Louisiana Medicaid

Provider Update

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Update on the National Provider Identifier

Louisiana Medicaid implemented the provisions of The Health Insurance Portability and Accountability Act (HIPAA) in 2003-2004. The implementation of a 10-digit National Provider Identification (NPI) number, a part of HIPAA, was delayed nationally until 2007.

NPI implementation has been mandated by law for May 23, 2007 for large health plans. Providers must obtain NPIs and begin using them for claims submission on and after May 23, 2007. Providers who do not provide medical services are exempt from this requirement (i.e. non-emergency transportation, case management, and some waiver services). Although HIPAA regulations address only electronic transactions, Louisiana Medicaid will require both the NPI number and the legacy 7-digit Medicaid provider number on **hard copy claims**.

Louisiana Medicaid has published Remittance Advice (RA) messages and used mail stuffers, web notices, and other means to notify providers of the mandate to use NPI numbers by May 23, 2007. Thus far, very few Louisiana Medicaid providers have registered their NPIs with our fiscal intermediary. Simply applying for and obtaining an NPI(s) is not the end of the process. It is the provider's responsibility to report and register all NPIs with any entity to which they submit claims. This function is not automatically done by the enumerator on behalf of the provider.

In an effort to make this reporting process as simple as possible, Louisiana Medicaid and Unisys developed a web application for provider registration of NPI(s). This application is housed on the secured side of the LA Medicaid web site, www.lamedicaid.com.

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Over the next few weeks, Unisys will "step-up" these outreach efforts to ensure that we have received NPI data from all Medicaid providers. Please understand that failure to obtain and register your NPI will cause claim denials after the mandated implementation date.

Please view the web site referenced above for information concerning the NPI and registering your NPI. Also, please watch your RA messages/stuffers, provider newsletters, association communications, and mail for additional outreach information.

Questions related to the Louisiana Medicaid implementation of NPI may be directed to our NPI Assistance line at 225-216-6400 or e-mail us at LAMedicaidNPI@Unisys.com.

All CMS 1500 (08-05) Claims Filers

Update on the CMS 1500 Claim Form

The Form CMS-1500 (08-05) will be accepted by Louisiana Medicaid for all dates of submission beginning March 5, 2007 but will not be mandated for use until June 4, 2007. This includes all rebilling of claims even though earlier submissions may have been on the Form CMS-1500 (12-90).

Health plans, clearinghouses, and other information support vendors must be able to handle and accept the Form CMS-1500 (08-05) by June 4, 2007.

Important Reminders for Completion of the Revised CMS 1500 Claim Form

As we transition to the new, revised CMS 1500 claim form, we have identified some areas of concern through the initial handling of the new forms. The following guidelines should be followed to ensure that claims are not rejected and are processed correctly.

- Claim forms are being submitted WITHOUT having software vendors adjust printer programs to allow information to be properly aligned and displayed on the new forms. Information **must appear within the appropriate boxes and be aligned in your printer** to ensure the correct horizontal and vertical placement of data elements.

- Some data elements have been relocated on the new form. It is imperative that your software vendor relocate this information to the new and appropriate field on the claim form.

- The 7-digit Medicaid provider number should NEVER be entered in the NPI number field(s). These provider numbers are not interchangeable.

All CMS 1500 (08-05) Claims Filers

- The **7-digit Medicaid number** for the attending provider should be entered in Field 24J **in the shaded portion of the field**. The **NPI number** for the attending provider should be entered in Field 24J **in the non-shaded portion of the field. Proper printer alignment is essential for this field.**

- The **7-digit Medicaid number** for the billing provider should be entered in **Field 33B**. The **NPI number**for the billing provider should be entered in **Field 33A**. **Proper printer alignment is essential for this field.**

- The NPI number IS NOT alpha-numeric; it must be a 10-digit number. Please enter your correct NPI in the appropriate field on the claim form.* For more information regarding the NPI, please refer to http://www.lamedicaid.com/provweb1/hipaa/npi.htm.

