Approved Date: November 25th,2009
Revision Date: January 25th, 2016

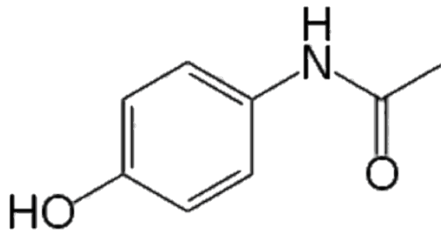
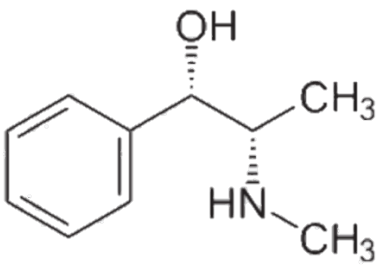
Package Insert of
Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II/ Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets.

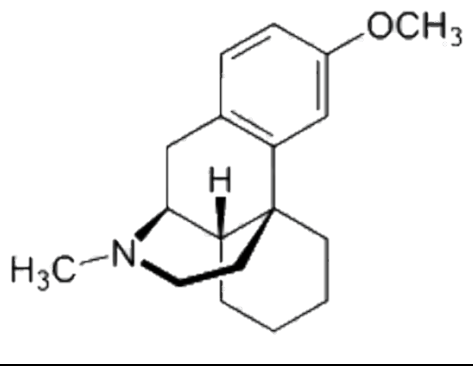
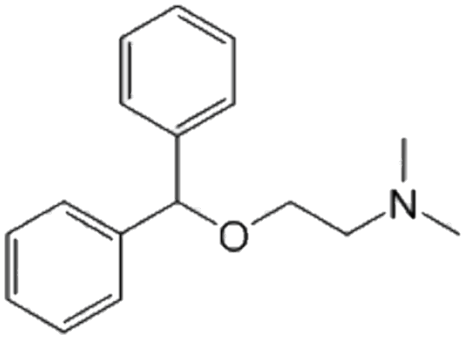
Please read the package insert carefully and use according to doctor's instructions.

[Drug Name]
Generic Name: Paracetamol, Pseudoephedrine and Dextromethorphan Hydrobromide Tablets II/Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets
Chinese Pinyin: Anfen Weima Meifen Pian II/ An Ma Ben Mei Pian

[Ingredients]
This product is a compound formulation:
Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II (DAY TABLETS):
Active ingredient: Acetaminophen 325 mg, Pseudoephedrine Hydrochloride 30 mg, Dextromethorphan Hydrobromide 15 mg.
Inactive ingredient: Corn starch, Low-Substituted Hydroxypropyl Cellulose, Povidone, Polyvinyl pyrrolidone, Magnesium Stearate, Film coating dry suspension.
Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets (NIGHT TABLETS):
Active ingredient: Acetaminophen 325 mg, Pseudoephedrine Hydrochloride 30 mg, Dextromethorphan Hydrobromide 15 mg, Diphenhydramine Hydrochloride 25 mg.
Inactive ingredient: Microcrystalline Cellulose, Low-Substituted Hydroxypropyl Cellulose, Povidone, Polyvinyl pyrrolidone, Magnesium Stearate, Film coating dry suspension.

Structure formula:

Acetaminophen	Pseudoephedrine
	
$C_8H_9NO_2$	$C_{10}H_{15}NO$
Molecular weight: 151.163	Molecular weight: 165.2322
Dextromethorphan	Diphenhydramine

	
$C_{18}H_{25}NO$	$C_{17}H_{21}NO$
Molecular weight: 271.40	Molecular weight: 255.355

[Properties]
This product is a film-coated tablets and the core inside is white or off-white.

[Classification]
OTC use for common cold.

[Indication]
This product is indicated for relieve of fever, headache, muscle pain, sneeze, rhinorrhea, nasal congestion, cough, pharyngalgia caused by common cold or flu.

[Strength]
Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II (DAY TABLETS): Acetaminophen 325 mg, Pseudoephedrine Hydrochloride 30 mg, Dextromethorphan Hydrobromide 15 mg.

Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets (NIGHT TABLETS): Acetaminophen 325 mg, Pseudoephedrine Hydrochloride 30 mg, Dextromethorphan Hydrobromide 15 mg, Diphenhydramine Hydrochloride 25 mg.

[Dosage and Administration]

Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II (DAY TABLETS):

Oral administration, adult or children above 12 years old, 1~2 tablets once, twice a day or every 6 hours during day time.

Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets (NIGHT TABLETS):

Oral administration, adult or children above 12 years old, 1~2 tablets before sleep.

