EFFIENT - prasugrel hydrochloride tablet, film coated
Physicians Total Care, Inc.

HIGHLIGHTS OF PRESCRIBING INFORMATION
These highlights do not include all the information needed to use Effient safely and effectively. See full prescribing information for Effient.
EFFIENT (prasugrel) tablets
Initial U.S. Approval: 2009

WARNING: BLEEDING RISK

See full prescribing information for complete boxed warning

Effient can cause significant, sometimes fatal, bleeding (5.1, 5.2, and 6.1).
Do not use Effient in patients with active pathological bleeding or a history of transient ischemic attack or stroke (4.1 and 4.2).
In patients ≥ 75 years of age, Effient is generally not recommended because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk patients (diabetes or prior MI), where its effect appears to be greater and its use may be considered (8.5).
Do not start Effient in patients likely to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue Effient at least 7 days prior to any surgery.
Additional risk factors for bleeding include:

- **body weight < 60 kg**
- **propensity to bleed**
- **concomitant use of medications that increase the risk of bleeding**

Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of Effient. If possible, manage bleeding without discontinuing Effient. Stopping Effient, particularly in the first few weeks after acute coronary syndrome, increases the risk of subsequent cardiovascular events (5.3).

RECENT MAJOR CHANGES

Contraindications, Hypersensitivity (4.3) 12/2010
Warnings and Precautions, Thrombotic Thrombocytopenic Purpura (5.4) 12/2010

INDICATIONS AND USAGE

Effient is a $P2Y_{12}$ platelet inhibitor indicated for the reduction of thrombotic cardiovascular events (including stent thrombosis) in patients with acute coronary syndrome who are to be managed with PCI as follows:

- Patients with unstable angina or, non-ST-elevation myocardial infarction (NSTEMI) (1.1).
- Patients with ST-elevation myocardial infarction (STEMI) when managed with either primary or delayed PCI (1.1).

DOSAGE AND ADMINISTRATION

- Initiate treatment with a single 60 mg oral loading dose (2).
- Continue at 10 mg once daily with or without food. Consider 5 mg once daily for patients <60 kg (2).
- Patients should also take aspirin (75 mg to 325 mg) daily (2).

DOSAGE FORMS AND STRENGTHS

5 mg and 10 mg tablets (3)

CONTRAINDICATIONS

- Active pathological bleeding (4.1)
- Prior transient ischemic attack or stroke (4.2)
- Hypersensitivity to prasugrel or any component of the product (4.3)

WARNINGS AND PRECAUTIONS

- CABG-related bleeding: Risk increases in patients receiving Effient who undergo CABG (5.2).
- Discontinuation of Effient: Premature discontinuation increases risk of stent thrombosis, MI, and death (5.3).
- Thrombotic thrombocytopenic purpura (TTP): TTP has been reported with Effient (5.4).

ADVERSE REACTIONS

Bleeding, including life-threatening and fatal bleeding, is the most commonly reported adverse reaction (6.1).
To report SUSPECTED ADVERSE REACTIONS, contact Eli Lilly and Company at 1-800-545-5979 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

See 17 for PATIENT COUNSELING INFORMATION and Medication Guide.

Revised: 3/2011

FULL PRESCRIBING INFORMATION: CONTENTS*

17.3 Other Signs and Symptoms Requiring Medical Attention
17.4 Invasive Procedures
17.5 Concomitant Medications

* Sections or subsections omitted from the full prescribing information are not listed.

FULL PRESCRIBING INFORMATION

WARNING: BLEEDING RISK

Effient can cause significant, sometimes fatal, bleeding *[see Warnings and Precautions (5.1 and 5.2) and Adverse Reactions (6.1)]*.

Do not use Effient in patients with active pathological bleeding or a history of transient ischemic attack or stroke *[see Contraindications (4.1 and 4.2)]*.

In patients ≥ 75 years of age, Effient is generally not recommended, because of the increased risk of fatal and intracranial bleeding and uncertain benefit, except in high-risk situations (patients with diabetes or a history of prior MI) where its effect appears to be greater and its use may be considered *[see Use in Specific Populations (8.5)]*.

Do not start Effient in patients likely to undergo urgent coronary artery bypass graft surgery (CABG). When possible, discontinue Effient at least 7 days prior to any surgery.

Additional risk factors for bleeding include:

- **body weight < 60 kg**
- **propensity to bleed**
- **concomitant use of medications that increase the risk of bleeding (*e.g.*, warfarin, heparin, fibrinolytic therapy, chronic use of non-steroidal anti-inflammatory drugs [NSAIDS])**

Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, percutaneous coronary intervention (PCI), CABG, or other surgical procedures in the setting of Effient.

If possible, manage bleeding without discontinuing Effient. Discontinuing Effient, particularly in the first few weeks after acute coronary syndrome, increases the risk of subsequent cardiovascular events *[see Warnings and Precautions (5.3)]*.

1 INDICATIONS AND USAGE

1.1 Acute Coronary Syndrome

Effient™ is indicated to reduce the rate of thrombotic cardiovascular (CV) events (including stent thrombosis) in patients with acute coronary syndrome (ACS) who are to be managed with percutaneous coronary intervention (PCI) as follows:

- Patients with unstable angina (UA) or non-ST-elevation myocardial infarction (NSTEMI).
- Patients with ST-elevation myocardial infarction (STEMI) when managed with primary or delayed PCI.

Effient has been shown to reduce the rate of a combined endpoint of cardiovascular death, nonfatal myocardial infarction (MI), or nonfatal stroke compared to clopidogrel. The difference between treatments was driven predominantly by MI, with no difference on strokes and little difference on CV death *[see Clinical Studies (14)]*.

It is generally recommended that antiplatelet therapy be administered promptly in the management of ACS because many cardiovascular events occur within hours of initial presentation. In the clinical trial that established the efficacy of Effient, Effient and the control drug were not administered to UA/NSTEMI patients until coronary anatomy was established. For the small fraction of patients that required urgent CABG after treatment with Effient, the risk of significant bleeding was substantial *[see Warnings and Precautions (5.2)]*. Because the large majority of patients are managed without CABG, however, treatment can be considered before determining coronary anatomy if need for CABG is considered unlikely. The advantages of earlier treatment with Effient must then be balanced against the increased rate of bleeding in patients who do need to undergo urgent CABG.

2 DOSAGE AND ADMINISTRATION

Initiate Effient treatment as a single 60 mg oral loading dose and then continue at 10 mg orally once daily. Patients taking Effient should also take aspirin (75 mg to 325 mg) daily *[see Drug Interactions (7) and Clinical Pharmacology (12.3)]*. Effient may be administered with or without food *[see Clinical Pharmacology (12.3) and Clinical Studies (14)]*.

Dosing in Low Weight Patients

Compared to patients weighing ≥ 60 kg, patients weighing < 60 kg have an increased exposure to the active metabolite of prasugrel and an increased risk of bleeding on a 10 mg once daily maintenance dose. Consider lowering the maintenance dose to 5 mg in patients < 60 kg. The effectiveness and safety of the 5 mg dose have not been prospectively studied.

3 DOSAGE FORMS AND STRENGTHS

Effient 5 mg is a yellow, elongated hexagonal, film-coated, non-scored tablet debossed with “5 MG” on one side and “4760” on the other side.

Effient 10 mg is a beige, elongated hexagonal, film-coated, non-scored tablet debossed with “10 MG” on one side and with “4759” on the other side.

4 CONTRAINDICATIONS

4.1 Active Bleeding

Effient is contraindicated in patients with active pathological bleeding such as peptic ulcer or intracranial hemorrhage *[see Warnings and Precautions (5.1) and Adverse Reactions (6.1)]*.

4.2 Prior Transient Ischemic Attack or Stroke

Effient is contraindicated in patients with a history of prior transient ischemic attack (TIA) or stroke. In TRITON-TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel), patients with a history of TIA or ischemic stroke (> 3 months prior to enrollment) had a higher rate of stroke on Effient (6.5%; of which 4.2% were thrombotic stroke and 2.3% were intracranial hemorrhage [ICH]) than on clopidogrel (1.2%; all thrombotic). In patients without such a history, the incidence of stroke was 0.9% (0.2% ICH) and 1.0% (0.3% ICH) with Effient and clopidogrel, respectively. Patients with a history of ischemic stroke within 3 months of screening and patients with a history of hemorrhagic stroke at any time were excluded from TRITON-TIMI 38. Patients who experience a stroke or TIA while on Effient generally should have therapy discontinued *[see Adverse Reactions (6.1) and Clinical Studies (14)]*.

4.3 Hypersensitivity

Effient is contraindicated in patients with hypersensitivity (e.g., anaphylaxis) to prasugrel or any component of the product *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS

5.1 General Risk of Bleeding

Thienopyridines, including Effient, increase the risk of bleeding. With the dosing regimens used in TRITON-TIMI 38, TIMI (Thrombolysis in Myocardial Infarction) Major (clinically overt bleeding associated with a fall in hemoglobin ≥ 5 g/dL, or intracranial hemorrhage) and TIMI Minor (overt bleeding associated with a fall in hemoglobin of ≥ 3 g/dL but < 5 g/dL) bleeding events were more common on Effient than on clopidogrel *[see Adverse Reactions (6.1)]*. The bleeding risk is highest initially, as shown in Figure 1 (events through 450 days; inset shows events through 7 days).