- The type of service (TOS) previously reported in field 24C has been deleted from the revised form and replaced with the Emergency Indicator (previously reported in field 24I). When appropriate, the CommunityCARE Emergency Indicator must now be entered in the field 24C. Please have your vendor make this software adjustment.

Please ensure that these guidelines are followed as you transition to the CMS 1500 revised claim form. The transition period is March 5, 2007 through June 3, 2007. Effective June 4, 2007, only the revised claim form will be accepted for processing regardless of the date of service on the bill. EFFECTIVE July 2, 2007, Unisys will no longer accept copies of any standard claims forms including the CMS 1500, both versions. All claims must be filed on an original, two-sided document. This includes original submissions, re-submissions of previous claims, and claim adjustments/voids. Copies will be returned to the provider.

WITH THE EXCEPTION OF SITUATIONS WHERE POLICY REQUIRES HARD COPY CLAIMS, ELECTRONIC CLAIMS SUBMISSION IS THE PREFERRED METHOD FOR TRANSMITTING MEDICAID CLAIMS TO UNISYS. IF YOU DO NOT CURRENTLY SUBMIT CLAIMS ELECTRONICALLY AND WOULD LIKE TO DISCUSS THIS OPTION, PLEASE CONTACT THE UNISYS EDI UNIT AT 225/216-6000, OPTION #2.

*NPI numbers are mandatory effective May 23, 2007. It is vital that providers obtain and register their NPI with Louisiana Medicaid. For assistance, please visit http://www.lamedicaid.com/provweb1/hipaa/npi.htm

Use of the UB-04 Claim Form Delayed

The National Uniform Billing Committee (NUBC) has given its stamp of approval to the new UB-04 Claim Form for hard copy billing, and it will be federally mandated effective May 23, 2007. The LA Medicaid claims processing system is currently being modified to accommodate the changes required for this new form. Providers will be notified when to begin submitting the new claim form to Unisys processing.

Please **DO NOT** submit new UB-04 claim forms to Unisys until you are notified of the effective date to do so. Continue to submit UB-92 forms at this time. Any new forms received by Unisys prior to the acceptance date will be rejected and returned to providers, which will cause a delay in processing your claims.

Once LA Medicaid mandates the use of the new form, all claims regardless of date of service must be submitted on that form. The UB-92 paper claim will no longer be accepted, even as an adjustment claim or for billing/re-billing older dates of service.

The new form accommodates the reporting of the National Provider Identifier (NPI) as well as several other changes. Providers must continue to use their 7-digit Medicaid Provider IDs. Once NPIs are mandated, providers will be required to enter NPIs also.

Complete instructions for completing the new UB-04 form for each provider type will be made available later on www.lamedicaid.com.

If applicable, it is very important that you communicate with your software vendor to ensure that any systems producing hard copy forms are updated for use of the new claim form and to capture data in the appropriate Form Locators as data is being relocated on the new form.

Please continue to read the RA messages, RA stuffers, *Provider Updates*, and the LA Medicaid web site for information concerning the system transition and the effective date of implementation for the UB-04 claim form.

HHS Launches New Online Toolkit for Medical Responses to Radiation Emergencies

This article is a press release from the U.S. Department of Health and Human Services.

The Department of Health and Human Services (HHS) Secretary Mike Leavitt has announced that HHS has developed a new downloadable online diagnostic and treatment toolkit designed for health care providers, primarily physicians, who may have to provide medical care during a radiation incident.

The new information package includes easy-to-follow procedures for diagnosis and management of radiation contamination and exposure, guidance for the use of radiation medical countermeasures, and a variety of other features to facilitate medical responses. All of this is now available on the Radiation Event Medical Management (REMM) Web site (http://REMM.NLM.GOV).

"The REMM toolkit is part of our effort to improve public health emergency preparedness and response," Secretary Leavitt said." It reflects the Department's commitment to help instill a spirit of preparedness throughout our nation."

