FULL PRESCRIBING INFORMATION

TYLENOL® Regular Strength (DIN 00559393)
Acetaminophen Tablets USP 325 mg

TYLENOL® Regular Strength Caplets (DIN 00723894)
Acetaminophen Tablets USP 325 mg

TYLENOL® Extra Strength (DIN 00559407)
Acetaminophen Tablets USP 500 mg

TYLENOL® Extra Strength Caplets (DIN 00723908)
Acetaminophen Tablets USP 500 mg

TYLENOL® Liquid Gels (DIN 02407612)
Acetaminophen Capsule 325 mg

TYLENOL® Rapid Release (DIN 00863270)
Acetaminophen Tablets USP 500 mg

Extra Strength TYLENOL® Easy Dissolve (DIN 02549417)
Acetaminophen Powder 500 mg (Berry)

TYLENOL® Arthritis Pain 8 (DIN 02238885)
Acetaminophen Tablets (Extended Release) 650 mg

TYLENOL® Muscle & Body (DIN 02246060)
Acetaminophen Tablets (Extended Release) 650 mg

Children's TYLENOL® Chewables (02241361)
Acetaminophen Tablets USP 160 mg
(Bubblegum and Grape)

Children's TYLENOL® Fastmelts (DIN 02347792)
Acetaminophen Tablets USP 160 mg (Grape)

Children's TYLENOL® (DIN 02046040)
Acetaminophen Suspension USP 160 mg/5 mL
(Banana Berry, Bubblegum, Grape, Dye-Free Cherry and Dye-Free Berry)

Infants' TYLENOL® (DIN 02046059)
Acetaminophen Suspension USP 80 mg / 1 mL
(Cherry and Dye-Free Grape)

Children's TYLENOL® Easy Dissolve (DIN02517280)
Acetaminophen Powder 160 mg (Wild Berry)

Analgesic / Antipyretic

McNeil Consumer Healthcare
division of Johnson & Johnson Inc.
88 McNabb Street
Markham, Ontario
L3R 5L2

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July 03, 2024

Control # 275388

TYLENOL®

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Acetaminophen
Analgesic – Antipyretic

HEALTH PROFESSIONAL INFORMATION

SUMMARY PRODUCT INFORMATION

Table 1: Product Information

Route of Administration	Dosage Form / Strength	Clinically Relevant Inactive Ingredients
Oral	Suspension / 80 mg/1 mL	Alcohol-, gluten-, lactose-, sucrose-, sulfite- and tartrazine-free *For a complete listing of inactive ingredients, see "Dosage Forms, Composition and Packaging" section*
Oral	Suspension / 160 mg/5mL	Alcohol-, gluten-, lactose-, sucrose-, sulfite- and tartrazine-free *For a complete listing of inactive ingredients, see "Dosage Forms, Composition and Packaging" section*
Oral	Tablet / 160 mg	**Fastmelts:** Gluten-, sucrose- and tartrazine-free; contains lactose *For a complete listing of inactive ingredients, see "Dosage Forms, Composition and Packaging" section*
Oral	Tablet / 160 mg	**Chewables (**grape; bubblegum)**:** aspartame-gluten-, lactose and tartrazine-free; contains dextrose. *For a complete listing of inactive ingredients, see "Dosage Forms, Composition and Packaging" section*
Oral	Tablet, Caplet and Liquid Gel Capsule / 325 mg	Gluten-, lactose- and tartrazine-free *For a complete listing of inactive ingredients, see "Dosage Forms, Composition and Packaging" section*
Oral	Tablet, Caplet and Gelcap / 500 mg	Gluten-, lactose- and tartrazine-free *For a complete listing of inactive ingredients, see Dosage Forms, Composition and Packaging section*
Oral	Caplet / 650 mg (325 mg Immediate Release/325 mg Extended Release)	Gluten-, lactose- and tartrazine-free *For a complete listing of inactive ingredients, see Dosage Forms, Composition and Packaging section*
Oral	Powder / 160 mg or 500 mg per Pack	Sucrose-free; contains sucralose and xylitol *For a complete listing of inactive ingredients, see Dosage Forms, Composition and Packaging section*

Indications and Clinical Use: As an analgesic-antipyretic for the temporary relief of mild to moderate pain in a wide variety of conditions involving musculoskeletal pain, as well as in other painful disorders such as headache pain (including mild to moderate migraine and tension headache), earache, low back pain, arthritis pain, dysmenorrhea, myalgias and neuralgias. Also indicated for the symptomatic reduction of fever due to the common cold, flu and other viral or bacterial infections.

Contraindications: Hypersensitivity to acetaminophen or to the ingredients of this formulation (see Dosage Forms, Composition and Packaging). Allergic reactions (primarily skin rash) or reports of hypersensitivity secondary to acetaminophen are rare and generally are controlled by discontinuation of the drug and, when necessary, symptomatic treatment. Do not use with any other product containing acetaminophen.

Warnings and Precautions:
General:
Adults and children 12 years and older should not exceed 4 g/day of acetaminophen or use more than one product containing acetaminophen at a time. Children under 12 years should not be given more than the maximum daily dosage stated on the product label. These limits include combination products that contain acetaminophen.

Overdose warning: Taking more than the recommended dose (overdose) may result in liver damage. In case of overdose, get medical help right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

Acetaminophen-containing products should be kept out of the reach of children.

Consumers who are chronic alcohol abusers or have hepatic disease should ask their doctor whether they should take acetaminophen or other pain relievers or fever reducers. Physicians should be cognizant of and supervise the use of acetaminophen in patients with chronic alcoholism, serious kidney or serious liver disease. Physicians should alert their patients who regularly consume large amounts of alcohol not to exceed the recommended doses of acetaminophen. Chronic heavy alcohol abusers may be at increased risk of liver toxicity from excessive doses of acetaminophen.

Patients should be counseled to stop use and consult a physician if redness or swelling is present in an area of pain, if symptoms do not improve or if they worsen; if pain or fever persists or gets worse; or if new symptoms such as high fever, rash, itching or persistent headache occur, as these may be signs of a condition which requires medical attention.

Acetaminophen should not be taken for pain for more than 5 days, for fever for more than 3 days or if new symptoms appear, without consulting a physician.

Hepatic:
Slower metabolism of acetaminophen, increased activity of the cytochrome P450 enzyme system, or depleted glutathione stores are cited as theoretical risk factors for

acetaminophen hepatotoxicity in patients with chronic liver disease. However, acetaminophen has been studied in both adults and children with a wide variety of liver diseases including various types of cirrhosis, hepatitis (including hepatitis C), nodular transformation, congenital hepatic fibrosis, and α1-antitrypsin deficiency. In none of these conditions is there evidence of an increased risk for hepatotoxicity at currently recommended acetaminophen doses but the studies were insufficiently powered to definitely establish the extent of risk. Patients with hepatic disease should consult a physician before use.

Forrest [1] compared acetaminophen metabolism following a single 1500 mg dose in normal subjects, patients with mild liver disease, and patients with severe liver disease. There were no significant differences in overall 24-hour urinary excretion of acetaminophen and glucuronide, sulfate, cysteine, and mercapturic acid conjugates, evidence that acetaminophen metabolism was similar to that in normal subjects. However, the elimination half-life was significantly prolonged in patients with severe liver disease.

