PRODUCT MONOGRAPH

INCLUDING PATIENT MEDICATION INFORMATION

ACET 120

ACET 160

ACET 325

ACET 650

Acetaminophen Suppositories

Suppositories 120 mg, 160 mg, 325 mg, 650 mg, Rectal

USP

Analgesic / Antipyretic

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Sections or subsections that are not applicable at the time of authorization are not listed.

PART I: HEALTH PROFESSIONAL INFORMATION

1 INDICATIONS

ACET 120 / ACET 160 / ACET 325 / ACET 650 (acetaminophen suppositories) is indicated for the treatment of mild to moderate pain and the reduction of fever.

1.1 Pediatrics

Pediatrics (1 to 18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of ACET in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use (see 4.2 Recommended Dose and Dosage Adjustment).

1.2 Geriatrics

Geriatrics (over 65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see 7.1.4 Geriatrics).

2 CONTRAINDICATIONS

- ACET is contraindicated in patients who are hypersensitive to this drug or to any ingredient in the formulation, including any non-medicinal ingredient, or component of the container. For a complete listing, see 6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING.

3 SERIOUS WARNINGS AND PRECAUTIONS BOX

Serious Warnings and Precautions
• Patients should not take more than the recommended dose of acetaminophen, or take it with other products containing acetaminophen, or while drinking 3 or more alcoholic drinks daily because severe or possibly fatal liver damage may occur (see 5 OVERDOSAGE, 4 DOSAGE AND ADMNISTRATION; 7 WARNINGS AND PRECAUTIONS)

4 DOSAGE AND ADMINISTRATION

4.1 Dosing Considerations

- A physician should be consulted for treatment regimens lasting longer than 5 days for pain and longer than 3 days for fever.

- The inherency in the rectal route of administration to an erratic absorption, lower blood concentrations and the possibility of lower bioavailability in some patients relative to the oral route of administration makes more frequent rectal administration acceptable when deemed necessary by the prescriber.

4.2 Recommended Dose and Dosage Adjustment

- *Adults and Children over 12 years*: One suppository (650 mg) every 4 - 6 hours. Maximum daily dosage is 6 suppositories.
- *Infants under 1 year*: Use only on the advice of a physician.
- *Children 1 to 2 years*: One suppository (120 mg) every 4 hours. Maximum daily dosage is 5 suppositories.
- *Children 2 to 4 years*: One suppository (160 mg) every 4 hours. Maximum daily dosage is 6 suppositories.
- *Children 4 to 6 years*: One suppository (325 mg) every 6 hours. Maximum daily dosage is 4 suppositories.
- *Children 6 to 12 years*: One suppository (325 mg) every 4 hours. Maximum daily dosage is 6 suppositories.

4.4 Administration

For rectal use only. Prior to administration wash hands with soap and water. Remove plastic wrapper and moisten suppository with cool water. Have patient lie on side with bottom leg straight and upper leg bent up toward chest. Gently push the suppository as high as possible into rectum. Wash hands with soap and water.

4.5 Missed Dose

If a dose is missed, patients are advised to take it as soon as they remember. If it is almost time for the next dose, patients are advised to skip the missed dose and continue with the next scheduled dose.

5 OVERDOSAGE

In adults, hepatotoxicity may occur after ingestion of a single dose of 10 to 15 g (200 to 250 mg/kg) of acetaminophen; a dose of 25 g or more is potentially fatal.

In adults, cases of non-fatal overdose (ranging from 12.5 to 31.5 g) have been reported; and one death after ingestion of 30 g of acetaminophen has been reported. A 13-year-old child is reported to have died after ingesting 15 g.

SYMPTOMS: The first 2 days of acute poisoning by acetaminophen do not reflect the potential seriousness of the intoxication, and hepatotoxicity is generally believed to occur only with

acute overdosage. Nausea, vomiting, anorexia and abdominal pain occur during the initial 24 hours and may persist for a week or more. Liver injury may become manifest the second day, initially by elevation of serum transaminase and lactic dehydrogenase activity, increased serum bilirubin concentration and prolongation of prothrombin time. Alkaline phosphatase activity and serum albumin concentration may remain normal. The hepatotoxicity may progress to encephalopathy, coma and death. Liver biopsy reveals centrilobular necrosis with sparing of the periportal area. In nonfatal cases, the hepatic lesions are reversible over a period of weeks or months. Transient azotemia is apparent in most patients and acute renal failure occurs in some.

