Date of preparation: July 2019

PRASUGREL EDUCATIONAL MATERIAL FOR PHYSICIANS ON THE RISK OF BLEEDING

This guidance note is an obligatory part of the prasugrel marketing authorisation. It has been included as an additional risk-minimisation measure to reduce the risk of serious adverse reactions such as bleeding and to increase the risk-benefit ratio of prasugrel.

IMPORTANT INFORMATION ON PRASUGREL KRKA (PRASUGREL)[1]

Indication
Prasugrel Krka (active substance prasugrel) is indicated in combination with acetylsalicylic acid (ASA) for the prevention of atherothrombotic events in adult patients with 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).

Pivotal study
The phase 3 TRITON study showed superior efficacy of prasugrel vs clopidogrel in the UA/NSTEMI cohort.

The efficacy and tolerability of prasugrel and clopidogrel were compared with regard to the reduction of atherothrombotic events (as a combined endpoint including cardiovascular death, non-fatal myocardial infraction or non-fatal stroke) in 13,608 patients with acute coronary syndrome (ACS) undergoing PCI.

Total ACS population
With a 9.4% incidence of the primary endpoint in the total ACS population, prasugrel+ASA) was superior to clopidogrel+ASA), which was associated with an 11.5% incidence of the primary endpoint (hazard ratio 0.812; 95% CI 0.732-0.902; p<0.001).

Serious bleeding events (classified as TIMI major bleeding) in the total ACS population, which were not caused by by-pass surgery, were significantly more frequent on prasugrel+ASA) therapy than on clopidogrel+ASA)/therapy (2.2% vs 1.7%).

[1] Summary of product characteristics for prasugrel

IMPORTANT INFORMATION ON THE USE OF PRASUGREL KRKA (ACTIVE SUBSTANCE: PRASUGREL)[1]

Annex: Copy of SmPC

Patients > 75 years of age or weighing < 60 kg:

- Severe haemorrhagic events (including fatal events) are more common in patients ≥ 75 years of age or those weighing < 60 kg.
- Treatment with prasugrel is generally not recommended in patients ≥ 75 years of age.
- If, after a careful individual risk-benefit assessment by the prescribing physician, treatment is deemed necessary in a patient in the ≥ 75 years age group then following a loading dose 60 mg, a reduced maintenance dose of 5 mg should be prescribed.
- Patients weighing < 60 kg should receive a single 60 mg loading dose and a reduced maintenance dose of 5 mg.

Patients weighing ≥ 60 kg and < 75 years of age, without a history of transient ischemic attack (TIA) or stroke:

- Reduction of atherothrombotic events, as a combined endpoint including cardiovascular death, non-fatal myocardial infraction or non-fatal stroke ($p < 0.001$).[2]
- No significant difference between prasugrel and clopidogrel in TIMI major bleeding events in these patients ($p = 0.17$).[2]

Table 1: Prescribing loading dose and maintenance dose

Patients:	**Loading dose**	**Maintenance dose**
≥ 60 kg and < 75 years	60 mg in a single dose	10 mg once daily
< 60 kg	60 mg in a single dose	5 mg once daily
The use of prasugrel in patients ≥ 75 years is generally not recommended (should only be used after a careful risk-benefit assessment)		
≥ 75 years	60 mg in a single dose	5 mg once daily
Contraindications:		
• Active pathological bleeding • History of TIA/stroke • Severe hepatic impairment (Child Pugh class C) • Hypersensitivity to the active substance or to any of the excipients listed in section		

[1] Summary of product characteristics for prasugrel
[2] Wiviott SD et al. NEJM. 2007; 357: 2001–2015.

Annex: Copy of a Summary of product characteristics for prasugrel (August 2018)