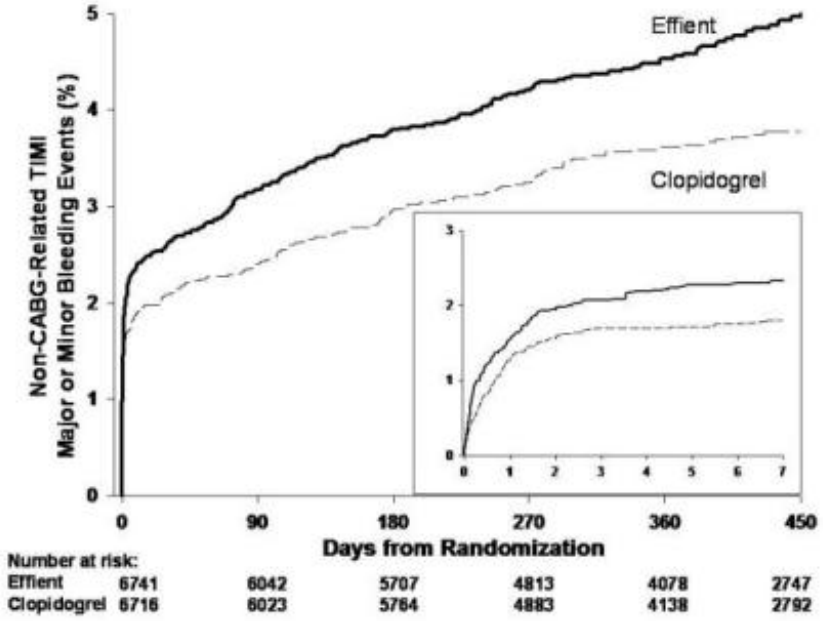


Figure 1: Non-CABG-Related TIMI Major or Minor Bleeding Events

Suspect bleeding in any patient who is hypotensive and has recently undergone coronary angiography, PCI, CABG, or other surgical procedures even if the patient does not have overt signs of bleeding.

Do not use Effient in patients with active bleeding, prior TIA or stroke *[see Contraindications (4.1 and 4.2)]*.

Other risk factors for bleeding are:

- Age ≥ 75 years. Because of the risk of bleeding (including fatal bleeding) and uncertain effectiveness in patients ≥ 75 years of age, use of Effient is generally not recommended in these patients, except in high-risk situations (patients with diabetes or history of myocardial infarction) where its effect appears to be greater and its use may be considered *[see Adverse Reactions (6.1), Use in Specific Populations (8.5), Clinical Pharmacology (12.3), and Clinical Trials (14)]*.
- CABG or other surgical procedure *[see Warnings and Precautions (5.2)]*.
- Body weight < 60 kg. Consider a lower (5 mg) maintenance dose *[see Dosage and Administration (2), Adverse Reactions (6.1), Use in Specific Populations (8.6)]*.
- Propensity to bleed (e.g., recent trauma, recent surgery, recent or recurrent gastrointestinal (GI) bleeding, active peptic ulcer disease, or severe hepatic impairment) *[see Adverse Reactions (6.1) and Use in Specific Populations (8.8)]*.
- Medications that increase the risk of bleeding (*e.g.*, oral anticoagulants, chronic use of non-steroidal anti-inflammatory drugs [NSAIDs], and fibrinolytic agents). Aspirin and heparin were commonly

used in TRITON-TIMI 38 *[see Drug Interactions (7), Clinical Studies (14)]*.

Thienopyridines inhibit platelet aggregation for the lifetime of the platelet (7-10 days), so withholding a dose will not be useful in managing a bleeding event or the risk of bleeding associated with an invasive procedure. Because the half-life of prasugrel's active metabolite is short relative to the lifetime of the platelet, it may be possible to restore hemostasis by administering exogenous platelets; however, platelet transfusions within 6 hours of the loading dose or 4 hours of the maintenance dose may be less effective.

5.2 Coronary Artery Bypass Graft Surgery-Related Bleeding

The risk of bleeding is increased in patients receiving Effient who undergo CABG. If possible, Effient should be discontinued at least 7 days prior to CABG.

Of the 437 patients who underwent CABG during TRITON-TIMI 38, the rates of CABG-related TIMI Major or Minor bleeding were 14.1% in the Effient group and 4.5% in the clopidogrel group *[see Adverse Reactions (6.1)]*. The higher risk for bleeding events in patients treated with Effient persisted up to 7 days from the most recent dose of study drug. For patients receiving a thienopyridine within 3 days prior to CABG, the frequencies of TIMI Major or Minor bleeding were 26.7% (12 of 45 patients) in the Effient group, compared with 5.0% (3 of 60 patients) in the clopidogrel group. For patients who received their last dose of thienopyridine within 4 to 7 days prior to CABG, the frequencies decreased to 11.3% (9 of 80 patients) in the prasugrel group and 3.4% (3 of 89 patients) in the clopidogrel group.

Do not start Effient in patients likely to undergo urgent CABG. CABG-related bleeding may be treated with transfusion of blood products, including packed red blood cells and platelets; however, platelet transfusions within 6 hours of the loading dose or 4 hours of the maintenance dose may be less effective.

5.3 Discontinuation of Effient

Discontinue thienopyridines, including Effient, for active bleeding, elective surgery, stroke, or TIA. The optimal duration of thienopyridine therapy is unknown. In patients who are managed with PCI and stent placement, premature discontinuation of any antiplatelet medication, including thienopyridines, conveys an increased risk of stent thrombosis, myocardial infarction, and death. Patients who require premature discontinuation of a thienopyridine will be at increased risk for cardiac events. Lapses in therapy should be avoided, and if thienopyridines must be temporarily discontinued because of an adverse event(s), they should be restarted as soon as possible *[see Contraindications (4.1 and 4.2) and Warnings and Precautions (5.1)]*.

5.4 Thrombotic Thrombocytopenic Purpura

Thrombotic thrombocytopenic purpura (TTP) has been reported with the use of Effient. TTP can occur after a brief exposure (< 2 weeks). TTP is a serious condition that can be fatal and requires urgent treatment, including plasmapheresis (plasma exchange). TTP is characterized by thrombocytopenia, microangiopathic hemolytic anemia (schistocytes [fragment red blood cells] seen on peripheral smear), neurological findings, renal dysfunction, and fever *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

6.1 Clinical Trials Experience

The following serious adverse reactions are also discussed elsewhere in the labeling:

- Bleeding *[see Boxed Warning and Warnings and Precautions (5.1, 5.2)]*
- Thrombotic thrombocytopenic purpura *[see Warnings and Precautions (5.4)]*

Safety in patients with ACS undergoing PCI was evaluated in a clopidogrel-controlled study, TRITON-

TIMI 38, in which 6741 patients were treated with Effient (60 mg loading dose and 10 mg once daily) for a median of 14.5 months (5802 patients were treated for over 6 months; 4136 patients were treated for more than 1 year). The population treated with Effient was 27 to 96 years of age, 25% female, and 92% Caucasian. All patients in the TRITON-TIMI 38 study were to receive aspirin. The dose of clopidogrel in this study was a 300 mg loading dose and 75 mg once daily.

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials cannot be directly compared with the rates observed in other clinical trials of another drug and may not reflect the rates observed in practice.

Drug Discontinuation

The rate of study drug discontinuation because of adverse reactions was 7.2% for Effient and 6.3% for clopidogrel. Bleeding was the most common adverse reaction leading to study drug discontinuation for both drugs (2.5% for Effient and 1.4% for clopidogrel).

Bleeding

Bleeding Unrelated to CABG Surgery - In TRITON-TIMI 38, overall rates of TIMI Major or Minor bleeding adverse reactions unrelated to coronary artery bypass graft surgery (CABG) were significantly higher on Effient than on clopidogrel, as shown in Table 1.

Table 1: Non-CABG-Related Bleeding[a] (TRITON-TIMI 38)

	Effient (%) (N=6741)	**Clopidogrel (%) (N=6716)**	**p-value**
TIMI Major or Minor bleeding	4.5	3.4	p=0.002
TIMI Major bleeding[b]	2.2	1.7	p=0.029
Life-threatening	1.3	0.8	p=0.015
Fatal	0.3	0.1	
Symptomatic intracranial hemorrhage (ICH)	0.3	0.3	
Requiring inotropes	0.3	0.1	
Requiring surgical intervention	0.3	0.3	
Requiring transfusion (≥4 units)	0.7	0.5	
TIMI Minor bleeding[b]	2.4	1.9	p=0.022

[a] Patients may be counted in more than one row.
[b] See 5.1 for definition.

Figure 1 demonstrates non-CABG related TIMI Major or Minor bleeding. The bleeding rate is highest initially, as shown in Figure 1 (inset: Days 0 to 7) *[see Warnings and Precautions (5.1)]*.

Bleeding rates in patients with the risk factors of age ≥ 75 years and weight < 60 kg are shown in Table 2.