Acetaminophen has also been studied in pediatric patients with liver disease. Following a single (10 mg/kg) dose of acetaminophen, the pharmacokinetic profiles in pediatric patients with mild, moderate, or severe liver disease were not significantly different [2]. Although the plasma half-life of acetaminophen was prolonged in patients with severe liver disease, there were no significant differences in the 36-hour (children) urinary excretion of acetaminophen or its conjugates.

At the currently recommended doses acetaminophen is a suitable analgesic choice for use in patients with chronic stable liver disease when used under physician supervision.

Acetaminophen may cause hepatotoxicity in situations of intentional overdose (e.g. attempted suicide), unintentional overdose (e.g. overdosing when pain relief is not satisfactory), simultaneous use of multiple acetaminophen-containing preparations, accidental overdose or in very rare cases, after recommended doses, although causality has not been determined. The hepatotoxic reaction can be severe and life-threatening. Early symptoms following a hepatotoxic overdose may include nausea, vomiting, diaphoresis, lethargy, and general malaise. If appropriate treatment is not instituted, these may progress to upper quadrant pain, confusion, stupor, and sequelae of hepatic necrosis, such as jaundice, coagulation defects, hypoglycemia, and encephalopathy. Renal failure and cardiomyopathy may also occur. In the event of known or suspected overdosage, treatment with N-acetyl cysteine should be instituted immediately (see OVERDOSAGE section below), even when there are no obvious symptoms. Failure to promptly treat acetaminophen hepatotoxicity with N-acetyl cysteine can result in liver failure, leading to liver transplantation and/or death.

Chronic Alcohol Use: Excessive alcohol use may increase risk of liver toxicity from acetaminophen overdose (acute or chronic) [3-5].

Prospective data from Kuffner [5, 6] demonstrate that chronic alcoholics can take recommended doses of acetaminophen without the added risk of liver injury. In these prospective, placebo-controlled studies, the researchers evaluated an actively drinking group of alcoholics with a high prevalence of malnourishment. The study participants abruptly stopped their daily alcohol intake and took acetaminophen the next day. This should theoretically make them vulnerable to acetaminophen injury because their CYP2E1 would be maximally induced from the alcohol and there would be no alcohol present to compete with acetaminophen for metabolism by CYP2E1. There was no statistically significant difference in mean values for AST, ALT, or INR for alcoholics given four grams per day of acetaminophen compared to placebo. Additionally, the researchers performed an analysis of the malnourished patients that showed there was no increase in AST or ALT levels in these patients. Study limitations include a limited duration of 2 days and exclusion of patients with preexisting AST or ALT elevations greater than 120 U/L. Study results do not preclude the possibility of an idiosyncratic hepatic reaction.

Renal:
Based on available clinical data, acetaminophen can be used in patients with chronic renal disease without dosage adjustment. Martin [7] found that patients with chronic renal failure had higher plasma concentrations of acetaminophen and the inactive glucuronide and sulfate metabolites than healthy subjects during repeated dosing up to ten days.

Several single-dose studies demonstrate accumulation of acetaminophen metabolites in patients with moderate chronic renal failure and in anephric patients [8-10] for whom hemodialysis appeared to be the major route of elimination [11].

The habitual consumption of acetaminophen should be discouraged. If indicated medically, the long-term use of acetaminophen should be supervised by a physician.

A National Kidney Foundation position paper notes that physicians preferentially recommend acetaminophen to patients with renal failure because of the bleeding complications associated with ASA in these individuals [12]. Acetaminophen was recommended as the non-narcotic analgesic of choice for episodic use in patients with underlying renal disease.

Skin:
Serious skin reactions such as acute generalized exanthematous pustulosis (AGEP), Stevens – Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN), have been reported very rarely in patients receiving acetaminophen. Patients should be informed about the signs of serious skin reactions, and use of the drug should be discontinued at the first appearance of skin rash or any other sign of hypersensitivity.

Special Populations:
Notwithstanding appropriate precautions, acetaminophen is a suitable analgesic choice for the majority of sub-populations at increased risk of adverse events from analgesic use. This includes asthmatics, elderly, patients taking multiple prescription drugs, patients

taking anti-coagulants, patients who are breast-feeding, as well as patients who may suffer from chronic alcoholism, serious kidney or liver disease.

Results of well-designed clinical studies indicate that a dose reduction of acetaminophen, to avoid potential increased risk for toxicity, is not necessary for elderly adults, and obese adults. Additionally, the weight of existing evidence does not indicate the need to adjust dosage in chronic renal disease or chronic stable liver disease.

Elderly Patients: Acetaminophen at currently recommended doses can be used safely by elderly patients. Results of well-designed clinical studies indicate that a dose reduction of acetaminophen, to avoid potential increased risk for toxicity, is not necessary. In a comprehensive metabolic study by Miners [13], the formation and clearance of glucuronide and glutathione conjugates were the same in young and elderly adults, although clearance of the sulphate conjugate and unchanged acetaminophen were reduced. This finding provides prospective scientific data that the amount of acetaminophen metabolized via the oxidative pathway, from which the highly reactive intermediate, NAPQI, is generated, does not increase with age. Recently, Bannwarth [14] evaluated the multiple-dose pharmacokinetics of acetaminophen in elderly patients. After seven days of repeat dosing, acetaminophen did not accumulate in the plasma, and the elimination half-life was the same as that reported for young adults.

Elderly patients who require therapy for longer than 5 days should consult their physician for condition monitoring; however, no reduction in recommended dosage is necessary. The American Geriatrics Society Clinical Practice Guidelines for the Management of Chronic Pain in Older Persons [15] recommend acetaminophen as the drug of choice for relieving mild to moderate musculoskeletal pain, with the maximum dosage not to exceed 4000 mg daily. Acetaminophen is safe for use in the elderly population as currently labeled.

Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency: In therapeutic doses, acetaminophen does not shorten the lifespan of red blood cells [16,17] and does not produce any clinically perceptible destruction of circulating red blood cells [18].

Obese Adults: Results of well-designed clinical studies indicate that a dose reduction of acetaminophen, to avoid potential increased risk for toxicity, is not necessary. O'Shea [19] studied the pharmacokinetics of chlorzoxazone (a putative probe for CYP2E1 activity) to evaluate the effect of obesity on CYP2E1 activity. The authors concluded that CYP2E1 is induced in obese adults and that this could impact the metabolic pathway of a number of drugs metabolized by CYP2E1, including acetaminophen. However, acetaminophen pharmacokinetic data have been investigated in obese adults [20]. In this prospective study, 650 mg acetaminophen was administered intravenously to obese men (297 lb), obese women (193 lb), control men (155 lb) and control women (121 lb). Acetaminophen distribution volume per total body weight was slightly lower in the obese adults but, more importantly, the half-life and metabolic clearance per total body weight did not differ among groups.

Pregnancy and Lactation

There are no adequate and well controlled clinical studies in pregnant or breast-feeding women.

Adverse Effects:
Central Nervous System Effects: Acetaminophen at recommended doses has no obvious effects on central nervous system function [21]. In an overdose situation, central nervous system effects are uncommon.