Hypoglycemia may occur, but glycosuria and impaired glucose tolerance have also been reported. Both metabolic acidosis and metabolic alkalosis have been noted, cerebral edema and non-specific myocardial depression have also occurred.

Since acetaminophen is metabolized primarily by the liver, in cases of acute poisoning following oral ingestion, prolongation of the plasma half-life beyond 3 hours may be indicative of liver injury. Hepatic necrosis should be anticipated if the half-life exceeds 4 hours, and hepatic coma is likely if the half-life is greater than 12 hours following oral ingestion. A single determination of serum acetaminophen concentration is a less reliable predictor of hepatic injury. However, only minimal liver damage has developed when the serum concentration was below 120 mcg/mL at 4 hours, or less than 50 mcg/mL at 12 hours after ingestion of the drug. Encephalopathy should be anticipated if serum bilirubin concentration exceeds 4 mg/100 mL during the first 5 days.

TREATMENT: Early diagnosis is vital in the treatment of overdose with acetaminophen. Vigorous supportive therapy is essential when intoxication is severe. Procedures to limit continuing absorption of the drug must be initiated promptly. When the oral route of administration is used, induction of vomiting or gastric lavage should be performed and should be followed by oral administration of activated charcoal (50 gm). Hemodialysis, if it can be initiated within the first 12 hrs, has been advocated for all patients with a plasma concentration of acetaminophen greater than 120 mcg/mL, 4 hrs after drug ingestion. If administered within the first few hours, ingestion of sulphydryl compounds, which replenish glutathione, have been shown to effectively prevent or reduce the hepatotoxic effects of acetaminophen. N-acetylcysteine, available commercially as a sterile 20% solution has been shown to be particularly effective and well tolerated when given orally as a 5% solution diluted with cola, fruit juice, or water. The accepted treatment regimen is a loading dose of 140 mg/kg followed by 70 mg/kg every 4 hrs for 17 doses or until plasma concentrations of acetaminophen are indicative of a low risk to hepatotoxicity.

For management of a suspected drug overdose, contact your regional poison control centre.

6 DOSAGE FORMS, STRENGTHS, COMPOSITION AND PACKAGING

Table 1 – Dosage Forms, Strengths, Composition and Packaging

Route of Administration	Dosage Form / Strength/Composition	Non-medicinal Ingredients
Rectal	Suppositories 120 mg	Novata (vegetable source triglycerides)
Rectal	Suppositories 160 mg	Novata (vegetable source triglycerides)
Rectal	Suppositories 325 mg	Novata (vegetable source triglycerides)
Rectal	Suppositories 650 mg	Novata (vegetable source triglycerides)

ACET 120: Each suppository, containing 120 mg acetaminophen, is individually sealed and available in boxes of 12.

ACET 160: Each suppository, containing 160 mg acetaminophen, is individually sealed and available in boxes of 12.

ACET 325: Each suppository, containing 325 mg acetaminophen, is individually sealed and available in boxes of 12.

ACET 650: Each suppository, containing 650 mg acetaminophen, is individually sealed and available in boxes of 12.

7 WARNINGS AND PRECAUTIONS

Please see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX.

General

When used as directed, acetaminophen is virtually free of severe toxicity or side effects. The incidence of gastrointestinal upset is less than after salicylate administration. If a rare sensitivity reaction occurs, usually manifested by a rash or urticaria, discontinue use of the drug.

Monitoring and Laboratory Tests

Acetaminophen may cause false measurements in blood glucose determinations.

Administration of acetaminophen prior to pancreatic function tests using bentiromide will invalidate test results.

Acetaminophen may cause falsely increased serum uric acid determinations when the phosphotungstate uric acid test method is used.

Acetaminophen may cause false positive results in qualitative screening tests of urine

5Bhydroxyindoleacetic acid (5-HIAA) determinations using nitrosonaphthol reagent.

In alcoholic patients taking hepatic enzyme inducers, or patients with pre-existing hepatic disease, when single toxic doses of acetaminophen are taken (or with prolonged use of lower doses), prothrombin time, serum bilirubin concentrations, serum lactate dehydrogenase activity, and serum transaminase activity may be increased.