Table 2: Bleeding Rates for Non-CABG-Related Bleeding by Weight and Age (TRITON-TIMI 38)

	Major/Minor		**Fatal**	
	Effient (%)	**Clopidogrel (%)**	**Effient (%)**	**Clopidogrel (%)**
Weight < 60 kg (N=308 Effient, N=356 clopidogrel)	10.1	6.5	0.0	0.3
Weight ≥ 60 kg (N=6373 Effient,	4.2	3.3	0.3	0.1

N=6299 clopidogrel)				
Age < 75 years (N=5850 Effient, N=5822 clopidogrel)	3.8	2.9	0.2	0.1
Age ≥ 75 years (N=891 Effient, N=894 clopidogrel)	9.0	6.9	1.0	0.1

Bleeding Related to CABG - In TRITON-TIMI 38, 437 patients who received a thienopyridine underwent CABG during the course of the study. The rate of CABG-related TIMI Major or Minor bleeding was 14.1% for the Effient group and 4.5% in the clopidogrel group (Table 3). The higher risk for bleeding adverse reactions in patients treated with Effient persisted up to 7 days from the most recent dose of study drug.

Table 3: CABG-Related Bleeding[a] (TRITON-TIMI 38)

	Effient (%) (N=213)	**Clopidogrel (%) (N=224)**
TIMI Major or Minor bleeding	14.1	4.5
TIMI Major bleeding	11.3	3.6
Fatal	0.9	0
Reoperation	3.8	0.5
Transfusion of ≥5 units	6.6	2.2
Intracranial hemorrhage	0	0
TIMI Minor bleeding	2.8	0.9

[a] Patients may be counted in more than one row.

Bleeding Reported as Adverse Reactions - Hemorrhagic events reported as adverse reactions in TRITON-TIMI 38 were, for Effient and clopidogrel, respectively: epistaxis (6.2%, 3.3%), gastrointestinal hemorrhage (1.5%, 1.0%), hemoptysis (0.6%, 0.5%), subcutaneous hematoma (0.5%, 0.2%), post-procedural hemorrhage (0.5%, 0.2%), retroperitoneal hemorrhage (0.3%, 0.2%), pericardial effusion/hemorrhage/tamponade (0.3%, 0.2%), and retinal hemorrhage (0.0%, 0.1%).

Malignancies

During TRITON-TIMI 38, newly diagnosed malignancies were reported in 1.6% and 1.2% of patients treated with prasugrel and clopidogrel, respectively. The sites contributing to the differences were primarily colon and lung. It is unclear if these observations are causally-related or are random occurrences.

Other Adverse Events

In TRITON-TIMI 38, common and other important non-hemorrhagic adverse events were, for Effient and clopidogrel, respectively: severe thrombocytopenia (0.06%, 0.04%), anemia (2.2%, 2.0%), abnormal hepatic function (0.22%, 0.27%), allergic reactions (0.36%, 0.36%), and angioedema (0.06%, 0.04%). Table 4 summarizes the adverse events reported by at least 2.5% of patients.

Table 4: Non-Hemorrhagic Treatment Emergent Adverse Events Reported by at Least 2.5% of Patients in Either Group

	Effient (%) (N=6741)	Clopidogrel (%) (N=6716)
Hypertension	7.5	7.1
Hypercholesterolemia/Hyperlipidemia	7.0	7.4
Headache	5.5	5.3
Back pain	5.0	4.5

Dyspnea	4.9	4.5
Nausea	4.6	4.3
Dizziness	4.1	4.6
Cough	3.9	4.1
Hypotension	3.9	3.8
Fatigue	3.7	4.8
Non-cardiac chest pain	3.1	3.5
Atrial fibrillation	2.9	3.1
Bradycardia	2.9	2.4
Leukopenia (< 4 x 10^9 WBC/L)	2.8	3.5
Rash	2.8	2.4
Pyrexia	2.7	2.2
Peripheral edema	2.7	3.0
Pain in extremity	2.6	2.6
Diarrhea	2.3	2.6

6.2 Postmarketing Experience

The following adverse reactions have been identified during post approval use of Effient. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Blood and lymphatic system disorders - Thrombocytopenia, Thrombotic thrombocytopenic purpura (TTP) *[see Warnings and Precautions (5.4) and Patient Counseling Information (17.3)]*

Immune system disorders - Hypersensitivity reactions including anaphylaxis *[see Contraindications (4.3)]*

7 DRUG INTERACTIONS

7.1 Warfarin

Coadministration of Effient and warfarin increases the risk of bleeding *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

7.2 Non-Steroidal Anti-Inflammatory Drugs

Coadministration of Effient and NSAIDs (used chronically) may increase the risk of bleeding *[see Warnings and Precautions (5.1)]*.

7.3 Other Concomitant Medications

Effient can be administered with drugs that are inducers or inhibitors of cytochrome P450 enzymes *[see Clinical Pharmacology (12.3)]*.

Effient can be administered with aspirin (75 mg to 325 mg per day), heparin, GPIIb/IIIa inhibitors, statins, digoxin, and drugs that elevate gastric pH, including proton pump inhibitors and H_2 blockers *[see Clinical Pharmacology (12.3)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Pregnancy Category B - There are no adequate and well-controlled studies of Effient use in pregnant women. Reproductive and developmental toxicology studies in rats and rabbits at doses of up to 30 times the recommended therapeutic exposures in humans (based on plasma exposures to the major

circulating human metabolite) revealed no evidence of fetal harm; however, animal studies are not always predictive of a human response. Effient should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

In embryo fetal developmental toxicology studies, pregnant rats and rabbits received prasugrel at maternally toxic oral doses equivalent to more than 40 times the human exposure. A slight decrease in pup body weight was observed; but, there were no structural malformations in either species. In prenatal and postnatal rat studies, maternal treatment with prasugrel had no effect on the behavioral or reproductive development of the offspring at doses greater than 150 times the human exposure *[see Nonclinical Toxicology (13.1)]*.

8.3 Nursing Mothers

It is not known whether Effient is excreted in human milk; however, metabolites of Effient were found in rat milk. Because many drugs are excreted in human milk, prasugrel should be used during nursing only if the potential benefit to the mother justifies the potential risk to the nursing infant.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established *[see Clinical Pharmacology (12.3)]*.

8.5 Geriatric Use

In TRITON-TIMI 38, 38.5% of patients were ≥65 years of age and 13.2% were ≥75 years of age. The risk of bleeding increased with advancing age in both treatment groups, although the relative risk of bleeding (Effient compared with clopidogrel) was similar across age groups.

Patients ≥ 75 years of age who received Effient had an increased risk of fatal bleeding events (1.0%) compared to patients who received clopidogrel (0.1%). In patients ≥ 75 years of age, symptomatic intracranial hemorrhage occurred in 7 patients (0.8%) who received Effient and in 3 patients (0.3%) who received clopidogrel. Because of the risk of bleeding, and because effectiveness is uncertain in patients ≥ 75 years of age *[see Clinical Studies (14)]*, use of Effient is generally not recommended in these patients, except in high-risk situations (diabetes and past history of myocardial infarction) where its effect appears to be greater and its use may be considered *[see Warnings and Precautions (5.1), Clinical Pharmacology (12.3), and Clinical Studies (14)]*.

8.6 Low Body Weight

In TRITON-TIMI 38, 4.6% of patients treated with Effient had body weight <60 kg. Individuals with body weight < 60 kg had an increased risk of bleeding and an increased exposure to the active metabolite of prasugrel *[see Dosage and Administration (2), Warnings and Precautions (5.1), and Clinical Pharmacology (12.3)]*. Consider lowering the maintenance dose to 5 mg in patients <60 kg. The effectiveness and safety of the 5 mg dose have not been prospectively studied.

8.7 Renal Impairment

No dosage adjustment is necessary for patients with renal impairment. There is limited experience in patients with end-stage renal disease *[see Clinical Pharmacology (12.3)]*.

8.8 Hepatic Impairment

No dosage adjustment is necessary in patients with mild to moderate hepatic impairment (Child-Pugh Class A and B). The pharmacokinetics and pharmacodynamics of prasugrel in patients with severe hepatic disease have not been studied, but such patients are generally at higher risk of bleeding *[see Warnings and Precautions (5.1) and Clinical Pharmacology (12.3)]*.

8.9 Metabolic Status

In healthy subjects, patients with stable atherosclerosis, and patients with ACS receiving prasugrel, there was no relevant effect of genetic variation in CYP2B6, CYP2C9, CYP2C19, or CYP3A5 on the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation.

10 OVERDOSAGE

10.1 Signs and Symptoms

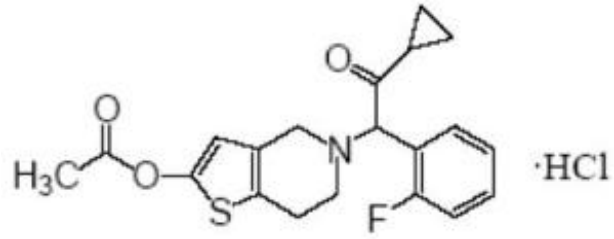
Platelet inhibition by prasugrel is rapid and irreversible, lasting for the life of the platelet, and is unlikely to be increased in the event of an overdose. In rats, lethality was observed after administration of 2000 mg/kg. Symptoms of acute toxicity in dogs included emesis, increased serum alkaline phosphatase, and hepatocellular atrophy. Symptoms of acute toxicity in rats included mydriasis, irregular respiration, decreased locomotor activity, ptosis, staggering gait, and lacrimation.

