

# encapsulate

## Welcome to 'encapsulate'

The ninth edition of **encapsulate** elaborates on a recent Medication Safety Alert regarding Heparin. We look at the influenza A(H1N1) virus. Also, we discuss the importance of correctly documenting and reporting adverse drug reactions, and explain some of the barriers that result in under reporting, with the example of the smoking cessation drug; Champix® (varenicline).

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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### Medication Safety Alert: Heparin

Unfractionated heparin (UFH) can be administered either by intravenous or subcutaneous injection. The intravenous route has an immediate onset of action, but short lasting effect (30 minutes-2 hours); whereas the subcutaneous route has a delayed onset of action (2 hours), but more prolonged effect (10 hours). The effects of heparin are monitored by measuring activated partial thromboplastin time (APTT). The importance of such monitoring should be emphasised, as patients can demonstrate up to a ten fold variance in response to a dose of heparin.

Critical incidents have been reported in Australia and overseas, involving errors in prescribing and administration of unfractionated heparin. One Australian patient suffered severe bleeding and cardiac arrest as the result of having their Hickman line locked with an inappropriate solution of heparin. The line had been inserted to facilitate administration of antibiotics, following a lung/kidney transplant. The patient suffered a coughing episode which resulted in the haemorrhage. Days after resuscitation, the patient sadly passed away.

In March, the Victorian Medicines Advisory Committee (VMAC) released a high risk

medicine alert regarding heparin. As such, Slade Pharmacy Services and Galen Health have released a Medication Safety Alert for Heparin.

The alert was distributed to all pharmacy, dispensary, nursing and medical staff to communicate the potential risks, contributing factors and recommendations to prevent future medication incidents with heparin. The recommendations are based on those published by VMAC. For further information please refer to the Medication Safety Alert – Heparin.

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### Adverse Drug Reactions: Reporting

Adverse drug reactions (ADRs) are an important cause of morbidity and mortality. The reporting of ADRs by health professionals is crucial to post-marketing surveillance. Clinical trials seldom identify all ADRs, as they only take place with a limited number of chosen participants, for short durations. For this reason, the reporting of ADRs, once a drug has been released for general prescribing, is extremely important. This is the time when time large sale prescribing will take place, when less commonly occurring adverse reactions may be observed. ADR reporting can, in some cases, lead to some drugs having their dosages altered to avoid adverse or unwanted effects after they have initially been released.

The Adverse Drug Reactions Advisory Committee (ADRAC) encourages the reporting of all suspected ADRs, particularly in all suspected reactions to newly marketed medicines, all suspected drug interactions and any unexplained reactions.

One French study showed that out of 3137 patients admitted to 200 hospitals, 1000 (3.19%) patients had been admitted as a result of an ADR. Interestingly the study highlighted that these patients tended to be older, demonstrating that elderly patients are more likely to suffer ADRs.

Newly marketed drugs are identified on 'Drugs of Current Interest' by ADRAC. An example of such a drug is varenicline (Champix®),

## encapsulate

indicated for smoking cessation therapy. Varenicline works by relieving cravings and withdrawal symptoms associated with nicotine withdrawal. Since varenicline's launch, ADRAC had received 339 related adverse reaction reports. In 255 (72%) of the reports psychiatric symptoms including depression, aggression, agitation, abnormal dreams, insomnia, hallucination and anger were recorded. There have also been reports of suicidal/self-injurious ideation or behaviour.

When an ADR is suspected, ensure the patients' doctor is alerted in the first instance, as treatment may be required. The clinical pharmacist should then be informed, so that they can record the necessary information and report to ADRAC accordingly.

#### References

1. Elland, I., Belton, K., Van Grootheest A., (1999) *Attitudinal survey of voluntary reporting of adverse drug reactions*, British Journal of Clinical Pharmacology, 1999, 48: 623-7.
2. Pouyanne, P., Haramburu, F., Imbs, J.L., Begaud, B., *Admissions to hospital caused by adverse drug reactions* - British Medical Journal, 2000.

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### Influenza A (H1N1)

Annually it is estimated that influenza infects between 5 and 20% of the Australian population; causing as many as 1,500 deaths, 18,000 hospitalisations and 300,000 GP consultations; a cost to the Australian health care system of \$85 million.

Influenza virus is an RNA virus, of which there are five main types. Only influenza viruses A, B and C infect humans.

The influenza A virus is further classified into serotypes based on human antibody response to its two main glycoproteins. These serotypes give rise to the H and N distinctions.

Influenza A(H1N1) is made up of genetic elements from four different viruses; produced by co-infection of a single cell by multiple viruses.

Symptoms are similar to other influenza viruses. In uncomplicated cases; acute symptoms last an average of 3-7 days although cough and malaise may persist beyond two weeks. The risk of complications,

hospitalisation and death from influenza are highest among the elderly, children and persons of any age with certain co-morbidities.

Presently there are two effective treatment options available on prescription: oral oseltamivir (Tamiflu®) or zanamivir (Relenza®) powder for inhalation. Treatment is currently recommended within 48 hours, following exposure to confirmed or probable cases of H1N1.

Generally flu symptoms are manageable at home. Symptomatic relief may be obtained from simple over-the-counter analgesics, such as paracetamol, which also exerts an antipyretic action. Good hygiene should always be practiced when flu like symptoms are displayed, with sufferers and their carers washing their hands frequently, covering nose and mouth whenever sneezing and disposing of tissues immediately after use.

