

ACETAMINOPHEN

THE MOST COMMON DRUG INGREDIENT IN AMERICA





USING IT

Acetaminophen is a **safe and effective pain reliever and fever reducer** when used as directed. Nearly 94% of the time, it is taken safely, appropriately, and according to the directions on the Drug Facts label.'



AVOIDING OVERDOSE

EXCEEDING THE MAXIMUM DAILY DOSE



of 4,000 mg is an overdose and can lead to liver damage² OF THOSE WHO EXCEED 4,000 MG IN 1 DAY, MOST DO SO BY



Taking the next dose too soon



Using multiple products containing acetaminophen



Taking too much at one time

A

PROMOTING SAFE USE & EDUCATING CONSUMERS

EDUCATION IS WORKING

More consumers understand that "exceeding the recommended daily dose of acetaminophen may lead to liver damage."



88% 2019

FOLLOW SAFE USE STEPS

- 1. Always read & follow the medicine label
- 2. Know if your medicines contain acetaminophen
- **3.** Never take two acetaminophencontaining medicines at the same time
- **4.** Ask your healthcare professional or pharmacist if you have questions
- Kaufman DW, Kelly JP, Battista DR, Malone MK, Weinstein RB, Shiffman S. Five-year trends in acetaminophen use exceeding the recommended daily maximum dose. Br J Clin Pharmacol 2019; 85:1028-1034.
- 2. Acetaminophen Dosage, last updated June 14, 2019. Accessed at https://www.drugs.com/dosage/acetaminophen.html
- 3. Shiffman S, Rohay JM, Battista D et al. Patterns of acetaminophen medication use associated with exceeding the recommended maximum daily dose. Pharmacoepidemiol Drug Saf 2015; 24:915-921.
- $4.\ https://www.chpa.org/about-consumer-healthcare/infographics/awareness-acetaminophen-safe-use-remains-high$



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EXECUTIVE SUMMARY

Every day, millions of Americans rely on over-thecounter (OTC) and prescription (Rx) medicines to improve or maintain their health and manage their pain. Chronic pain and its management are of increasing concern: more than one in four Americans ages 45-64 live with chronic pain. By age 85, that number increases to one in every three. In fact, chronic pain prevalence in older adults 65-84 years old is twice as great as in younger adults 24-44 years old.1,2 With the number of Americans ages 65 and older projected to nearly double from 52 million in 2018 to 95 million by 20603, this will likely lead to an increased demand for safe and effective pain relief. Adding another layer of complexity, three guarters of adults 65 years and older have two or more chronic conditions such as heart disease or diabetes, which poses additional risk with taking pain medicines.4 For some consumers, including older adults with persistent pain, patients with stomach conditions such as ulcers or other chronic conditions, acetaminophen is the recommended option for pain relief.

There has been a shift in the use of Rx pain medications and U.S. healthcare professional (HCP) prescribing behavior. Following an increase in Rx opioid overdoses in America, there was a 34 percent decline in opioid prescriptions in 2018 compared to 2012.⁵ HCPs want to provide adequate pain control for their patients, but balancing the risks

and benefits of all pain treatment options can be challenging. Additionally, the HCP-patient dialogue and HCP counseling are becoming increasingly more important to ensuring medicines are used responsibly, including those available over the counter. As the pain management landscape continues to evolve, everyone within the healthcare sector—from manufacturer, to HCP, to patient/consumer—has a part to play in managing and treating pain safely.

Acetaminophen is one of the most commonly used drug ingredients in the U.S. for pain relief and fever reduction, and is found in more than 600 different OTC and Rx medicines.⁶ More than 50 million Americans use an acetaminophen-containing medicine each week to treat pain, fever, and minor aches such as those due to the common cold, headache, backache, minor pain of arthritis, toothache, muscular aches, and premenstrual and menstrual cramps.⁷

Acetaminophen has long been proven to be safe and effective when taken as directed, but there is a limit to how much should be taken in one day. The maximum daily limit for acetaminophen is 4,000 milligrams (mg) over a 24-hour period, although some acetaminophen labels specify a maximum limit as low as 3,000 mg in 24 hours unless directed by a doctor. It's important to always read the Drug Facts label and follow the provided dosing directions to avoid exceeding the daily dosing limit.

Taking more acetaminophen than directed is an overdose and can lead to adverse health outcomes. There are two types of overdose scenarios: intentional overdoses involve purposefully taking more than directed to relieve symptoms or attempt suicide; unintentional overdoses occur when a subject unknowingly takes more acetaminophen than directed. If the overdose is large enough, this can lead to severe liver damage. Though total instances are rare in the context of the ingredient's widespread use, acetaminophen overdose is commonly recognized as a cause of acute liver failure. Research shows that three dosing patterns involving deviations from label directions account for the majority of unintentional overdoses: redosing too soon, taking multiple acetaminophen-containing medicines at the same time, and/or taking too much acetaminophen at one time.8 For these reasons, it is critically important that we understand how people use acetaminophen, understand how it's misused, and advance educational interventions to promote safe use.



50 MILLION AMERICANS

use acetaminophen each week.

This is equivalent to **5,000 PEOPLE PER MINUTE.**⁷

In 2010, a group of leading health and consumer organizations and HCPs came together to form the Acetaminophen Awareness Coalition (Coalition). The Coalition's objective is to educate consumers on the importance of knowing the ingredients in their medicines and following labeled directions to prevent unintentional acetaminophen overdose. In 2011, the Coalition launched a public education campaign called *Know Your Dose* to reach consumers, patients, and HCPs with safe use education and resources. The *Know Your Dose* campaign and the Coalition continue this important education work today.

This report is a compilation of recent research on acetaminophen that explores how it is used; how misuse leading to unintentional overdose can occur; and what HCPs, drug manufacturers, health advocates, regulators, media, and other stakeholder groups have accomplished together to promote safe use among consumers and patients. Though uncommon, liver damage related to acetaminophen overdose is serious. Reducing liver injuries begins



with understanding the problem and risk factors, then developing and implementing research-based solutions targeted to those risk factors. It is essential to reinforce the need for everyone who uses acetaminophen-containing medicines to take them safely, as well as to emphasize the importance of reading and following medicine labels. Coordinated, comprehensive educational initiatives and product innovations—described in this report—have been put in place to promote safe use across multiple channels, via the collaboration of many stakeholders. The Coalition urges continued collaboration and education to further spread the word about the importance of using acetaminophen appropriately.

