommended. However, its true lethal potential is often underestimated, especially by adolescents. Overdosage can lead to serious, even fatal, liver damage. Not uncommonly, an attention-getting "suicidal" gesture using acetaminophen becomes a tragic reality. It is estimated that acute doses of more than 6 g (20 tablets) are necessary for liver toxicity to occur. In children under ten years of age, multiple miscalculated overdoses administered by their parents (as in the pediatric aspirin overdose scenario) have also led to severe liver damage.

To prevent permanent liver injury or death, the importance of administering the antidote, N-acetylcysteine, within 16 hours of acetaminophen ingestion cannot be overemphasized. The major problem in dealing with an acetaminophen overdose is the delay in observable symptoms. During the first 12 to 24 hours after an acetaminophen overdose, few if any symptoms occur, even with large ingestions. The patient is not perceived as ill, and unfortunately the first 24 hours represents the period when the antidote

will be of most benefit. It is not until after 24 hours that symptoms of nausea and vomiting and abnormal liver function become evident. So while a highly effective antidote exists, the overdose is often diagnosed too late.

Like other drugs that have gained OTC approval after prescription use, a marked increase in reports of overdose reactions occurred following ibuprofen's 1984 OTC approval. However, there has not been any evidence to contradict ibuprofen's prescription claims of relatively low toxicity. In adult cases of intentional overdose, there appear to be few serious risks if less than 6 g (30 tablets) is ingested. In addition, all patients who become symptomatic do so within four hours of an acute ibuprofen overdose. This is unlike the slow, insidious nature of acetaminophen overdose.

Acute overdose reactions to naproxen and naproxen sodium have rarely been reported. Even patients ingesting very high doses (up to 35 g) completely recovered with appropriate medical care. As with other OTC analgesics, naproxen sodium appears to be safe when used as directed.

## *Precautions, Contraindications, and Drug Interactions*

Although OTC pain relievers are generally considered safe, even low-dose and short-duration exposure may place certain patients at risk. Patient information provided for OTC pain relievers specifically list three warnings, concerning aspirin allergy, pregnancy, and concomitant alcohol use. In addition, aspirin products carry a warning about bleeding disorders and Reye's syndrome. There are also risks in combining the use of pain relievers and certain other pharmaceuticals.

Aspirin and the other NSAIDs have been associated with an allergic reaction whose symptoms range from stuffy nose and rash to severe asthma. In the overall population, this syndrome has a low incidence, of less than 1%. However, it has been estimated that 10% to 28% of adult asthma patients may be intolerant to aspirin. Patients with a history of aspirin-sensitive asthma or allergy must avoid naproxen sodium, ibuprofen, and ketoprofen, because these drugs

also may precipitate a serious allergic reaction. While acetaminophen is usually considered a safe alternative in these patients, it was recently reported that as many as one third of those aspirin-sensitive asthmatics are also sensitive to high doses of acetaminophen.

The use of aspirin or any of the other NSAIDs should be avoided by pregnant women. NSAIDs can inhibit labor and prolong pregnancy and may also increase bleeding risk associated with delivery. Additionally, maternal NSAID use can result in circulatory problems in the newborn. Aspirin should be avoided during pregnancy, particularly late in pregnancy, because it is associated with delivery complications and excessive bleeding after delivery. Earlier in pregnancy, chronic use of aspirin has been associated with anemia in expectant mothers. Acetaminophen is generally considered the best choice for managing minor pains and fever in pregnancy.

Long-term, high-dose use of the newer NSAIDs has been implicated in counteracting the blood pressure–lowering effects of many antihypertensive agents. This interaction has not, in general, been associated with short-term low-dose OTC therapy.

Mixing alcohol with pain relievers presents a number of potential hazards. The combined use of alcohol and NSAIDs can significantly increase the risk of ulcers and blood loss. The use of NSAIDs should be separated from alcohol consumption by at least 12 hours. The FDAhas mandated that manufacturers of all OTC aspirin-containing and NSAID-containing products include in their labeling the warning that patients who consume three or more alcoholic drinks per day should contact their physician before ingesting aspirin, naproxen sodium, ibuprofen, or ketoprofen because the combination may increase the risk of stomach bleeding.

Prolonged use of alcohol and acetaminophen can cause severe liver damage. The FDA has mandated that manufacturers of acetaminophen-containing products include in their labeling the warning that patients who consume three or more alcoholic drinks per day should contact their physician before ingesting acetaminophen because the combination may increase the risk of liver damage.

Serious bleeding, or hemorrhage, can be a complication of anticoagulant ("blood-thinning") therapy. Thirty percent of patients requiring long-term treatment with these medications, which inhibit blood clotting, suffer this side effect. The combination of anticoagulants and NSAIDs can be dangerous. Careful physician monitoring of this combination is required.

## *New and Potential Future Indications*

Aspirin has been approved as a daily therapy to prevent life-threatening cardiovascular problems, such as heart attack (M.I.) and stroke. Aspirin and the other NSAIDs are also being investigated for their potential to prevent colorectal cancer and to prevent or lessen the symptoms of Alzheimer's disease. NSAIDS may also be effective in dental and periodontal (gum) disease, which can result in tooth loss.