The current annual seasonal influenza vaccination is recommended for at risk individuals; however it is not expected to confer any immunity to the H1N1 subtype.

There are a number of sources providing up to date information on the progress of the spread of A(H1N1), including the Australian Government's Health Emergency website ([www.healthemergency.gov.au](http://www.healthemergency.gov.au)). Alternatively speak to your pharmacist if you require any further information or advice.

#### References

1. [http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/health-swine\\_influenza-index.htm](http://www.healthemergency.gov.au/internet/healthemergency/publishing.nsf/Content/health-swine_influenza-index.htm)
2. Therapeutic Guidelines
3. Australian Medicines Handbook, July 2008 Edition
4. Basler C.F., et al., Sequence of the 1918 pandemic influenza virus nonstructural gene (NS) segment and characterization of recombinant viruses bearing the 1918 NS genes, Proceedings of the National Academy of Sciences of the United States of America. 2001; 98(5):2115-6.

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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.*

# Medication Safety Alert - Unfractionated Heparin

## Safe Practice Recommendation No. 10

***Inappropriate administration of heparin can cause major bleeding events, potentially resulting in death.***

Unfractionated heparin (UFH) can be administered either by intravenous or subcutaneous injection. The intravenous route has an immediate onset of action, but short lasting effect (30 minutes-2 hours); whereas the subcutaneous route has a delayed onset of action (2 hours), but more prolonged effect (10 hours). The effects of heparin are monitored by measuring activated partial thromboplastin time (APTT).

Critical incidents have been reported in Australia and overseas involving errors in prescribing and administration of unfractionated heparin.

The types of errors that have been reported include:

- Inappropriate dose prescribed for patients' condition or delayed or inappropriate dose adjustment in response to APTT results; and
- Incorrect dose administered due to incorrect product selection, incorrect concentration of infusion or incorrect infusion rate.

Contributing factors in these errors include:

- UFH is prescribed for multiple indications, with varying dose ranges. Indications include prevention and treatment of venous thromboembolism (VTE), prevention and treatment in acute coronary syndrome, to maintain catheter patency, or to maintain extracorporeal circulation.
- UFH has a narrow therapeutic range and can produce unpredictable adverse reactions at therapeutic doses. For example, UFH can cause heparin induced thrombocytopenia syndrome (HITS). Regular monitoring is important. This involves:
  - Baseline and ongoing APTT (at least daily), haemoglobin, and platelet counts.
  - Being aware of the risks and observing for bleeding.
  - Assessing renal function. UFH excretion is proportional to glomerular filtration rate.
- Requirement for increased monitoring when using heparin in combination with interacting drugs (or complementary medicines), or when the patient has certain co-existing medical conditions. An accurate and current medication history must be recorded and the patient asked about over the counter medicines and complementary medicines (for example, St John's Wort and Gingko).
- There are many presentations of UFH available that may look alike and therefore lead to selection error.

Slade Pharmacy Services recommend the following action to reduce the risk of error with heparin. They are based on recommendations by the Victorian Medicines Advisory Committee (VMAC), released in March 2009.

## encapsulate

1. Ensure both medical and nursing staff are sufficiently aware of unfractionated heparin, low molecular weight heparin (LMH) and fondaparinux's indications for use, contraindications and potential adverse events resulting from their use.
  - Prior to prescribing UFH or a LMW heparin, the patient must specifically be asked if they have a history of heparin induced thrombocytopenia (HIT) or previous allergy to heparin and the response documented in the patient's medical history and where appropriate on the medication chart.
  - Recent trauma, surgery and co-existing medical conditions should be documented in patients notes.
  - Prescribers should document the indication and therapeutic goal for antithrombotic therapy in the patient's medical record and medication chart.
  - Devise clearly defined weight-based dosing regimens for prophylaxis and treatment. Identify whether the patient's ideal body weight, actual weight or a medical staff-approved dosing corrected weight is to be used. Include a dosing maximum where appropriate.
  - Devise a dosing table for adjusting infusion rates in response to APTT results and the frequency of ongoing APTT monitoring.
  - Use a standard concentration for infusions; for example, consider a maximum concentration 50 Units/mL for premixed infusions. Adjust the rate of infusion, not the concentration, to achieve dose changes.
  - Devise an agreed local process for withholding or resuming UFH pre- and post invasive procedures.
  - Devise an agreed local procedure for managing UFH or LMW heparin overdose with reversal agents.
  - Advise that doses of UFH, low molecular weight heparin products and fondaparinux require dose confirmation if prescribed within 6-12 hours of each other.
2. Develop strict monitoring guidelines for frequent and timely review of the patient's status.
  - Results, documented in a standardised way, should accompany monitoring requirements (noting frequency of blood tests required) when UFH is prescribed.
  - Ensure that staff alter infusion rates in a timely manner in accordance with the prescriber's order, APTT results and guidelines.
3. Ensure dosing tables are readily accessible to all staff at the point of heparin prescribing and administration and that staff are aware of heparin doses for common indications and ensure they are confident with managing non-standard or unusual unfractionated heparin orders.
4. Rationalise and minimise the concentrations of UFH stocked on clinical area. This can be achieved by storing only one strength of heparin in each clinical area unless there is a specific requirement for more than one presentation, or storing heparinised saline separately from other heparin products and sodium chloride 0.9% ampoules to minimise risk of selection error.