10.2 Recommendations about Specific Treatment

Platelet transfusion may restore clotting ability. The prasugrel active metabolite is not likely to be removed by dialysis.

11 DESCRIPTION

Effient contains prasugrel, a thienopyridine class inhibitor of platelet activation and aggregation mediated by the $P2Y_{12}$ ADP receptor. Effient is formulated as the hydrochloride salt, a racemate, which is chemically designated as 5-[(1RS)-2-cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl acetate hydrochloride. Prasugrel hydrochloride has the empirical formula $C_{20}H_{20}FNO_3S$•HCl representing a molecular weight of 409.90. The chemical structure of prasugrel hydrochloride is:



Prasugrel hydrochloride is a white to practically white solid. It is soluble at pH 2, slightly soluble at pH 3 to 4, and practically insoluble at pH 6 to 7.5. It also dissolves freely in methanol and is slightly soluble in 1- and 2-propanol and acetone. It is practically insoluble in diethyl ether and ethyl acetate.

Effient is available for oral administration as 5 mg or 10 mg elongated hexagonal, film-coated, non-scored tablets, debossed on each side. Each yellow 5 mg tablet is manufactured with 5.49 mg prasugrel hydrochloride, equivalent to 5 mg prasugrel and each beige 10 mg tablet with 10.98 mg prasugrel hydrochloride, equivalent to 10 mg of prasugrel. During manufacture and storage, partial conversion from prasugrel hydrochloride to prasugrel free base may occur. Other ingredients include mannitol, hypromellose, croscarmellose sodium, microcrystalline cellulose, and vegetable magnesium stearate. The color coatings contain lactose, hypromellose, titanium dioxide, triacetin, iron oxide yellow, and iron oxide red (only in Effient 10 mg tablet).

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action

Prasugrel is an inhibitor of platelet activation and aggregation through the irreversible binding of its

active metabolite to the $P2Y_{12}$ class of ADP receptors on platelets.

12.2 Pharmacodynamics

Prasugrel produces inhibition of platelet aggregation to 20 µM or 5 µM ADP, as measured by light transmission aggregometry. Following a 60-mg loading dose of Effient, approximately 90% of patients had at least 50% inhibition of platelet aggregation by 1 hour. Maximum platelet inhibition was about 80% (Figure 2). Mean steady-state inhibition of platelet aggregation was about 70% following 3 to 5 days of dosing at 10 mg daily after a 60-mg loading dose of Effient.

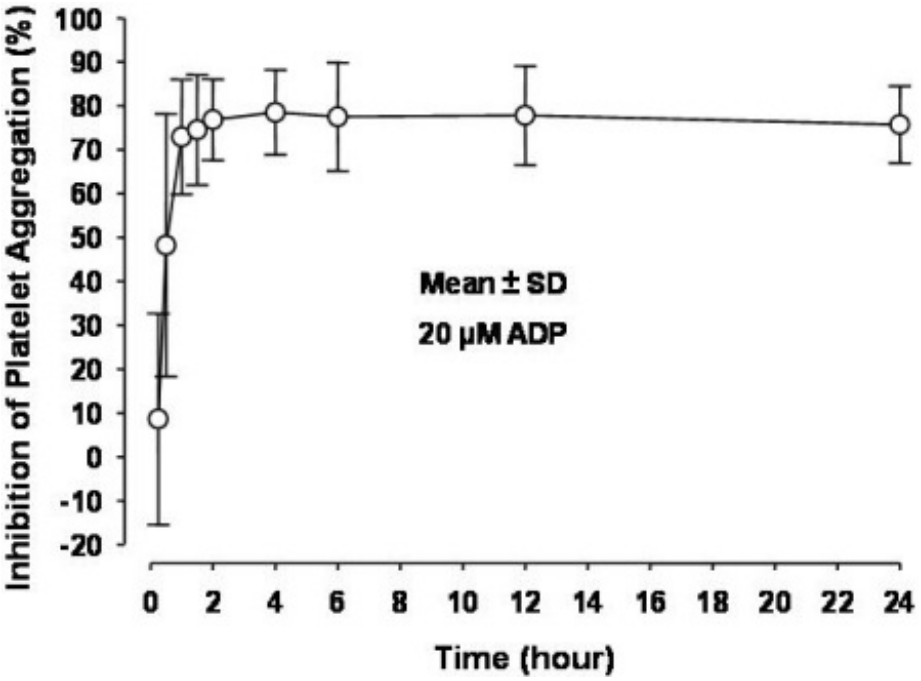


Figure 2: Inhibition (Mean±SD) of 20 µM ADP-induced Platelet Aggregation (IPA) Measured by Light Transmission Aggregometry after Prasugrel 60 mg

Platelet aggregation gradually returns to baseline values over 5-9 days after discontinuation of prasugrel, this time course being a reflection of new platelet production rather than pharmacokinetics of prasugrel. Discontinuing clopidogrel 75 mg and initiating prasugrel 10 mg with the next dose resulted in increased inhibition of platelet aggregation, but not greater than that typically produced by a 10 mg maintenance dose of prasugrel alone. The relationship between inhibition of platelet aggregation and clinical activity has not been established.

12.3 Pharmacokinetics

Prasugrel is a prodrug and is rapidly metabolized to a pharmacologically active metabolite and inactive metabolites. The active metabolite has an elimination half-life of about 7 hours (range 2-15 hours). Healthy subjects, patients with stable atherosclerosis, and patients undergoing PCI show similar pharmacokinetics.

Absorption and Binding - Following oral administration, ≥ 79% of the dose is absorbed. The absorption and metabolism are rapid, with peak plasma concentrations (C_{max}) of the active metabolite occurring approximately 30 minutes after dosing. The active metabolite's exposure (AUC) increases slightly more than proportionally over the dose range of 5 to 60 mg. Repeated daily doses of 10 mg do not lead to accumulation of the active metabolite. In a study of healthy subjects given a single 15 mg dose, the AUC of the active metabolite was unaffected by a high fat, high calorie meal, but C_{max} was decreased by 49% and T_{max} was increased from 0.5 to 1.5 hours. Effient can be administered without regard to food. The active metabolite is bound about 98% to human serum albumin.

Metabolism and Elimination - Prasugrel is not detected in plasma following oral administration. It is rapidly hydrolyzed in the intestine to a thiolactone, which is then converted to the active metabolite by a single step, primarily by CYP3A4 and CYP2B6 and to a lesser extent by CYP2C9 and CYP2C19. The estimates of apparent volume of distribution of prasugrel's active metabolite ranged from 44 to 68 L and the estimates of apparent clearance ranged from 112 to 166 L/hr in healthy subjects and patients with stable atherosclerosis. The active metabolite is metabolized to two inactive compounds by S-methylation or conjugation with cysteine. The major inactive metabolites are highly bound to human plasma proteins. Approximately 68% of the prasugrel dose is excreted in the urine and 27% in the feces as inactive metabolites.

Specific Populations

Pediatric - Pharmacokinetics and pharmacodynamics of prasugrel have not been evaluated in a pediatric population *[see Use in Specific Populations (8.4)]*.

Geriatric - In a study of 32 healthy subjects between the ages of 20 and 80 years, age had no significant effect on pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation. In TRITON-TIMI 38, the mean exposure (AUC) of the active metabolite was 19% higher in patients ≥75 years of age than in patients <75 years of age *[see Warnings and Precautions (5.1), Adverse Reactions (6.1), and Use in Specific Populations (8.5)]*.

Body Weight - The mean exposure (AUC) to the active metabolite is approximately 30 to 40% higher in subjects with a body weight of <60 kg than in those weighing ≥60 kg *[see Dosage and Administration (2), Warnings and Precautions (5.1), Adverse Reactions (6.1), and Use in Specific Populations (8.6)]*.

Gender - Pharmacokinetics of prasugrel's active metabolite are similar in men and women.

Ethnicity - Exposure in subjects of African and Hispanic descent is similar to that in Caucasians. In clinical pharmacology studies, after adjusting for body weight, the AUC of the active metabolite was approximately 19% higher in Chinese, Japanese, and Korean subjects than in Caucasian subjects.

Smoking - Pharmacokinetics of prasugrel's active metabolite are similar in smokers and nonsmokers.

Renal Impairment - Pharmacokinetics of prasugrel's active metabolite and its inhibition of platelet aggregation are similar in patients with moderate renal impairment (CrCL=30 to 50 mL/min) and healthy subjects. In patients with end stage renal disease, exposure to the active metabolite (both C_{max} and AUC(0-t_{last})) was about half that in healthy controls and patients with moderate renal impairment *[see Use in Specific Populations (8.7)]*.

Hepatic Impairment - Pharmacokinetics of prasugrel's active metabolite and inhibition of platelet aggregation were similar in patients with mild to moderate hepatic impairment compared to healthy subjects. The pharmacokinetics and pharmacodynamics of prasugrel's active metabolite in patients with severe hepatic disease have not been studied *[see Warnings and Precautions (5.1) and Use in Specific Populations (8.8)]*.

Drug Interactions

Potential for Other Drugs to Affect Prasugrel

Inhibitors of CYP3A - Ketoconazole (400 mg daily), a selective and potent inhibitor of CYP3A4 and CYP3A5, did not affect prasugrel-mediated inhibition of platelet aggregation or the active metabolite's AUC and T_{max}, but decreased the C_{max} by 34% to 46%. Therefore, CYP3A inhibitors such as verapamil, diltiazem, indinavir, ciprofloxacin, clarithromycin, and grapefruit juice are not expected to have a significant effect on the pharmacokinetics of the active metabolite of prasugrel *[see Drug Interactions (7.3)]*.