Guidance on diagnosis and treatment will help health care providers by describing: types of radiation emergencies they may face, initial medical actions at the incident site and/or medical facility, and key steps in patient care.

Critical information is presented in a format that will quickly and efficiently orient and guide health care providers during a mass casualty radiation event. In addition to online access, federal, state and local medical response teams will be able to download REMM information on laptop computers for quick access when they are deployed to a radiation incident or for training sessions. Users can also register for automatic e-mail updates whenever information is changed or added to the REMM Web site.

Future plans include formatting the REMM material for use on Personal Digital Assistant (PDA) devices, additional multimedia graphics, and more topic areas, such as follow-up patient care of radiation's chronic effects.

A team of subject matter experts from the HHS Office of the Assistant Secretary for Preparedness and Response, the National Institutes of Health's National Cancer Institute and National Library of Medicine and the Centers for Disease Control and Prevention collaborated on the development and design of the REMM tool.

Reporting Recipient Fraud or Abuse

The unauthorized use of a Louisiana Medicaid Card constitutes recipient fraud. The misrepresentations of facts in order to become or to remain eligible to receive benefits are grounds for recipient fraud referral. In cases of fraud or abuse, providers should contact the Medicaid Fraud Hotline at **1-800-488-2917**.

Implanon Implant Policy

Effective for dates of service on or after August 9, 2006, the following reimbursement policy applies to the insertion and removal of the Implanon (etonogestrel) implant:

Clinically trained providers obtain the contraceptive implant (one per recipient per 3 years) from a specialty pharmacy authorized by the manufacturer. The physician will not be reimbursed by Medicaid for the implant itself. The implant will be reimbursed as a pharmacy benefit.

Provider claims for the insertion, removal, or removal with reinsertion of the implant are to be submitted using the appropriate CPT procedure codes (11981-11983) and ICD -9 diagnosis codes (V25.5, V25.43, or V45.52. If nationally approved changes occur to diagnoses or CPT codes that relate to this implant at a future date, providers are to use the most accurate coding available for the particular date of service. [Other procedural and diagnosis codes may also be appropriate on this date of service, and providers are to use the codes that most accurately describe the service(s) provided.]

Claims submitted for this contraceptive implant and its insertion in excess of the manufacturer's recommended guidelines are subject to review and action by the Department.

Documentation in the physician's recipient record is to include evidence of recipient education regarding this long-acting contraceptive.

CommunityCARE Immunization Pay for Performance Initiative

Effective February 9, 2007, CommunityCARE PCPs interested in the Immunization Pay-for-Performance (P4P) initiative can begin registering to participate by using the Louisiana Medicaid website at www.lamedicaid.com. Registration for P4P can be completed only through this website. Providers are to login using the established login procedures for "Provider Login". Once logged in, follow the instructions in the Immunization Pay-for-Performance (P4P) link. To qualify for participation in P4P retroactive to July 1, 2006, CommunityCARE PCPs had until March 11, 2007, to complete the P4P registration process. PCPs that register after March 11, 2007, will not be eligible for retroactive participation but will be eligible to participate in P4P starting with the month that their registration is completed (except PCPs with registrations from March 12 to March 31, 2007, who were eligible for participation in P4P starting April 1, 2007). Details, including contact information, can be found at the P4P link mentioned above.

Supports Waiver Providers

This is to advise that the Department of Health and Hospitals, Office for Citizens with Developmental Disabilities Waiver Supports and Services Unit issued a new form for the Supports Waiver Program effective March 27, 2007. The Job Assessment, Job Discovery, and Job Development Completion Form is to be used for all requests for Job Assessment, Job Discovery, and Job Development. The form is available via the website www.lamedicaid.com under the "new Medicaid information" link. Providers are encouraged to visit the OCDD website at http://www.ocdd.dhh.louisiana.gov (click on OCDD waiver unit link) for more information.