Hepatic/Biliary/Pancreatic

Acetaminophen may cause hepatotoxicity in situations of intentional overdose, unintentional overdose, simultaneous use of multiple acetaminophen-containing preparations, accidental overdose or in very rare cases, after recommended doses, although causality has not been determined.

In adults, hepatotoxicity may occur after ingestion of a single dose of 10 to 15 g (200 to 250 mg/kg) of acetaminophen. An 18 month-old child and a 3 year-old child each ingested 3 g of acetaminophen with no ill effects. One adult ingested 35 and another 17.5 g, and both recovered after developing symptoms and signs of hepatotoxicity. On the other hand, fatalities have been reported from large overdosage of 15, 25 and 75 g.

Early symptoms of hepatotoxicity may include yellowing of the skin/eyes, dark urine, sweating, nausea, vomiting, stomach pain, unusual tiredness, and loss of appetite. Do not exceed the maximum recommended daily dose of acetaminophen (see 3 SERIOUS WARNINGS AND PRECAUTIONS BOX, 5 OVERDOSAGE and 4.2 Recommended Dose and Dose Adjustment).

Renal

Uremia has been reported as an adverse reaction, especially with prolonged use of high doses in patients with severe renal function impairment. Although a causal association has not been established, a retrospective study has suggested that long-term daily use of acetaminophen may be associated with an increased risk of chronic renal disease (analgesic nephropathy) in individuals without pre-existing renal function impairment.

Skin

In rare cases, serious skin reactions such as Stevens-Johnson syndrome, toxic epidermal necrolysis, exfoliative dermatitis, DRESS (Drug Reaction with Eosinophilia and Systemic Symptoms), AGEP (Acute Generalized Exanthematous Pustulosis) and erythema multiforme have been associated with the use of acetaminophen. Causality is not clear due to the low frequency noted during post-marketing. Symptoms may include skin reddening, skin blisters, rash, hives, severe itching, swelling of eyes and mouth, and difficulty breathing. If any of the above noted symptoms occur, stop use and seek medical help right away.

7.1 Special Populations

7.1.1 Pregnant Women

It is not known whether acetaminophen suppositories can cause fetal harm when administered to a pregnant woman.

7.1.2 Breast-feeding

Acetaminophen crosses the placenta and is excreted in breast milk in low concentrations. Caution should be exercised in prescribing ACET 120/160/325/650 to women who are breast-feeding.

7.1.3 Pediatrics

Pediatrics (1 to 18 years of age): Based on the data submitted and reviewed by Health Canada, the safety and efficacy of ACET 120/160/325/650 in pediatric patients has been established. Therefore, Health Canada has authorized an indication for pediatric use in patients from 1 to 18 years of age. For infants under 1 year of age, use ACET 120/160/325/650 only on the advice of a physician (see 4.2 Recommended Dose and Dosage Adjustment).

7.1.4 Geriatrics

Geriatrics (over 65 years of age): Evidence from clinical studies and experience suggests that use in the geriatric population is associated with differences in safety or effectiveness (see 7 WARNINGS AND PRECAUTIONS, Renal).

8 ADVERSE REACTIONS

8.1 Adverse Reaction Overview

Although the incidence of adverse reactions is rare, the following adverse reactions may have clinical significance (possible signs and symptoms in parentheses):

- Agranulocytosis (unexplained sore throat and fever)
- Anemia (unusual tiredness or weakness)
- Dermatitis, allergic (skin rash, hives, or itching)
- Hepatitis (yellow eyes or skin)
- Renal colic (pain, severe and/or sharp, in lower back and/or side) with prolonged use of high doses in patients with severe renal function impairment.
- Renal failure (sudden decrease in amount of urine)

- Sterile pyuria (cloudy urine)
- Thrombocytopenia (usually asymptomatic: rarely, unusual bleeding or bruising; black, tarry stools; blood in urine or stools; pinpoint red spots on skin).

8.2 Clinical Trial Adverse Reactions

The clinical trial data on which the original indication was authorized is not available.

8.5 Post-Market Adverse Reactions

This information is not available for this drug product.

9 DRUG INTERACTIONS

9.2 Drug Interactions Overview

Patients should be advised not to take ACET 120/160/325/650 with other drugs containing acetaminophen.

9.3 Drug-Behavioural Interactions

Risk of hepatotoxicity with single toxic doses or prolonged use of high doses of acetaminophen may be increased in alcoholics. The effect of other lifestyle choices (e.g., smoking) on the use of ACET 120/160/325/650 has not been established.

