PRASUGREL

TARGET AUDIENCE: All Canadian health care professionals.

OBJECTIVE:

To provide practical point of care knowledge on the optimal utilization and management of prasugrel in clinical practice.

ABBREVIATIONS:

ACS	acute coronary syndrome
ADP	adenosine diphosphate
ARR	absolute risk reduction
ASA	acetyl salicylic acid
CABG	coronary artery bypass graft
MI	myocardial infarction
NNH	number needed to harm
NNT	number needed to treat
PCI	percutaneous coronary intervention
TIA	transient ischemic attack

MECHANISM OF ACTION:

Prasugrel (Effient®) is an irreversible inhibitor of platelet activation and aggregation through the irreversible binding of its active metabolite to the P2Y12 adenosine diphosphate (ADP) receptor on platelets.

INDICATION:

Prasugrel, co-administered with acetyl salicylic acid (ASA), is indicated for the secondary prevention of ischemic cardiac events in patients with an acute coronary syndrome (ACS) (i.e. unstable angina, ST elevation myocardial infarction or non-ST elevation myocardial infarction) with defined coronary anatomy and managed with percutaneous coronary intervention (PCI).

Use of prasugrel should be considered because:

a) a large phase 3 randomized trial demonstrated a significant 2.2% absolute risk reduction (ARR) with prasugrel in the combined rate of myocardial infarction (MI), cardiovascular death and stroke (driven mostly by MI) compared with clopidogrel, in patients presenting with ACS managed by PCI (number needed to treat (NNT) = 46). MI and stent thrombosis were also significantly reduced (ARR 2.3%; NNT = 43 and ARR 1.3%; NNT = 77, respectively).
b) the benefit of prasugrel has been demonstrated only in patients with ACS undergoing PCI.

DOSING:

In patients with ACS, a loading dose of 60 mg of should be administered. Following hospital discharge, prasugrel should be administered at a dose of 10 mg daily, or 5 mg may be considered in patients weighing < 60 kg or age ≥ 75 years. Absorption is not affected by food intake and no dosing adjustment is required in patients with chronic renal disease or in patients with mild to moderate hepatic impairment. Patients taking prasugrel should also take ASA 81 mg daily, unless specifically contraindicated.

MONITORING:

No monitoring of prasugrel is required.

ADVERSE EFFECTS:

As with all antiplatelet agents, prasugrel increases the risk of major bleeding including intra-cerebral hemorrhage. In TRITON-TIMI 38, a 1-year study of 13,608 ACS patients undergoing PCI, non-coronary artery bypass graft (CABG)-related major bleeding occurred in approximately 2.4% of subjects, a significant absolute increase of 0.6% compared with clopidogrel (number needed to harm [NNH] = 167). Fatal bleeding, although rare, was also significantly increased compared with clopidogrel (0.4% vs 0.1%; NNH = 333). Although intracranial hemorrhage was not increased, patients with a history of stroke or transient ischemic attack were at significantly greater risk. Major bleeding was also increased, and net clinical benefit was lost, in patients 75 years of age or over, or with a body weight < 60 kg.

PERI-PROCEDURAL MANAGEMENT:

The peri-procedural use of antiplatelet agents may increase the risk of bleeding and transfusion requirements associated with surgery and other invasive procedures. However, discontinuation of dual antiplatelet therapy within 12 months of drug-eluting stent implantation or within 6 weeks of bare-metal stent implantation is associated with a large increased risk of major adverse cardiovascular events and stent thrombosis. For this reason, procedures associated with significant bleeding risk should be delayed beyond these time frames if possible, and, if not possible, done with the patient remaining on therapy. If prasugrel can be stopped safely, it should be discontinued 7 days prior to surgery. In general, consultation with a specialist is advised before discontinuing prasugrel in patients with a coronary stent. In patients undergoing a minor procedure (e.g. dental, skin, cataract, arthrocentesis), discontinuation may not be necessary.

SPECIAL CONSIDERATIONS:

Due to increased risk of fatal and intracranial bleeding, prasugrel should be avoided in patients with a history of stroke or transient ischemic attack (TIA). In patients age ≥75 years or weight <60 kg a dose of 5 mg once daily may be considered.

PEDIATRICS:

There are no studies evaluating the use of prasugrel in children. Use of prasugrel in children is not recommended until dosing, safety and efficacy are confirmed.

REFERENCES:

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