Inducers of Cytochromes P450 - Rifampicin (600 mg daily), a potent inducer of CYP3A and CYP2B6 and an inducer of CYP2C9, CYP2C19, and CYP2C8, did not significantly change the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation. Therefore, known CYP3A

inducers such as rifampicin, carbamazepine, and other inducers of cytochromes P450 are not expected to have significant effect on the pharmacokinetics of the active metabolite of prasugrel *[see Drug Interactions (7.3)]*.

Drugs that Elevate Gastric pH - Daily coadministration of ranitidine (an H_2 blocker) or lansoprazole (a proton pump inhibitor) decreased the C_{max} of the prasugrel active metabolite by 14% and 29%, respectively, but did not change the active metabolite's AUC and T_{max}. In TRITON-TIMI 38, Effient was administered without regard to coadministration of a proton pump inhibitor or H_2 blocker *[see Drug Interactions (7.3)]*.

Statins - Atorvastatin (80 mg daily), a drug metabolized by CYP450 3A4, did not alter the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation *[see Drug Interactions (7.3)]*.

Heparin - A single intravenous dose of unfractionated heparin (100 U/kg) did not significantly alter coagulation or the prasugrel-mediated inhibition of platelet aggregation; however, bleeding time was increased compared with either drug alone *[see Drug Interactions (7.3)]*.

Aspirin - Aspirin 150 mg daily did not alter prasugrel-mediated inhibition of platelet aggregation; however, bleeding time was increased compared with either drug alone *[see Drug Interactions (7.3)]*.

Warfarin - A significant prolongation of the bleeding time was observed when prasugrel was coadministered with 15 mg of warfarin *[see Drug Interactions (7.1)]*.

Potential for Prasugrel to Affect Other Drugs

In vitro metabolism studies demonstrate that prasugrel's main circulating metabolites are not likely to cause clinically significant inhibition of CYP1A2, CYP2C9, CYP2C19, CYP2D6, or CYP3A, or induction of CYP1A2 or CYP3A.

Drugs Metabolized by CYP2B6 — Prasugrel is a weak inhibitor of CYP2B6. In healthy subjects, prasugrel decreased exposure to hydroxybupropion, a CYP2B6-mediated metabolite of bupropion, by 23%, an amount not considered clinically significant. Prasugrel is not anticipated to have significant effect on the pharmacokinetics of drugs that are primarily metabolized by CYP2B6, such as halothane, cyclophosphamide, propofol, and nevirapine.

Effect on Digoxin - The potential role of prasugrel as a Pgp substrate was not evaluated. Prasugrel is not an inhibitor of Pgp, as digoxin clearance was not affected by prasugrel coadministration *[see Drug Interactions (7.3)]*.

12.5 Pharmacogenomics

There is no relevant effect of genetic variation in CYP2B6, CYP2C9, CYP2C19, or CYP3A5 on the pharmacokinetics of prasugrel's active metabolite or its inhibition of platelet aggregation.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis - No compound-related tumors were observed in a 2-year rat study with prasugrel at oral doses up to 100 mg/kg/day (>100 times the recommended therapeutic exposures in humans (based on plasma exposures to the major circulating human metabolite). There was an increased incidence of tumors (hepatocellular adenomas) in mice exposed for 2 years to high doses (>250 times the human metabolite exposure).

Mutagenesis - Prasugrel was not genotoxic in two *in vitro* tests (Ames bacterial gene mutation test, clastogenicity assay in Chinese hamster fibroblasts) and in one *in vivo* test (micronucleus test by intraperitoneal route in mice).

Impairment of Fertility - Prasugrel had no effect on fertility of male and female rats at oral doses up to

300 mg/kg/day (80 times the human major metabolite exposure at daily dose of 10 mg prasugrel).

14 CLINICAL STUDIES

The clinical evidence for the effectiveness of Effient is derived from the TRITON-TIMI 38 (TRial to Assess Improvement in Therapeutic Outcomes by Optimizing Platelet InhibitioN with Prasugrel) study, a 13,608-patient, multicenter, international, randomized, double-blind, parallel-group study comparing Effient to a regimen of clopidogrel, each added to aspirin and other standard therapy, in patients with ACS (UA, NSTEMI, or STEMI) who were to be managed with PCI. Randomization was stratified for UA/NSTEMI and STEMI.

Patients with UA/NSTEMI presenting within 72 hours of symptom onset were to be randomized after undergoing coronary angiography. Patients with STEMI presenting within 12 hours of symptom onset could be randomized prior to coronary angiography. Patients with STEMI presenting between 12 hours and 14 days of symptom onset were to be randomized after undergoing coronary angiography. Patients underwent PCI, and for both UA/NSTEMI and STEMI patients, the loading dose was to be administered anytime between randomization and 1 hour after the patient left the catheterization lab. If patients with STEMI were treated with thrombolytic therapy, randomization could not occur until at least 24 hours (for tenecteplase, reteplase or alteplase) or 48 hours (for streptokinase) after the thrombolytic was given.

Patients were randomized to receive Effient (60 mg loading dose followed by 10 mg once daily) or clopidogrel (300 mg loading dose followed by 75 mg once daily), with administration and follow-up for a minimum of 6 months (actual median 14.5 months). Patients also received aspirin (75 mg to 325 mg once daily). Other therapies, such as heparin and intravenous glycoprotein IIb/IIIa (GPIIb/IIIa) inhibitors, were administered at the discretion of the treating physician. Oral anticoagulants, other platelet inhibitors, and chronic NSAIDs were not allowed.

The primary outcome measure was the composite of cardiovascular death, nonfatal MI, or nonfatal stroke in the UA/NSTEMI population. Success in this group allowed analysis of the same endpoint in the overall ACS and STEMI populations. Nonfatal MIs included both MIs detected solely through analysis of creatine kinase muscle-brain (CK-MB) changes and clinically apparent (investigator-reported) MIs.

The patient population was 92% Caucasian, 26% female, and 39% ≥65 years of age. The median time from symptom onset to study drug administration was 7 hours for patients with STEMI and 30 hours for patients with UA/NSTEMI. Approximately 99% of patients underwent PCI. The study drug was administered after the first coronary guidewire was placed in approximately 75% of patients.

Effient significantly reduced total endpoint events compared to clopidogrel (*see* Table 5 and Figure 3). The reduction of total endpoint events was driven primarily by a decrease in nonfatal MIs, both those occurring early (through 3 days) and later (after 3 days). Approximately 40% of MIs occurred peri-procedurally and were detected solely by changes in CK-MB. Administration of the clopidogrel loading dose in TRITON-TIMI 38 was delayed relative to the placebo-controlled trials that supported its approval for ACS. Effient produced higher rates of clinically significant bleeding than clopidogrel in TRITON-TIMI 38 *[see Adverse Reactions (6.1)]*. Choice of therapy requires balancing these differences in outcome.

The treatment effect of Effient was apparent within the first few days, and persisted to the end of the study (Figure 3). The inset shows results over the first 7 days.

