SANIC **CV. SANIC OFFSET**		DIAJUKAN TANGGAL :	NO :
RELASI	**PT MITSUBISHI TANABE PHARMA**	**10 / 05 / 2023**	000
NAMA ITEM	**BROCHURE EFFIENT (DEPAN 1)**	HASIL ACC DITERIMA OLEH :	
UK JADI	**18,5 X 28 CM**		CATATAN :
WARNA	**HITAM** ■		**REVISI 3**
LAIN-LAIN		(.....)	

18,5 cm

28,0 cm

Antiplatelet agent

EFFIENT® Tablets 3.75mg
EFFIENT® Tablets 5mg

(COMPOSITION AND DESCRIPTION)

PHYSICOCHEMISTRY

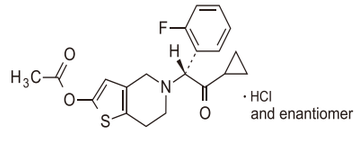
Non-proprietary name : Prasugrel hydrochloride

Chemical name : 5-[(1*RS*)-2-Cyclopropyl-1-(2-fluorophenyl)-2-oxoethyl]-4,5,6,7-tetrahydrothieno[3,2-c]pyridin-2-yl acetate monohydrochloride

Molecular formula : $C_{20}H_{20}FNO_3S$•HCl

Molecular weight : 409.90

Structural formula :



Description : White to brownish white crystals or crystalline powder.
Soluble in water and sparingly soluble in *N,N*-dimethylformamide and ethanol (99.5%).

Melting point : 178°C to 179°C (decomposition)

DESCRIPTION

Brand name	EFFIENT Tablets 3.75 mg			EFFIENT Tablets 5 mg		
Active ingredient (per tablet)	Prasugrel hydrochloride 4.12 mg (prasugrel 3.75 mg)			Prasugrel hydrochloride 5.49 mg (prasugrel 5 mg)		
Inactive ingredient	Lactose monohydrate, microcrystalline cellulose, low substituted hydroxypropylcellulose, hydroxypropylcellulose, magnesium stearate, hypromellose, titanium oxide, talc, and red ferric oxide			Lactose monohydrate, microcrystalline cellulose, low substituted hydroxypropylcellulose, hydroxypropylcellulose, magnesium stearate, hypromellose, titanium oxide, talc, yellow ferric oxide, and red ferric oxide		
Description / Dosage form	Slightly reddish white/ Film-coated tablet (oblong shape)			Slightly yellowish red/ Film-coated tablet with a debossed line for scoring (oblong shape)		
Appearance						
Size / Weight	Diameter (mm) 7.3 (major axis) 5.1 (minor axis)	Thickness (mm) Approx. 3.2	Weight (mg) Approx. 107.5	Diameter (mm) 8.7 (major axis) 4.7 (minor axis)	Thickness (mm) Approx. 2.9	Weight (mg) Approx. 107.5

(ACTION)

PHARMACOLOGY

1. Mechanism of Action[11-14]

Prasugrel hydrochloride is a prodrug. It is converted to its active metabolite, which inhibits platelet aggregation by binding to the $P2Y_{12}$ ADP receptors on platelets selectively and irreversibly.

2. Pharmacological effects

(1) Antiplatelet Activity[2, 11, 14, 15]

Oral administration of prasugrel suppressed ADP-induced platelet aggregation in animal studies (rats, dogs, and monkeys). Twenty-three healthy adults were administered a loading dose of 20 mg of prasugrel on the first day, followed by 3.75-mg maintenance doses daily for 6 days. The inhibitory effect on platelet aggregation rapidly emerged 1 hour after the loading dose. The inhibition of platelet aggregation after administration of the loading dose was 34% at 1 hour post dose and 52% (maximum) at 8 hours post dose. The inhibition of platelet aggregation remained at similar percentages during treatment with the maintenance dose.

(2) Antithrombotic Activity[11, 15]

Oral administration of prasugrel demonstrated inhibition of thrombus formation in a dose-related manner in a rat model of arterio-venous shunt thrombosis and in a rat model of electrical stimulation-induced arterial thrombosis. In the rat model of arterio-venous shunt thrombosis, the antithrombotic effect of prasugrel was enhanced in combination with aspirin.

(3) Effect in Disease Models[14, 16]

In a rat model of myocardial infarction, oral administration of prasugrel hydrochloride reduced the size of myocardial infarction. Oral administration of prasugrel reduced the size of cerebral infarction in rat models of thrombotic and embolic cerebral infarction and inhibited the progression of lesions in the hind legs in a rat model of peripheral arterial occlusive diseases.

PHARMACOKINETICS

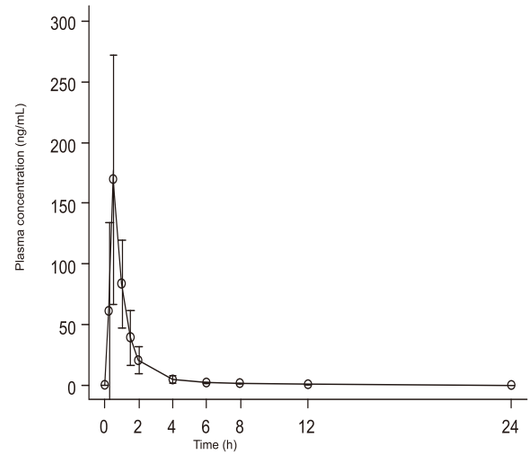
1. Plasma Concentrations

Because prasugrel is metabolized rapidly following oral dosing, unchanged EFFIENT was not detected in plasma, and plasma concentrations of the active metabolite R-138727 were therefore measured.