Copies of Standard Claim Forms Will No Longer be Accepted

In accordance with a recent DHH directive, Unisys will no longer accept copies of standard claim forms, effective July 2, 2007. The regulations do not allow the copying of hardcopy claim forms. This includes the UB-92, UB-04, CMS 1500 (12-90), CMS 1500 (08-05), and ADA claims forms as well as the NCPDP Universal Claim Form. Any hard copy claims submitted to Unisys for processing must be an original, standard claim form and must meet the licensure/copyright requirements of the particular organization that regulates that claim form. This includes original submissions, re-submissions of previous claims, and claim adjustments/voids.

With the implementation of this requirement, providers who are routinely billing all claims hard copy may want to consider transitioning to electronic claims submission. Questions concerning EDI billing may be directed to the Unisys EDI Department at 225/216-6000, Option 2. A complete listing of approved EDI vendors is available on the LA Medicaid web site, www.lamedicaid.com, link HIPAA Information Center/link VBC List. Please contact the vendors for specific information on their services as a wide range of packages/fees are available.

Acetaminophen Overuse

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Issues

- ...acetaminophen (commonly known as Tylenol®) has become the most widely used antipyretic and analgesic because of its efficacy and relative safety

- Although it is relatively safe when used at therapeutic doses, intentional and unintentional overdoses of acetaminophen have been recognized to cause fatal and nonfatal hepatic necrosis which can lead to acute liver failure.

Introduction

Since its introduction in 1950, acetaminophen (commonly known as Tylenol®) has become the most widely used antipyretic and analgesic because of its efficacy and relative safety. It is readily available in hundreds of over-the-counter and prescription medications. Although it is relatively safe when used at therapeutic doses, intentional and unintentional overdoses of acetaminophen have been recognized to cause fatal and nonfatal hepatic necrosis which can lead to acute liver failure. [1, 2, 3]

In 2005, 138,602 acetaminophen exposures were reported by the American Association of Poison Control Centers Toxic Exposure Surveillance System. Approximately one-half (49%) of these exposures were from acetaminophen alone, and one-half (51%) were from acetaminophen in combination with other drugs. Forty-six percent (46%) of the exposures were intentional. Thirty-one percent (31%) of the exposures occurred among children younger than six years, and twenty percent (20%) among children between 6 and 19 years of age. Additionally, 187 deaths were reported where acetaminophen was believed to be the primary responsible agent. Of these fatalities, 48 were associated with acetaminophen as a single agent, 47 with acetaminophen plus one or two other products, and 92 with acetaminophen in a combination product, usually containing an opioid. [4]

Pharmacokinetics

Acetaminophen is available over-the-counter in both immediate and sustained-release formulations. Acetaminophen, in varying strengths, is contained in over-the-counter cough, flu and cold, allergy and sinus, and sleep preparations. [1] Depending on the formulation, the liquid preparations may range in concentration from 32 mg/mL to 65 mg/mL (syrups, elixirs) to 100 mg/mL (infant drops), and the strength may range from 80 mg to 650 mg for pills, capsules, or suppositories. [5]

Immediate release acetaminophen is rapidly and completely absorbed from the gastrointestinal tract, with peak plasma concentrations being reached from 70 to 160 minutes following ingestion of a therapeutic dose. However, following ingestion of extended-release preparations or with co-ingestion of other drugs or high carbohydrate foods which delay gastric emptying, peak serum concentrations may be delayed beyond four hours. The various suppository preparations have different absorption characteristics, and reach peak concentration at variable times. [1]

Following oral doses, acetaminophen is metabolized extensively in the liver via three main pathways: glucuronidation, sulphation, and oxidation. At therapeutic doses, 90% of acetaminophen is metabolized in the liver to sulfate and glucuronide conjugates that are then excreted in the urine or bile. One-half of the remaining acetaminophen, or 5%, is oxidized via the hepatic cytochrome P450 mixed function pathway to N-acetyl-p-benzoquinoeimine (NAPQI), which is a toxic metabolite. With normal doses, the small amount of NAPQI formed after ingestion is promptly detoxified by conjugation to hepatic glutathione, forming nontoxic compounds that are excreted in the urine. However, when toxic doses are ingested, the sulfate and glucuronide pathways become saturated resulting in an increased fraction of acetaminophen being metabolized by cytochrome P450 enzymes. As large amounts of NAPQI are formed, glutathione stores in the body are depleted. When approximately 70% of glutathione stores are depleted, unconjugated NAPQI begins to accumulate and hepatic injury ensues. [1, 2, 6]

