Note:
This guideline provides advice of a general nature. This statewide guideline has been prepared to promote and facilitate standardisation and consistency of practice, using a multidisciplinary approach. The guideline is based on a review of published evidence and expert opinion.

Information in this statewide guideline is current at the time of publication.
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Health practitioners in the South Australian public health sector are expected to review specific details of each patient and professionally assess the applicability of the relevant guideline to that clinical situation.

If for good clinical reasons, a decision is made to depart from the guideline, the responsible clinician must document in the patient’s medical record, the decision made, by whom, and detailed reasons for the departure from the guideline.

This statewide guideline does not address all the elements of clinical practice and assumes that the individual clinicians are responsible for discussing care with consumers in an environment that is culturally appropriate and which enables respectful confidential discussion. This includes:

- The use of interpreter services where necessary,
- Advising consumers of their choice and ensuring informed consent is obtained,
- Providing care within scope of practice, meeting all legislative requirements and maintaining standards of professional conduct, and
- Documenting all care in accordance with mandatory and local requirements

### Dose and Indications

**Consult Haematology prior to use.** Do not allow this to lead to delayed administration in the case of bleeding. Contact the appropriate senior person immediately

**Treatment of overdose or bleeding induced by intravenous unfractionated heparin (UFH)**

**Intravenous**

Dose is based on the amount of UFH received in the previous 2 hours

<table>
<thead>
<tr>
<th>Time since last UFH dose (min)</th>
<th>Protamine sulfate dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 30</td>
<td>1mg per 100units heparin received</td>
</tr>
<tr>
<td>30 – 60</td>
<td>0.5-0.75mg per 100units heparin received</td>
</tr>
<tr>
<td>60 – 120</td>
<td>0.375-0.5mg per 100units heparin received</td>
</tr>
<tr>
<td>Greater than 120</td>
<td>0.25-0.375mg per 100units heparin received</td>
</tr>
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</table>
Treatment of overdose or bleeding induced by subcutaneous enoxaparin, a low molecular weight heparin (LMWH)

**Intravenous**

Dose is dependent on the dose and time of administration of enoxaparin

Maximum dose 50mg protamine sulfate

<table>
<thead>
<tr>
<th>Time since last LMWH dose received</th>
<th>Protamine sulfate dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 8 hours</td>
<td>First dose: 1mg per 1mg enoxaparin received</td>
</tr>
<tr>
<td></td>
<td>Second dose: (if required*) 0.5 mg per 1mg enoxaparin received</td>
</tr>
<tr>
<td>8 to 12 hours</td>
<td>1mg per 1mg enoxaparin received</td>
</tr>
<tr>
<td>Greater than 12 hours</td>
<td>Dose may not be necessary</td>
</tr>
</tbody>
</table>

Protamine reverses most, but not all, of the effects of LMWH

*e.g. if aPTT remains prolonged (measured 2 to 4 hours after the first infusion)*

**Preparation and Administration**

**Intravenous**

Protamine sulfate may be administered undiluted (10mg/mL). Alternatively, dilute protamine sulfate (10mg/mL) with equal parts sodium chloride 0.9%. This results in a solution of 5mg/mL protamine sulfate.

Infuse over at least 10 minutes. Maximum infusion rate 5mg/minute. Too rapid administration can cause hypotension, dyspnoea and bradycardia, as well as increase the risk of severe hypersensitivity reactions

**Compatible Fluids**

Sodium chloride 0.9%, glucose 5%

**Adverse Effects**

**Common**

Flushing, vomiting

**Infrequent**

Hypotension, bradycardia, dyspnoea, rebound bleeding with excessive doses

**Unknown**

Severe hypersensitivity reactions (hypotension, cardiovascular collapse, non-cardiogenic pulmonary oedema, pulmonary vasoconstriction, pulmonary hypertension)
Protamine sulfate
50mg/5mL ampoule

Monitoring

> Close monitoring of aPTT
  > At baseline (if possible)
  > 5 to 15 minutes after administration of antidote
  > Repeat aPTT again at 2 to 8 hours post antidote
  > Consider further testing at 18 hours post antidote if aPTT did not normalise or there is continued risk of bleeding
> Continuous cardio-respiratory monitoring
> Continuous invasive blood pressure monitoring or 15 minute non-invasive blood pressure monitoring for 2 hours
> Observe for bleeding

Practice Points

> If UFH needs to be discontinued for clinical reasons, termination of the infusion will usually suffice because of the rapid clearance of UFH. If immediate reversal is required, protamine rapidly neutralises UFH activity
> Protamine is a basic protein which combines with heparin to form a stable inactive complex, reversing its anticoagulant effect
> Due to UFH’s short half-life, the dose of protamine sulfate required reduces over time
> Consider the need for protamine and the original indication for heparin, as re-heparinisation may not be effective until the protamine has been eliminated
> Protamine neutralizes the anti-thrombin (anti-IIa) activity of LMWH (e.g. enoxaparin), but result in only partial (60-75%) neutralization of its anti-Xa activity.
> In excessive doses, protamine may bind to platelets and fibrinogen producing a bleeding tendency

Reference

Protamine sulfate
50mg/5mL ampoule

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If so, which policy (title)?

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<th>Who approved New/Revised Version</th>
<th>Reason for Change</th>
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<td>6/8/2019</td>
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