Gastrointestinal Effects: Acetaminophen at recommended doses does not cause gastric irritation, gastric erosions, occult or overt gastrointestinal blood loss or ulcers [22,23].

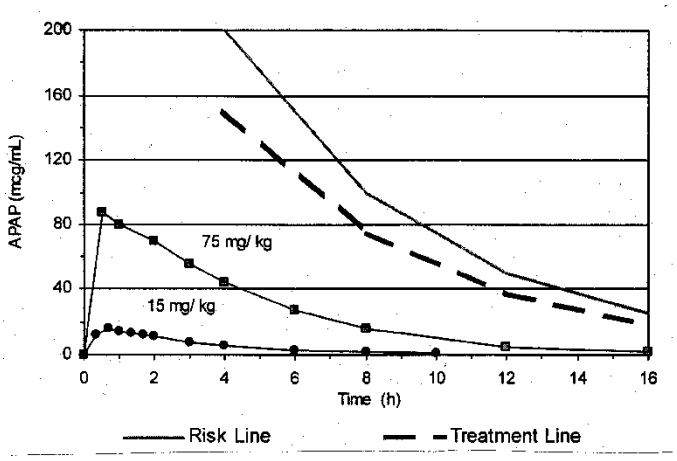
Blot and McLaughlin[24] conducted an independent analysis of case-control data from a study conducted by the American College of Gastroenterology. The risk of gastrointestinal bleeding increased two to three-fold among recent users of ASA, ibuprofen and other NSAIDs at OTC doses, and the risk was also dose-related. In contrast, the use of acetaminophen was not associated with an increased risk of gastrointestinal bleeding.

Hematologic Effects: Acetaminophen does not have any immediate or delayed effects on small vessel hemostasis, as measured by bleeding time. In normal volunteers receiving a single dose of acetaminophen (975 or 1950 mg) or multiple doses of acetaminophen (1950 mg daily for 6 weeks), no change in bleeding time or platelet aggregation was observed [25]. In another study, a single 1000 mg dose of acetaminophen was given to normal volunteers and did not affect bleeding time or platelet aggregation [26]. Patients with hemophilia receiving multiple doses of acetaminophen showed no significant changes in bleeding time [27,28].

Haematological reactions including thrombocytopenia, leucopenia, pancytopenia, neutropenia, and agranulocytosis have been reported, although these are rare and causality has not been established.

Hepatic Effects: As an illustration of the margin of safety of acetaminophen at supratherapeutic doses, a comparison of serum concentrations of acetaminophen over time for a standard 15 mg/kg dose and for a dose exceeding the standard by a multiple of 5 (75 mg/kg) are shown in Figure 1. The serum concentrations are drawn relative to the risk line for hepatotoxicity and treatment line of the Rumack-Matthew nomogram used to manage acute overdoses. The mean plasma concentrations for this supratherapeutic dose are well below the risk and treatment lines of the nomogram at all times. However, to minimize the risk for adverse effects, the maximum recommended dose should not be exceeded.

Figure 1: Mean Data for a Standard (1 g, 15 mg/kg) and Higher (5.6 g, 75 mg/kg) Dose Relative to Risk and Treatment Lines of the Acetaminophen Nomogram



Acetaminophen in overdosage may cause hepatotoxicity. In adults and adolescents, hepatotoxicity may occur following ingestion of greater than 150 mg/kg over a period of 8 hours or less. Fatalities are infrequent (less than 3% to 4% of untreated cases in which blood levels exceed the treatment line) and have rarely been reported with overdoses less than 7.5 g. In children, amounts less than 150 mg/kg are unlikely to produce hepatotoxicity.

In both adults and children, toxicity associated with acetaminophen is usually caused by ingestion of quantities of the drug that are significantly above the recommended dosage range. Hepatotoxicity, ranging from transient sharp transaminase elevations to fatal, fulminant hepatic failure, is the most common result of clinically significant overdosage [29].

In a double-blind, placebo-controlled clinical study, healthy adults were given 4, 6 and 8 g/d of acetaminophen over 3 days [30]. Plasma concentrations did not accumulate with repeat doses. Clinically all doses were well tolerated by the subjects and aminotransferase values stayed within normal limits throughout the study. These data provide information related to the margin of safety but are not intended to support dosing beyond the maximum recommended dose of 4 g/day.

A report has suggested that hepatotoxicity following greater than the recommended dose of acetaminophen may be enhanced by both prolonged fasting and/or chronic alcohol abuse [31].

Acute Alcohol Use: Acute alcohol ingestion refers to the occasional or intermittent use of alcohol. When taken together, alcohol competes with acetaminophen for CYP2E1. CYP2E1 accepts alcohol more readily than acetaminophen; therefore, less NAPQI is produced [32]. In the presence of alcohol, acetaminophen may be diverted to the glucuronidation and sulfation pathways. The overall result is that a smaller percentage of acetaminophen may be expected to be metabolized to the toxic intermediate, NAPQI,

than would otherwise be the case [33]. NAPQI production is increased above baseline for the period up to 18-24 hours post ethanol clearance from the body. In healthy adults, at normal labeled doses of acetaminophen, the temporary increase in NAPQI production is more than accommodated by normal glutathione stores in the liver.

Hypersensitivity: Sensitivity reactions are rare and may manifest as rash, urticaria, dyspnea, hypotension, laryngeal edema, angioedema, bronchospasm, or anaphylaxis. Cross-reactivity in ASA-sensitive persons has been rarely reported. If sensitivity is suspected, discontinue use of the drug.

Renal Effects: Acute nephrotoxicity has been reported following massive overdose either as a sequela of hepatic failure or, occasionally, in the absence of hepatic failure [34].

Clinical data have established that acetaminophen in recommended doses is not nephrotoxic [21].

Some studies suggest an association between the chronic long-term use of acetaminophen and renal effects. Results, however, are conflicting, limited by recall bias and confounded by the inability to determine whether analgesic use preceded or followed the onset of renal disease [35-40].

Case control studies have suggested a weak association between habitual acetaminophen use and prevalence of chronic renal failure and end stage renal disease [12]. This National Kidney Foundation position paper concludes that acetaminophen has been preferentially recommended by physicians to patients with renal failure and that there is no evidence that occasional use of acetaminophen caused renal injury. In this position paper, acetaminophen was recommended as the non-narcotic analgesic of choice for episodic use in patients with underlying renal disease.

Special Populations:
Pediatric: Lesko and Mitchell [41] enrolled more than 84,000 febrile children in a randomized, double blind, acetaminophen-controlled trial to assess the risks of rare but serious adverse events following use of pediatric ibuprofen. Of the children included in the analysis, 28,130 received acetaminophen and none experienced anaphylaxis, or serious hepatic, gastrointestinal or renal effects.

Pregnancy and Lactation: As with any drug, patients who are pregnant or nursing a baby should consult a physician before taking this product.

