AUSTRALIAN COMMISSION ON SAFETY AND QUALITY IN HEALTH CARE

D19-39152

Ms Anna Dalling
Coroner's Solicitor
Coroners Court of Victoria
65 Kavanagh St
SOUTHBANK VIC 3006

Dear Ms Dalling

Investigation into the death of Ms C – Court ref: COR2017 005367

Thank you for your letter of 27 November 2019 concerning the recommendation of the Coroners Court of Victoria (the Coroner) regarding the death of Ms C on 21 October 2017. The Commission has considered the Coroner's recommendation.

The Coroner recommended that the Australian Commission on Safety and Quality in Health Care (the Commission) evaluate firstly, whether an increased dose of medicines to prevent venous thromboembolism (VTE) should be considered in the obese population and, secondly, whether a specific dosage for obese patients should be included in *Therapeutic Guidelines*.

The Commission has considered the Coroner's recommendation by reviewing current evidence-based guideline recommendations and other clinical resources for the dosing of medicines for the prevention of VTE in obese people (BMI>30kg/m^2). As there is insufficient evidence to recommend specific dosages, the Commission recommends clinicians consider the need for dose adjustment of VTE prophylaxis in obese people and consult with specialists on a case-by-case basis.

The United Kingdom's National Institute for Health and Care Excellence (NICE) guideline *Venous Thromboembolism in over 16s: reducing the risk of hospital-acquired deep vein thrombosis or pulmonary embolism (2018)*, lists obesity as a risk factor for developing VTE. While it specifies that current practice is to administer a higher than usual dose of pharmacological prophylaxis for obese people, it states this may not be required. Specifically in regard to dosing of low molecular weight heparins (LMWH) for VTE prophylaxis in people who are obese, the NICE evidence review found no evidence to support dose adjustment in terms of clinical outcomes and recommended that further research was required to better understand the effect of different dosing strategies on clinical outcomes in this patient group. No recommendation was made by NICE regarding the use of unfractionated heparins, such as those prescribed to Ms C.

The NSW Clinical Excellence Commission (CEC) VTE risk assessment tool lists obesity as a risk factor for VTE. It recommends that specialist advice be sought regarding dosing of pharmacological prophylaxis in people with extremities of body weight (< 50kg or > 120 kg or BMI >35) as evidence for dosing is limited.

Therapeutic Guidelines: Cardiovascular specifies that optimal anticoagulation in obese people has not been fully determined and limited information is available to guide dosing. Some considerations for dosing LMWH and Direct Oral Anticoagulants (DOACs) in this patient group are provided, however definitive dosages are not recommended. As in the NICE guideline, no guidance is provided for dose adjustment of unfractionated heparin. (Attachment 1). The

Commission will continue dialogue with Therapeutic Guidelines Limited (TGL) to further clarify this issue.

The above findings are consistent with the research conducted by the Commission at the time of developing the *Venous Thromboembolism Prevention Clinical Care Standard (2018)*, and suggest that that there is still little evidence to guide dose adjustments of medicines to prevent VTE in obese people.

The Commission will update the *Venous Thromboembolism Prevention Clinical Care Standard* to note the need for clinicians to seek specialist advice regarding doses of medicines to prevent VTE in obese people.

Please direct any further enquiries to:

Ms Alice Bhasale
Director – Clinical Care Standards
(02) 9126 3515 or alice.bhasale@safetyandquality.gov.au

Yours sincerely

Adjunct Professor Debora Picone AO
Chief Executive Officer
Australian Commission on Safety and Quality in Health Care

17 Dec 2019

Considerations for anticoagulation of obese patients

Optimal anticoagulation in obese patients has not been fully determined and limited evidence is available to guide dosing.

Based on limited data and until further evidence is available, it may be reasonable to dose enoxaparin or dalteparin according to actual body weight, for patients up to 150 kg or with a body mass index (BMI) up to 40 kg/m^2. Consider a dose-adjusted approach above this weight, using anti-Xa monitoring to achieve target anticoagulation levels. Twice-daily dosing is preferred in these patients.

Non–vitamin K antagonist oral anticoagulant (NOAC) (apixaban, dabigatran, rivaroxaban) studies included only a minority of obese patients so clinical data on efficacy and safety of NOACs for obese patients are limited. Available pharmacokinetic data suggest that in obese patients, there may be decreased drug exposure, reduced peak drug concentration and shorter half-lives of NOACs. This raises concerns about underdosing. Consequently, the International Society on Thrombosis and Haemostasis (ISTH) recommends standard dosing in patients up to 120 kg or with a BMI up to 40 kg/m^2, and recommends avoiding use of NOACs in patients who exceed these levels.

If NOACs are used at higher body weight or BMI, ISTH recommends testing a drug-specific peak and trough level, and only continuing the NOAC if the results are in the expected range [Note 10]. If the NOAC levels are inadequate for anticoagulation, ISTH recommends changing to warfarin rather than adjusting the NOAC dose, because the anticoagulant effect of warfarin can be monitored using the international normalised ratio (INR).

Note 10: At the time of writing, measurement of drug-specific peak and trough levels for NOACs is not readily available in Australia; seek specialist haematologist advice.