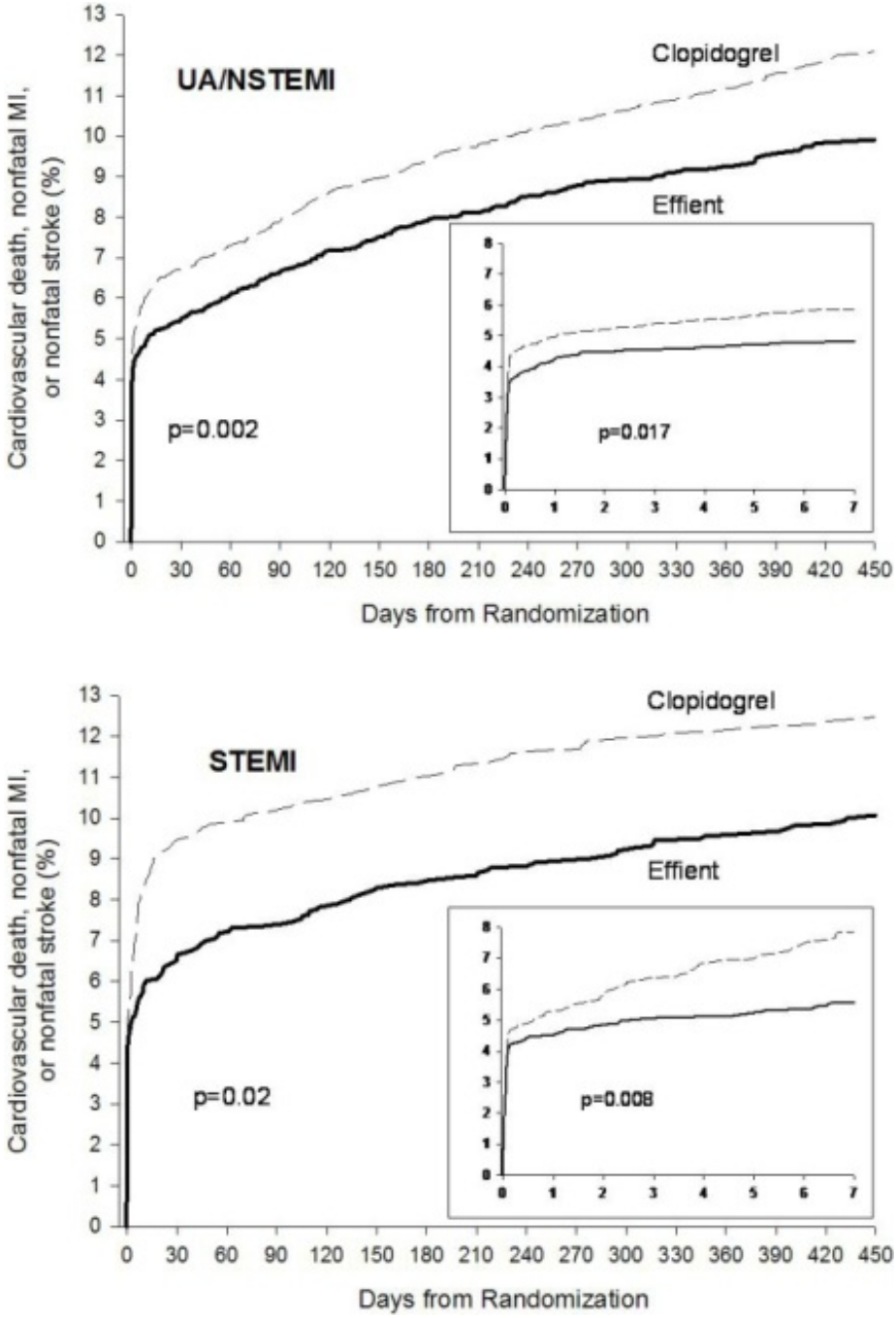


Figure 3: Time to first event of CV death, MI, or stroke (TRITON-TIMI 38)

The Kaplan-Meier curves (Figure 3) show the primary composite endpoint of CV death, nonfatal MI, or nonfatal stroke over time in the UA/NSTEMI and STEMI populations. In both populations, the curves separate within the first few hours. In the UA/NSTEMI population, the curves continue to diverge throughout the 15 month follow-up period. In the STEMI population, the early separation was maintained throughout the 15 month follow-up period, but there was no progressive divergence after the first few weeks.

Effient reduced the occurrence of the primary composite endpoint compared to clopidogrel in both the UA/NSTEMI and STEMI populations (*see* Table 5). In patients who survived an on-study myocardial infarction, the incidence of subsequent events was also lower in the Effient group.

Table 5: Patients with Outcome Events (CV Death, MI, Stroke) in TRITON-TIMI 38

	Patients with events	From Kaplan-Meier analysis

	Effient (%)	Clopidogrel (%)	Relative Risk Reduction (%)[a] (95% CI)	p-value
UA/NSTEMI	**N=5044**	**N=5030**		
CV death, nonfatal MI, or nonfatal stroke	9.3	11.2	18.0 (7.3, 27.4)	0.002
CV death	1.8	1.8	2.1 (-30.9, 26.8)	0.885
Nonfatal MI	7.1	9.2	23.9 (12.7, 33.7)	<0.001
Nonfatal Stroke	0.8	0.8	2.1 (-51.3, 36.7)	0.922
STEMI	**N=1769**	**N=1765**		
CV death, nonfatal MI, or nonfatal stroke	9.8	12.2	20.7 (3.2, 35.1)	0.019
CV death	2.4	3.3	26.2 (-9.4, 50.3)	0.129
Nonfatal MI	6.7	8.8	25.4 (5.2, 41.2)	0.016
Nonfatal Stroke	1.2	1.1	-9.7 (-104.0, 41.0)	0.77

[a] RRR = (1-Hazard Ratio) x 100%. Values with a negative relative risk reduction indicate a relative risk increase.

The effect of Effient in various subgroups is shown in Figures 4 and 5. Results are generally consistent across pre-specified subgroups, with the exception of patients with a history of TIA or stroke *[see Contraindications (4.2)]*. The treatment effect was driven primarily by a reduction in nonfatal MI. The effect in patients ≥75 years of age was also somewhat smaller, and bleeding risk is higher in these individuals *[see Adverse Reactions (6.1)]*. See below for analyses of patients ≥75 years of age with risk factors.

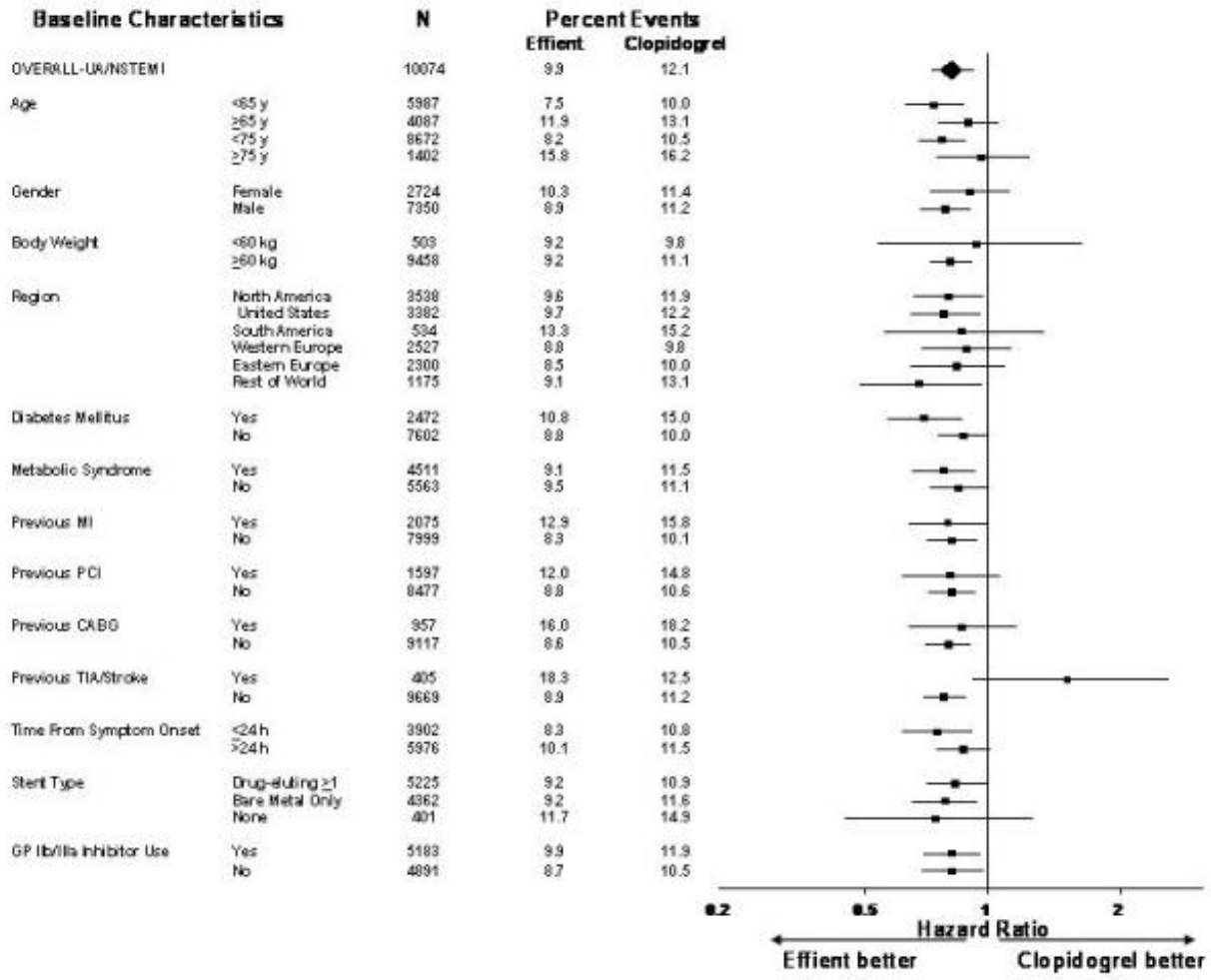


Figure 4: Subgroup analyses for time to first event of CV death, MI, or stroke (HR and 95% CI; TRITON-TIMI 38) – UA/NSTEMI Patients.