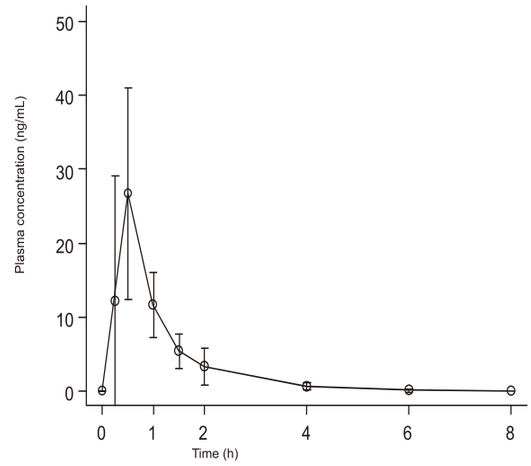
(1) Healthy Adults[2]

Plasma concentration profiles and pharmacokinetic parameters that were obtained for the active metabolite R-138727 when healthy adults were orally administered 20 mg of prasugrel on Day 1 of treatment and 3.75 mg of prasugrel once daily on Days 2 to 7 are presented below.

The Time Course of the Plasma Concentration of the Active Metabolite R-138727 After Administration of 20 mg: Day 1



The Time Course of the Plasma Concentration of the Active Metabolite R-138727 After Administration of 3.75 mg: Day 7



Pharmacokinetic Parameters of the Active Metabolite R-138727

Dose (mg)	n	C_{max} (ng/mL)	t_{max} (h)	AUC_{last} (ng·h/mL)	$t_{1/2}$ (h)
20 (Day 1)	23	177.1 ± 96.3	0.6 ± 0.2	185.1 ± 66.5	4.9 ± 5.8
3.75 (Day 7)	23	29.2 ± 15.5	0.6 ± 0.4	26.3 ± 9.2	0.9 ± 0.4

Data are expressed as mean ± SD.

(2) Patients With Renal Impairment[4]

No notable difference was found in pharmacokinetics of the active metabolite R-138727 after a single oral administration of a dose of 60 mg of prasugrel between patients with moderate renal impairment (creatinine clearance = 30 mL/min to 50 mL/min) and healthy adult subjects. AUC of the active metabolite R-138727 decreased by approximately 31% to 47%, and C_{max} decreased by approximately 20% to 52% in patients with end-stage renal impairment who required dialysis in comparison with healthy adult subjects. (Non-Japanese data)

(3) Patients With Hepatic Impairment[5]

No notable difference was found in pharmacokinetics of the active metabolite R-138727 after a single oral prasugrel dose of 60 mg on Day 1 and once daily oral prasugrel dose of 10 mg on Days 2 to 6 between patients with moderate hepatic impairment (Child–Pugh Class B) and healthy adult subjects. (Non-Japanese data)

(4) Geriatric Patients[2]

In the elderly (age ≥ 75 years), compared to nonelderly patients, no differences were found in the pharmacokinetic

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profiles of the active metabolite R-138727 when elderly patients (age ≥ 75 years) were orally administered 20 mg of prasugrel on Day 1 of treatment and 3.75 mg of prasugrel once daily on Days 2 to 7.

2. Distribution

(Reference: animal studies)

In rats that were administered a single oral dose of ^{14}C-prasugrel, the concentration of radioactivity reached the maximum at 1 hour post-dose in many tissues. The levels of radioactivity were higher in the stomach, small intestine, liver, kidney, and urinary bladder than in the blood. At 72 hours post the dose, the thyroid gland and aorta showed higher levels of radioactivity than blood. The levels in other tissues were similar to or lower than those in the blood. The tissue distribution of radioactivity reached a steady state on Day 14 of repeated dosing.

3. Metabolism

Orally administered prasugrel hydrochloride is rapidly metabolized to R-95913 by carboxylesterases in human small intestine, and R-138727, the active metabolite, is formed following additional metabolism by cytochrome P450 (CYP) drug metabolizing enzymes in the small intestine and liver. In vitro studies suggest that CYP3A and CYP2B6 isozymes are primarily involved in metabolizing prasugrel to R-138727.

4. Excretion

In healthy male adults that were administered a single oral 15-mg dose of ^{14}C-prasugrel, the 240-hour cumulative excretion rate of radioactivity was ≥ 95%. Approximately 68% of the radioactivity was excreted in the urine and approximately 27% in the feces.

(Non-Japanese data)

5. Effect of Food

Considering the pharmacokinetics of the active metabolite R-138727 following single oral dosing with 20 mg of prasugrel in healthy adult males, C_{max} was approximately 3.3 times higher following dosing in a fasted condition than in a fed condition, and no appreciable difference was found in AUC.

6. Drug interactions

When prasugrel hydrochloride was administered in combination with ketoconazole, a CYP3A4 inhibitor, the C_{max} of the active metabolite R-138727 decreased by approximately 46% at the loading dose (60 mg) and by approximately 34% at the maintenance dose (15 mg) in comparison with prasugrel hydrochloride monotherapy; however, no effects were observed on the $AUC_{0\text{-}24h}$. No effects of concomitant ketoconazole were observed on the rate of inhibition of platelet aggregation (20 μM ADP-induced) at the loading dose or maintenance dose. No effects of prior therapy with rifampicin, a CYP3A4 inducer, were observed on R-138727 exposure.