1) ACETAMINOPHEN: AN OVERVIEW

Acetaminophen (pronounced: a·seet·a·MIN·o·fen), also known in other parts of the world as paracetamol (para·SEET·a·mol), is the active ingredient in medicines widely used to reduce fever and temporarily relieve minor aches and pains, such as those due to the common cold, headache, backache, minor pain of arthritis, toothache, muscular aches, and premenstrual and menstrual cramps. It is one of the most commonly used drug ingredients in the U.S., available in OTC as well as Rx products, either as a single ingredient or in combination with other drug ingredients.9 More than 60 years of consumer use and scientific investigation have established acetaminophen as safe and effective when used as directed at recommended doses. As with any medicine, however, there is a limit to how much should be taken in one day. For acetaminophen, the maximum daily dose is 4,000 mg.¹⁰

COMMON MEDICINES THAT MAY CONTAIN ACETAMINOPHEN

Over-the-Counter

And store brands

Actifed®
Advil Dual Action
Alka-Seltzer Plus®
Cepacol®
Contac®
Coricidin® HPB
DayQuil®/NyQuil®
Dimetapp®
Dristan®
Excedrin®
FeverAll®
Formula 44®

Goody's Powders®

Panadol®
Robitussin®
Saint Joseph®
Aspirin-Free
Singlet
SUDAFED®
Theraflu®
Triaminic®
TYLENOL®
Vanquish®
Vicks®

Prescription Brand Name Medicines

And generic drugs

ALLZITAL™ Oxycodone
Anexsia® Percocet®
Bultalbital Phenaphen®
Butapap™ ROXICET®
Codeine or Codeine with acetaminophen Tapanol®
Endocet® TREZIX™
Fioricet® Tramadol

Hycotab TYLENOL® with Codeine

Hydrocet® Tylox®
Hydrocodone Ultracet®
Lortab® Vicodin®
MIDRIN® XARTEMIS
NORCO® Zydone®

Oxycet[®]

Many OTC and Rx medicines have store-brand or generic versions. For example, there are many store-brand products that are similar to brands such as TYLENOL*, NyQuil*, and Robitussin*. Rx medicines that come in generic form may list the ingredients in place of a drug name. For example, the generic version of Vicodin* has "hydrocodone and acetaminophen" written on its label. Rx labels may list the ingredients, the brand name, or both. This list is just a sample of the more than 600 different medicines that contain acetaminophen.

SINGLE-INGREDIENT AND COMBINATION MEDICINES CONTAINING ACETAMINOPHEN

There are more than 600 medicines that contain acetaminophen, including OTC medicine brands such as Excedrin®, Midol®, Mucinex® Sinus Max products, NyQuil®, Robitussin®, Sudafed®, Triaminic®, and TYLENOL®, and Rx medicines, such as Endocet®, Percocet®, and Vicodin®. Sometimes, acetaminophen is the only active drug ingredient in a medicine. These are "single-ingredient" medicines and include products such as Regular Strength TYLENOL® and Extra Strength TYLENOL®. Acetaminophen can also be found in many products with more than one active ingredient ("combination medicines"), such as NyQuil® or Percocet®. These may also be sold under generic or store brand names.

HOW ACETAMINOPHEN IS LISTED ON THE LABEL

If acetaminophen is in an OTC medicine, it will be listed on the product packaging and on the Drug Facts label. Acetaminophen is always prominently written on the front of the box or packaging and will often be highlighted or bolded in the active ingredients section of the Drug Facts label.

Acetaminophen historically has been commonly identified on Rx labels as "APAP," "acetam," or other abbreviated versions of the word. In 2011, the pharmacy standards development organization National Council for Prescription Drug Programs (NCPDP) initiated a task group of government, manufacturers, and professional and consumer advocacy organizations to encourage pharmacies to fully spell out "acetaminophen" on Rx drug labels to avoid consumer confusion. Today, NCPDP estimates that more than 95 percent of U.S. pharmacies are working to fully spell out "acetaminophen" on Rx labels.¹¹



KNOW YOUR MILLIGRAMS

Strength*

325 mg (Every 4-6 hours)

Alka-Seltzer Plus® Cough & Cold Liquid Gels Excedrin® Sinus Headache Mucinex® Fast-Max Cold & Sinus Caplets Nyquil® Cold & Flu Nighttime Relief LiquiCaps Percocet (Rx)
Robitussin® Peak Cold Nasal Relief TYLENOL® Regular Strength Vicodin (Rx)
Mucinex®

500 mg (Every 6 hours)

Contac[®] Cold & Flu Coricidin[®] HBP Maximum Strength Flu Midol[®] Complete TYLENOL[®] Extra Strength

650 mg (Every 8 hours)

TYLENOL® 8-HR Arthritis Pain
TYLENOL® 8-HR Muscle Aches & Pain

NOTE: This information also applies to the generic/store brand versions of these products. Always read and follow the Drug Facts label and ask your pharmacist or other healthcare professional if you have questions about the ingredients in your medicine.

*Acetaminophen in mg. Based on one tablet, capsule, caplet, or gel cap.

ACETAMINOPHEN DOSING

In the U.S., acetaminophen is available in different dosage strengths measured in mg: 325 mg, 500 mg, and 650 mg (extended release). The specific dosage strength will be listed on the label. As this may vary across many different types of medicine—both Rx and OTC—it is critical to read and follow the Drug Facts labels to understand dosage strength and unique dosing directions for each product (including when to take). Each strength has its own duration, length of time before the next dose can be taken, and total maximum daily dose. For example, 325 mg is directed to be taken as needed every 4-6 hours and not to exceed the total daily dose of 10 caplets (3,250 mg) in 24 hours; 500 mg is directed to be taken as needed every 6 hours and not to exceed the total daily dose of 6 caplets (3,000 mg) in 24 hours; and 650 mg is directed to be taken as needed every 8 hours and not to exceed the total daily dose of 6 caplets (3,900 mg) in 24 hours. It is also important not to take more than one acetaminophen-containing medicine at the same time.