Pregnancy: Issues of risks in pregnancy are multifactorial. The information provided cannot be substituted for direct patient consultation. Acetaminophen is believed to be non-teratogenic in humans. However, existing studies have not assessed the effect of very high doses. The Motherrisk Collaborative Perinatal project monitored 50,282 mother-child pairs, of which 226 had first trimester exposure to acetaminophen and 781 had used acetaminophen at any time during their pregnancy. No evidence was found to suggest a relationship between acetaminophen use and major or minor malformations [42]. In a

surveillance study of Michigan Medicaid recipients conducted between 1985 and 1992 involving 229,101 completed pregnancies, 9,146 newborns had been exposed to acetaminophen during the first trimester [42]. This data do not support an association between acetaminophen use and the occurrence of birth defects. Another cohort study, using prescription monitoring, found no excess risk for malformation, and no evidence that acetaminophen influenced fetal growth [43]. Finally, as part of a larger study, 697 women used acetaminophen with or without codeine in their first trimester. No teratogenic risk was found [44].

A prospective study investigated the outcome of pregnancy in 300 women who had self-administered an overdose of acetaminophen, either alone, or as part of a combined preparation. Exposure to overdose occurred in all trimesters. The majority of the pregnancies had normal outcomes. The malformation rate was within the expected range. There was no obvious relationship between the time of exposure and the time of delivery. The overall conclusion was that acetaminophen overdose is not an indication for termination of pregnancy [45].

In a long-term developmental follow-up study [46], acetaminophen did not adversely affect IQ or behavior measures at four years of age. Height, weight and head circumference were also not affected by exposure to acetaminophen in-utero.

Unlike ASA, which has been shown to profoundly affect platelet function, there does not seem to be a risk of hemorrhage associated with acetaminophen use at term [47,48].

Currently there is no evidence to suggest that acetaminophen is teratogenic when used as recommended. However, data for continuous high daily doses are not sufficient, and safety during pregnancy has not yet been established.

Lactation: Following a typical therapeutic dose, acetaminophen is excreted in breast milk in very low concentrations. Based on a number of published reports [49-52], infant exposure levels are at most 4.5% of a weight adjusted pediatric therapeutic dose. In addition, acetaminophen is considered compatible with breast-feeding by the American Academy of Pediatrics [53].

Post-Marketing Data

Adverse drug reactions (ADRs) identified during post-marketing experience with paracetamol are included in Table 2. The frequencies are provided according to the following convention:

Very common	1/10
Common	1/100 and <1/10
Uncommon	1/1000 and <1/100
Rare	1/10,000 and <1/1,000
Very rare	<1/10,000
Not known	(cannot be estimated from the available data)

Table 2: Adverse Drug Reactions Identified during Post-Marketing Experience with Therapeutic Doses of Acetaminophen by Frequency Category Estimated from Spontaneous Reporting Rates

System Organ Classification Frequency	**Adverse Event Preferred Term**
Investigations	
Very rare	Transaminases increased†
Immune System Disorders	
Very rare	Anaphylactic reaction
Very rare	Hypersensitivity
Skin and Subcutaneous Tissue Disorders	
Very rare	Fixed eruption
Very rare	Urticaria
Very rare	Pruritic rash
Very rare	Rash

†Low level transaminase elevations may occur in some patients taking labeled doses of acetaminophen; these elevations are not accompanied with liver failure and usually resolve with continued therapy or discontinuation of acetaminophen.

Drug Interactions:

Analgesics
Caution is recommended when analgesic products are used in combination because of possible increases in adverse events (e.g. nephrotoxicity, gastrointestinal lesions, bleeding).

Alcohol: Studies evaluating the metabolism of doses up to 20 mg/kg of acetaminophen in chronic alcohol abusers and a study evaluating the effects of 2 days of acetaminophen dosing at 4000 mg/d in chronic alcoholics undergoing detoxification, have yielded inconsistent results with regard to effects on acetaminophen pharmacokinetics and demonstrate no evidence of adverse effect on liver function tests [3-6, 54,55].

Anticoagulants - Oral: Patients who concomitantly medicate with warfarin-type anticoagulants and regular doses of acetaminophen have occasionally been reported to have unforeseen elevations in their INR. Physicians should be cognizant of this potential interaction and monitor the INR in such patients closely while therapy is established. Many factors, including diet, medications, and environmental and physical states, may affect how a patient responds to anticoagulant therapy [56]. There have been several reports that suggest that acetaminophen may produce hypoprothrombinemia (elevated international normalized ratio [INR] or prothrombin time) when administered with coumarin derivatives [57-59]. In other studies, prothrombin time did not change [60-62]. Reported changes have been generally of limited clinical significance, however, periodic evaluation of prothrombin time should be performed when these agents are administered concurrently.

In the period immediately following discharge from the hospital or whenever other medications are initiated, discontinued, or taken regularly, it is important to monitor patient response to anticoagulation therapy with additional prothrombin time or INR determinations [56]. Despite the potential for interaction, acetaminophen is the least likely OTC analgesic to interfere with anticoagulant therapy and thereby remains the OTC analgesic of choice for concomitant use.

Patients should be instructed to ask a physician or pharmacist before use if they are taking the blood thinning drug warfarin or other coumarin derivatives.

Anticonvulsants: Some reports have suggested that patients taking long-term anticonvulsants, who overdose on acetaminophen, may be at increased risk of hepatotoxicity because of accelerated metabolism of acetaminophen [63,64]. Available data are conflicting. A 7-year retrospective study of acetaminophen overdose admissions indicates that the overall mortality rate was not significantly different for patients taking concomitant anticonvulsant medications [65].

> ***Hydantoins:*** At usual oral therapeutic doses of acetaminophen and hydantoins, no special dosage adjustment or monitoring is generally required. Pharmacokinetic studies indicate that phenytoin primarily induces the glucuronidation pathway, whereas glutathione-derived metabolites are not increased in patients on chronic phenytoin therapy [66]. Additionally, recent data demonstrate that phenytoin is metabolized primarily by CYP2C9 and CYP2C19 [67], whereas acetaminophen is primarily metabolized by CYP2E1 [68]. These data indicate that there is no increased risk of acetaminophen hepatotoxicity in patients on chronic hydantoin therapy who use the recommended dose of acetaminophen.
>
> ***Carbamazepine:*** At usual oral therapeutic doses of acetaminophen and carbamazepine, no special dosage adjustment is generally required. Carbamazepine is primarily metabolized by CYP3A4 [67], whereas acetaminophen is metabolized primarily via CYP2E1. It is not known whether there is increased risk from an acetaminophen overdose in patients on chronic carbamazepine therapy.

Diflunisal: Professional literature from the manufacturer of diflunisal cautions that concomitant administration with acetaminophen produces an approximate 50% increase in plasma levels of acetaminophen in normal volunteers [56]. Acetaminophen had no effect on diflunisal plasma levels. The clinical significance of these findings has not been established. However, caution should be used with concomitant administration of diflunisal and acetaminophen and patients should be monitored carefully.

Isoniazid: Some reports suggest that patients on chronic isoniazid therapy may be at risk for developing hepatotoxicity from an acetaminophen overdose [69-71]. Since patients on isoniazid therapy may develop hepatic effects from isoniazid alone, data from individual case reports are unclear as to whether chronic administration of isoniazid may increase

the risk of acetaminophen toxicity. Isoniazid is primarily metabolized by CYP2E1 [72,73] and induces CYP2E1 [63,72,74,75]. Studies in healthy subjects demonstrate that isoniazid blocks the formation of the toxic metabolite NAPQI when administered concomitantly with acetaminophen, but increase NAPQI formation when acetaminophen is administered one day after discontinuation of isoniazid [76,77]. Thus, concomitant use of isoniazid is unlikely to potentiate the risk of acetaminophen-induced hepatotoxicity at recommended doses. The isoniazid induction of CYP2E1 is short-lived, lasting only 12 to 48 hours after the discontinuation of isoniazid [77,78]; it is during this period the toxicity of an acetaminophen overdose may be potentiated.