When prasugrel was administered at 60 mg in combination with lansoprazole, a proton pump inhibitor, or ranitidine, a H_2 receptor antagonist, the C_{max} of R-138727 decreased by approximately 14% to 29% in comparison with prasugrel hydrochloride monotherapy; however, no effects were observed on the AUC. No effects of these combinations were observed on the inhibitory effect on platelet aggregation (inhibition of platelet activation).[5, 7]

(Non-Japanese data)

Note) The approved doses of EFFIENT are 20 mg as the loading dose and 3.75 mg/day as the maintenance dose.

CLINICAL STUDIES

1. Japanese Clinical Studies

(1) Acute Coronary Syndromes (unstable angina, non-ST-segment elevation myocardial infarction, and ST-segment elevation myocardial infarction)[8]

In the Japanese phase 3 study in 1385 patients with ACS (UA, NSTEMI, and STEMI) who undergo PCI, the incidence of major adverse cardiovascular events during the period from initiation of treatment with investigational drug to Week 24 was as follows.

Incidence of Major Adverse Cardiovascular Events [a] During the Period From Initiation of Treatment With Investigational Drug to Week 24 in Patients With ACS (UA, NSTEMI, or STEMI) Who Undergo PCI (Japanese Phase 3 Study)

	Prasugrel [b]	Clopidogrel [c]	Hazard Ratio (95% CI)
Incidence (No. of events)	9.3% (64/685)	11.8% (80/678)	0.773 (0.557, 1.074)

a) Composite endpoint of cardiovascular death, nonfatal myocardial infarction, or nonfatal ischaemic stroke
b) Prasugrel loading dose of 20 mg and maintenance dose of 3.75 mg/day, in combination with aspirin at 81–100 mg/day
c) Clopidogrel loading dose of 300 mg and maintenance dose of 75 mg/day, in combination with aspirin at 81–100 mg/day

The incidence of non-coronary artery bypass grafting (CABG)-related major or minor bleeding was 5.7% (39 of 685 subjects) in the prasugrel group and 4.3% (29 of 678 subjects) in the clopidogrel group. The incidence of PCI complications in these subjects was 2.8% (19 of 685 subjects) in the prasugrel group and 1.8% (12 of 678 subjects) in the clopidogrel group.

The incidence of non-CABG-related major, minor, or clinically significant bleeding was 9.6% (66 of 685 subjects) in the prasugrel group and 9.6% (65 of 678 subjects) in the clopidogrel group. In patients who underwent CABG within 14 days following the end of EFFIENT therapy, major, minor, or clinically significant bleeding occurred in 9 of 10 subjects in the prasugrel group and 7 of 9 subjects in the clopidogrel group.

As a rule, EFFIENT was taken after food, except for the loading dose.

(2) Stable Angina and Old Myocardial Infarction[9]

The incidence of major adverse cardiovascular events during the period from initiation of treatment with investigational drug to Week 24 in the Japanese phase 3 study in 774 patients with stable angina and old myocardial infarction was as follows.

Incidence of Major Adverse Cardiovascular Events [a] During the Period From Initiation of Treatment With Investigational Drug to Week 24 in Patients With Stable Angina and Old Myocardial Infarction (Japanese Phase 3 Study)

	Prasugrel [b]	Clopidogrel [c,d]
Incidence (No. of events)	4.1% (15/370)	6.7% (25/372)

a) Composite endpoint of cardiovascular death, nonfatal myocardial infarction, or nonfatal ischaemic stroke
b) Prasugrel loading dose of 20 mg and maintenance dose of 3.75 mg/day, or skip prasugrel loading dose and administer prasugrel maintenance dose of 3.75 mg/day, in combination with aspirin at 81–100 mg/day
c) Clopidogrel loading dose of 300 mg and maintenance dose of 75 mg/day, or skip clopidogrel loading dose and administer clopidogrel maintenance dose at 75 mg/day, in combination with aspirin at 81–100 mg/day
d) Group used for reference; not used in statistical comparisons

The incidence of non-CABG-related major, minor, or clinically significant bleeding was 5.4% (20 of 370 subjects) in the prasugrel group and 6.2% (23 of 372 subjects) in the clopidogrel group. In patients who underwent CABG within 14 days following the end of EFFIENT therapy, major, minor, or clinically significant bleeding occurred in 3 of 3 subjects in the prasugrel group and 1 of 1 subject in the clopidogrel group.

As a rule, EFFIENT was taken after food, except for the loading dose.

In addition, the incidence of major cardiovascular events (composite endpoint comprising all deaths, nonfatal myocardial infarction, nonfatal stroke, myocardial ischemia requiring rehospitalization, and revascularization) up to Week 12 in elderly (age ≥ 75 years) or low-body-weight (body weight ≤ 50 kg) subjects in the Japanese phase 2 study was 5.4% (2 of 37 subjects) in the prasugrel 2.5 mg group,[a] 10.8% (4 of 37 subjects) in the prasugrel 3.75 mg group,[b] and 11.1% (4 of 36 subjects) in the clopidogrel group.[c,d]

The incidence of non-CABG-related major or minor bleeding was 0% (0 of 37 subjects) in the prasugrel 2.5 mg group, 2.7% (1 of 37 subjects) in the prasugrel 3.75 mg group, and 2.8% (1 of 36 subjects) in the clopidogrel group.

a) Prasugrel loading dose of 20 mg and maintenance dose of 2.5 mg/day, in combination with aspirin at 81–100 mg/day
b) Prasugrel loading dose of 20 mg and maintenance dose of 3.75 mg/day, in combination with aspirin at 81–100 mg/day
c) Clopidogrel loading dose of 300 mg and maintenance dose of 75 mg/day, in combination with aspirin at 81–100 mg/day
d) Group used for reference; not used in statistical comparisons

2. Overseas Clinical Studies[10]

In the overseas phase 3 study in 13619 patients with ACS (UA, NSTEMI, and STEMI) who undergo PCI, the incidence of major adverse cardiovascular events was as follows.