ACETAMINOPHEN AND LIVER DAMAGE

Taking more acetaminophen than directed and exceeding the maximum daily dose of 4,000 mg is considered an overdose and can lead to severe liver damage.¹⁰

Acetaminophen is metabolized in the liver, an essential organ that filters blood coming from the digestive tract. While the majority of a therapeutic dose of acetaminophen is metabolized and eventually excreted in urine, a very small amount is metabolized into NAPQI, a compound harmful to liver cells if present in large amounts. When acetaminophen is taken as directed, NAPQI is rendered harmless (detoxified) as part of the body's natural processes. However, very high NAPQI levels resulting from an acetaminophen overdose can damage the liver or, in severe cases, result in acute liver failure (ALF; i.e., the rapid loss of liver function), or even lead to death.

While the percent of overall acetaminophen users who exceed the maximum daily labeled dose when using the medicine is very low, and in the vast majority of instances it does not result in side effects or adverse events, it remains critical to continue working to improve safe use to reduce the potential for overdose.

EXCEEDING THE LABELED DOSE:

COMMON ACETAMINOPHEN DOSING MISTAKES



Taking the next dose **too soon**



Using multiple acetaminophen-containing products at the same time



Taking more than the recommended dose at a single time⁸

2) FACTORS ASSOCIATED WITH EXCEEDING RECOMMENDED DOSING AMOUNTS

According to research, nearly 94 percent of the time, acetaminophen is taken safely, appropriately, and according to the directions on Drug Facts labels. There are still some consumers, however, who exceed recommended amounts of acetaminophen, either for a single dose or the maximum daily amount (4,000 mg). This section explores research into ingredient awareness and behaviors contributing to exceeding recommended dosing amounts.

A study examining patterns associated with exceeding the maximum labeled dose of 4,000 mg per day found that for nearly 97 percent of the days for which acetaminophen dosage was recorded, the recommended maximum dose of acetaminophen was not exceeded.⁸ For the small number of cases involving use of more than 4,000 mg a day, there are three underlying dosing patterns that account for the majority of unintentional overdoses:

- 1) Taking the next dose too soon (2.2 percent of usage days);
- 2) Using multiple products containing acetaminophen (1.8 percent of usage days); and/or
- **3)** Taking too much at one time (1 percent of usage days).

REDOSING TOO SOON

Redosing too soon is the result of not following the labeled guidance to wait a set period of time before taking the next dose and may happen when someone is trying to achieve greater relief from pain symptoms. People living with and treating pain symptoms are encouraged to have an ongoing dialogue with their HCP to find a pain management solution that is safe and effective. Reduced pain can often be achieved by adjusting medication regimen or ensuring the patient is using the right dosage strength, as well as implementing other non-medicine alternatives—such as meditation and stretching—under the guidance of a HCP.

Consumers are significantly more likely to exceed the 4,000 mg maximum daily dose on days when they are taking both OTC and Rx acetaminophen-containing medicines.¹²

DOUBLING UP: USING MULTIPLE ACETAMINOPHEN-CONTAINING PRODUCTS AT THE SAME TIME

Approximately one in three older adults (ages 60-79) in the U.S. is taking five or more Rx medicines.¹⁴ Using more than one medicine at the same time can be appropriate and safe when these medicines do not contain the same active ingredient and have no drugdrug interactions. The use of multiple acetaminophencontaining products at the same time, or "doubling up," typically occurs when consumers or patients do not realize their medicines contain acetaminophen or do not read and follow the Drug Facts label. This behavior can result in an unintentional overdose and often involves the use of multiple acetaminophencontaining OTC medicines (e.g., a pain medicine with a cold medicine), multiple acetaminophen-containing Rx pain medicines, or a combination of both an acetaminophen-containing Rx and an OTC medicine (an Rx pain medication with an OTC cold medicine).8

Research illustrates that taking multiple acetaminophen-containing medicines at the same time is a risk factor for acetaminophen overdose. Consumers are significantly more likely to exceed the 4,000 mg maximum daily dose on days when they are taking both OTC and Rx acetaminophen-containing medicines, compared to days in which they are only taking OTC medicines with acetaminophen.⁸

When consumers can identify acetaminophen in their medicines, they are less likely to accidentally overdose. In a 2018 study, 74 percent of patients taking a single-ingredient medication could correctly identify acetaminophen; when taking combination medications, however, this number ranged from 61 percent (for sleep or other non-pain medicines) down to 39 percent (for cough/cold medicines). Only about one-third of patients knew the importance of only taking one medicine with acetaminophen at once.¹⁵ This illustrates that there is still work to be done to ensure that all patients and consumers know when acetaminophen is in their medicines.

TAKING TOO MUCH ACETAMINOPHEN AT ONCE

Sometimes, consumers take more acetaminophen than directed simply by exceeding the one-time recommended dose of an acetaminophen-containing product. Although research has found that this occurs relatively infrequently, according to a 2015 study⁸, factors associated with this behavior include lack of knowledge of the one-time dose and the presence of chronic pain conditions.

In a study examining attitudes and knowledge associated with use of acetaminophen-containing medicines among U.S. adults, 4.5 percent of users took more than 4,000 mg on at least one day in a week. Subjects aware that their medications contained acetaminophen or those with knowledge of the maximum one-time dose were significantly less likely to exceed the maximum daily dose. 16 Virtually all acetaminophen users in the study who exceeded the 4,000 mg maximum daily dose reported having some ongoing pain during the diary period, with 64 percent reporting chronic pain (i.e., occurring for ≥6 months). Another study examining knowledge of acetaminophencontaining medication directions found that those subjects with knowledge of the maximum one-time dose were significantly less likely to take too much at one time compared to those who were unaware of the maximum one-time dose. 15 In a separate study, the overall percentage of subjects exceeding the recommended one-time dose of acetaminophen was low and did not change over the 2011-2016 period.¹³ However, this behavior underscores the need to ensure that consumers and patients understand the maximum daily dose and risks involved with taking too much acetaminophen at one time.

SEASONAL TRENDS: ACETAMINOPHEN OVERDOSE DURING COLD AND FLU SEASON

Certain seasonal factors can lead to increased patterns of heightened unintentional misuse. A 2018 study looked at the likelihood of consumers exceeding the maximum daily dose of acetaminophen during cold and flu season (as identified using Google Trends data) when compared to off-season use. Respondents were 23 percent more likely to take more than the maximum daily dose of acetaminophen during cold and flu season than they were during off season (6.5 percent vs. 5.3 percent). This is largely due to increased use of OTC combination medications treating upper respiratory cold and flu symptoms. 17 This trend emphasizes the need to provide education during the cold and flu season, specifically about the importance of knowing the ingredients in the medicine one is taking and following the label to avoid unintentional overdose.