Dosage and Administration:

Immediate Release:
Adults and children 12 years of age and older

325 mg tablet/caplet or liquid gel capsule: Take 1 every 4 to 6 hours. If pain or fever does not respond to 1 tablet/caplet or liquid gel, take 2 tablets/caplets or liquid gels at next dose. Do not take more than 12 tablets/caplets or liquid gels per day.

500 mg tablet/caplet or sachet: 500 mg to 1000 mg every 4 to 6 hours, as required, not to exceed 1000 mg per single dose. Taken in divided doses, not greater than 4000 mg acetaminophen in 24 hours.

Doses may be administered with or without food.

Children under 12 years of age: 10 to 15 mg/kg every 4 to 6 hours, as required, not to exceed 50-75 mg/kg/24 hours. For children weighing more than 53 kg do not exceed the maximum allowed daily dose of 4000 mg acetaminophen. Alternatively, the following single doses (see Table 3) may be given every 4 to 6 hours not to exceed 5 doses in 24 hours. Doses may be given with or without food (i.e. milk, formula, juices, etc.). Dose determination based on weight is preferred over dose determination based on age.

Sustained Release:
TYLENOL® Arthritis Pain 8H Extended Release Tablets:
Adults and children 12 years of age and over: Not greater than 2 sustained release caplets (1300 mg) every 8 hours, not to exceed 6 caplets (3900 mg) in 24 hours. Swallow each caplet whole with water on an empty stomach. Do not crush, chew or dissolve the caplet.

TYLENOL® Muscle and Body Extended Release Tablets:
Adults and children 12 years of age and older: Not greater than 2 sustained release caplets (1300 mg) every 8 hours, not to exceed 6 caplets (3900 mg) in 24 hours. Swallow each caplet whole with water on an empty stomach. Do not crush, chew or dissolve the caplet.

Table 3: TYLENOL®

Dosage in Children					
Weight (kg)	**Age Group**	**Single Dose (mg)**	**Concentration of Available Products**		
2.5-5.4	0-3 mos[a]	40	Infants' Suspension Drops (80 mg/mL)	Children's Suspension Liquid (160 mg/5 mL)	Children's Tablets[b] (160 mg/tablet)
5.5-7.9	4-11 mos	80			
8-10.9	12-23 mos	120			
11-15.9	2-3 yrs	160			
16-21.9	4-5 yrs	240			
22-26.9	6-8 yrs	320			
27-31.9	9-10 yrs	400			
32-43.9	11-12 yrs	480			

[a] Consumer labeling for Infants' and Children's TYLENOL® acetaminophen does not offer dosing information for children less than 4 months of age; therefore, this dose is provided as a guideline for professional recommendations to the consumer. Note: Data not available to define appropriate adjustments, if any, needed for the immediate neonatal period. Use of antipyretics in the immediate neonatal period is extremely limited.
[b] TYLENOL® solid dosage forms may not be appropriate for children under 2 years of age.

Children's TYLENOL® Easy Dissolve (Acetaminophen Powder 160 mg): Children aged 6-11 years: Tear pack and pour powder on child's tongue. Single dose may be repeated every 4 to 6 hours, as needed. Do not give more than 5 doses in 24 hours.

Weight		Age	Single Oral Dose
Lbs	Kg	Years	Packs
48-59	22-26.9	6-8	2
60-71	27-31.9	9-10	2
72-95	32-43.9	11	3

Overdosage:
Symptoms and Treatment: Acetaminophen: Typical Toxidrome: Hepatic injury is the principal toxic effect of a substantial acetaminophen overdose. In adults and adolescents (12 years of age and older), hepatic toxicity may occur following ingestion of greater than 7.5 to 10 grams over a period of 8 hours or less. Fatalities are infrequent (less than 3-4% of untreated cases) and have rarely been reported with overdoses of less than 15 grams. In children (<12 years of age), an acute overdosage of less than 150 mg/kg has not been associated with hepatic toxicity. Early symptoms following a potentially hepatotoxic overdose may include: anorexia, nausea, vomiting, diaphoresis, pallor and general malaise. Clinical and laboratory evidence of hepatic toxicity may not be apparent until 48 to 72 hours post-ingestion [110].

If an acetaminophen extended release product is involved, it may be appropriate to obtain an additional plasma acetaminophen level 4-6 hours following the initial acetaminophen level.

Serious toxicity or fatalities have been extremely infrequent following an acute acetaminophen overdose in young children, possibly because of differences in the way they metabolize acetaminophen [110].

The physician should be mindful that there is no early presentation that is pathognomic for the overdose. A high degree of clinical suspicion must always be maintained.

Untreated acetaminophen overdoses may produce hepatotoxicity. Acetaminophen hepatotoxicity occurs as a threshold effect and is characterized by a lack of toxicity at lower/therapeutic doses. Acetaminophen hepatotoxicity occurs after major depletion of glutathione, an endogenous detoxifying substance. Once the threshold is exceeded, increasing acetaminophen doses may produce increasing degrees of hepatotoxicity, unless N-acetylcysteine (NAC) is administered. Situations in which acetaminophen overdose and resultant hepatotoxicity may occur include acute intentional overdose and repeated supratherapeutic overdose in adults and acute accidental ingestion or overdose and repeated supratherapeutic overdose in children.

The clinical course of acetaminophen overdose generally occurs in a three-phase sequential pattern. The first phase begins shortly after ingestion and lasts for 12 to 24 hours. The patient may manifest signs of gastrointestinal irritability, nausea, vomiting, anorexia, diaphoresis, pallor and general malaise. If toxicity continues, there is a latent phase of up to 48 hours. During this second phase, initial symptoms abate and the patient may feel better. However, hepatic enzymes, bilirubin, and prothrombin time or INR values will progressively rise. Right upper quadrant pain may develop as the liver becomes enlarged and tender. Most patients do not progress beyond this phase, especially if given N-acetylcysteine (NAC) treatment early in the course. Signs and symptoms of the third phase depend on the severity of hepatic damage and usually occur from three to five days following overdose ingestion. Symptoms may be limited to anorexia, nausea, general malaise, and abdominal pain in less severe cases or may progress to confusion, stupor and sequelae of hepatic necrosis including jaundice, coagulation defects, hypoglycemia, and encephalopathy, as well as renal failure and cardiomyopathy. Death, if it occurs, is generally the result of complications associated with fulminant hepatic failure. Mortality rates in patients with toxic plasma levels who do not receive antidote therapy range from 3% to 4%.

Due to the wide availability of acetaminophen, it is commonly involved in single and mixed drug overdose situations and the practitioner should screen for its presence in a patient's serum. Acute toxicity after single dose overdoses of acetaminophen can be anticipated when the overdose exceeds 150 mg/kg. Chronic alcohol abusers, cachectic individuals, and persons taking pharmacologic inducers of the hepatic P450 microsomal enzyme system may be at risk with lower exposures.