Incidence of Major Adverse Cardiovascular Events [a] in Patients With ACS (UA, NSTEMI, or STEMI) Who Undergo PCI (Overseas Phase 3 Study)

	Incidence (No. of Events)	Hazard Ratio (95% CI)	*P* Value [d]
	Prasugrel [b] / Clopidogrel [c]		
Overall ACS	9.44% (643/6813) / 11.49% (781/6795)	0.812 (0.732, 0.902)	*P* < 0.001
UA, NSTEMI	9.30% (469/5044) / 11.23% (565/5030)	0.820 (0.726, 0.927)	*P* = 0.002
STEMI	9.84% (174/1769) / 12.24% (216/1765)	0.793 (0.649, 0.968)	*P* = 0.019

a) Composite endpoint of cardiovascular death, nonfatal myocardial infarction, or nonfatal stroke
b) Prasugrel loading dose of 60 mg and maintenance dose of 10 mg/day administered for 6 months to 15 months, in combination with aspirin at 75–325 mg/day
c) Clopidogrel loading dose of 300 mg and maintenance dose of 75 mg/day administered for 6 months to 15 months, in combination with aspirin at 75–325 mg/day
d) Gehan–Wilcoxon test. First, analysis was conducted in patients with UA/NSTEMI. In cases in which superiority of prasugrel was verified, analysis was conducted in patients with overall ACS including patients with STEMI.

The incidence of non-CABG-related major or minor bleeding was 4.5% (303 of 6741 subjects) in the prasugrel group and 3.4% (231 of 6716 subjects) in the clopidogrel group. The incidence of major bleeding in CABG patients was 11.3% (24 of 213 subjects) in the prasugrel group, and 3.6% (8 of 224 subjects) in the clopidogrel group.

Note) The approved doses of EFFIENT are 20 mg as the loading dose and 3.75 mg/day as the maintenance dose.

(INDICATION)

EFFIENT, co-administered with acetylsalicylic acid (ASA), is indicated for acute coronary syndrome (i.e. unstable angina, non-ST segment elevation myocardial infarction [UA/NSTEMI] or ST segment elevation myocardial infarction [STEMI]) undergoing primary or delayed percutaneous coronary intervention (PCI), and stable angina requiring elective PCI.

(DOSAGE AND ADMINISTRATION)

EFFIENT should be initiated with a single 20-mg oral dose and then continued at a 3.75-mg once daily oral dose as a maintenance dose.

(CONTRAINDICATIONS)

EFFIENT is contraindicated for use in the following patients:

1. Patients with bleeding (with hemophilia, intracranial hemorrhage, gastrointestinal hemorrhage, urinary tract hemorrhage, hemoptysis, vitreous hemorrhage, etc). [EFFIENT may enhance bleeding.]
2. Patients with a history of hypersensitivity to any component of the product.

(PRECAUTIONS)

1. Precaution related to indications

EFFIENT can be administered to patients with ischemic heart disease who are to undergo PCI.

Administration of EFFIENT should be discontinued when the surgeon decides to adopt conservative therapy or coronary

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18,5 cm

28,0 cm

9. Precautions Concerning Administration

At the time of dispensing blister packs, instruct the patient to take the tablets out of the packaging for ingestion. (Cases of mediastinitis and other serious complications were reported when the hard edge of a blister pack was swallowed by mistake, which became embedded in the esophageal mucosa and led to perforation.)

10. Other Precautions

An increased incidence of hepatic tumors in male and female mice orally exposed for 2 years to ≥ 300 mg/kg/day and ≥ 100 mg/kg/day, respectively, was noted. However, no treatment-related tumors were noted in a 2-year oral rat study.

(STORAGE)

Do not store above 30°C.

(SHELF LIFE)

Please refer to outer carton, pillow, or blister package

ON DOCTOR PRESCRIPTION ONLY
HARUS DENGAN RESEP DOKTER

(PACKAGING)

EFFIENT Tablets 3.75 mg	: Box, pouch, desiccant, 2 blisters @ 14 tablets	Reg. No: DKI2056600117A1
EFFIENT Tablets 5 mg	: Box, pouch, desiccant, 2 blisters @ 8 tablets	Reg. No: DKI2056600117B1

REFERENCES

1. References:

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Bandung, Indonesia

PI/SO/EFF-DOM/02-2021/01

DISETUJUI OLEH BPOM : 24/8/2025 DEPAN 2

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artery bypass grafting instead of PCI based on the coronary angiography.