Evaluation of Suspected Acetaminophen Toxicity

Prompt recognition of toxicity is essential to preventing morbidity and mortality associated with overuse of acetaminophen. [7] Therefore, a careful assessment and a detailed medical history of the patient are important when evaluating the potential for toxicity of an ingestion of acetaminophen. Important components include, but are not limited to, the age of the patient, concomitant medications or substances that may have been ingested, and risk factors that could increase the potential for toxicity, such as chronic alcohol abuse or malnutrition. The clinician should also consider contacting the local poison control center for reporting the toxicity and also to obtain any information that may assist in the proper treatment of the patient. Evidence suggests that children under the age of 6 years are less susceptible to the same amount of acetaminophen per unit of body weight than would be associated with severe toxicity in older patients. [8] An acute ingestion is often discovered quickly in younger patients, whereas older patients that may be attempting self-harm are more likely to conceal such an attempt.

The amount ingested, as well as the pattern and duration in which the medication was taken, must be determined as quickly and accurately as possible in order to correctly interpret laboratory values and administer appropriate therapy. The range of toxicity largely depends on how the medication was taken in terms of whether the ingestion was acute or chronic.

Acute Ingestion of Acetaminophen

Acute toxicity of acetaminophen is generally regarded as a single ingestion over less than a 4 hour time period. [7] The risk of toxicity is best predicted by relating the time of ingestion to the serum acetaminophen concentration. Current guidelines recommend emergency room referral for an acute, single ingestion of acetaminophen under the following circumstances: [9, 10]

- The patient has symptoms of apparent acetaminophen toxicity such as protracted vomiting, upper right quadrant pain or mental status changes.
- The patient is less than 6 years old and has ingested 200 mg/kg or more.
- The patient is 6 years old or more and has ingested at least 10 g or 200 mg/kg (whichever is lower).
- The patient has ingested an unknown amount of acetaminophen.
- All patients should be referred to the emergency department for ingestions involving unknown intent, suspected or stated self-harm or possible malicious administration.

Table 1 [5]

Acetaminophen Dosing for Children

Age of Child	Weight of Child	Dosage Recommendation	Acetaminophen Drops (80mg/tsp)	Acetaminophen 160 mg/tsp	Chewable Tablets (80 mg)	Adult Tablets
≤ 3 months	6 – 11 lbs	40 mg	½ dropperful (0.4 mL)	----------	----------	----------
4 – 11 months	12 – 17 lbs	80 mg	1 dropperful (0.8 mL)	½ tsp (2.5 mL)	1 tablet	----------
12 – 23 months	18 – 23 lbs	120 mg	1 ½ dropperful (1.2 mL)	¾ tsp (3.75 mL)	1 ½ tablets	----------
2 – 3 years	24 – 35 lbs	160 mg	2 droppersful (1.6 mL)	1 tsp (5 mL)	2 tablets	----------
4 – 5 years	36 – 47 lbs	240 mg	3 droppersful (2.4 mL)	1 ½ tsp (7.5 mL)	3 tablets	----------
6 – 8 years	48 – 59 lbs	320 mg	----------	2 tsp (10 mL)	4 tablets	1 adult tablet
9 – 10 years	60 – 71 lbs	400 mg	----------	2 ½ tsp (12.5 mL)	5 tablets	1 ½ adult tablets
11 – 12 years	72 – 95 lbs	480 mg	----------	3 tsp (15 mL)	6 tablets	1 ½ adult tablets