3) PROMOTING SAFE USE OF ACETAMINOPHEN

Research shows that adults with knowledge of the ingredients in their medicines and the appropriate dose have a lower likelihood of exceeding the maximum daily dose of 4,000 mg of acetaminophen.¹⁵

This data point, along with the specific dosing patterns identified in this report, identifies why educational initiatives, as well as product and packaging changes, are key to preventing unintentional acetaminophen overdose and the rare but concerning liver failure that can result. There have been many innovative, root-cause-based interventions that have helped promote the safe use of acetaminophen in both adult and pediatric populations.

PRODUCT CHANGES TO PROMOTE SAFE USE

Over the last 15 years, manufacturers and pharmacies have worked closely with the Food and Drug Administration (FDA), HCP and pharmacist groups, and consumer health advocates to promote safe acetaminophen use by making changes to products, packaging, and labeling. Consistency and visibility across OTC and Rx drug labels are a critical step to ensuring that consumers and patients can identify and compare ingredients and take steps to improve the safe use of acetaminophen. Such changes have included:

- Enhanced visibility of acetaminophen in OTC medicines via labeling changes: All OTC medicines containing acetaminophen now prominently display the word "acetaminophen" on the front panel of packaging to make it easier for consumers to identify this ingredient. OTC medicines with acetaminophen also highlight or bold "acetaminophen" on the Drug Facts label, and liver and concomitant use warnings are standardized across all products.
- Limited levels of acetaminophen in Rx products: The amount of acetaminophen in Rx combination products is limited to 325 mg per unit dose.¹⁸
- Improved communication of duration for extendedrelease products: The naming of extended-release acetaminophen products has been updated to prominently communicate the 8-hour limit (e.g., TYLENOL® 8-Hour Arthritis).
- Improved Rx labeling: An estimated 95 percent of U.S. pharmacies have removed the "APAP" abbreviation, and the majority of Rx container labels for combination acetaminophen-opioid prescriptions contain the full spelling of acetaminophen, per the recommendations of the NCPDP. 10 As a result, the word "acetaminophen" is now more visible on labels of Rx medicines that contain acetaminophen and is accompanied by a standard concomitant use warning, such as: "This has acetaminophen. Don't take with other medicines that have acetaminophen (prescription or nonprescription). Too much can cause liver damage."

PEDIATRIC ACETAMINOPHEN PRODUCT CHANGES

Among children under six, unintentional ingestion of acetaminophen causes more emergency room (ER) visits than any other oral liquid medicine. From 2012-2015, accidental ingestion of OTC liquid acetaminophen caused an estimated 2,500 ER visits each year. Standardization of the acetaminophen concentration (160 mg/5 mL) and packaging improvements for OTC pediatric liquid products have resulted in a reduced incidence of dosing errors, as well as a 40 percent reduction in accidental unsupervised ingestions.

- Introduced flow restrictors: In 2011, OTC acetaminophen manufacturers voluntarily introduced flow restrictors into pediatric liquid acetaminophen products. Following the introduction of flow restrictors, researchers monitored reported accidental unsupervised ingestions (AUIs) involving single-ingredient liquid acetaminophen among children under the age of 12. Reported exposures decreased steadily following the introduction, dropping by 40 percent from 2010 to 2015. Additionally, flow restrictors led to lower doses ingested among reported exposures, as well as decreased risk of hospital admission.²¹
- Standardized concentration levels in pediatric medicines: The introduction of flow restrictors was coupled with a voluntary standardization of pediatric liquid acetaminophen concentrations. Prior to 2011, liquid acetaminophen products for infants had a different concentration than liquid acetaminophen products for older children. To standardize concentration and dosing across all single-ingredient pediatric liquid acetaminophen products, industry voluntarily combined both infants' products and children's acetaminophen products to one concentration (strength) of 160 mg per 5 mL. In the years following the standardization (2012-2016), the rate of exposures reported to poison centers fell by 19 percent.²⁰ In 2017, manufacturers of pediatric acetaminophen solid dose medicines began to voluntarily transition their products to a single concentration of 160 mg, consistent with the concentration of liquid acetaminophen (160 mg/5 mL).

EDUCATIONAL CAMPAIGNS TO PROMOTE SAFE USE

Consumer Education

Several ongoing national education campaigns are focused on increasing consumer awareness about acetaminophen, its risks, and how to use it appropriately and within the recommended daily dose.

The Know Your Dose Campaign

In 2010, leading HCP and pharmacy organizations came together with consumer and public health advocates to form the Acetaminophen Awareness Coalition. The Coalition includes the Alliance for Aging Research, American Association of Nurse Practitioners, American Pharmacists Association, BeMedWise Program at NeedyMeds, Caregiver Action Network, Consumer Healthcare Products Association Educational Foundation, National Association of Boards of Pharmacy, National Association of Chain Drug Stores Foundation, National Community Pharmacists Association, and National Consumers League. The Centers for Disease Control and Prevention and U.S. FDA serve as advisors to the Coalition.

In 2011, the Coalition launched the *Know Your Dose* campaign to educate patients and consumers on how to safely and appropriately use medicines that contain acetaminophen to avoid unintentional overdose.

At its outset, the Coalition conducted research to establish a baseline understanding of consumer awareness, perceptions surrounding acetaminophen, and the behaviors that drive unintentional overdose, as well as to validate campaign messaging and materials. This research helped to ensure that campaign messages would motivate audiences to act. On a continual basis, the Coalition conducts research to ensure that campaign communications alert consumers to the importance of safe use without undermining confidence in the safety and effectiveness of the ingredient when used appropriately.

The *Know Your Dose* campaign reaches consumers in places where medicine safety is contextually relevant and more likely to be top of mind: at points of care in health clinics and HCP offices; at points of purchase

in retail pharmacies and in OTC aisles; and at points online when consumers are likely to be searching for relevant information. The campaign promotes four key steps for safe acetaminophen use:

- 1) Always read and follow the medicine label
- 2) Know if your medicines contain acetaminophen
- 3) Only take one medicine with acetaminophen at the same time
- **4)** Ask your healthcare professional or pharmacist if you have questions

To date, *Know Your Dose* messages in English and Spanish have reached consumers and HCPs more than 700 million times. In all efforts, the campaign aims to target people in key moments—at points of purchase, points of care, points of consideration, and seasonal moments of increased acetaminophen use such as cold and flu season. Additionally, *Know Your Dose* continually seeks to place messaging in the hands of populations that are known to be at risk for unintentional overdose, such as the chronic pain community, older adults, Spanish-speaking community, and teenagers.

