Regarding Tenecteplase (TNKase®) Temporary Drug Shortage: Considerations from Canadian Cardiology and Emergency Medicine Health Care Providers

Issue:

From approximately October 2014 to January 2015, Roche Canada anticipates a temporary **drug shortage of tenecteplase (TNKase®, TNK)** due to capacity constraints within the manufacturing supply chain.

Document background:

On July 17 and August 14, 2014, Roche Canada convened meetings bringing together Canadian cardiologists, an emergency physician and emergency department nurses, pharmacists, an emergency medical services (EMS) specialist, and representatives from the Cardiac Care Network of Ontario to discuss the impact of the temporary tenecteplase shortage and develop suggestions for Canadian health care providers (HCPs) to consider with regards to this shortage.

Proposed therapeutic substitution:

If tenecteplase is not available at your centre during the shortage period, alteplase (**ACTIVASE® rt-PA, tPA),** indicated for treatment of acute myocardial infarction (AMI) and acute ischemic stroke (AIS), is available as a therapeutic substitution. You may want to provide resources for HCPs on dosing and administration for alteplase in AMI as it differs from that of alteplase in AIS and from tenecteplase for AMI.

Proposed Therapeutic Substitution Strategies With ACTIVASE in Hospital

Strategy 1: Therapeutic Substitution	Use all available tenecteplase stock until depleted, then administer alteplase to all patients with AMI who are eligible for fibrinolytic therapy.
Strategy 2: Reserved Use of Tenecteplase	**Reserve tenecteplase for select patients who may benefit most, and start administering alteplase now to the remainder of patients with AMI who are eligible for fibrinolytic therapy.** The following factors may be considered when deciding allocation of tenecteplase: geographic access and need for patient transport (or other situations when primary percutaneous coronary intervention (PCI) cannot be performed in a timely manner) and clinical patient characteristics. **Bleeding risk should be considered in certain patient populations, e.g. elderly patients and low body weight females.**[1,2]

Alteplase supply:

Please ensure that your centre has an adequate supply of alteplase prior to October 2014, and that it is approved by your hospital formulary for use in AMI.

Tenecteplase stock currently available in hospital:

Ensure that tenecteplase vials with the earliest expiry date are used first.

EMS/Prehospital:

If your region has a prehospital fibrinolytic treatment program in place, consider reallocating or prioritizing existing tenecteplase stock to EMS for prehospital use.

Additional Information and Considerations for Use of Alteplase

<table>
<tr><td>Alteplase for Acute Myocardial Infarction (AMI): Dosage and Administration[1]</td><td colspan="2">Dosing of alteplase for AMI is based on patient weight. Administer alteplase to patients with AMI who are eligible for fibrinolytic therapy as soon as possible after the onset of symptoms. The maximum total dose is 100 mg.

The administration requires an initial partial dose given as an IV bolus over 1-2 minutes. DO NOT PUSH the initial bolus dose or the full dose of alteplase for AMI.

There are two dose regimens for alteplase for use in the management of AMI. The comparative efficacy of these two regimens has not been evaluated.

As it is the most commonly used regimen, the 90-minute accelerated infusion regimen is shown below:</td></tr>
<tr><td></td><td>Weight greater than 67 kg
Initial IV bolus over 1-2 minutes: 15 mg
First 30 minutes: 50 mg
Next 60 minutes: 35 mg
Total dose: 100 mg</td><td>Weight less than or equal to 67 kg
Initial IV bolus over 1-2 minutes: 15 mg
First 30 minutes: 0.75 mg/kg to a maximum of 50 mg
Next 60 minutes: 0.50 mg/kg to a maximum of 35 mg
Total dose is based on patient weight, not to exceed 100 mg</td></tr>
<tr><td>Alteplase for Acute Ischemic Stroke (AIS): Dosage and Administration[2]</td><td colspan="2">NB: This is not the recommended dosing for AMI.
Dosing of alteplase for AIS is based on patient weight.
The recommended dose is 0.9 mg/kg (maximum of 90 mg) infused over 60 minutes with 10% of the total dose administered as an initial IV bolus over 1 minute.</td></tr>
<tr><td>Rescue or Planned Transfers</td><td colspan="2">Many EMS systems may not be able to transfer a patient with the fibrinolytic infusion still running. When possible, adhere to current transfer protocols while considering that transfer may be delayed until fibrinolytic infusion is completed or alternatively, may require additional personnel en route.</td></tr>
<tr><td>Adjunctive Therapies (Antiplatelets/ Anticoagulants)</td><td colspan="2">Limited data are available on the use of alteplase in AMI with current adjunctive therapy regimens (i.e. antiplatelets and anticoagulants). However, the ACCF/AHA 2013 STEMI guidelines do not distinguish between fibrin-specific lytic agents with respect to adjunctive therapies.[3]</td></tr>
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REFERENCES

1. ACTIVASE rt-PA (alteplase) Product Monograph for Acute Myocardial Infarction. Hoffmann-La Roche Limited. December 9, 2013. http://www.rochecanada.com/PMs/Activase/Activase_AMI_PM_E.pdf
2. ACTIVASE rt-PA (alteplase) Product Monograph for Acute Ischemic Stroke. Hoffmann-La Roche Limited. December 9, 2013. http://www.rochecanada.com/PMs/Activase/Activase_AIS_PM_E.pdf
3. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. J Am Coll Cardiol. 2013;61(4):e78-140.