Repeated Supratherapeutic Ingestion of Acetaminophen

Repeated supratherapeutic ingestions of acetaminophen (RSTI), frequently referred to as subacute or chronic, take place over a period longer than 4 hours. [8] Most commonly they are unintentional and could occur from (a) self-medication for pain or fever in doses exceeding professional medical recommendations or the package recommendation of 4 grams/day, (b) dose calculation and administration errors, and (c) use of multiple products that contain acetaminophen, any of which can lead to liver injury. [3, 11] Prevention of inappropriate dosing of acetaminophen includes education of patients, parents, and caregivers of the appropriate dosing for children (Table 1) and awareness of other products that contain acetaminophen (Table 2).

Table 2

Over-the-Counter and Prescription Drugs That Contain Acetaminophen*	
Anacin®-3	Lortab® 5/500
Anacin®-3 Extra Strength	Lortab® 7.5/500
Aspirin Free Anacin®	Lortab® 10/500
Aspirin-Free Excedrin® Caplets	Midol® Menstrual Formula Maximum Strength Caplets
Bayer® Select Maximum Strength Headache pain Relief Formula	Midol® Menstrual Formula Maximum Strength Gelcaps
Benadryl® Severe Allergy and Sinus Headache Maximum Strength Caplets	Midol® PMS Maximum Strength Caplets
Darvocet-N® 50	Norco® 5/325
Darvocet-N® 100	Norco® 7.5/325
Excedrin P.M. ® Caplets	Norco® 10/325
Excedrin P.M. ® Geltabs	Oxycet®
Excedrin P.M. ® Tablets	Percocet® 2.5/325
Excedrin® Caplets	Percocet® 5/325
Excedrin® Extra Strength Caplets	Percocet® 7.5/325
Excedrin® Extra Strength Tablets	Percocet® 7.5/500
Feverall® Junior Strength	Percocet® 10/325
Feverall® Sprinkle Caps Junior Strength	Percocet® 10/500
Feverall® Sprinkle Caps, Children's	Roxicet® Elixir
Feverall®, Children's	Roxicet® 5/325
Feverall®, Infant's	Roxicet® 5/500
Goody's® Fast Pain Relief Tablets	Sinutab® Sinus Medication Maximum Strength Without Drowsiness Tablets
Goody's® Headache Powders	Sudafed® Sinus and Headache Caplets
Goody's® Extra Strength Tablets	Sudafed® Sinus & Headache Maximum Strength Tablets
Lorcet® 10/650	Talacen®
Lorcet Plus®	Tylox®
Lorcet-HD®	Vicodin®
Lortab® Elixir	Wygesic®
Lortab® 2.5/500	

* The foregoing list should not be construed to be all inclusive.

Current guidelines recommend emergency room referral under the following circumstances surrounding RSTI of acetaminophen:

- Patients under 6 years of age:
    - 200 mg/kg or more over a single 24-hour period, or
    - 150 mg/kg or more per 24-hour period for the preceding 48 hours, or
    - 100 mg/kg or more per 24-hour period for the preceding 72 hours or longer
- Patients 6 years of age or older:
    - 10 g or 200 mg/kg (whichever is lower) over a single 24-hour period
    - 6 g or 150 mg/kg (whichever is lower) per 24-hour period for the preceding 48 hours or longer
- For patients with conditions that may increase susceptibility to acetaminophen toxicity (i.e. alcoholism, malnutrition, isoniazid use)

Chronic or repeated-supratherapeutic ingestions of acetaminophen are often insidious, and, therefore, present the potential for misdiagnosis. Serum acetaminophen levels are essential for evaluating toxicity for acute exposures, but are not an accurate monitoring parameter for supratherapeutic exposures or for acute ingestions that present late for treatment. The ability to interpret the trends in hepatic enzymes becomes essential in such cases. [12]