2.Precaution related to dosage and administration

(1) EFFIENT should be used in combination with aspirin (81 –100 mg/day; up to 324 mg may be used as a loading dose).
(2) Before administering EFFIENT to patients implanted with a stent, carefully read the instructions on the label for the stent.
(3) The loading dose (ie, the 20-mg dose on the first day of treatment) is not necessary in patients who have received doses of 3.75 mg of EFFIENT for approximately 5 days before undergoing PCI. (It is expected that EFFIENT-induced inhibition of platelet aggregation would reach a steady state in 5 days.)
(4) It is not recommended to administer EFFIENT in a fasted condition (except for the administration of the loading dose). (See the "Pharmacokinetics" and "Clinical Studies" sections.)

3.Precautions

1. Careful Administration: EFFIENT should be administered with care to the following patients:
   (1) Patients with a propensity to bleed or predisposition to bleeding (patients with a medical history of intracranial hemorrhage) [EFFIENT may cause bleeding.]
   (2) Patients with severe hepatic impairment [EFFIENT may increase the risk of bleeding because patients with severe hepatic impairment produce low levels of coagulation factors.]
   (3) Patients with severe renal impairment [EFFIENT may increase the risk of bleeding.]
   (4) Patients with continued high blood pressure (see Important Precautions)
   (5) Elderly patients [EFFIENT may increase the risk of bleeding (see Geriatric Use).
   (6) Low-body weight patients [Low-body-weight patients may be at an increased risk of bleeding. In patients with body weight ≤ 50 kg, the risk of thrombotic events and other risk factors for bleeding, such as age and renal function, should be evaluated, and, if necessary, dose reduction to a maintenance dose of 2.5 mg once daily should be considered. (See the "Clinical Studies" section.)]
   (7) Patients with a history of cerebral infarction or transient ischemic attack (TIA) [Overseas clinical studies reported an increased risk of bleeding when EFFIENT was administered at the loading dose of 60 mg and maintenance dose of 10 mg/day with concomitant aspirin.]
   Note) The approved doses of EFFIENT are 20 mg as the loading dose and 3.75 mg/day as the maintenance dose.
   (8) Patients with a history of hypersensitivity to other thienopyridines (eg, clopidogrel). [Hypersensitivity including angioedema has been reported in patients receiving EFFIENT, including patients with a history of hypersensitivity to other thienopyridines.]

2. Important Precautions
   (1) Pay attention to the possibility that the loading dose and the concurrent use of aspirin could increase the risk of bleeding.
   (2) In the case where the loading dose is given prior to coronary angiography, pay attention to the increased risk of bleeding, such as puncture site bleeding, due to the EFFIENT-induced inhibition of platelet aggregation. [In an overseas clinical study in NSTEMI patients (the ACCOAST Study[1]), compared to a standard loading dose of 60 mg given at the time of PCI, a split loading dose of 30 mg given on average 4 hours prior to coronary angiography followed by an additional 30 mg at the time of PCI resulted in an increased risk of serious peri-procedural bleeding with no additional benefit.]
   Note) The approved doses of EFFIENT are 20 mg as the loading dose and 3.75 mg/day as the maintenance dose.
   (3) In the case where EFFIENT-induced inhibition of platelet aggregation may be problematic for patients undergoing surgery, the prescribing physician is recommended to discontinue EFFIENT at least 14 days prior to surgery (see the "Clinical Studies" section). Patients who cannot have a sufficient washout period should be closely observed for elevated risks of serious bleeding. Appropriate measures should be taken to prevent thrombosis and embolism in discontinued patients who are at a high risk of developing these disorders. For postoperative patients restarting EFFIENT, confirm cessation of surgical-site bleeding before resuming therapy.
   (4) Patients with continued high blood pressure will require careful administration of EFFIENT and appropriate measures for blood pressure control during treatment.
   (5) Anticoagulant, aspirin, and EFFIENT should be coadministered with caution, as such use may result in an increased risk of bleeding.
   (6) If a patient is believed to be at a high risk of bleeding, consideration should be given to discontinuing treatment. If clinical symptoms suggesting bleeding are suspected, appropriate tests, such as blood cell assessments, should be performed immediately (see the "Adverse Drug Reactions" section).
   (7) Explain to patients that EFFIENT can make them more prone to bleeding than usual, and instruct them to contact their physician if an abnormal bleeding develops. Instruct patients to inform their physician that they are taking EFFIENT when they visit other hospital departments or clinics.
   (8) EFFIENT may cause thrombotic thrombocytopenic purpura (TTP) and other significant adverse drug reactions. Consider having blood testing approximately once a fortnight during the first 2 months after initiating the treatment with EFFIENT (see the "Adverse Drug Reactions" section).

3.Drug Interactions

[Precautions for Concomitant Medications] Attention should be paid to the concomitant use of the following drugs:

Drugs	Signs, Symptoms, and Treatment	Mechanism of Action and Risk Factors
Anticoagulants eg, warfarin, heparin, and edoxaban Antiplatelet drugs eg, aspirin Thrombolytic drugs eg, urokinase and alteplase	EFFIENT may increase the risk of bleeding when administered with these medications. Pay attention to the conditions of patients when administering EFFIENT in combination with these medications.	EFFIENT and these medications may mutually enhance the antithrombotic effect.
NSAIDS eg, loxoprofen and naproxen		

4. Adverse Reactions

In the Japanese phase 3 clinical studies of EFFIENT Tablets, adverse drug reactions (including laboratory abnormality) were reported in 487 of 1055 subjects (46.2%). Major adverse drug reactions included haemorrhage subcutaneous (n = 109, 10.3%), epistaxis (n = 72, 6.8%), haematuria (n = 58, 5.5%), vessel puncture site haematoma (n = 44, 4.2%), and subcutaneous haematoma (n = 41, 3.9%) [Data at approval].

