Midazolam for Conscious Sedation in Adults

1. Introduction:
Midazolam is a benzodiazepine that is widely used as an intravenous injection for the purpose of conscious sedation of a patient prior to a variety of procedures. In December 2008 the National Patient Safety Agency (NPSA) released a Rapid Response Report regarding the use of midazolam following a number of incidents of overdose and over reliance on flumazenil for reversal of midazolam effects. Following on from this, this guidance has been produced.

2. Target Group:
Any patient receiving midazolam for conscious sedation in Wirral University Teaching Hospitals NHS Foundation Trust (WUTH). It does not cover the sedation of agitated patients, the use of midazolam in critical care or in syringe drivers in palliative care or the use of midazolam in paediatrics.

3. Definitions:
Conscious sedation has been defined by the British Society of Gastroenterologists as:
“A technique in which the use of drug or drugs produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation. The drug and techniques used to provide conscious sedation should carry a margin of safety wide enough to render loss of consciousness unlikely”.

4. Midazolam information
Side-effects:
Midazolam is a sedative and as such depresses the central nervous system; this has the potential to cause cardiac/respiratory depression. The most common undesirable effects are loss of respiratory volume and or fall in respiratory rate or apnoea.
Respiratory depression and arrest can occur particularly if the dose is given too quickly or in elderly patients or those with pre existing respiratory dysfunction.
Changes in the cardiovascular system are less frequent but include a decrease in cardiac output, stroke volume and systemic vascular resistance. Can also cause bigeminy, premature ventricular contractions, tachycardia or vasovagal episodes.
Contra-indications:
Midazolam is contra indicated in patients with:
- Hypersensitivity to benzodiazepines or any excipient of the product.
- Severe respiratory failure or acute respiratory depression.
- Marked neuromuscular respiratory weakness including unstable myasthenia gravis.

Cautions:
Myastheina gravis
Impaired respiratory function
Acute intoxication with alcohol and/or other CNS depressants
Patients who are pregnant or breast feeding
Severe liver or renal failure
Severe cardiovascular problems that are not well controlled.

Sleep apnoea syndrome
Severe cerebrovascular disease.

High-risk patients:
Special caution should be exercised when administering midazolam to high-risk patients:
- adults over 70 years of age
- chronically ill or debilitated patients, e.g.
  - patients with chronic respiratory insufficiency
  - patients with chronic renal failure, impaired hepatic function or with impaired cardiac function

These high-risk patients require lower dosages (see prescribing section) and should be continuously monitored for early signs of alterations of vital functions.

Drug interactions:
Clinical interactions may occur between midazolam and substances that inhibit specific liver enzymes. These substances are capable of influencing midazolam pharmacokinetics and can lead to deeper and longer lasting sedation.
- The hypotensive effects of antihypertensives may be potentiated by midazolam.
- Midazolam should be given with caution in patients who are taking either erythromycin or clarithromycin as they can significantly reduce clearance, increasing sedation.
- High dose cimetidine >800mg per day can also lead to delayed recovery.
- Carbamazepine may lower the plasma concentration of midazolam, reducing the response.

Please refer to the current BNF for a full list of drug interactions.

5. Staff Training and Records of Training
Anaesthetists will be exempt from the need for regular training and documentation as conscious sedation is part of their normal clinical practice.
Doctors and Nurses performing Endoscopy and Colonoscopy are accredited as part of their JAG training and those certified in this way, or who are trained and monitored using JAG standards will not require this further WUTH accreditation.

Doctors other than Anaesthetists and Endoscopists will be assessed as competent to perform conscious sedation by the Clinical Lead for Sedation.
Refer to Essential Training Matrix for details of training.

6. Prescribing:
Conscious sedation is not without risk. Conscious Sedation is under the responsibility of senior clinician/anaesthetist. The prescriber is responsible for identifying patients who are vulnerable to the risks associated with administration of midazolam and taking the appropriate action.
Use of other agents:
For non-painful procedures, ideally, a single agent (midazolam being the preferred choice), should be used to sedate the patient. If a combination of drugs is used there should be a clear understanding of the synergistic effects of benzodiazepines and opioids and the increased potential for causing respiratory depression. If concomitant opioids are to be used the opioids should be given first and the midazolam administered as detailed in table 1 below.
The most commonly used sedative drugs include midazolam, diazepam, fentanyl, alfentanil, pethidine, morphine and diamorphine. Propofol and ketamine should only be used by anaesthetists.
Prior to prescribing midazolam for conscious sedation the prescriber should have an understanding of the drug and its characteristics. Section 4 of this guidance provides some information. The prescriber should check the following:
• Does the patient have any contraindications to receiving midazolam? If yes the use of midazolam will need to be reviewed.
• Does the patient have any cautions to receiving midazolam or is the patient taking any medication that interacts with midazolam? If yes, a clinical decision needs to be made based upon an assessment of the risks and benefits and what alternative options in the given case are available. In most cases it is likely that using the dose for high risk patients and careful monitoring will be possible.
• Does the patient fall into the category for high risk? If yes, use the reduced dose as described below in table 1.