Treatment

Interpretation of Laboratory Values

Following a recent acute single ingestion, the decision to treat potential hepatotoxicity with the antidote, acetylcysteine, is determined by interpretation of the serum acetaminophen level as plotted on the Rumack-Matthew nomogram. [13] An acetaminophen level obtained less than 4 hours post an acute ingestion is generally not considered accurate, because the medication is still in absorption and distribution phases. Moreover, a serum level obtained greater than 24 hours after the ingestion cannot be accurately interpreted and is often misinterpreted as being subtoxic or even therapeutic. The most reliable levels are obtained 4-12 hours after an acute ingestion. It is also important to note that the nomogram is not useful for accurately evaluating toxicity in patients with chronic or repeated acetaminophen ingestions. [12, 14]

A reliable monitoring parameter for late or chronic acetaminophen toxicity involves following the trend of the hepatic enzymes, aspartate aminotransferase (AST) and alanine aminotransferase (ALT), to monitor the degree of hepatic injury, as well as the PT and INR. Aminotransferase levels may begin to increase as early as 8 hours, but typically become elevated within 24-36 hours after a toxic acute ingestion of acetaminophen. Unlike a large acute ingestion, patients that ingest smaller multiple doses over a period of hours or days are likely to present with elevated aminotransferase levels. [12]

Decontamination

Though generally not helpful for chronic ingestions, effective gastrointestinal decontamination may obviate the need for further treatment and extended hospital admission for the patient that is discovered soon after an acute ingestion of acetaminophen. [15] Acetaminophen usually absorbs very quickly, therefore lavage is typically not very effective in preventing systemic absorption. Furthermore, the time it takes to perform lavage delays the administration of activated charcoal. Activated charcoal effectively adsorbs acetaminophen and can be administered to rapidly prevent systemic absorption of the drug. The use of activated charcoal alone has been shown to be as effective as the combination of lavage and charcoal; however, the activated charcoal is significantly less effective when given 2 hours post ingestion of acetaminophen versus 1 hour post. [16] This emphasizes the importance of early intervention with gastrointestinal decontamination. However, some published data provides evidence that suggests some efficacy of administering activated charcoal more than four hours after an acetaminophen overdose, and thus could offer benefit for late-presenting acute or supratherapeutic cases. [17]

Antidotal Therapy

The agent of choice for the treatment of acetaminophen overdose is N-acetylcysteine. As a substitute for glutathione, N-acetylcysteine binds directly to the toxic metabolite, NAPQI. Clear evidence states that treatment with acetylcysteine administered within 8 hours of ingestion is superior to treatment started beyond 8 hours. However, published data indicates that acetylcysteine may offer benefit if initiated between 15 - 24 hours after the time of ingestion. [18, 19]
Currently, both the oral and intravenous routes are FDA approved. The most common protocol used in the U.S. for prevention of acetaminophen-induced hepatotoxicity is the 72-hour oral N-acetylcysteine protocol. The 21-hour intravenous N-acetylcysteine protocol is currently used in the U. S. as well. [9]

Oral N-acetylcysteine

An extemporaneous solution using inhaled N-acetylcysteine is prepared and administered orally according to a 72-hour protocol as follows:

Loading Dose:	Give a single dose 140 mg/kg as a five percent (5%) solution in water, juice or soda.
Maintenance Doses:	4 hours after the loading dose, give doses of 70 mg/kg as a five percent (5%) solution in water, juice or soda every 4 hours, for 17 doses. [9]

Emesis during the administration of the oral regimen often develops due to the unpleasant taste and odor of the antidote. General recommendations to address this issue include administering each dose via nasogastric tube and antiemetic prophylaxis with metoclopramide or ondansetron. [20, 21] Emesis that persists in spite of these efforts should prompt the clinician to consider the intravenous option.

Intravenous N-acetylcysteine

Though the practice is not FDA approved, intravenous use of the inhaled N-acetylcysteine has been administered due to a lack of an approved intravenous formulation. An FDA approved intravenous formulation of N-acetylcysteine is currently available under the trade name of Acetadote®. Though rare, anaphylactic reactions have occurred following the administration of intravenous N-acetylcysteine.