(1) Significant Adverse Drug Reactions

1) **Bleeding**: EFFIENT may cause intracranial hemorrhage (early symptoms include headache, nausea/vomiting, consciousness disorder, hemiplegia, etc), gastrointestinal hemorrhage, pericardial haemorrhage, and other bleeding (incidence = 1.2%). Observe patients closely, and if any abnormalities are found, treatment should be discontinued, and appropriate action should be taken.
2) **TTP (frequency unknown[Note])**: If malaise, anorexia, bleeding (eg, purpura), neuropsychiatric manifestations (eg, consciousness disorder), thrombocytopenia, hemolytic anemia with fragmented erythrocytes, pyrexia, renal impairment, or other early signs of TTP occur, discontinue EFFIENT therapy immediately and perform blood tests (reticulocytes and fragmented erythrocytes). Conduct plasma exchange or other appropriate measures, where relevant.
3) **Hypersensitivity (frequency unknown [Note])**: Hypersensitivity including angioedema has been reported. Observe patients closely, and if any abnormalities are found, treatment should be discontinued, and appropriate action should be taken.

(2) Significant Adverse Drug Reactions (Similar Drugs of the Same Class)

The following events were reported as significant adverse drug reactions for several antiplatelet medications. Carefully observe for these events and take appropriate measures if detected.

1) Hepatic function disorder and jaundice
2) Agranulocytosis, aplastic anaemia, and other forms of pancytopenia

(3) Other Adverse Drug Reactions

EFFIENT may cause the following adverse drug reactions. If one or more of these signs are observed, take appropriate measures for treatment.

	≥1%	≥0.1% to <1%
Blood	Anemia	Platelet count decreased, eosinophil count increased, and white blood cell count decreased
Propensity to bleed	Hemorrhage subcutaneous (10.3%), epistaxis, hematuria, vessel puncture site hematoma, subcutaneous hematoma, puncture site hemorrhage, hematoma, procedural hemorrhage, gingival bleeding, occult blood, conjunctival hemorrhage, hemorrhoidal hemorrhage, and wound hemorrhage	Hemoptysis, gastrointestinal hemorrhage, retinal hemorrhage, hemorrhage, upper gastrointestinal hemorrhage, mouth hemorrhage, catheter site hemorrhage, purpura, vitreous hemorrhage, diverticulum intestinal hemorrhagic, lower gastrointestinal hemorrhage, petechiae, and vascular pseudoaneurysm
Hepatic	Hepatic function disorder	γ-GTP increased, ALP increased, ALT (GPT) increased, and AST (GOT) increased
Renal		Renal impairment
Nervous system and psychiatric		Dizziness
Gastrointestinal		Diarrhea, constipation, nausea/vomiting, gastroesophageal reflux disease, abdominal pain, abdominal discomfort, and gastritis
Hypersensitivity	Rash	Erythema
Other		Uric acid increased, edema peripheral, back pain, vessel puncture site swelling, blood thyroid stimulating hormone increased, and angina pectoris

Note: Frequencies for these adverse drug reactions reported overseas were unknown.

5. Geriatric Use

Elderly patients generally have compromised physiological functions. Carefully administer EFFIENT and observe their conditions.

6. Use in Pregnant, Parturient, and Lactating Women

(1) Administer EFFIENT in pregnant and possibly pregnant women only when the expected therapeutic benefits outweigh the possible risks. [Safety in pregnant women has not been established, and it was noted that EFFIENT metabolites were excreted in the fetus of rats.]
(2) Nursing mothers should refrain from breastfeeding while taking EFFIENT. [It was noted that EFFIENT metabolites were excreted in the breast milk of rats.]

7. Pediatric Use

Safety in low birth-weight infants, newborns, nursing infants, infants, or pediatric patients has not been established. [There is no clinical experience with the use of EFFIENT in Japanese children.]

8. Overdosage

Overdosage may cause bleeding. Take appropriate measures if bleeding occurs. There is no specific antidote. Consider platelet transfusion in case of emergency.

DISETUJUI OLEH BPOM : 24/8/2023

BELAKANG 2

ID : EREG10002812500043
EREG10002812500044

CV. SANIC OFFSET		DIAJUKAN TANGGAL :	NO :
RELASI	PT MITSUBISHI TANABE PHARMA	26 / 01 / 2021	000
NAMA ITEM	BROCHURE EFFIENT (DEPAN 3)	HASIL ACC DITERIMA OLEH :	
UK JADI	18,1 X 28 CM		CATATAN :
WARNA	HITAM ■		REVISI 2
LAIN-LAIN		(.....)	

18,1 cm

28,0 cm

Leaflet: Informasi Produk Untuk Pasien

EFFIENT 3,75 mg Tablet
EFFIENT 5 mg Tablet

Prasugrel hydrochloride

Mohon leaflet ini dibaca baik-baik sebelum Anda mulai mengonsumsi obat ini karena mengandung informasi penting untuk Anda.

- Simpan leaflet ini setelah Anda baca. Anda mungkin perlu membacanya lagi.
- Jika Anda memiliki pertanyaan lebih lanjut, tanyakan pada dokter atau tenaga kesehatan lainnya.
- Jika Anda mengalami efek samping, konsultasikan kepada dokter atau tenaga kesehatan lainnya. Termasuk kemungkinan efek samping yang tidak tercantum di leaflet ini. Lihat Bagian 4.