9.4 Drug-Drug Interactions

- Risk of hepatotoxicity with single toxic doses or prolonged use of high doses of acetaminophen may be increased in patients regularly taking other hepatotoxic medications or hepatic enzyme inducers.
- Concurrent chronic high-dose administration of acetaminophen may increase the anticoagulant effect of anticoagulants, coumarin-type (e.g. warfarin) or andantino-derivative.
- Prolonged concurrent use of acetaminophen and anti-inflammatory drugs, nonsteroidal (NSAIDs) or aspirin or other salicylates is not recommended because recent evidence suggests that chronic high-dose administration of combined analgesics significantly increases the risk of analgesic nephropathy, renal papillary necrosis, end-stage renal disease, and cancer of the kidney or urinary bladder.
- Diflusinal may increase the plasma concentration of acetaminophen by 50%, leading to increased risk of acetaminophen-induced hepatotoxicity.
- Acetaminophen may competitively inhibit the hepatic glucoronidation and decrease the clearance of zidovudine; zidovudine may also inhibit the hepatic glucoronidation of acetaminophen.

9.5 Drug-Food Interactions

As rectal medication, studies evaluating interactions with food are not relevant.

9.6 Drug-Herb Interactions

Interactions with herbal products have not been established.

9.7 Drug-Laboratory Test Interactions

Please see 7 WARNINGS AND PRECAUTIONS, Monitoring and Laboratory Tests.

10 CLINICAL PHARMACOLOGY

10.1 Mechanism of Action

Acetaminophen is the major metabolite of phenacetin and acetanilid. Animal and clinical studies have shown acetaminophen to have antipyretic and analgesic activity equal to that of acetylsalicylic acid. Acetaminophen lacks anti-inflammatory effects.

10.2 Pharmacodynamics

Unlike the salicylates, acetaminophen does not interfere with tubular secretion of uric acid nor does it affect acid-base balance if taken in therapeutic doses. Acetaminophen does not interfere with hemostasis and, in particular, does not inhibit platelet aggregation. Allergic reactions are rare and thus the drug is useful in patients who cannot tolerate salicylates and those with an allergic diathesis, including bronchial asthmatics.

It has been shown that glutathione precursors such as N-acetylcysteine, cysteine, cysteamine and methionine can decrease experimental acetaminophen induced hepatic necrosis when administered promptly after a toxic dose of acetaminophen.

10.3 Pharmacokinetics

Absorption / Distribution

Rectal absorption of acetaminophen, as with most rectally administered drugs, is more erratic than absorption following oral administration. Absorption rate is generally slower. Higher rectal doses or more frequent administration may be required to achieve and/or maintain blood concentrations of acetaminophen comparable to those obtained following oral administration.

With doses up to 650 mg the peak plasma concentrations are from 5 to 20 mcg/mL. The time to reach peak effect is 1 to 3 hours and the duration of action is 3 to 4 hours. The plasma half-life of unchanged drug is about 2 hrs with approximately 85% of a 1 gm oral dose being recovered in the urine in 24 hrs.

The rate of acetaminophen absorption from the gastrointestinal tract following oral administration is a function of stomach emptying rate and is generally rapid and complete with

peak plasma concentrations of free drug being achieved in 1/2 to 2 hours following administration.

Metabolism

A small portion of the administered acetaminophen is converted by hepatic microsomal enzymes to reactive metabolite. At therapeutic doses this minor metabolite is rapidly inactivated by conjugation with glutathione and eliminated by renal excretion. However, where hepatic glutathione has been depleted, covalent binding of the reactive metabolite to liver-cell macromolecules occurs and hepatic cell necrosis ensues.

Elimination

Acetaminophen metabolites are mainly excreted in the urine, with approximately 85% of a 1 gm oral dose being recovered in the urine in 24 hrs. Approximately 3% is excreted unchanged with the balance being eliminated principally as the glucoronide and sulfate conjugates.

11 STORAGE, STABILITY AND DISPOSAL

Store between 15 and 25°C. Keep out of reach and sight of children. This package contains enough medicine to seriously harm a child.