As previously discussed, aspirin irreversibly blocks the COX enzyme system that causes platelets to clump. This is the rationale for long-term aspirin therapy in the prevention of heart attack and stroke (caused by blood clots in the brain) in certain high-risk patients. On October 23, 1998, the FDA published a new set of expanded indications with definitive dosing guidelines for each condition. They are described in detail in **Table 3** (page 21). Low doses of aspirin (325 mg—one pill—or less per day) are recommended for people who have already suffered a heart attack, those with angina, and those who have undergone procedures such as coronary bypass. Aspirin is also recommended for patients in the acute stages of a heart attack. Taking aspirin for these and other conditions has proved effective in reducing the risk of future cardiovascular events. However, use of aspirin for these indications requires the supervision of a physician or other licensed practitioner.

There is considerable interest in the possibility that aspirin and the other NSAIDs may retard or prevent the development of colorectal cancer. Studies demonstrate that the consumption of aspirin on 16 or more days a month over a period of six years and the use of ibuprofen, naproxen sodium, and ketoprofen for a period of at least 12 months have both been associated with roughly a 40% decrease in the inci-

dence of colorectal cancer. Perhaps one or more of these drugs will gain FDA approval as a "colorectal cancer protectant." However, controlled clinical trials will first be required.

A number of studies suggest that the long-term administration of aspirin or other NSAIDs, including naproxen sodium and ibuprofen, reduces both the risk of developing Alzheimer's disease and the severity of Alzheimer symptoms. NSAID inhibition of prostaglandin production may be responsible. As with colorectal cancer, the potential labeling of NSAIDs as "Alzheimer's disease protectants" would likely be considered prescription use of these drugs, because of the need for long-term use.

Bacteria are the primary cause of human periodontal disease. But prostaglandins as mediators of inflammation have been associated with gum disease and subsequent tooth loss. Ibuprofen, naproxen, and ketoprofen applied directly to the gums or taken orally have been shown to reduce the severity of gingivitis (a precursor of periodontal disease) and lessen bone and tooth loss in the mouth. Although there is considerable information supporting the use of NSAIDs as treatment for periodontal disease, no NSAID formulation has been granted FDA approval for this indication. Studies are necessary to evaluate the relationship between benefits and side effects.

## *CONCLUSION*

Over-the-counter pain relievers provide great benefits to American consumers. This statement, while true enough before the arrival of the new NSAIDs, is even more so now with the addition of naproxen sodium, ibuprofen, and ketoprofen to the old standbys, aspirin and acetaminophen.

Aspirin, with its long history of safety and effectiveness, has been the most relied-upon analgesic. Now it also has been given new indications, for heart disease prevention and treatment. What acetaminophen lacks in anti-inflammatory characteristics is compensated for by its safety profile. The new NSAIDs—which include naproxen sodium, ibuprofen, and ketoprofen—are remarkable for their speed, efficacy, and duration of effect. Their use is likely to increase as news of their effectiveness and safety continues to spread.

As with all medications, there are small but definite risks associated with OTC analgesic use. Even the safest drug can do harm when prescribed or ingested without regard to appropriate safeguards. Caution must be used in certain specific population groups, notably children, the elderly**,** and those with pre-existing kidney, gastrointestinal, or liver disease. The good news, however, is evident. After literally billions of doses, the record of safety and efficacy of the medications reviewed in this document, when they are used according to OTC guidelines, is extremely favorable.

Table 2. **Some Convenience Combinations**

| Proprietary Name | Constituents |
|---|---|
| Actifed Cold and Sinus | Acetaminophen 500 mg<br>Pseudoephedrine HCl 30 mg<br>Tripolidine HCl 1.25 mg |
| Advil Cold and Sinus | Ibuprofen 200 mg<br>Pseudoephedrine bitartrate 30 mg |
| Alka-Seltzer | Aspirin 325 mg<br>Sodium bicarbonate 1916 mg<br>Citric Acid 1000 mg |
| Alka-Seltzer plus Cold and Cough | Aspirin 325 mg<br>Chlorpheniramine maleate 2 mg<br>Phenylpropanolamine bitartrate 20 mg<br>Dextromethorphan hydromine 10 mg |
| Excedrin PM | Acetaminophen 500 mg<br>Diphenhydramine citrate 38 mg |
| Robitussin Night-Time Cold Formula | Acetaminophen 325 mg<br>Pseudoephedrine HCl 30 mg<br>Dextromethorphan HBr 15 mg<br>Doxylamine succinate 6.25 mg |

Table 3. **Expanded Antiplatelet Indications and Dosing Guidelines of Aspirin**

| Indications | Recommended Daily Dose | Duration of Therapy |
|---|---|---|
| **Vascular Indications:** | | |
| Ischemic Stroke and TIA | 50–325 mg | Indefinitely |
| Suspected Acute MI (heart attack) | 160–162.5 mg taken as soon as infarction is suspected; then once daily | For 30 days post infarction (after 30 days consider further daily treatment based on indication for previous MI) |
| Prevention of Recurrent MI | 75–325 mg | Indefinitely |
| Unstable Angina Pectoris | 75–325 mg | Indefinitely |
| Chronic Stable Angina Pectoris | 75–325 mg | Indefinitely |

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