

# encapsulate

## Welcome to 'encapsulate'

The tenth edition of **encapsulate** highlights current concerns over a possible link between insulin glargine and cancer. We also introduce Rivaroxaban, the first of a new class of drug; an oral factor Xa inhibitor.

You can obtain further copies of **encapsulate** via our website - [www.slade.net.au](http://www.slade.net.au). Please forward any comments or suggested topics for our next issue to [marketing@slade.net.au](mailto:marketing@slade.net.au).

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## Cancer Fears with Insulin Glargine: More Evidence Needed

Recently the publication of four studies in *Diabetologia*, The journal of the European Association for the Study of Diabetes (EASD), has sparked fears of a possible link between insulin glargine, used to treat both Type 1 and Type 2 diabetes, and cancer.

Three of four studies, conducted in various European member States, reported that there appears to be a relationship between insulin glargine and the development of cancer.

The German study observed a positive association between cancer incidence and insulin dose for all insulin types. In addition, a dose-dependent increase in cancer risk was seen for treatment with insulin glargine compared with human insulin. This study also indicated a dose-dependent increase in cancer risk; 10 Units of insulin glargine increased the risk by 9% whereas 50 Units increased the risk by 31%.

The Swedish study reported women taking insulin glargine had an increased incidence of breast cancer compared with women using other types of insulin.

Findings from a Scottish study indicate a higher cancer rate for all cancers and a higher rate for breast cancer specifically, in people receiving insulin glargine as their only insulin

compared with those using non-glargine plus glargine insulin or non-glargine insulin alone.

Meanwhile, the UK study suggests insulin analogues are not associated with an increased cancer risk compared with human insulin.

EASD emphasises that the studies reported are far from conclusive, but they do indicate the need for further investigation of this issue.

Following the publication, the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP) carried out an in-depth review of all available information about the possible link between insulin analogues and the risk of cancer by looking at the four studies and their outcomes. The EMA advised that due to limitations the studies were found to be inconclusive, inconsistent and did not confirm or deny a relationship between insulin glargine and cancer. The committee has requested that insulin glargine (Lantus®) manufacturer, Sanofi-Aventis, conducts further studies to confirm the safety of insulin glargine.

Medical practitioners are being urged to continue prescribing insulin glargine and reassure any concerned patients, and await the findings of any further investigations.

### References

1. <http://www.diabetologia-journal.org/cancer.html#published> [Accessed 27/7/2009]
2. Tuffs, A., *The British Medical Journal*, 2009 Vol., 339, b2774

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## Rivaroxaban

Rivaroxaban (Xarelto®) is the first in a new class of drugs: oral factor Xa inhibitors. By inhibiting factor Xa, thrombin production and the formation of clots are ultimately inhibited. Onset of action is seen around 3 hours post dose and lasts between 8 to 12 hours but factor Xa activity does not return to normal within 24 hours allowing once daily dosing.

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Factor Xa inhibitor rivaroxaban was shown to be superior to the standard dose of enoxaparin when used to prevent venous thromboembolism (VTE) in people undergoing hip or knee replacement, a recently published paper indicates. Overall results from three studies (the RECORD programme), demonstrated 9,581 patients were randomised to receive either oral rivaroxaban 10mg daily, starting six to eight hours after elective total hip replacement or total knee replacement surgery, or subcutaneously injected enoxaparin 40mg daily, started 12 hours before their procedure. VTE was observed in fewer patients receiving rivaroxaban than in those receiving enoxaparin.<sup>1</sup>

Trials administered rivaroxaban for 14 days after knee replacement surgery or for 35 days after hip replacement surgery, durations consistent with current recommendations for other anticoagulants. There was no statistically significant benefit in extending prophylaxis in knee replacement surgery.<sup>2</sup>

Guidelines recommend that surgery patients receive graduated compression/antiembolism stockings from the time of admission, to further reduce the risk of venous thromboembolism. Patients should continue to wear their stockings after discharge until they return to their usual level of mobility.<sup>2</sup>

From 1<sup>st</sup> August, rivaroxaban will be available on the PBS, through Authority prescriptions, for patients who have undergone hip or knee replacements, possibly marking the end of daily post operative enoxaparin injections for orthopaedic patients.