To provide consumers with messaging at points of purchase, the *Know Your Dose* campaign has partnered with retail pharmacies including Costco, Walmart, and Sam's Club to display posters, brochures, and "shelf-talkers" throughout OTC medicine aisles and at Rx counters. The campaign has also included inserts in pickup bags for acetaminophen-containing prescriptions, as well as targeted purchasers of OTC acetaminophen medicines via messaging printed on in-store purchase receipts.

To reach consumers when they are considering purchasing or taking a pain medicine, *Know Your Dose* continuously ensures that people searching online for information about acetaminophen receive campaign safe use steps, and places hyper-targeted media buys that raise awareness and drive traffic to KnowYourDose.org.

Know Your Dose maintains a presence at points of care through its ongoing contact with HCPs, who use the free patient educational materials provided at KnowYourDose.org in discussion with their patients at pharmacy counters and exam rooms. To date, Know Your Dose has disseminated more than 11 million free English and Spanish educational materials.

Organizational partnerships are another critical component anchoring *Know Your Dose* efforts. Currently, 27 health and consumer organizations have adopted and shared *Know Your Dose* acetaminophen safe use messages with their constituents and communities, including the American Association of Poison Control Centers, American Liver Foundation, National Fibromyalgia & Chronic Pain Association, National Headache Foundation, U.S. Pain Foundation, and more.

The Coalition's *Know Your Dose* campaign is one of many ongoing, coordinated educational initiatives that work in concert to drive appropriate acetaminophen use and prevent overdose. Aligned acetaminophen safe use education efforts also include:

Alliance for Aging Research: OTC Pain Medication Safe Use Educational Film Campaign

A series of educational "pocket films" from the nonprofit Alliance for Aging Research help consumers select, take, store, and dispose of OTC pain medications.

- What You Need to Know Before You Reach for OTC Pain Medication guides users in choosing the medication that's right for them and their loved ones and gives tips on taking the medication safely.
- Safely Taking and Storing OTC Pain Medication
 helps viewers learn where to store their medications,
 how to keep them up and away and out of sight of
 young children, how to prevent misuse, and what to
 do when the medication is no longer needed.
- Safe Medication Disposal gives a simple step-by-step guide on how to dispose of OTC and Rx medications in a way that keeps them out of the hands of young children, prevents abuse, and is safe for the environment.

These films have been translated into Spanish, turned into public service announcements, reduced to topic specific chapters, produced with closed captioning, and shared through dozens of outreach channels. The films have reached an estimated audience of more than 100 million and can be found online at https://www.agingresearch.org/health-topic/medication-safety/. They are also being shared through a comprehensive education program for older adults on safely managing their pain.

The BeMedWise Program at NeedyMeds

BeMedWise.org, "Talk About Your Medicines" Month, Medication Use Safety Training (MUST) for Seniors, the Acetaminophen Safe Use Toolkits, and the SCOUTStrong BeMedWise Award are public education initiatives promoting safe and appropriate medication use, storage, and disposal. These initiatives are led by BeMedWise, a program of the national nonprofit NeedyMeds, a health education-focused forum of consumer, HCP, business, patient advocacy, government, and public health organizations working together to improve health outcomes through the adoption of responsible medication practices. BeMedWise was formerly the National Council on Patient Information and Education (NCPIE), founded in 1982.

Approximately one in three older adults (ages 60-79) in the U.S. is taking five or more Rx medicines. ¹⁴ Additionally, one in 10 Americans (10 percent) over the age of 65 has Alzheimer's disease or related dementia, potentially making daily medicine decisions difficult. ²² A broad medicine safety campaign, the MUST for Seniors program, provides a ready-to-use PowerPoint presentation with presenter notes and downloadable tips for taking medications safely for use by older adults, caregivers, and HCPs to self-educate and present in their communities. MUST for Seniors includes the "Tips for Using Acetaminophen Safely," "Questions to Ask Your Healthcare Professional About Acetaminophen," and more.

The "Acetaminophen Safe Use College Resource Guide" and the "Acetaminophen Safe Use Program for Teen Influencers" offer customized content for educators, coaches, student leaders, school-based HCPs, and others, including education modules on label-reading in general and specific instructions on the safe use of acetaminophen. The interactive SCOUTStrong BeMedWise Award and patch program educates members of the Boy Scouts of America program, and American youth, about the benefits of OTC medicines and the harm that they can cause if they are misused.

Talk About Your Medicines Month, celebrated in October, is a well-recognized annual health observance month that has grown for more than three decades to stimulate conversations between patients and HCPs about all types of medicines they may take, with a focus on what to know about a medication in terms of expected health outcomes, possible side effects, benefits, and potential risks.

National Consumers League: Script Your Future

The National Consumers League (NCL) leads the medicine adherence education campaign Script Your Future. Script Your Future is a public education program designed to raise awareness among consumers, family caregivers, and HCPs about the importance of medication adherence and taking medicines as directed. Poor medicine adherencefrom delaying refills, to not following the dosing instructions on a medicine label-leads to morbidity, mortality, and avoidable healthcare costs. Script Your Future brings together stakeholders in healthcare, business, and government in six targeted cities. For HCPs, the campaign offers guidance on how to improve communication with patients. For patients, the campaign offers practical tools to improve medication adherence.

Get Relief Responsibly®

Individual drug manufacturers are also conducting educational campaigns. For example, Johnson & Johnson Consumer Inc., manufacturer of several OTC products containing acetaminophen, launched the Get Relief Responsibly® education initiative in 2011 to educate consumers about the appropriate use of OTC medicines and help them safely choose, use, store, and dispose of OTC medicines for themselves and their loved ones. Grounded in comprehensive consumer behavior research, Get Relief Responsibly® aims to increase awareness of OTC medicine safety and reduce OTC medication errors. The initiative also addresses the needs of specific audiences, such as older adults, whose OTC medicine choices may change over time; parents administering OTC medicines to infants and children; and adults who want to teach tweens and teens how to use OTC medicines safely.