Specific Antidote: Any individual presenting with a possible acetaminophen overdose should be treated with N-acetylcysteine (NAC), even if the amount of acetaminophen ingested is unknown or questionable. A blood sample for determination of the plasma acetaminophen concentration should be obtained as early as possible, but no sooner than four hours following ingestion. Do not await the results of assays for plasma acetaminophen levels before initiating treatment NAC. If the acetaminophen plasma level is found to plot above the treatment line on the acetaminophen overdose nomogram, NAC treatment should be continued for a full course of therapy. NAC is used clinically to treat acute acetaminophen overdose, and acts by interacting with the oxidative intermediate, NAPQI. NAC administered by either the i.v. or the oral route is known to be a highly effective antidote for acetaminophen poisoning. It is most effective when administered within 8 hours of a significant overdose but reports have indicated benefits to treatment initiated well beyond this time period. It is imperative to administer the antidote as early as possible in the time course of acute intoxication to reap the full benefits of the antidote's protective effects. For full prescribing information, consult the product monograph for NAC.

General Management: When the possibility of acetaminophen overdose exists, treatment should begin immediately and include appropriate decontamination of the gastrointestinal tract, proper supportive care, careful assessment of appropriately timed serum acetaminophen estimations evaluated against the Rumack-Matthew nomogram, timely administration of NAC as required and appropriate follow-up care. Liver function tests should be performed initially and repeated at 24-hour intervals.

Overdose During Pregnancy:
Acetaminophen is one of the most common overdoses in pregnancy. Hepatic toxicity of acetaminophen follows the formation of the highly reactive metabolite N-acetyl-p-benzoquinoneimine produced by acetaminophen metabolism through the cytochrome P450 mixed-function oxidase system. Hepatic failure can be prevented by timely administration of NAC either orally for 72 hours, or intravenously (IV) for 20 hours[79,80].

Acetaminophen crosses the human placenta[81] though the fetus is theoretically at risk when maternal overdose of acetaminophen occurs. Acetaminophen can be transformed to its toxic metabolite since the oxidative capacity of fetal microsomes is present in the fetus by 14 weeks gestation[82].

Studies on placental transfer of NAC in rats and sheep yielded conflicting results[83]. Placental transfer of N-acetylcysteine in humans was demonstrated in 4 women treated with NAC for acetaminophen overdose during labour. NAC blood levels in the fetuses were within the range associated with therapeutic doses of NAC administered to adults with acetaminophen poisoning[84].

Fetal toxicity and stillbirth after a large (e.g. 30 g) acetaminophen overdose has been reported, but others observed a normal outcome for the offspring after acetaminophen overdose in pregnancy. A large case series investigated the pregnancy outcome in 300 women who had overdosed with acetaminophen. In this group, 118 cases occurred in the

first trimester, 103 in the second trimester and 79 in the third trimester. Forty-nine of these mothers were treated with specific antidotes (33 with NAC and 16 with methionine). There were 219 live-born infants, 11 have malformations (including minor); none had been exposed to acetaminophen during the first trimester. Nine women were treated with NAC during the first trimester; there were two elective terminations; two spontaneous abortions, and five healthy babies in this group[85].

In summary, acetaminophen overdose during pregnancy should be treated according to regular protocols in order to prevent maternal and potentially fetal toxicity. Unless severe maternal toxicity develops, an acetaminophen overdose does not increase the risk for birth defects or adverse pregnancy outcomes.

Physicians unfamiliar with the current management of acetaminophen overdose should consult with a Poison Control Centre immediately. Telephone numbers for local Poison Control Centres are available in the local phone directory. Delays in initiation of appropriate therapy may jeopardize the patient's chances for full recovery.

The following are clinical events associated with acetaminophen overdose that if seen with overdose are considered expected, including fatal events due to fulminant hepatic failure or its sequelae.

Table 4: Adverse Drug Reactions Identified with Overdose of Acetaminophen

Metabolism and Nutrition Disorders: Anorexia **Gastrointestinal Disorders:** Vomiting, Nausea, Abdominal discomfort **Hepatobiliary disorders:** Hepatic necrosis, Acute hepatic failure, Jaundice, Hepatomegaly, Liver tenderness **General disorders and Administration Site Conditions:** Pallor, Hyperhidrosis, Malaise **Investigations:** Blood bilirubin increased, Hepatic enzymes increased, International normalized ratio increase, Prothrombin time prolonged, Blood phosphate increased, Blood lactate increased

The following clinical events are sequelae to acute hepatic failure and may be fatal. If these events occur in the setting of acute hepatic failure [111, 112] associated with acetaminophen overdose (adults and adolescents: ≥ 12 years of age: > 7.5 g within 8

hours; children < 12 years of age: >150 mg/kg within 8 hours), they are considered expected.

Table 5: Expected Sequelae to Acute Hepatic Failure Associated with Acetaminophen Overdose

Infections and Infestations: Sepsis, Fungal infection, Bacterial infection **Blood and Lymphatic System Disorders:** Disseminated intravascular coagulation, Coagulopathy, Thrombocytopenia **Metabolism and Nutrition Disorders:** Hypoglycemia, Hypophosphatemia, Metabolic Acidosis, Lactic Acidosis **Nervous System Disorders:** Coma (with massive acetaminophen overdose or multiple drug overdose), Encephalopathy, Brain edema **Cardiac Disorders:** Cardiomyopathy **Vascular Disorders:** Hypotension **Respiratory, Thoracic and Mediastinal Disorders:** Respiratory failure **Gastrointestinal Disorders:** Pancreatitis, Gastrointestinal hemorrhage **Renal and Urinary Disorders:** Acute renal failure **General Disorders and Administration Site Conditions:** Multi-organ failure

Action and Clinical Pharmacology:

Mechanism of Action: Acetaminophen is a centrally acting analgesic and antipyretic drug. Although the precise mechanism of action is not totally understood, work by Boutaud [86] suggests acetaminophen is an inhibitor of the peroxidase portion of cyclooxygenase (prostaglandin H synthase inhibitor). Depending on the redox state and substrate concentrations surrounding the enzymes, acetaminophen may or may not have a

significant inhibitory effect. This accounts for its selective activity on pain and fever with little anti-inflammatory effect [87].

It is postulated that the analgesic effect is produced by elevation of the pain threshold and the antipyretic effect is produced through action on the hypothalamic heat-regulating centre.

The optimal effective analgesic dose of acetaminophen was demonstrated in dental pain studies and is 1000 mg every four to six hours, up to 4000 mg daily. At least 500 published and unpublished controlled clinical trials in adults and children have evaluated acetaminophen for the relief of pain or fever. These studies include single and multiple dose treatments. Most studies were less than 14 days in duration, although the longest study duration was two years. No significant safety issues were reported in any of these studies.

Moreover, at recommended doses, acetaminophen has not been shown to increase the risk of developing renal diseases [21,35,88,89] or upper gastrointestinal ulceration/bleeding [22,23,90-92]. This observation is consistent with its minimal inhibitory effect on peripheral prostaglandin synthesis [93] and on gastric prostaglandin synthesis [94].