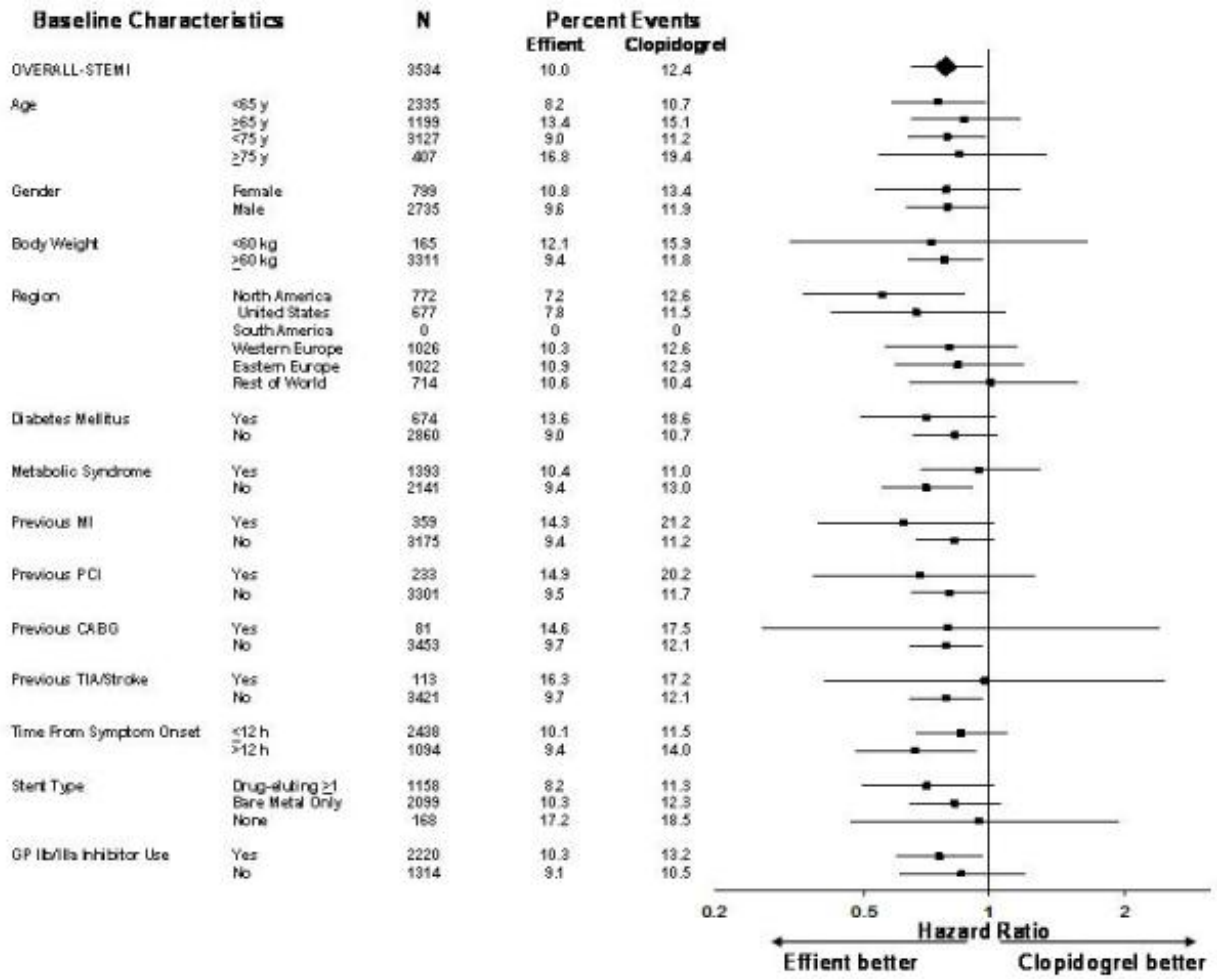


Figure 5: Subgroup analyses for time to first event of CV death, MI, or stroke (HR and 95% CI; TRITON-TIMI 38) – STEMI Patients.

Effient is generally not recommended in patients ≥75 years of age, except in high-risk situations (diabetes mellitus or prior MI) where its effect appears to be greater and its use may be considered. These recommendations are based on subgroup analyses (Table 6) and must be interpreted with caution, but the data suggest that Effient reduces ischemic events in such patients.

Table 6: Subgroup Analyses for Time to First Event of CV Death, MI, or Stroke: Patients < or ≥75 Years of Age, ± Diabetes, ± Prior History of MI, All ACS Patient Population

	Effient		Clopidogrel			
	N	% with events	N	% with events	Hazard Ratio (95% CI)	p-value
Age ≥75						
Diabetes - yes	249	14.9	234	21.8	0.64 (0.42, 0.97)	0.034
Diabetes - no	652	16.4	674	15.3	1.1 (0.83, 1.43)	NS
Age <75						
Diabetes - yes	1327	10.8	1336	14.8	0.72 (0.58, 0.89)	0.002
Diabetes - no	4585	7.8	4551	9.5	0.82 (0.71, 0.94)	0.004
Age ≥75						

Prior MI - yes	220	17.3	212	22.6	0.72 (0.47, 1.09)	0.12
Prior MI - no	681	15.6	696	15.2	1.05 (0.80, 1.37)	NS
Age <75						
Prior MI - yes	1006	12.2	996	15.4	0.78 (0.62, 0.99)	0.04
Prior MI - no	4906	7.7	4891	9.7	0.78 (0.68, 0.90)	<0.001

There were 50% fewer stent thromboses (95% C.I. 32% - 64%; p< 0.001) reported among patients randomized to Effient (0.9%) than among patients randomized to clopidogrel (1.8%). The difference manifested early and was maintained through one year of follow-up. Findings were similar with bare metal and drug-eluting stents.

In TRITON-TIMI 38, prasugrel reduced ischemic events (mainly nonfatal MIs) and increased bleeding events *[see Adverse Reactions (6.1)]* relative to clopidogrel. The findings are consistent with the intended greater inhibition of platelet aggregation by prasugrel at the doses used in the study *[see Clinical Pharmacology (12.2)]*. There is, however, an alternative explanation: both prasugrel and clopidogrel are pro-drugs that must be metabolized to their active moieties. Whereas the pharmacokinetics of prasugrel's active metabolite are not known to be affected by genetic variations in CYP2B6, CYP2C9, CYP2C19, or CYP3A5, the pharmacokinetics of clopidogrel's active metabolite are affected by CYP2C19 genotype, and approximately 30% of Caucasians are reduced-metabolizers. Moreover, certain proton pump inhibitors, widely used in the ACS patient population and used in TRITON-TIMI 38, inhibit CYP2C19, thereby decreasing formation of clopidogrel's active metabolite. Thus, reduced metabolizer status and use of proton pump inhibitors may diminish clopidogrel's activity in a fraction of the population, and may have contributed to prasugrel's greater treatment effect and greater bleeding rate in TRITON-TIMI 38. The extent to which these factors were operational, however, is unknown.

16 HOW SUPPLIED/STORAGE AND HANDLING

Effient (prasugrel) 10 mg is supplied as a beige, elongated hexagonal, film-coated, non-scored tablet debossed with “10 MG” on one side and “4759” on the other side.

Bottles of 30	NDC 54868-6238-0

Store at 25°C (77°F); excursions permitted to 15° to 30°C (59° to 86°F).

Dispense and keep product in original container. Keep container closed and do not remove desiccant from bottle. Do not break the tablet.

17 PATIENT COUNSELING INFORMATION

See Medication Guide

17.1 Benefits and Risks

- Summarize the effectiveness features and potential side effects of Effient.
- Tell patients to take Effient exactly as prescribed.
- Remind patients not to discontinue Effient without first discussing it with the physician who prescribed Effient.
- Recommend that patients read the Medication Guide.

17.2 Bleeding

Inform patients that they:

- will bruise and bleed more easily.
- will take longer than usual to stop bleeding.
- should report any unanticipated, prolonged, or excessive bleeding, or blood in their stool or urine.

17.3 Other Signs and Symptoms Requiring Medical Attention

- Inform patients that TTP is a rare but serious condition that has been reported with Effient.
- Instruct patients to get prompt medical attention if they experience any of the following symptoms that cannot otherwise be explained: fever, weakness, extreme skin paleness, purple skin patches, yellowing of the skin or eyes, or neurological changes.

17.4 Invasive Procedures

Instruct patients to:

- inform physicians and dentists that they are taking Effient before any invasive procedure is scheduled.
- tell the doctor performing the invasive procedure to talk to the prescribing health care professional before stopping Effient.

17.5 Concomitant Medications

Ask patients to list all prescription medications, over-the-counter medications, or dietary supplements they are taking or plan to take so the physician knows about other treatments that may affect bleeding risk (*e.g.*, warfarin and NSAIDs).

Literature Revised: December 6, 2010

Manufactured by Eli Lilly and Company, Indianapolis, IN, 46285

Marketed by Daiichi Sankyo, Inc. and Eli Lilly and Company

PV 7311 AMP

Relabeling of "**Additional barcode label**" by:
Physicians Total Care, Inc.
Tulsa, OK 74146

MEDICATION GUIDE

Effient™ (Ef′-fee-ent)

(prasugrel)

Tablets

Read this Medication Guide before you start taking Effient and each time you get a refill. There may be new information. This Medication Guide does not take the place of talking with your doctor about your medical condition or your treatment.

What is the most important information I should know about Effient?

- Effient is used to lower your chance of having a heart attack or other serious problems with your heart or blood vessels. But, Effient can cause bleeding, which can be serious, and sometimes lead to death. You should not start to take Effient if it is likely that you will have heart bypass surgery (coronary artery bypass graft surgery or CABG) right away. You have a higher risk of bleeding if you take Effient and then have heart bypass surgery.
- **Do not take Effient if you:**

- currently have abnormal bleeding, such as stomach or intestinal bleeding, or bleeding in your head
- have a history of stroke, or “mini-stroke” (transient ischemic attack or TIA)
- are allergic to prasugrel or any of the ingredients in Effient. See the end of this Medication Guide for a list of ingredients in Effient.