Consumers can visit GetReliefResponsibly.com for online tools, videos, and quizzes including information on how to read a Drug Facts label, dosing charts, and resources to use with their doctor. There is also a platform for HCPs on GetReliefResponsiblyProfessional.com. This HCP website includes information on OTC analgesic interactions and considerations, dosing, peer-to-peer tools, and patient counseling resources.²³

U.S. Food and Drug Administration

The FDA has promoted appropriate use of acetaminophen to consumers and HCPs through a Use Acetaminophen Safely education campaign

that includes consumer safety updates, educational videos, and content within its Medicines in My Home campaign. Additionally, the agency's Safe Use Initiative focuses on reducing the preventable risk from acetaminophen overdose via public and private collaborations, including partnerships with the NCPDP, the Acetaminophen Awareness Coalition, and others.²⁴

Most recently, the FDA Safe Use Initiative funded a study conducted by Rocky Mountain Poison & Drug Safety, which was completed in 2018. The study used poison control center data to calculate the impact of flow restrictors on the number and severity of AUIs involving acetaminophen products in children less than 6 years of age. The rate of AUI for single ingredient acetaminophen products was significantly lower (325.6 exposures/million units sold) after flow restrictors were introduced compared to before (507.2 exposures/million units sold). An estimated 19,836 exposures and 115 clinically significant outcomes were prevented. This work established that flow restrictors, recommended in an August 2015 FDA Guidance (Over the Counter Pediatric Oral Liquid Drug Products Containing Acetaminophen), were effective.²⁵

Healthcare Professional Education

Numerous HCP organizations have hosted continuing professional education focused on acetaminophen and made resources available to members. For example, the American Pharmacists Association (APhA) has partnered with the American Academy of PAs (AAPA) to develop a continuing education program that prepares providers to engage and communicate with patients on the safe and effective use of acetaminophen. In addition, APhA has a full module, case studies, and faculty materials associated with acetaminophen toxicity on Pharmacotherapy First and chapters on OTC analgesics in their Pharmacy Library platform. The NCPDP has published white papers, and educational resources for HCPs have been made available by groups including the FDA, Alliance for Aging Research and its Silver Book series, and the Gerontological Society of America.

EDUCATION IS WORKING

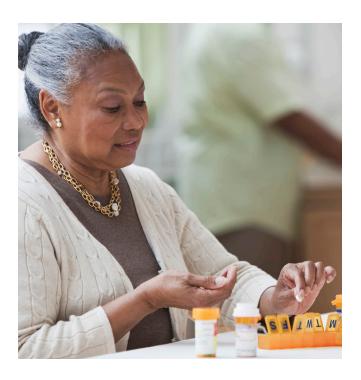
More consumers are aware that "exceeding the recommended dose can lead to liver damage."²⁶



IMPACT OF EFFORTS

Education campaigns are having an impact on consumer knowledge of acetaminophen safe use. When it comes to treating pain, current research indicates that more consumers report knowing how to safely use medicines with acetaminophen and avoid accidental overdose and liver damage. Nationwide surveys of U.S. adult pain medicine users show that safe use knowledge and risk awareness have increased over a nine-year period (2010-2019):²⁶

- Label reading: The number of consumers who agree that it is "important to check the label to find out the maximum daily dose" of medicines increased from 95 percent in 2010 to 97 percent in 2019.
- Following dosing instructions: The number of consumers who agree it is "important not to exceed the dosing directions on the label" of pain relievers increased from 92 percent in 2010 to 94 percent in 2019.
- Awareness of risk: The number of consumers who understand that "exceeding the recommended daily dose of acetaminophen may lead to liver damage" increased from 81 percent in 2010 to 88 percent in 2019.
- Avoidance of "doubling up:" Knowledge that "acetaminophen can be found in many OTC and Rx pain medicines" increased from 84 percent in 2010 to 87 percent in 2019, and understanding that "it is possible to exceed the maximum daily dose when taking an OTC acetaminophen product at the same time as an Rx pain medicine" increased from 79 percent in 2010 to 81 percent in 2019.



4) CONCLUSION

WORKING TOGETHER: HEALTHCARE PROFESSIONALS AND PATIENTS

As the healthcare landscape continues to evolve, more advances and innovations in medicines to meet the health needs of Americans will emerge. Ensuring patients and consumers use medicines safely will remain a top priority. This will require ongoing commitment and engagement from all sectors—HCPs, drug manufacturers, government agencies, pharmacies, and patients. There is a role for everyone to play to make sure patients and consumers use Rx and OTC medicines safely, read and follow the information on their medicine labels, and become familiar with the active ingredients in the medicines they take.

Product innovations and educational initiatives are effective tools to reduce unintentional acetaminophen overdose. Ongoing coordinated, comprehensive educational initiatives have successfully been put in place and created a "surround sound" of educational messages promoting safe use across multiple channels. Over the last decade, these efforts have had demonstrated impact on consumer knowledge and attitudes. In addition, packaging and product interventions have proven effective in reducing acetaminophen overdose in the pediatric population.

All consumers, regardless of which medicines they take to treat their health conditions, will be well-served by reminders and reinforcements that urge them to always read and follow the labels or product inserts that come with each medicine. For all sectors, it is crucial to adopt and share consistent and tested educational messages that are understandable, relevant, and actionable. We encourage more pharmacies, more HCPs, and more health-involved stakeholder groups to work together to disseminate safe medicine use education and resources. The Acetaminophen Awareness Coalition provides educational materials, including posters and brochures in English and Spanish, for display and distribution in waiting rooms, exam rooms, and pharmacy counters. These are available free of charge and can be ordered at KnowYourDose.org/order.

When taken as directed, acetaminophen is safe and effective and an important and trusted pain reliever and fever reducer option for many. Used for decades by millions of people, it is one of the most widely used medicines in the U.S, and for some with chronic conditions, is the most appropriate or only option for OTC pain relief. But when taken in excess, it can cause liver damage and even death. Although very rare, particularly in the context of acetaminophen's widespread use, liver injury from acetaminophen remains a public health concern. We have solid insights into the behaviors associated with exceeding labeled doses of acetaminophen, as well as evidence that education increases safe use knowledge and awareness of risks. This is key, as increased knowledge of medicine ingredients and dosing instructions decreases the risk of acetaminophen overdose. With this understanding, we must continue our collaboration and education efforts about the importance of using acetaminophen appropriately. When education is readily accessible, and patients and HCPs are communicating openly and clearly about acetaminophen safety, we can continue to increase consumer awareness and knowledge.