[Adverse Reactions]

Acetaminophen:

Common

Dermatologic: Pruritus (5% or greater)

Gastrointestinal: Constipation (5% or greater), Nausea (adult, 34%; pediatric, 5% or greater), Vomiting (adult, 15%; pediatric, 5% or greater)

Neurologic: Headache (1% to 10%), Insomnia (1% to 7%)

Psychiatric: Agitation (5% or greater)

Respiratory: Atelectasis (5% or greater)

Serious

Dermatologic: Generalized exanthematous, pustulosis, acute, Stevens-Johnson syndrome, Toxic epidermal necrolysis.

Hepatic: Liver failure

Respiratory: Pneumonitis

Pseudoephedrine:

Common

Cardiovascular: Hypertension, Tachyarrhythmia

Neurologic: Insomnia

Psychiatric: Anxiety, Feeling nervous, Restlessness

Serious

Cardiovascular: Atrial fibrillation, Myocardial infarction, Ventricular premature beats

Dextromethorphan:

Common

Neurologic: Dizziness (mild), Somnolence (mild)

Other: Fatigue (mild)

Diphenhydramine:

Common

Gastrointestinal: Xerostomia

Neurologic: Dizziness, Dyskinesia, Sedated

Psychiatric: Somnlence

Respiratory: Nasal mucosa dry, Pharyngeal dryness, Thick sputum, Bronchial

Serious

Immunologic: Anaphylaxis

[Contraindications]
Acetaminophen:
Active and severe hepatic disease
Hypersensitivity to acetaminophen and other components of this product
Severe hepatic impairment

Pseudoephedrine:
Coronary artery disease, severe
Hypersensitivity to pseudoephedrine or sympathomimetics

Hypertension, severe
Monoamine oxidase inhibitor (MAOI) therapy

Dextromethorphan:
Concurrent or within 14 days of Monoamine oxidase inhibitors (MAOIs) use.

Diphenhydramine Hydrochloride
Hypersensitivity to diphenhydrAMINE and other similar antihistamines.
Newborns or premature infants
Nursing mothers
Use as a local anesthetic

[Precautions]
Acetaminophen

Hepatotoxicity: Do not exceed the maximum recommended daily dose (>4 g daily in adults). In addition, chronic daily dosing may also result in liver damage in some patients.

Hypersensitivity/anaphylactic reactions: Hypersensitivity and anaphylactic reactions have been reported; discontinue immediately if symptoms of allergic or hypersensitivity reactions occur.

Skin reactions: Serious and potentially fatal skin reactions, including acute generalized exanthematous pustulosis (AGEP), Stevens-Johnson syndrome (SJS), and toxic epidermal necrolysis (TEN) have occurred rarely with acetaminophen use. Discontinue therapy at the first appearance of skin rash.

Ethanol use: Use with caution in patients with alcoholic liver disease; consuming ≥ 3 alcoholic drinks/day may increase the risk of liver damage.

G6PD deficiency: Use with caution in patients with known G6PD deficiency.

Hepatic impairment: Use with caution in patients with hepatic impairment or active liver disease.

Malnutrition: Use with caution in patients with chronic malnutrition.

Renal impairment: Use with caution in patients with severe renal impairment; consider dosing adjustments.

Aspartame: Some products may contain aspartame, which is metabolized to phenylalanine and must be avoided (or used with caution) in patients with phenylketonuria.

When used for self-medication, if symptoms get worse or new symptoms appear, redness or swelling is present in the painful area, fever lasts > 3 days (all ages), or pain (excluding sore throat) lasts longer than: Adults: 10 days, Children and Adolescents: 5 days, Infants: 3 days. When treating children with sore throat, if sore throat is severe, persists for > 2 days, or is followed by fever, rash, headache, nausea, or vomiting, consult health care provider immediately.

Pseudoephedrine

Cardiovascular disease: Use with caution in patients with cardiovascular disease (including hypertension and ischemic heart disease).

Diabetes: Use with caution in patients with diabetes mellitus.

Increased intraocular pressure/glaucoma: Use with caution in patients with increased intraocular pressure or angle-closure glaucoma.

Prostatic hyperplasia/urinary obstruction: Use with caution in patients with prostatic hyperplasia and/or GU obstruction.

Renal impairment: Use caution in patient with renal impairment; consider dosage adjustments.

Seizure disorder: Use with caution in patients with seizure disorder; may produce CNS stimulation.

Thyroid dysfunction: Use with caution in patients with thyroid dysfunction.

Special populations: Elderly: Use with caution in the elderly; may be more sensitive to adverse effects.

Self-medication (OTC use): If symptoms do not improve within 7 days or are accompanied by fever. Discontinue and contact healthcare provider if nervousness, dizziness, or sleeplessness occur. Not for OTC use in children < 4 years of age.