PART II: SCIENTIFIC INFORMATION

13 PHARMACEUTICAL INFORMATION

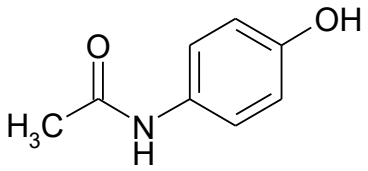
Drug Substance

Proper name: Acetaminophen

Chemical name: N-Acetyl-p-Aminophenol 4'-Hydroxyacetanilide N-(4-Hydroxyphenyl) Acetamide

Molecular formula and molecular mass: $C_8H_9NO_2$ / 151.2 g/mol

Structural formula:



Physicochemical properties: Acetaminophen is a white odourless crystalline powder with a slightly bitter taste. Soluble 1 in 70 of water, 1 in 20 in boiling water and, 1 in 7-10 in alcohol; very soluble in chloroform and ether.

14 CLINICAL TRIALS

14.3 Comparative Bioavailability Studies

A double-blind, single dose, randomized, cross-over study was conducted on healthy adults (average weight 75.2 kg) to evaluate and compare the rate and extent of absorption and comparative bioavailability between ACET 120 (120 mg) suppository (test product), and ABENOL (120 mg) suppository, a Canadian marketed formulation (reference product). Comparative bioavailability between formulations was evaluated on statistical comparison of areas under the plasma concentrations versus time curves (AUC's), peak concentrations (C_{max}) and time to reach peak concentrations (T_{max}).

The summary of the results obtained are as follows:

Table 2 Results of Comparative Pharmacokinetic Study of Unchanged Acetaminophen in Blood Following Administration of 120 mg Suppositories

	Mean values (± CV%)	
	Reference*	**Test****
Observed C_{MAX} (mcg/mL)	1.07 (31.5)	1.21 (21.4)
Observed T_{MAX} (h)	1.1 (37.4)	1.2 (25.5)
AUC_{CUM} (mcg.h/mL)	4.48 (29.8)	4.65 (20.4)
AUC (mcg.h/mL)	5.12 (32.1)	5.38 (25.6)
Ratio AUC_{CUM}/AUC (%)	87.93 (4.7)	87.59 (7.7)
MRT (h)	3.0 (9.5)	3.0 (8.6)
Elimination $T_{1/2}$ (h^{-1})	3.1 (19.8)	3.3 (43.9)

* ABENOL 120 (120 mg) suppository (BEECHAM Laboratories Inc.)
** ACET 120 (120 mg) suppository (PENDOPHARM, Division of Pharmascience Inc.)
AUC_{CUM} = Cumulative area under the plasma concentration time curve calculated from 0 to time of last quantifiable concentration.
MRT = Mean Residence Time

From this study, no statistical difference could be detected between the two formulations for all the pharmacokinetic parameters under study; the relative bioavailability was 106.4%.

A similar double-blind, single dose, randomized, cross-over study was conducted on healthy adults (average weight 74.3 kg) to evaluate and compare the rate and extent of absorption and comparative bioavailability between ACET 650 (650 mg) suppository (test product) and ABENOL 650 (650 mg) suppository, a Canadian marketed formulation (reference product). Comparative bioavailability between formulations was evaluated on statistical comparison of areas under the plasma concentrations versus time curves (AUCs), peak concentrations (C_{max}) and time to reach peak concentrations (T_{max}).

The summary of the results obtained are as follows:

Table 3 Results of Comparative Pharmacokinetic Study of Unchanged Acetaminophen in Blood Following Administration of 650 mg Suppositories

	Mean values (± CV%)	
	Reference*	**Test****
Observed C_{MAX} (mcg/mL)	3.20 (26.9)	4.13 (28.1)
Observed T_{MAX} (h)	4.1 (50.3)	2.8 (65.2)
AUC_{CUM} (mcg.h/mL)	24.07 (27.1)	27.72 (28.9)
AUC (mcg.h/mL)	26.89 (30.8)	30.71 (28.5)
Ratio AUC_{CUM}/AUC (%)	90.4 (5.4)	90.4 (5.9)
MRT (h)	5.6 (13.1)	5.2 (10.6)
Elimination $T_{1/2}$ (h^{-1})	7.0 (40.7)	6.1 (57.0)

* ABENOL 650 (650 mg) suppository (BEECHAM Laboratories Inc.)
** ACET 650 (650 mg) suppository (PENDOPHARM, Division of Pharmascience Inc.)
AUC_{CUM} = Cumulative area under the plasma concentration time curve calculated from 0 to time of last quantifiable concentration.
MRT = Mean Residence Time

Peak blood levels of free acetaminophen are not reached until 3 hours following rectal administration of ACET Suppositories and the peak concentration in the blood is approximately 50% of that observed following an equivalent oral dose (10-20 mcg/mL). The percentage of a rectal dose of acetaminophen absorbed also varies, giving wide variances in the bioavailability. No adverse reactions were reported and all physical, medical and laboratory evaluations were judged to be clinically normal.