EDUCATIONAL RESOURCES

HOW TO READ YOUR MEDICINE LABEL

Knowing how to read the labels on prescription and over-the-counter medicines is an important step in making sure you use medicines appropriately. Always keep your medicine in the original packaging so that you have proper dosing information on hand.

PRESCRIPTION LABEL

Warnings

Warnings are specific to the medicine you are taking. Always read the warnings before taking your medicine.

 May cause drowsiness. Use care when operating a car or dangerous machines. Don't drink alcohol when taking this medicine.

This has acetaminophen. Don't take with other medicines that have acetaminophen (prescription or nonprescription). Too much can cause liver damage. Questions? Ask your doctor or pharmacist.

Taking more of this medicine than recommended may cause serious breathing problems.

Orig: 10/31/2011
 Date filled: 10/31/2011
 Discard after: 10/31/2012

This is a white, oval-shaped tablet with no imprint

CAUTION: FEDERAL LAW PROHIBITS THE TRANSFER OF THIS DRUG TO ANY PERSON OTHER THAN THE PATIENT FOR WHOM IT WAS PRESCRIBED.

Pharmacy Information

Your local pharmacy name, address and phone number and the name of the doctor who prescribed your medicine will be listed. Contact your pharmacist if you have any questions about your prescription.

Your prescription (Rx) number is unique to your medicine and helps the pharmacist ensure you go home with the correct prescription.

Local Pharmacy

1234 Winding Street Fort Washington, PA 12345

John Smith

3254 Maple Street Fort Washington, PA,12345

Brandname

hydrocodone/acetaminophen X mg / XXX mg

Take 1 tablet by mouth every 4-6 hours as needed for pain

Qty: 30 Refills: Ø

Pharmacy phone: (609) 555-5562

Rx # A123456

Prescriber: Dr. Johnson

Expiration

Date

Medicines expire. You should not take a medicine after the expiration date.

OVER-THE-COUNTER LABEL

Active Ingredient

This section indicates the ingredient or ingredients that make the medicine work. It is especially important to pay attention to this section if you are taking more than one medicine—whether OTC or prescription—to make sure you are not taking an excessive amount of the same active ingredient. Too much of an active ingredient can be harmful.

Uses

This section explains the symptoms or illnesses for which the product should be used. Only use products that treat the symptom(s) you have. If you need help choosing a product, ask your pharmacist or other healthcare professional.

Warnings

There are times you should not take a medicine. The warnings section explains these situations, and also tells you possible side effects, when a doctor or other healthcare professional needs to be consulted, and when to stop taking a product. If you have questions, ask a pharmacist or other healthcare provider.

Directions

This section tells you exactly how and when to take a medicine. Remember that these directions are not suggestions or recommendations. They should be followed exactly, except under a doctor's specific advice. Taking a higher dose of a medicine more often or for a longer period of time than the medicine label says can be dangerous.

Other Information

This section tells you other important information about your medicine, such as where to store it and at what temperature ranges. Most medicines should be kept away from heat and humidity to help them stay effective longer. Always keep medicines out of the reach and sight of children.

Inactive Ingredients

The inactive ingredients section includes important information about what is in your medicine in addition to the active drug ingredients. It is especially important if you or a loved one has a known allergy.

Questions?

Always talk to your healthcare professional if you have any questions. You can also call the toll-free number listed in this section.

Purpose

This section tells you what treatment type—or category—of medicine the product is in, such as a pain reliever or fever reducer.

Drug Facts

Active ingredient (in each caplet)

Purpose

Acetaminophen XXX mg .

.Pain relieve/fever reduce

Uses

- temporarily relieves minor aches and pains due to:
 - the common cold
- toothache
- headache
- muscular achespremenstrual and menstrual cramps
- backacheminor pain of arthritis
- temporarily reduces fever

Warnings

Liver Damage: This product contains acetaminophen. Severe liver damage may occor if you:

- take more than X caplets in 24 hours, which is the maximum daily amount
- take with other drugs containing acetaminophen
- drink 3 or more alcoholic drinks every day while using this product

Do not use:

- with any other drug containing acetaminophen (prescription or nonprescription). If you are not sure whether a drug contains acetaminophen ask a doctor or pharmacist
- if you are allergic to acetaminophen or any of the inactive ingredients in the product

Ask a doctor before use if you have: liver disease

Ask a doctor or pharmacist before use if you are: taking the blood thinning drug warfarin

Stop use and ask a doctor if:

- pain gets worse or lasts more than 10 days
- fever gets worse or lasts more than 3 days
 These could be signs of a serious condition.
- new symptoms occur
- redness or swelling is present

If pregnant or breast-feeding, ask a health professional before use.

Keep out of reach of children.

Overdose warning: Taking more than the recommended dose (overdose) may cause liver damage. In case of overdose, get medical help or contact a Poison Control Center right away (1-800-222-1222). Quick medical attention is critical for adults as well as for children, even if you do not notice any signs or symptoms.

Directions

do not take more than directed (see overdose warning)

adults and children 12 years and over	 take X caplets every X to X hours while symptoms last do not take more than X caplets in 24 hours do not use for more than 10 days unless directed by a doctor
children under 12 years	do not use this adult product in children under 12 years of age; this will provide more than the recommended dose (overdose) and may cause liver damage

Other information

- store between 20-25° C (68-77° F)
- do not use if carton is opened or neck wrap or foil inner seal imprinted with "Safety Seal[®]" is broken or missing
- see end panel for a lot number and expiration date

Inactive Ingredients

carrnauba wax*, castor oil*, corn starch, FD&C red #40 aluminum lake, hypromellose, magnesium stearate, polyethylene glycol*, powdered cellulose, pregelatinized starch, proylene glycol, shellac, sodium starch glycolate, titanium dioxide *contains one or more of these ingredients

Questions or comments?

call **1-877-XXX-XXXX**

KNOW YOUR DOSE ENGLISH CAMPAIGN POSTER



Acetaminoph is in more medicines than you might think

It's the most common drug ingredient in America, found in more than 600 different prescription and over-the-counter medicines, including pain relievers, fever reducers, and sleep aids as well as cough, cold, and allergy medicines. On prescription labels, acetaminophen is sometimes listed as "APAP," "acetam," or other shortened versions of the word. When used as directed, acetaminophen is safe and effective, but there is a limit to how much you can take in one day. Taking more than directed is never take two medicines that contain acetaminophen at the same time.