Acetaminophen is considered equipotent to ASA and ibuprofen, within the recommended OTC dosing ranges, in its analgesic and antipyretic effects. Acetaminophen at recommended doses does not cause the type of gastrointestinal complications associated with NSAID-containing products, such as gastric irritation, gastric erosions, occult or overt gastrointestinal blood loss, or ulcers. Unlike these drugs, however, it has no anti-inflammatory effect at clinically relevant doses in humans.

Pharmacokinetics:

A. Absorption: Oral acetaminophen is rapidly and almost completely absorbed from the gastrointestinal tract primarily in the small intestine. This absorption process occurs by passive transport. Peak plasma concentrations occur within 0.4 to 1 hour depending on the product formulation. Although high-fat foods delay the time to peak concentration for up to an hour, the dose is completely absorbed.

B. Distribution: Acetaminophen is uniformly distributed throughout most body fluids, but not in fatty tissue. As a result, the volume of distribution in adults ranges between 0.8 and 1.0 L/kg [32,95]. Since acetaminophen has low protein binding in plasma of only 10% to 25%, it does not compete with drugs that are highly protein bound [96,97].

C. Metabolism: Acetaminophen is primarily metabolized by the liver via three principal separate pathways [68]:

a) Conjugation with glucuronide
b) Conjugation with sulfate
c) Oxidation via the cytochrome P450 mixed function oxidase system.

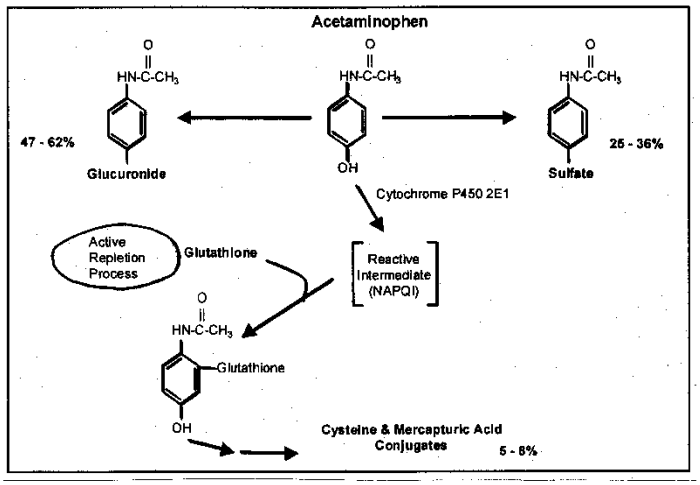
Both the glucuronic and oxidative pathways adhere to a first-order rate process, which means the concentration of acetaminophen metabolized increases as the concentration in the liver increases. The sulfate pathway adheres to Michaelis-Menten kinetics, which means the concentration of acetaminophen metabolized remains constant once the concentration in the liver increases above a saturation level. A schematic of acetaminophen metabolism is shown in Figure 2.

The major metabolic pathway is glucuronidation, where 47% to 62% of the acetaminophen dose conjugates with glucuronide. These glucuronide conjugates are inactive and nontoxic, and are secreted in bile and eliminated in the urine.

The second major pathway is sulfation, where 25% to 36% of the dose conjugates with sulfate. These sulfate ester conjugates are also inactive and nontoxic and are excreted in the urine.

The third pathway is oxidation, where 5% to 8% of the dose is metabolized via the cytochrome P450 enzyme system. The cytochrome P450 isoenzyme that is primarily responsible is CYP2E1. When acetaminophen is metabolized by CYP2E1, it forms a highly reactive intermediate, N-acetyl-p-benzoquinoneimine (NAPQI). Since NAPQI is highly reactive, it cannot be measured outside the liver nor can it accumulate. This intermediate is rapidly inactivated by hepatocellular stores of glutathione to form cysteine and mercapturate conjugates, which are both inactive and nontoxic. These conjugates are excreted in the urine.

Figure 2: Acetaminophen Metabolism



D. Elimination: Acetaminophen undergoes first-order elimination from the body, and has a short plasma half-life that ranges from 2 to 3 hours in healthy young and elderly adults [13, 98-104] and from 1.5 to 2.9 hours in children [105-109]. Since acetaminophen clears rapidly from the body, repeated doses do not lead to accumulation of acetaminophen plasma concentrations.

Storage:
Store at room temperature (15 to 30°C). TYLENOL® Rapid Release (Gelcaps) should additionally be protected from high heat and humidity. Infants' and Children's TYLENOL® Suspensions should additionally be protected from light.

Dosage Forms, Composition and Packaging:

Adults

Tablets

TYLENOL® Regular Strength (325 mg Tablets): Each round, white tablet, engraved "TYLENOL" on one side and "325" on the other side, contains: acetaminophen 325mg. Inactive ingredients: cellulose, corn starch, magnesium stearate and sodium starch glycolate.Vials of 12 and plastic bottles of 24, 50, 100.

TYLENOL® Extra Strength (500 mg eZ TABS/Tablets): Each round, red, sweet-coated tablet, printed "TYLENOL 500" contains: acetaminophen 500 mg. Inactive ingredients: carnauba wax, cellulose, corn starch, FD&C red no. 40, FD&C yellow no. 6, hypromellose, iron oxide black, polyethylene glycol, polysorbate 80, povidone, sodium starch glycolate, stearic acid, sucralose, titanium dioxide.
Plastic bottles of 24, 50, 100, 150, 200. See next entry for vials.

TYLENOL® Extra Strength (500 mg eZ TABS/Tablets): Each round, red, sweet-coated tablet, printed "TYLENOL 500", contains: acetaminophen 500 mg. Inactive ingredients: carnauba wax, cellulose, corn starch, FD&C red no. 40, FD&C yellow no. 6, hypromellose, iron oxide black, magnesium stearate, polyethylene glycol, polysorbate 80, sodium starch glycolate, sucralose, titanium dioxide.
Vials of 10.

Caplets

TYLENOL® Regular Strength Caplets (325 mg): Each elongated, capsule-shaped white tablet, engraved "TYLENOL" on one side and "325" on the other side, contains: acetaminophen 325 mg. Inactive ingredients: cellulose, corn starch, hypromellose, magnesium stearate, polyethylene glycol and sodium starch glycolate.
Plastic bottles of 24, 50, 100 and 200.

TYLENOL® Extra Strength Caplets (500 mg): Each elongated, capsule-shaped white tablet, engraved "TYLENOL" on one side and "500" on the other side, contains: acetaminophen 500 mg. Inactive ingredients: cellulose, corn starch, hypromellose, magnesium stearate, polyethylene glycol and sodium starch glycolate.
Vials of 10 and plastic bottles of 24, 50, 100 and 150.

Liquid Gel Capsules

TYLENOL® Liquid Gels (325 mg liquid-filled capsules): Each red liquid capsule is printed with "TY 325" on one side in white ink, contains: acetaminophen 325 mg. Inactive ingredients: ascorbyl palmitate, caprylic/capric triglycerides, dl-α-tocopherol, FD&C red no. 40, gelatin, glycerin, lecithin, medium chain triglycerides, mono-diglycerides, oleic acid, phosphatidylcholines (soya), polyethylene glycol, polyvinyl acetate phthalate, potassium acetate, povidone, propylene glycol, purified water, sorbitol sorbitan solution, titanium dioxide. Bottles of 32 and 115.