- You should stop taking Effient if you have a stroke.
- **Whenever possible, you should stop taking Effient at least 7 days before any surgery, as instructed by the doctor who prescribed Effient for you.**

You may also have a higher risk of bleeding if you take Effient and:

- have had trauma, such as an accident or surgery
- have stomach or intestine bleeding that is recent or keeps coming back, or you have a stomach ulcer
- have severe liver problems
- weigh less than 132 pounds
- take other medicines that increase your risk of bleeding, including:
  - warfarin sodium (Coumadin*, Jantoven*)
  - a medicine that contains heparin
  - other medicines to prevent or treat blood clots
  - non-steroidal anti-inflammatory drugs (NSAIDs) for a long time

Tell your doctor if you take any of these medicines. Ask your doctor if you are not sure if your medicine is one listed above.

- Effient increases your risk of bleeding because it lessens the ability of your blood to clot. While you take Effient:
  - you will bruise and bleed more easily
  - you are more likely to have nose bleeds
  - it will take longer for any bleeding to stop
- Call your doctor right away if you have any of these signs or symptoms of bleeding:
  - unexpected bleeding or bleeding that lasts a long time
  - bleeding that is severe or you can not control
  - pink or brown urine
  - red or black stools (looks like tar)
  - bruises that happen without a known cause or get larger
  - cough up blood or blood clots
  - vomit blood or your vomit looks like “coffee grounds”
- **Do not stop taking Effient without talking to the doctor who prescribes it for you. People who are treated with angioplasty and have a stent, and stop taking Effient too soon, have a higher risk of a blood clot in the stent, having a heart attack, or dying. If you must stop Effient because of bleeding, your risk of a heart attack may be higher. See “What are the possible side effects of Effient?” for more information about side effects.**

What is Effient?

Effient is a prescription medicine used to treat people who:

- have had a heart attack or severe chest pain that happens when your heart does not get enough oxygen, and
- have been treated with a procedure called “angioplasty” (also called balloon angioplasty).

Effient is used to lower your chance of having another serious problem with your heart or blood vessels, such as another heart attack, a stroke, blood clots in your stent, or death.

Platelets are blood cells that help with normal blood clotting. Effient helps prevent platelets from sticking together and forming a clot that can block an artery or a stent.

It is not known if Effient is safe and works in children.

What should I tell my doctor before taking Effient?

Effient may not be right for you. Tell your doctor about all of your medical conditions, including if you:

- have any bleeding problems
- have a history of stomach ulcers, colon polyps, diverticulosis
- have liver problems
- have had any recent severe injury or surgery
- plan to have surgery or a dental procedure. See "What is the most important information I should know about Effient?"
- pregnant, or are planning to get pregnant. It is not known if Effient will harm your baby.
- if you are breast-feeding. It is not known if Effient passes into your breast-milk. You and your doctor should decide if you will take Effient or breast-feed. You should not do both without talking with your doctor.

Tell all of your doctors and dentists that you are taking Effient. They should talk to the doctor who prescribed Effient for you, before you have **any** surgery or invasive procedure.

Tell your doctor about all the medicines you take, including prescription and non-prescription medicines, vitamins, and herbal supplements. Certain medicines may increase your risk of bleeding. See "What is the most important information I should know about Effient?"

Know the medicines you take. Keep a list of them and show it to your doctor and pharmacist when you get a new medicine.

How should I take Effient?

- Take Effient exactly as prescribed by your doctor.
- Take Effient one time each day.
- You can take Effient with or without food.
- Take Effient with aspirin as instructed by your doctor.
- Your doctor will decide how long you should take Effient. Do not stop taking Effient without first talking to the doctor who prescribed it for you. See "What is the most important information I should know about Effient?"
- If you miss a dose, take Effient as soon as you remember. If it is almost time for your next dose, skip the missed dose. Just take the next dose at your regular time. Do not take two doses at the same time unless your doctor tells you to.
- If you take too much Effient, call your local emergency room or poison control center right away.

What are the possible side effects of Effient?

Effient can cause serious side effects, including:

- **See "What is the most important information I should know about Effient?"**
- **A blood clotting problem called Thrombotic Thrombocytopenic Purpura (TTP).** TTP can happen with Effient, sometimes after a short time (less than 2 weeks). TTP is a blood clotting problem where blood clots form in blood vessels and can happen all over the body. TTP needs to be treated in a hospital right away, because you may die. Get medical help right away if you have any of these symptoms and they can not be explained by another medical condition:
- purplish spots called purpura on the skin or mucous membranes (such as on the mouth) due to bleeding under the skin
- paleness or jaundice (a yellowish color of the skin or eyes)
- feeling tired or weak
- fever
- fast heart rate or feeling short of breath

- headache, speech changes, confusion, coma, stroke, or seizure
- low amount of urine, or urine that is pink-tinged or has blood in it
- stomach area (abdominal) pain, nausea, vomiting, or diarrhea
- visual changes

Tell your doctor if you have any side effect that bothers you or that does not go away.

These are not all of the possible side effects of Effient. For more information, ask your doctor or pharmacist.

Call your doctor for medical advice about side effects.

You may report side effects to FDA at 1-800-FDA-1088.

How should I store Effient?

- Keep Effient at room temperature between 59°F to 86°F (15°C to 30°C).
- Keep Effient in the container it comes in.
- Keep the container closed tightly with the gray cylinder inside.
- Protect Effient from moisture.

Keep Effient and all medicines out of the reach of children.

General Information about Effient

Medicines are sometimes prescribed for purposes other than those listed in a Medication Guide. Do not use Effient for a condition for which it was not prescribed. Do not give your Effient to other people, even if they have similar symptoms. It may harm them.

This Medication Guide summarizes the most important information about Effient. If you would like more information about Effient, talk with your doctor or pharmacist. For more information, call 1-800-545-5979 or go to the following website: www.Effient.com

What are the ingredients in Effient?

Active Ingredient: prasugrel

Inactive Ingredients: mannitol, hypromellose, croscarmellose sodium, microcrystalline cellulose, and vegetable magnesium stearate. The color coatings contain lactose, hypromellose, titanium dioxide, triacetin, iron oxide yellow, and iron oxide red (only in Effient 10 mg tablet).

*The brands listed are trademarks of their respective owners and are not trademarks of Daiichi Sankyo, Inc. or Eli Lilly and Company.

Revised: December 6, 2010

Manufactured by Eli Lilly and Company, Indianapolis, IN, 46285

Marketed by Daiichi Sankyo, Inc. and Eli Lilly and Company

This Medication Guide has been approved by the U.S. Food and Drug Administration.

PV 6181 AMP

PACKAGE LABEL – Effient 10 mg 30 Tablets

Effient $_{TM}$

(prasugrel) tablets

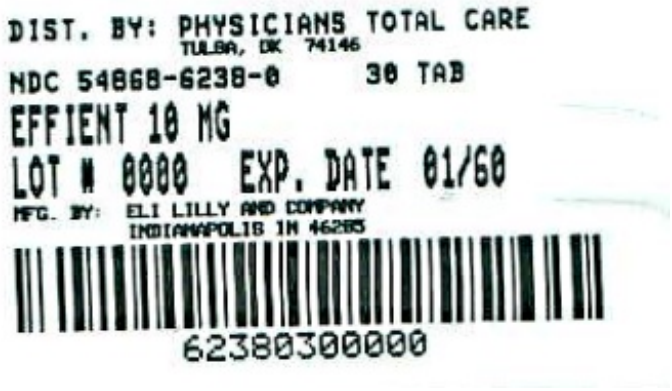
10 mg

Rx only

Each tablet contains prasugrel hydrochloride* equivalent to 10 mg prasugrel

*see package insert section 11

Dispense accompanying Medication Guide to each patient.



EFFIENT

prasugrel hydrochloride tablet, film coated

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:54868-6238(NDC:0002-4759)
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
PRASUGREL HYDROCHLORIDE (UNII: G89JQ59I13) (PRASUGREL - UNII:34K66TBT99)	PRASUGREL	10 mg

Inactive Ingredients	
Ingredient Name	**Strength**
MANNITOL (UNII: 3OWL53L36A)	
HYPROMELLOSES (UNII: 3NXW29V3WO)	
CROSCARMELLOSE SODIUM (UNII: M28OL1HH48)	
CELLULOSE, MICROCRYSTALLINE (UNII: OP1R32D61U)	
MAGNESIUM STEARATE (UNII: 70097M6I30)	
LACTOSE (UNII: J2B2A4N98G)	
TITANIUM DIOXIDE (UNII: 15FIX9V2JP)	
TRIACETIN (UNII: XHX3C3X673)	
FERRIC OXIDE YELLOW (UNII: EX438O2MRT)	
FERRIC OXIDE RED (UNII: 1K09F3G675)	

Product Characteristics			
Color	brown (beige)	**Score**	no score

Shape	HEXAGON (6 sided) (double-arrow)	**Size**	11mm
Flavor		**Imprint Code**	10;mg;4759
Contains			

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:54868-6238-0	30 in 1 BOTTLE		

Marketing Information

Marketing Category	Application Number or Monograph Citation	Marketing Start Date	Marketing End Date
NDA	NDA022307	03/15/2011	

Labeler - Physicians Total Care, Inc. (194123980)

Establishment

Name	Address	ID/FEI	Business Operations
Physicians Total Care, Inc.		194123980	relabel

Revised: 1/2011 Physicians Total Care, Inc.