The 21-hour I.V. N-acetylcysteine Protocol for adult administration using the FDA approved intravenous formulation is as follows:

Loading Dose:	150 mg/kg in 200 mL 5% Dextrose infused intravenously over 60 minutes
Second Dose:	50 mg/kg in 500 mL 5% Dextrose infused intravenously over 4 hours
Third Dose:	100 mg/kg in 1000 mL 5% Dextrose infused intravenously over 16 hours

Though the calculations for dosing are the same as the above protocol, parenteral volumes must be appropriately adjusted for pediatric administration to prevent complication associated with hyponatremia. (See manufacturer recommendations). [19]

Special Consideration for Acute Ingestions

- A serum acetaminophen level should be drawn 4 hours after ingestion or as soon as possible. If the level plotted on the Rumack-Matthew nomogram crosses above the "treatment" line the patient is at risk for hepatotoxicity and should receive the full course of the antidote, N-acetylcysteine therapy as indicated.
- If a patient arrives 8 hours or more post ingestion, the N-acetylcysteine should be started until the serum level results indicate whether or not it should be continued.
- Patients that present 24 hours or more after ingestion should receive N-acetylcysteine if they have a measurable acetaminophen level or other evidence of hepatotoxicity.
- Patients who develop hepatotoxicity should receive N-acetylcysteine until hepatotoxicity improves. [9]

Special Considerations for Repeated-Supratherapeutic Ingestions

- Patients are at an increased risk of hepatotoxicity with chronic acetaminophen ingestions. N-acetylcysteine should be administered for any evidence of hepatotoxicity or for an acetaminophen level of greater than 10 mcg/mL upon presentation.
- The Rumack-Matthew nomogram cannot be used for chronic ingestions.
- N-acetylcysteine should be administered until hepatic enzymes are near normal and the acetaminophen level is undetectable; many clinicians recommend N-acetylcysteine for at least 24 - 36 hours from the last time of ingestion. Discontinue if hepatic enzymes remain normal and the acetaminophen level is undetectable.

Prognosis

If a patient is at risk for developing acetaminophen toxicity and begins N-acetylcysteine prior to the onset of symptoms, then the patient has an excellent chance of survival. Of course, this is dependent upon early detection of the risk with a serum acetaminophen level accurately plotted on the nomogram indicating antidotal therapy is necessary. An incidence and outcome study that observed the frequency of acetaminophen overdose-related emergency department cases determined that a group of patients whose risk could not be estimated using the Rumack-Matthew nomogram had the poorest outcome. These atypical presenters represented 44% of the hospitalized patients and 83% of those who suffered hepatic injury. [22] Those patients with greatest chance of dying without a liver transplant present with a pH < 7.3, or with a combination of creatinine > 3.3mg/dL, PT > 100 seconds, and grade III or IV encephalopathy. Patients that meet these criteria are identified to be placed on the "super-urgent" transplant list. [23, 24] Patients with repeated-supratherapeutic ingestions or late presenters of acute overdose are at the greatest risk of hepatic injury and death. Early recognition using prognostic markers and patient education may help prevent many of these serious cases.

Conclusion

Acetaminophen had proven to be a safe and effective antipyretic/analgesic when used as recommended. However, because of the multitude of preparations, it is necessary that health care providers and patients be familiar with appropriate acetaminophen dosing. The Food and Drug Administration is currently proposing to make the warnings on over-the-counter analgesics clearer and stricter. The proposed regulations would require manufacturers to display on product packaging the safety information in a consistent manner. For example, acetaminophen packaging would contain the warning about liver damage, and product labels would have generic as well as the brand name of the product visible. Education to patients regarding the indication for their medication, appropriate use, and what is in the preparation they are taking is essential to minimize harm to patients.

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Provider Relations	**1-800-473-2783**
	(225) 924-5040
REVS Line	**1-800-776-6323**
	(225) 216-REVS(7387)
Point of Sale Help Desk	**1-800-648-0790**
	(225) 216-6381