Gelcaps

TYLENOL® Rapid Release (500 mg Gelcaps): Each solid, capsule-shaped tablet, coated with red gelatin on one end, blue gelatin on the other end, a gray band between the two gelatin-coated ends, printed "TY" on one gelatin-coated end and "500" on the other gelatin-coated end, contains: acetaminophen 500 mg. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, corn starch, D&C yellow no. 10, edetate calcium disodium, FD&C blue no. 1, FD&C red no. 40, gelatin, hypromellose, iron oxide black, iron oxide red, iron oxide yellow, magnesium stearate, methylparaben, polyethylene glycol, polysorbate 80, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide. Bottles of 20, 40 and 80.

Powder

Extra Strength TYLENOL® Easy Dissolve (Acetaminophen Powder 500 mg each pack) (Berry): Each stick pack contains: acetaminophen 500 mg as a white to off-white free flowing granular powder with a characteristic berry odour. Inactive ingredients: Citric acid, ethylcellulose, flavour, magnesium stearate, sodium bicarbonate, sucralose, xylitol. Carton containing 12 or 32 stick packs.

Extended Release

TYLENOL® Arthritis Pain 8Hour (650 mg Extended Release Tablet): Each elongated, bilayer yellow and white, extended release tablet, engraved "TYLENOL ART" on one side, contains: acetaminophen 650 mg (325 mg immediate release acetaminophen and 325 mg delayed release acetaminophen in a slow dissolving matrix). Inactive ingredients: carnauba wax, cellulose, corn starch, D&C yellow no. 10, FD & C yellow no. 6, hydroxyethyl cellulose, hypromellose, magnesium stearate, povidone, sodium starch glycolate, and triacetin.Bottles of 24, 50 and 100.

TYLENOL® Muscle & Body (650 mg Extended Release Tablet): Each elongated, bilayer red and white, extended release tablet, engraved "TYLENOL ER" on one side, contains: acetaminophen 650 mg (325 mg immediate release acetaminophen and 325 mg delayed release acetaminophen in a slow dissolving matrix). Inactive ingredients: carnauba wax, cellulose, corn starch, FD&C red no. 40, hydroxyethyl cellulose,

hypromellose, magnesium stearate, microcrystalline cellulose, povidone, sodium starch glycolate and triacetin. Bottles of 16and 72.

Children

Tablets

Children's TYLENOL® Chewables (160 mg) (Bubblegum): Round tablet, pink, one side debossed "TY" over "160", the other side debossed with "HALF" over "HALF" and a center score line contains: acetaminophen 160 mg. Inactive ingredients: cellulose acetate, citric acid anhydrous, crospovidone, dextrose, D&C red no. 7 calcium lake, flavour, magnesium stearate, povidone, sucralose. Bottles of 20 tablets.

Children's TYLENOL® Chewables (160 mg) (Grape): Round tablet, purple, one side debossed "TY" over "160", the other side debossed with "HALF" over "HALF" and a center score line, contains: acetaminophen 160 mg. Inactive ingredients: cellulose acetate, citric acid anhydrous, crospovidone, D&C red no. 7 calcium lake, D&C red no. 30 aluminum lake, dextrose, FD&C blue no. 1 aluminum lake, flavour, magnesium stearate, povidone, sucralose. Bottles of 20 tablets.

Children's TYLENOL® Fastmelts 160 mg (Grape): Each round, white tablet with characteristic grape odour, debossed with "TYG 160" on one side and scored on the other side contains: acetaminophen 160 mg. Inactive ingredients: citric acid, copovidone, corn starch, crospovidone, ethylcellulose, flavour, lactose, magnesium stearate, mannitol, silicon dioxide, sorbitol, sucralose. Bottles of 20 tablets.

Suspension

Children's TYLENOL® (Suspension Liquid 160 mg/5 mL) (Banana Berry): Each 5 mL contains: acetaminophen 160 mg in a pink liquid vehicle with a strawberry-banana flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, corn syrup, FD&C red no. 40, flavour, glycerin, propylene glycol, purified water, sodium benzoate, sorbitol and xanthan gum.
Plastic bottles of 100 mL.

Children's TYLENOL® (Suspension Liquid 160 mg/5 mL)(Bubblegum): Each 5 mL contains: acetaminophen 160 mg in a dark pink liquid vehicle with a bubble gum-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, corn syrup, D&C red no. 33, FD&C red no. 40, flavour, glycerin, propylene glycol, purified water, sodium benzoate, sorbitol and xanthan gum.
Plastic bottles of 24 and 100 mL.

Children's TYLENOL® (Suspension Liquid 160 mg/5 mL) (Grape): Each 5 mL contains: acetaminophen 160 mg in a purple liquid vehicle with a grape-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, corn syrup, D&C red no. 33, FD&C blue no. 1, flavour, glycerin, propylene glycol, purified water, sodium benzoate, sorbitol and xanthan gum. Plastic bottles of 100 mL.

Children's TYLENOL® (Suspension Liquid 160 mg/5 mL) (Dye-Free Cherry): Each 5 mL contains: acetaminophen 160 mg in a pink liquid vehicle with a cherry-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, flavours, glycerin, propylene glycol, propylparaben, purified water, sodium citrate, sorbitol, sucralose, sucrose and xanthan gum.
Plastic bottles of 100 mL.

Children's TYLENOL® (Suspension Liquid 160 mg/5 mL) (Dye-Free Berry): Each 5 mL contains: acetaminophen 160 mg in a pink liquid vehicle with a berry-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, flavours, glycerin, propylene glycol, propylparaben, purified water, sorbitol, sucralose powder, sucrose and xanthan gum. Plastic bottles of 100 mL.

Powder

Children's TYLENOL® Easy Dissolve (Acetaminophen Powder 160 mg each pack) (Wild Berry): Each stick pack contains: acetaminophen 160 mg as a white to off-white free flowing granular powder with a characteristic berry odour. Inactive ingredients: Citric acid, ethylcellulose, flavour, magnesium stearate, sodium bicarbonate, sucralose, xylitol.
Carton containing 16 stick packs.

Suspension Drops

Infants' TYLENOL® (Suspension Drops 80 mg/1 mL)(Cherry): Each mL contains: acetaminophen 80 mg in a red liquid vehicle with a cherry-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, corn syrup, FD&C red no. 40, flavour, glycerin, propylene glycol, purified water, sodium benzoate, sorbitol and xanthan gum. Plastic bottles of 15 mL and 24 mL with a calibrated syringe and push-in bottle applicator technology (SIMPLE MEASURE®).

Infants' TYLENOL® (Suspension Drops 80 mg/1 mL)(Dye-Free Grape): Each mL contains: acetaminophen 80 mg in a white to off-white liquid vehicle with a grape-flavoured taste. Inactive ingredients: butylparaben, carboxymethylcellulose sodium, cellulose, citric acid, corn syrup, flavour, glycerin, propylene glycol, purified water, sodium benzoate, sorbitol and xanthan gum.
Plastic bottles of 15 mL, 24 mL and 24 mL(institutional use only) with a calibrated syringe and push-in bottle applicator technology (SIMPLE MEASURE®).

All packages are safety sealed.

McNeil Consumer Healthcare
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