Apa yang ada dalam leaflet ini

1. Apa itu EFFIENT dan apa kegunaannya

EFFIENT mengandung zat aktif prasugrel hydrochloride.

Obat ini diberikan bersama dengan asam asetilsalisilat (ASA) yang digunakan untuk

- sindrom koroner akut, yaitu
  - angina tidak stabil, yakni kondisi dimana otot-otot jantung kurang mendapatkan asupan oksigen dari darah.
  - Infark miokard tanpa peningkatan segmen ST atau
  - Infark miokard dengan peningkatan segmen ST

  yang menjalani Intervensi Koroner Perkutan/ *Percutaneous Coronary Intervension (PCI)* primer atau tertunda, yakni suatu prosedur untuk menangani penyempitan arteri koroner.
- angina stabil yang membutuhkan PCI elektif

2. Apa yang perlu Anda tahu sebelum menggunakan EFFIENT

Jangan menggunakan EFFIENT:

- Jika Anda pasien dengan perdarahan (dengan hemofilia /kekurangan faktor pembekuan darah, perdarahan intrakranial/perdarahan di dalam tulang tengkorak, perdarahan gastrointestinal/saluran pencernaan, perdarahan saluran kemih/urin, hemoptisis/ batuk berdarah, perdarahan vitreus/bagian pada mata, dll). [EFFIENT mungkin dapat meningkatkan perdarahan].
- Jika Anda pasien dengan riwayat alergi atau hipersensitif terhadap bahan atau komposisi produk ini (Lihat Bagian 6)

Jika hal-hal di atas berlaku untuk Anda, jangan gunakan EFFIENT dan beri tahu dokter atau tenaga kesehatan lainnya. Jika Anda tidak yakin, konsultasikan kepada dokter atau tenaga kesehatan lain sebelum menggunakan EFFIENT.

Peringatan dan Perhatian

- Dokter akan memberikan perhatian terhadap kemungkinan *loading dose* (dosis awal yang diberikan agar mencapai konsentrasi obat yang cukup secara tepat di dalam darah sehingga tercapai dosis terapi) dan penggunaan EFFIENT dengan aspirin secara bersamaan dapat meningkatkan risiko perdarahan.
- Penggunaan EFFIENT pada saat *loading dose* jika diberikan sebelum angiografi koroner/tindakan kateterisasi dapat meningkatkan risiko perdarahan.
- EFFIENT dapat menghambat pelepasan trombosit/keping darah sehingga sangat berisiko pada pasien yang menjalani operasi, dokter yang meresepkan dianjurkan untuk menghentikan EFFIENT setidaknya 14 hari sebelum pembedahan.
- Pasien dengan tekanan darah tinggi memerlukan pemantauan penggunaan EFFIENT secara cermat untuk mengontrol tekanan darah selama pengobatan.
- Antikoagulan, aspirin, dan EFFIENT jika digunakan bersamaan harus dengan hati-hati, karena penggunaan tersebut dapat mengakibatkan peningkatan risiko perdarahan.

Sebelum menggunakan obat ini, ceritakan pada dokter atau tenaga kesehatan lain:

- Jika Anda mempunyai kecenderungan perdarahan atau predisposisi perdarahan (pasien dengan riwayat medis perdarahan intrakranial/tengkorak)
- Jika Anda mengalami gangguan hati berat
- Jika Anda mengalami gangguan ginjal berat
- Jika Anda mengalami hipertensi/tekanan darah tinggi
- Jika Anda pasien dengan usia lanjut
- Jika Anda pasien dengan berat badan rendah
- Jika Anda pasien dengan riwayat infark serebral atau *transient ischemic attack* (TIA) / kematian sel-sel otak akibat kekurangan oksigen
- Jika Anda pasien dengan riwayat alergi/hipersensitif terhadap tienopiridin/ golongan obat anti-platelet lainnya (misalnya klopidogrel)

Jika Anda tidak yakin jika hal-hal di atas berlaku untuk Anda, konsultasikanlah dengan dokter atau tenaga kesahatan lain Anda sebelum menggunakan EFFIENT.

Obat lain dan EFFIENT

Ceritakan kepada dokter Anda jika Anda sedang menggunakan atau baru saja menggunakan obat lain. Termasuk obat-obatan yang Anda beli tanpa resep dan obat-obatan herbal.

Kehamilan, Proses Persalinan dan Menyusui

Wanita hamil dan mungkin hamil boleh menggunakan EFFIENT hanya jika manfaat terapeutik yang diharapkan lebih besar daripada risiko yang mungkin terjadi. [Keamanan pada wanita hamil belum ditetapkan, dan tercatat bahwa metabolit EFFIENT dikeluarkan pada janin tikus.]

Ibu menyusui harus menahan diri dari menyusui saat menggunakan EFFIENT. [Telah dicatat bahwa metabolit EFFIENT dikeluarkan dalam ASI tikus.]

Penggunaan EFFIENT pada usia lanjut

Perlu pemantauan khusus untuk penggunaan EFFIENT pada usia lanjut karena pasien dengan usia lanjut umumnya memiliki fungsi fisiologis yang rendah.

Penggunaan EFFIENT pada Pediatrik

Keamanan pada bayi berat lahir rendah, bayi baru lahir, bayi menyusui, bayi, atau pasien anak belum ditetapkan.