Dextromethorphan

Serotonin syndrome: Symptoms of agitation, confusion, hallucinations, hyper-reflexia, myoclonus, shivering, and tachycardia may occur with concomitant proserotonergic drugs (ie, SSRIs/SNRIs or triptans); especially with higher dextromethorphan doses.

Special populations:

CYP2D6 poor metabolizers: Dextromethorphan is metabolized by hepatic CYP2D6. Poor metabolizers of CYP2D6 may have exaggerated or prolonged effects of dextromethorphan. Increased risk may be seen with concomitant use of potent CYP2D6 inhibitors; use with caution.

Debilitated patients: Use with caution in patients who are sedated, debilitated or confined to a supine position.

Pediatric: Use with caution in atopic children. Not for OTC use in children < 4 years of age.

Abuse/misuse: Be alert to problems of abuse or misuse. Abuse can cause death, brain damage, seizure, loss of consciousness, and irregular heartbeat.

Self-medication (OTC use): When used for self-medication (OTC) if symptoms do not improve within 7 days, or are accompanied by fever, rash or persistent headache. Do not use for persistent or chronic cough (as with smoking, asthma, chronic bronchitis, emphysema) or if cough is accompanied by excessive phlegm unless directed to do so by healthcare provider.

Diphenhydramine

CNS depression: May cause CNS depression, which may impair physical or mental abilities; patients must be cautioned about performing tasks which require mental alertness (eg, operating machinery or driving).

Asthma: Use with caution in patients with a history of asthma.

Cardiovascular disease: Use with caution in patients with cardiovascular disease (including hypertension and ischemic heart disease).

Increased intraocular pressure/glaucoma: Use with caution in patients with increased intraocular pressure or angle-closure glaucoma.

Prostatic hyperplasia/urinary obstruction: Use with caution in patients with prostatic hyperplasia, bladder neck obstruction, and/or GU obstruction.

Pyloroduodenal obstruction: Use with caution in patients with pyloroduodenal obstruction (including stenotic peptic ulcer).

Thyroid dysfunction: Use with caution in patients with thyroid dysfunction.

Potentially significant interactions may exist, requiring dose or frequency adjustment, additional monitoring, and/or selection of alternative therapy. Consult drug interactions database for more detailed information.

Special populations: Pediatric: Antihistamines may cause excitation in young children. Toxicity (overdose) in pediatric patients may result in hallucinations, convulsions, or death; neonates and young children are highly sensitive to depressive effects of diphenhydramine; use is contraindicated in neonates and premature infants.

Self-medication (OTC use): Do not use with other products containing diphenhydramine, even ones used on the skin. Oral products are not for OTC use in children < 6 years of age.

[Use in Pregnant and Lactation]

Acetaminophen:

Acetaminophen crosses the placenta and can be detected in cord blood, newborn serum, and urine immediately after delivery. An increased risk of teratogenic effects has not been observed following maternal use of acetaminophen during pregnancy. Prenatal constriction of the ductus arteriosus has been noted in case reports following maternal use during the third trimester. The use of acetaminophen in normal doses during pregnancy is not associated with an increased risk of miscarriage or still birth; however, an increase in fetal death or spontaneous abortion may be seen following maternal overdose if treatment is delayed. Frequent maternal use of acetaminophen during pregnancy may be associated with wheezing and asthma in early childhood.

Acetaminophen is excreted in breast milk.
Acetaminophen can be detected in the urine of nursing infants. Except for a single case report of a rash, adverse reactions have generally not been observed in nursing infants. Current guidelines note that nonopioid analgesics are preferred for the treatment of pain in breastfeeding women and acetaminophen is one of the preferred nonopioid agents. Acetaminophen is considered compatible with breast-feeding when used in usual recommended doses.

Pseudoephedrine:
Use of pseudoephedrine during the first trimester may be associated with a possible risk of gastroschisis, small intestinal atresia, and hemifacial microsomia due to pseudoephedrine's vasoconstrictive effects; additional studies are needed to define the magnitude of risk. Single doses of pseudoephedrine were not found to adversely affect the fetus during the third trimester of pregnancy (limited data); however, fetal tachycardia was noted in a case report following maternal use of an extended release product for multiple days. Decongestants are not the preferred agents for the treatment of rhinitis during pregnancy. Oral pseudoephedrine should be avoided during the first trimester.

Pseudoephedrine is present in breast milk. Irritability and agitation has been reported in infants exposed to pseudoephedrine via breast milk.
The relative infant dose (RID) of pseudoephedrine is 6.7%. In general, breastfeeding is considered acceptable when the RID is <10%.