15 MICROBIOLOGY

No microbiological information is required for this drug product.

16 NON-CLINICAL TOXICOLOGY

General Toxicology:

The LD_{50} in mice has been reported to be 338 mg/kg orally and 500 mg/kg i.p.

PATIENT MEDICATION INFORMATION

READ THIS FOR SAFE AND EFFECTIVE USE OF YOUR MEDICINE

ACET 120

ACET 160

ACET 325

ACET 650

Acetaminophen Suppositories USP

Read this carefully before you start taking **ACET 120 / ACET 160 / ACET 325 / ACET 650** and each time you get a refill. This leaflet is a summary and will not tell you everything about this drug. Talk to your healthcare professional about your medical condition and treatment and ask if there is any new information about **ACET 120 / ACET 160 / ACET 325 / ACET 650**.

Serious Warnings and Precautions

Liver warning: Acetaminophen may cause severe or possibly fatal liver damage:

- If you take more than the recommended dose in 24 hours
- If you take ACET 120 / ACET 160 / ACET 325 / ACET 650 with other drugs containing acetaminophen
- If you take ACET 120 / ACET 160 / ACET 325 / ACET 650 while drinking 3 or more alcoholic drinks every day

Symptoms of liver damage may include:

- Yellowing of the skin / eyes, dark urine
- Sweating, nausea, vomiting, stomach pain
- Unusual tiredness, and/or loss of appetite

What is ACET 120 / ACET 160 / ACET 325 / ACET 650 used for?

ACET 120 / ACET 160 / ACET 325 / ACET 650 suppositories are used to relieve mild to moderate pain, and to reduce fever.

How does ACET work?

It is not completely understood how acetaminophen works in your body. Some explanations involve chemical messengers of inflammation and pain. Other explanations involve aspects of the way nerves interact (neurotransmission) in the brain and spinal cord.

What are the ingredients in ACET 120 / ACET 160 / ACET 325 / ACET 650?

Medicinal ingredients: Acetaminophen

Non-medicinal ingredients: Novata (vegetable source triglycerides)

ACET 120 / ACET 160 / ACET 325 / ACET 650 comes in the following dosage forms:

Suppositories: 120 mg, 160 mg, 325 mg, 650 mg

Do not use ACET 120 / ACET 160 / ACET 325 / ACET 650 if:

- You are allergic or hypersensitive to acetaminophen or any other ingredient in this product.
- You are taking other drugs containing acetaminophen. (If you are not sure whether a drug contains acetaminophen, ask your healthcare professional.)

To help avoid side effects and ensure proper use, talk to your healthcare professional before you take ACET 120 / ACET 160 / ACET 325 / ACET 650. Talk about any health conditions or problems you may have, including if you:

- have liver disease
- have kidney disease
- take blood thinning drugs such as warfarin
- are pregnant or breastfeeding

Other warnings you should know about:

Stop using ACET 120 / ACET 160 / ACET 325 / ACET 650 and contact your healthcare professional if:

- you develop a severe allergic reaction (difficulty in breathing, skin rash and itching, swelling of the face and throat, runny nose)
- your pain lasts for more than 5 days
- your fever lasts for more than 3 days

Acetaminophen may cause serious skin reactions. Symptoms may include skin reddening, blisters and rash

Tell your healthcare professional about all the medicines you take, including any drugs, vitamins, minerals, natural supplements or alternative medicines.