For more information, talk to your healthcare professional or visit KnowYourDose.org

KNOW YOUR DOSE SPANISH CAMPAIGN POSTER



El acetaminofén está en más medicinas de lo que usted cree

El acetaminofén (también llamado paracetamol) se encuentra en más de 600 medicinas diferentes, incluyendo las medicinas de venta libre y con receta para la fiebre, la tos, la gripe, las alergias y el insomnio, además de las medicinas para el dolor (analgésicos). Si se siguen las instrucciones de uso, el acetaminofén es seguro y eficaz. Pero hay un límite a la cantidad que se puede tomar en un día. Si se toma más acetaminofén de lo indicado, se produce una sobredosis que puede causar daño al hígado.

Siga estos tres pasos simples para usar acetaminofén de manera segura:

- ▶ Siempre lea la etiqueta de la medicina y siga las instrucciones.
- Averigüe si sus medicinas contienen acetaminofén.
- Nunca tome al mismo tiempo dos medicinas que contengan acetaminofén.

Para más información, hable con su proveedor de servicios de salud, visite KnowYourDose.org, o llame a Su Familia, la línea de ayuda en español al 1-866-783-2645





ACETAMINOPHEN DOSING FOR INFANTS AND CHILDREN

It is important to always read and follow the label each time you give medicine to your child. This guide will help you give your child the right amount of acetaminophen. If possible, use weight to dose your child; otherwise, use age.





Use formulations made for infants and children, not adult products.



Dose by weight when possible, according to the instructions on the medicine label. Otherwise, use age.



Put all medicine up and away and out of sight after every use to avoid accidentalingestion by curious children.

CHILD'S WEIGHT AND AGE INFANTS' ACETAMINOPHEN SUSPENSION LIQUID

160 MG/5 ML

CHILDREN'S
ACETAMINOPHEN
SUSPENSION
LIQUID

160 MG/5 ML

CHILDREN'S ACETAMINOPHEN TABLETS

80 MC

CHILDREN
AND JUNIOR'S
ACETAMINOPHEN
TABLETS

160 MG

UNDER 2 YEARS If your child is under 2 years of age, be sure to ask your healthcare provider for the right dose.



1 tablet

1-1/2 tablets

2 tablets

2-1/2 tablets

3 tablets

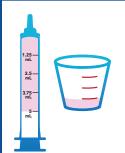
LIQUIDS: In 2011, manufacturers standardized the concentration of infants and children's single-ingredient liquid acetaminophen products. The current standard concentration on liquid products is 160 mg/5 ml.

CHEWABLES: In order to align with the liquid concentration, in 2017 the makers of Children's TYLENOL® began transitioning to a single strength of 160 mg chewables in the U.S. (now called "Children's TYLENOL®"). While 80 mg Children's TYLENOL® tablets tablets will no longer be sold, there are still some chewable products on shelves and in medicine cabinets at the 80 mg strength. All pediatric acetaminophen products currently on the market can continue to be used as labeled.

Ask your healthcare provider if you have any questions and always read and follow the label of the specific medicine you are using.

LA DOSIS DE ACETAMINOFÉN PARA SU BEBÉ O SU NIÑO

Cada vez que le de un medicamento a su bebe o a su niño, es importante que usted lea la etiqueta del medicamento y sigua las instrucciones. Esta guía le ayudará a administrar una dosis correcta de acetaminofén. Utilice el peso del niño para determinar la dosis. Si esto no es posible, utilice la edad del niño.



72 A 95 LIBRAS **11** AÑOS

Siempre use el medidor (una jeringa o vaso plástico) que viene con la medicina.



Use fórmulas para bebés y niños. No use los productos para adultos.



Determine la dosis según el peso, cuando sea posible, y sique las instrucciones de la etiqueta del medicamento. Si no, use la edad.



Ponga los medicamentos fuera del alcance y lejos de la vista después de cada uso. Los niños son curiosos. Evite que ingieran un medicamento accidentalmente.

TABLETAS DE

ACETAMINOFÉN PARA

NIÑOS

TABLETAS DE

ACETAMINOFÉN

PARA NIÑOS Y

JÓVENES

y media

v media

JARABE CON **JARABE CON PESO Y ACETAMINOFÉN ACETAMINOFÉN EDAD DEL PARA BEBÉS PARA NIÑOS** NIÑO 0 A 23 MESES If your child is under 2 years of age, be sure to ask your healthcare provider for the right dose. **24 A 35** LIBRAS 2. 25 25 26 2 A 3 AÑOS 5mL (1tsp) **36 A 47** LIBRAS 4 A 5 AÑOS **48 A 59** LIBRAS 6 A 8 AÑOS Consulte con su proveedor de servicios de salud **60 A 71** LIBRAS **9 A 10** AÑOS



JARABES: En el 2011, los fabricantes estandarizaron la concentración en los productos líquidos de un solo ingrediente con acetaminofén para los bebes y niños. La concentración estandarizada actual en estos productos líquidos es de 160 mg/5 mL.

TABLETAS MASTICABLES: Para concordar con la concentración en líquidos, en el 2017, los fabricantes de Children's TYLENOL® comenzaron la transición a una dosis de 160 mg en los productos masticables en EE. UU. (estos productos ahora se conocen como "Children's TYLENOL®"). Mientras que las tabletas Children's TYLENOL® de 80 mg ya no se venderán, quedan algunos productos masticables de 80 mg en estantes y botiquines. Todos los productos pediátricos de acetaminofén actualmente en el mercado pueden seguir siendo utilizados según su etiqueta.

Si tiene alguna pregunta, consulte con su proveedor de servicios de salud y siempre lea y siga las instrucciones de la etiqueta del medicamento que esté utilizando.

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The Acetaminophen Awareness Coalition is a diverse group of organizations representing healthcare professionals and consumers whose members are committed to ensuring that acetaminophen is used only as labeled or directed. Coalition members include the Alliance for Aging Research, American Association of Nurse Practitioners, American Pharmacists Association, BeMedWise Program at NeedyMeds, Caregiver Action Network, CHPA Educational Foundation, National Association of Boards of Pharmacy, National Association of Chain Drug Stores Foundation, National Community Pharmacists Association, and National Consumers League.

The Coalition's Know Your Dose campaign is advised by the FDA's Safe Use Initiative, the Center for Disease Control and Prevention, and the American Academy of Pediatrics.





















KnowYourDose.org Acetaminophen Awareness Coalition