If no to all of the above use the standard dose as described in table 1 below.

Prescribing – the concentration of midazolam injection to be used for conscious sedation is 1mg/ml. It is given by intravenous injection. The dose is shown in the table 1 below.

### Table 1: Dosing of midazolam for conscious sedation

<table>
<thead>
<tr>
<th>Initial dose (given 5-10mins pre-procedure)</th>
<th>Wait</th>
<th>Additional dose increments</th>
<th>Total dose should not normally exceed</th>
<th>Ampoule size</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard dose</td>
<td>2 mins</td>
<td>0.5mg to 1mg may be given every 2 minutes until desired level attained.</td>
<td>5mg</td>
<td>5ml</td>
</tr>
<tr>
<td>Dose for high risk patients, i.e.: Age ≥70years OR chronically ill/debilitated patients (e.g.: patients with chronic respiratory insufficiency, chronic renal failure, impaired hepatic function, impaired cardiac function, high alcohol intake or users of benzodiazepines).</td>
<td>0.5mg to 1mg over 30 seconds</td>
<td>3.5mg (or 2mg if given with concomitant opioids)</td>
<td>2ml</td>
<td></td>
</tr>
</tbody>
</table>

A Trust Patient Safety Incident form should be completed if more than 5mg is given.

7. Administration:
Prior to administration of midazolam check the following:
• Patients need to fast prior to conscious sedation. Refraining from solid food for 6 hours and from clear fluids 2 hours before the procedure.
• The patient has someone to accompany them upon discharge from the hospital and for 12 hours after the procedure.
• Flumazenil is available (see section 9)
• Midazolam is being administered in an area where resuscitation equipment and facilities are available.
• The patient should be given a patient information leaflet covering conscious sedation and any questions they may have answered.
• There should be a minimum of one trained nurse in addition to the practitioner in the room with the sedated patient.
• The prescriber has assessed the patient and prescribed the midazolam in accordance with table 1 (see section 6).
• Patient will have given informed and valid consent.
• Pulse oximetry monitoring will be used in all sedated patients.
• All sedated patients will have a cannula inserted, which will remain in situ, until patient has fully recovered.
• Oxygen 24-26% will be given via nasal cannulae at a rate of 2 litres per minute.
• Midazolam will be titrated in accordance with table 1 above with a reduced dose given to patients who are vulnerable to its effects.
• Midazolam drawn up into syringes need to be labelled in accordance with the Trust Injectable Medicines Policy (Ref 45c). Only the midazolam 1mg/ml strength should be used.

8. Monitoring:
Any deterioration in patients' condition which causes concern for the practitioner will result in termination of the procedure. Reversal of sedation should occur in accordance with section 9. The patient should be monitored and this documented during the procedure every 5 minutes in accordance with the appended Trust Sedation Chart. In Endoscopy monitoring will be recorded on the Endoscopy Record Chart. The monitoring should be continued every 5 minutes after the procedure until the practitioner is satisfied that the patient is stable.

9. Reversal of Sedation:
Flumazenil can be used for the reversal of sedative effects of benzodiazepines such as midazolam. It must be available in all areas where conscious sedation is performed in case of excessive sedation. If flumazenil is used a Trust Patient Safety Incident form must be completed.
Flumazenil dose:
By intravenous injection, 200 micrograms over 15 seconds;
Then 100 micrograms at 60 second intervals if required.
Usual dose range: 300-600micrograms; total maximum dose 1mg (2mg in intensive care).
If flumazenil is used it is essential that the patient is not left unattended. Flumazenil has a shorter duration of action than midazolam and the patient can lose consciousness again. These patients should remain in recovery for at least an hour.

10. Documentation:
All drugs administered to the patient must be recorded in their medical notes, with the times of administration. The entry must be signed by the prescriber. The level of consciousness and respiratory rate should be recorded on the Trust Sedation Chart.

References
6. BNF September 2009