The following may interact with ACET 120 / ACET 160 / ACET 325 / ACET 650:

- Anticoagulants to thin your blood such as warfarin and coumarin
- Anti-inflammatory drugs, nonsteroidal drugs (NSAIDs) or aspirin or other salicylates
- Diflusinal
- Zidovudine

How to take ACET 120 / ACET 160 / ACET 325 / ACET 650:

- Wash hands with soap and water
- Remove plastic wrapper
- Moisten suppository with cool water
- Lie on side with bottom leg straight and upper leg bent up toward chest
- Gently push suppository as high as possible into rectum
- Do not use immediately before bowel movement
- Wash hands with soap and water

Usual dose (children aged 1 to 12):

Use ACET 120, ACET 160 or ACET 325 according to the dose chart below:

Age (Years)	Single Dose	Maximum Daily Dose
Under 1	Use only on the advice of a physician.	
1 to 2	1 **ACET 120** suppository (120 mg) every 4 hours	5 suppositories
2 to 4	1 **ACET 160** suppository (160 mg) every 4 hours	6 suppositories
4 to 6	1 **ACET 325** suppository (325 mg) every 6 hours	4 suppositories
6 to 12	1 **ACET 325** suppository (325 mg) every 4 hours	6 suppositories

Usual dose (adults and children over 12 years):

Use ACET 650 according to the dose chart below:

Adults and Children over 12 years	Single Dose	Maximum Daily Dose
	1 **ACET 650** suppository (650 mg) every 4 to 6 hours	6 suppositories

Overdose:

If you think you, or a person you are caring for, have taken too much ACET 120 / ACET 160 / ACET 325 / ACET 650, contact a healthcare professional, hospital emergency department, or regional poison control centre immediately, even if there are no symptoms.

- **Signs of overdose:** nausea or vomiting, stomach cramps or pain, and unusual increases in sweating, diarrhea, loss of appetite. Onset may be delayed 24 hours after intake.
- **If emergency help is not available**: vomiting should be induced at once (within 30 minutes) by ipecac syrup. Vomiting should never be induced in unconscious individuals or in children younger than 1 year old without medical help.

Missed Dose:

If you forget to take a dose, take it as soon as you remember. If it is almost time for your next dose, do not take the missed dose and just carry on as before. Do not take a double dose to make up for a forgotten dose.

What are possible side effects from using ACET 120 / ACET 160 / ACET 325 / ACET 650?

These are not all the possible side effects you may have when taking ACET 120 / ACET 160 / ACET 325 / ACET 650. If you experience any side effects not listed here, tell your healthcare professional.

Side effects may include:

- Unexplained sore throat and fever
- Unusual tiredness or weakness
- Skin rash, hives, or itching

Serious side effects and what to do about them			
Symptom / effect	**Talk to your healthcare professional**		**Stop taking drug and get immediate medical help**
	Only if severe	**In all cases**	
RARE			
Allergic reaction (symptoms like swelling of the face, lip or throat, red and lumpy skin, rash, itchiness, hives, difficulty breathing or wheezing)			√
Serious skin reactions (skin reddening, blisters, and rash)			√
Hepatitis (yellow eyes or skin)			√

Serious side effects and what to do about them			
Symptom / effect	Talk to your healthcare professional		Stop taking drug and get immediate medical help
	Only if severe	In all cases	
Renal colic (pain, severe and / or sharp, in lower back and / or side)			√
Renal failure (sudden decrease in amount of urine)			√
Sterile pyuria (cloudy urine)			√
Thrombocytopenia (unusual bleeding or bruising; black, tarry stools; blood in urine or stools; pinpoint red spots on skin)			√

If you have a troublesome symptom or side effect that is not listed here or becomes bad enough to interfere with your daily activities, tell your healthcare professional.

Reporting Side Effects

You can report any suspected side effects associated with the use of health products to Health Canada by:

- Visiting the Web page on Adverse Reaction Reporting (https://www.canada.ca/en/health-canada/services/drugs-health-products/medeffect-canada.html) for information on how to report online, by mail or by fax; or
- Calling toll-free at 1-866-234-2345.

NOTE: Contact your health professional if you need information about how to manage your side effects. The Canada Vigilance Program does not provide medical advice.

Storage:

- Store between 15°C and 25°C.
- Keep out of reach and sight or children.

If you want more information about ACET 120 / ACET 160 / ACET 325 / ACET 650:

- Talk to your healthcare professional

- Find the full product monograph that is prepared for healthcare professionals and includes this Patient Medication Information by visiting the Health Canada website: (https://www.canada.ca/en/health-canada/services/drugs-health-products/drug-products/drug-product-database.html; or by calling 1-888-550-6060.

This leaflet was prepared by PENDOPHARM, Division of Pharmascience Inc.

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