Dextromethorphan:
When an antitussive is needed during pregnancy, dextromethorphan standard at standard OTC doses is generally considered acceptable.
Information related to the presence of dextromethorphan in breast milk has not been located. Data are not available to make recommendations for use in breastfeeding women (WHO 2002).

Diphenhydramine:
Adverse events have not been observed in animal reproduction studies. Diphenhydramine crosses the placenta. In general, the use of first generation antihistamines immediately before parturition may cause respiratory depression in the newborn. Diphenhydramine may be used for the treatment of allergic conditions in pregnant women when a first generation antihistamine is indicated. Antihistamines are not recommended for treatment of pruritus associated with intrahepatic cholestasis in pregnancy.

Diphenhydramine is present in breast milk. Drowsiness and irritability have been reported in breastfed infants exposed to antihistamines; of these effects, drowsiness was reported in infants exposed to diphenhydramine In general, if a breastfed infant is exposed to a first generation antihistamine via breast milk, they should be monitored for irritability or drowsiness.

[Drug Interactions]
Dasatinib: ACETAMINOPHEN may enhance the hepatotoxic effect of Dasatinib. Dasatinib may increase the serum concentration of Acetaminophen.
SORAfenib: ACETAMINOPHEN may enhance the hepatotoxic effect of SORAfenib. SORAfenib may increase the serum concentration of Acetaminophen.
Benzylpenicilloyl Polylysine: PSEUDOEPHEDRINE may diminish the diagnostic effect of Benzylpenicilloyl Polylysine.
Ergot Derivatives: May enhance the hypertensive effect of PSEUDOEPHEDRINE. Ergot Derivatives may enhance the vasoconstricting effect of PSEUDOEPHEDRINE. **Exceptions: Ergoloid Mesylates, Avoid combination.**
Iobenguane Radiopharmaceutical Products: PSEUDOEPHEDRINE (Indirect-Acting) may diminish the therapeutic effect of Iobenguane Radiopharmaceutical Products.
Monoamine Oxidase Inhibitors: May enhance the hypertensive effect of PSEUDOEPHEDRINE (Indirect-Acting). While linezolid is expected to interact via this mechanism, management recommendations differ from other monoamine oxidase inhibitors. **Linezolid, Avoid combination**.
Serotonin/Norepinephrine Reuptake Inhibitors: May enhance the tachycardic effect of PSEUDOEPHEDRINE.

[Pharmacology]

Acetaminophen	Pseudoephedrine Hydrochloride	Dextromethorphan Hydrobromide	Diphenhydramine Hydrochloride

Although not fully elucidated, the analgesic effects are believed to be due to activation of descending serotonergic inhibitory pathways in the CNS. Interactions with other nociceptive systems may be involved as well. Antipyresis is produced from inhibition of the hypothalamic heat-regulating center.	Directly stimulates alpha-adrenergic receptors of respiratory mucosa causing vasoconstriction; directly stimulates beta-adrenergic receptors causing bronchial relaxation, increased heart rate and contractility	Decreases the sensitivity of cough receptors and interrupts cough impulse transmission by depressing the medullary cough center through sigma receptor stimulation; structurally related to codeine	Competes with histamine for H1-receptor sites on effector cells in the gastrointestinal tract, blood vessels, and respiratory tract; anticholinergic and sedative effects are also seen

[Storage]
Seal and store away from direct sunlight.

[Packaging]
Aluminum-plastic blister packaging, DAY TABLETS: 10 tablets/plate, one plate/carton
NIGHT TABLETS: 5 tablets/plate, one plate/carton
Aluminum-plastic blister packaging, DAY TABLETS: 12 tablets/plate, one plate/carton
NIGHT TABLETS: 6 tablets/plate, one plate/carton
Aluminum-plastic blister packaging, DAY TABLETS: 7 tablets/plate, two plates/carton
NIGHT TABLETS: 7 tablets/plate, one plate/carton
Aluminum-plastic blister packaging, DAY TABLETS: 8 tablets/plate, two plates/carton
NIGHT TABLETS: 8 tablets/plate, one plate/carton

[Shelf-Life]
24 months

[Executive Standard]
Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II (DAY TABLET):
National Medical Products Agency Standard YBH09522009

Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets (NIGHT TABLET):
National Medical Products Agency Standard YBH09482009

[Approval Number]
Paracetamol, Pseudoephedrine Hydrochloride and Dextromethorphan Hydrobromide Tablets II (DAY TABLET):
Guo Yao Zhun Zi H20094121

Paracetamol, Pseudoephedrine Hydrochloride, Diphenhydramine Hydrochloride and Dextromethorphan Hydrobromide Tablets (NIGHT TABLET):
Guo Yao Zhun Zi H20094117

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