### References

1. Eriksson, B.I., Kakkar, A.K., Turpie, A.G.G., Bandel, T-J., Misselwitz, F., and Lassen, M.R., Oral rivaroxaban for the

*prevention of symptomatic venous thromboembolism after elective hip and knee replacement, Journal of Bone and Joint Surgery, Vol 91-B; Issue 5; 636-644.*

*Eikelboom J.W., Quinlan D.J., Douketis J.D. Extended-duration prophylaxis against venous thromboembolism after total hip or knee replacement: a meta-analysis of the randomised trials. Lancet 2001;358:9-15.*

2. National Institute for Health and Clinical Excellence. Venous thromboembolism. Reducing the risk in surgical inpatients. NICE clinical guideline 46. 2007. <http://www.nice.org.uk/guidance/CG46/Guidance/pdf/English> (accessed 29 July 2009).

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## Medication Safety Alert: Routine Flushing of Intravenous Lines

There have been incidences of patients unexpectedly suffering respiratory depression, respiratory arrest and even death in Australia and overseas, when their intravenous (IV) lines have not been suitably flushed at the end of surgical cases. These adverse events occur when residual amounts of highly potent drugs are unexpectedly introduced into the systemic circulation. These situations have the potential to occur when an IV line, used to administer a muscle relaxant or similar, has not been flushed through and is later used to administer fluid replacement or further drug therapy. Slade Pharmacy Service and Galen Health have taken the initiative to define guidelines to reduce the likelihood of the aforementioned scenarios occurring. For more information please refer to Medication Safety Alert: Routine Flushing of Intravenous Lines

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*This publication is intended to provide a general outline and is not intended to be and is not a complete or definitive statement of the information on the subject matter. Further professional advice should be sought before any action is taken in relation to the matters described in this publication. To obtain further copies of all documents referred to in this publication please see your pharmacist*

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### Safe Practice Recommendation No. 11

***Respiratory depression, respiratory arrest and even death can occur when intravenous lines are not flushed following administration of muscle relaxants, and other high potency medications.***

The intravenous route is the preferred method of delivery for a number of medications. When drugs are administered intravenously, the external length of the line, preceding the cannula, provides a void. This void can act as a reservoir of previously administered drug, if not flushed.

Introduction of a subsequent medication or fluid therapy into the line will force the remaining medication into the systemic circulation. Adverse events occur when there is unexpected delivery of highly potent medications in this manner.

General anaesthesia, which is induced by achieving a balance of hypnosis, analgesia and muscle relaxation, takes advantage of the intravenous route of administration. Pressured environments within operating theatres, especially at the end of cases, may result in anaesthetists inadvertently not flushing a line which has been used to deliver a drug, such as those listed below:

- Muscle relaxants;
- Respiratory depressants; and
- High dose anticoagulants.

Recently clinical incidents, regarding high potency drugs delivered by the intravenous route, have been brought to the attention of The Australian Commission on Safety and Quality in Health Care.

Slade Pharmacy recommends the following action be taken to reduce the risk of adverse events occurring as a result of intravenous access lines not being appropriately flushed:

1. Any person administering a drug to a patient must assume responsibility for the management of both the patient and intravenous line.
2. The last person to deliver a drug, via the intravenous line, must assume responsibility for any remaining pharmaceutical agent present.
3. If an intravenous line has not been flushed, appropriate action must be taken by the last person to have used it. I.e. aspiration or removal of line.
4. When handing over a patient following surgery, both nurse and anaesthetist must confirm that the intravenous line has been flushed, or otherwise suitably dealt with.

Intravenous lines should be flushed with saline, or other appropriate fluid, following administration of any medication. This is especially important at the end of a case, when it is likely that highly potent agents will have been administered through the line.