3. Bagaimana cara penggunaan EFFIENT

EFFIENT digunakan secara oral, diberikan dengan dosis tunggal dengan dosis awal 20 mg, kemudian dilanjutkan dengan dosis 3,75 mg sehari sekali sebagai dosis pemeliharaan.

Selalu minum EFFIENT seperti yang diinstruksikan oleh dokter Anda.

4. Kemungkinan efek samping

Seperti semua obat-obatan, obat ini dapat menyebabkan efek samping meskipun tidak semua orang mengalaminya.

Efek samping berikut dapat terjadi. Jika terjadi, dokter Anda akan memberi Anda perawatan yang tepat.

Efek samping yang signifikan

- Perdarahan
- *Thrombotic thrombocytopenic purpura* (TTP) atau kelainan darah
- Hipersensitifitas/alergi

Efek samping yang signifikan (obat sejenis dari kelas yang sama)

- Gangguan fungsi hati
- Jaundice atau perubahan warna kuning pada kulit dan mata
- Agranulositosis, anemia aplastik, dan bentuk pansitopenia lainnya

Efek samping lain

- Anemia (kekurangan sel darah merah)
- Jumlah trombosit menurun, jumlah eosinofil meningkat, dan jumlah sel darah putih menurun
- Kecenderungan mengalami perdarahan
- Gangguan fungsi hati
- Gangguan ginjal
- Pusing
- Diare
- Konstipasi atau sembelit
- Mual/muntah
- *Gastroesophageal Reflux Disease* (GERD) atau penyakit asam lambung yang ditandai dengan nyeri pada ulu hati atau sensasi terbakar di dada akibat naiknya asam lambung menuju esofagus (kerongkongan)
- Nyeri perut

DISETUJUI OLEH BPOM : 24/8/2025 DEPAN 3

ID : EREG10002812500043
EREG10002812500044

SANIC **CV. SANIC OFFSET**		DIAJUKAN TANGGAL :	NO : 000
RELASI	**PT MITSUBISHI TANABE PHARMA**	**26 / 01 / 2021**	
NAMA ITEM	**BROCHURE EFFIENT (BELAKANG 3)**	HASIL ACC DITERIMA OLEH :	
UK JADI	**18,1 X 28 CM**		CATATAN : **REVISI 2**
WARNA	**HITAM** ■		
LAIN-LAIN		(.....)	

18,1 cm

28,0 cm

- Gastritis atau iritasi lambung
- Ruam
- Asam urat meningkat
- Edema perifer/pembengkakan pada kaki
- Sakit punggung
- Pembengkakan pembuluh darah
- Hormon stimulasi tiroid (kelenjar pada bagian depan leher/kelenjar gondok) darah meningkat
- Angina pektoris/kekurangan pasokan darah pada otot jantung

Jika Anda berpikir Anda memiliki efek samping atau jika Anda mengalami efek samping yang tidak tercantum dalam leaflet ini, harap beri tahu dokter atau tenaga kesehatan lain Anda.

Pelaporan efek samping

Jika Anda mengalami efek samping, konsultasikan dengan dokter, apoteker, atau perawat Anda. Ini termasuk semua kemungkinan efek samping yang tidak tercantum dalam leaflet ini. Dengan melaporkan efek samping Anda dapat membantu memberikan informasi lebih lanjut tentang keamanan obat ini.

5. Bagaimana cara penyimpanan EFFIENT

- Simpan obat ini tidak lebih dari suhu 30^0C.
- Jauhkan obat ini dari pandangan dan jangkauan anak-anak.
- Jangan gunakan EFFIENT setelah tanggal kadaluwarsa yang tercantum pada karton.

6. Isi kemasan dan informasi lainnya

Apa kandungan EFFIENT

Zat aktifnya adalah prasugrel 3,75 mg dan 5 mg dalam setiap tablet.

Bahan lainnya adalah Lactose monohydrate, microcrystalline cellulose, low substituted hydroxypropylcellulose, hydroxypropylcellulose, magnesium stearate, hypromellose, titanium oxide, talc, red ferric oxide, dan yellow ferric oxide.

Seperti apa EFFIENT dan isi kemasannya

EFFIENT 3,75 mg adalah tablet salut selaput berbentuk lonjong berwarna putih kemerahan dalam kemasan dus, pouch, dessicant, 28 tablet (2 blister @ 14 tablet).

EFFIENT 5 mg adalah tablet salut selaput dengan garis tengah berbentuk lonjong berwarna merah sedikit kekuningan dengan kemasan dus, pouch, dessicant, 16 tablet (2 blister @ 8 tablet).

7. Nomor Izin Edar

EFFIENT 3,75 mg Tablet Reg. No: DKI2056600117A1

EFFIENT 5 mg Tablet Reg. No: DKI2056600117B1

8. Peringatan khusus

HARUS DENGAN RESEP DOKTER

Dibawah lisensi oleh:

DAIICHI SANKYO CO., LTD.

3-5-1, Nihonbashi Honcho, Chuo-ku, Tokyo, Japan

Dibuat dan dikemas primer oleh:

TAIYO Pharma Tech Co., Ltd.

4-38, Aketacho, Takatsuki, Osaka, Japan

Diimpor, dikemas sekunder dan dirilis oleh:

PT Mitsubishi Tanabe Pharma Indonesia

Bandung, Indonesia

Leaflet ini direvisi terakhir di Jakarta<{06/2020}>

DISETUJUI OLEH BPOM : 24/8/2020

BELAKANG 3

ID : EREG10002812500043
EREG10002812500044