INTRODUCTION

The purpose of this clinical protocol is to aid compliance with the National Patient Safety Alert RRR018 Preventing fatalities from medication loading doses (November 2010)

A loading dose is an initial large dose of medicine used to ensure a quick therapeutic response. It is usually administered for a short period before therapy continues on a lower maintenance dose. The use of loading doses of medicines can be complex and prone to errors. Incorrect use of loading doses or subsequent maintenance regimens may lead to severe harm or death National Patient Safety Agency (NPSA 2010).

Review of evidence from the National Reporting and Learning System (NRLS) between 1st January 2005 and 30th April 2010 highlighted the highest incidents of loading dose errors involved warfarin, amiodarone, digoxin and phenytoin.

It is recognised that health professionals working within Wirral Community NHS Trust, (with the exception of the DVT service), are not routinely involved in the preparation or administration of loading doses of medication. However, all health professionals need to be made aware of the potential for loading doses to be inadvertently continued, as patients are discharged from secondary care into the community setting or where treatments are initiated in the community by another health professional.

This protocol will therefore highlight usual loading and maintenance doses for the identified high risk medicines and the potential side effects suggestive of elevated serum levels.

TARGET GROUP

All health professionals employed by the Trust who are involved in the care and treatment of patients who may potentially be prescribed warfarin, amiodarone, digoxin or phenytoin.
ESSENTIAL INFORMATION

DIGOXIN

Digoxin belongs to a group of medicines called cardiac glycosides, these slow down the rate of the heart, but increase the force with which the heart muscle contracts, making the heart work more efficiently.

Digoxin tablets are used to treat:
- Atrial fibrillation or flutter.
- Heart failure.

Digoxin Loading Doses for Adults

Rapid digitalisation, for atrial fibrillation or flutter, by mouth 0.75 to 1.5mg (750 micrograms to 1500 micrograms) over 24 hours in divided doses.

Digoxin Maintenance Doses for Adults

For atrial fibrillation or flutter, by mouth
According to renal function and plasma-digoxin concentrations after initial loading dose; usual range is 125 to 250 micrograms daily.
Heart failure (for patients in sinus rhythm),
By mouth, 62.5 to 125 micrograms daily

Renal Impairment

Reduce dose and monitor plasma-digoxin concentration; toxicity is increased by electrolyte disturbances.

Doses of digoxin greater than 250 microgram daily in adults and greater than 125 microgram in people over 70 years of age should rarely be seen and should be challenged.

Side Effects

Digoxin is a medicine with a narrow therapeutic index; this means that there is very little difference between toxic and therapeutic doses. Side effects that patients may complain of that could indicate excessive serum levels include: loss of appetite, nausea, vomiting, diarrhoea, blurred or yellow vision, confusion, drowsiness, insomnia, nightmares, agitation or depression. For a full list of side effects, see British National Formulary (BNF) or Summary of Product Characteristics.
Interactions

For a list of medications that interact with digoxin see appendix 1 of current BNF. Please note the interactions for digoxin are listed under cardiac glycosides.

Monitoring

Regular monitoring of plasma-digoxin concentration during maintenance treatment is not necessary unless problems are suspected.

AMIODARONE

Amiodarone tablets belong to a group of medicines called anti-arrhythmics. They work by regulating the heart rate. Amiodarone should only be initiated in hospital or under specialist supervision.

Amiodarone Loading Doses for Adults

By mouth, 200mg three times a day for up to 1 week, then reduced to 200mg twice a day for a further week.

Amiodarone Maintenance Doses for Adults

After the initial period the dose should be reduced to 200mg a day or lower. Elderly patients may be given a lower dose.

Amiodarone doses higher than 200mg daily should be queried (the maximum licensed dose for maintenance is 200mg daily)

Side Effects

Reported side effects include: nausea, vomiting, taste disturbances, raised serum transaminases (may require dose reduction or withdrawal if accompanied by acute liver disorders). Impaired vision due to optic neuritis or optic neuropathy (if vision is impaired amiodarone should be stopped and specialist advice sought). For a full list of side effects, see BNF or Summary of Product Characteristics.

Interactions

Amiodarone has a long half-life; there is therefore a potential for interactions with other medicines to occur for several weeks (or even months) after treatment has stopped. For a list of medications that interact with amiodarone see appendix 1 of current BNF.
Monitoring

Amiodarone contains iodine and can cause disorders of thyroid function. Thyroid function tests should therefore be performed every 6 months. Pneumonitis should always be suspected if new or progressive shortness of breath develops. Fresh neurological symptoms should raise the possibility of peripheral neuropathy. Amiodarone is also associated with hepatotoxicity and treatment should be discontinued if severe liver function abnormalities or clinical signs of liver disease develop.

PHENYTOIN

Phenytoin is used to control all forms of epilepsy, except absence seizures. It is also occasionally used to treat trigeminal neuralgia if carbamazepine is inappropriate. Phenytoin has a narrow therapeutic index and the relationship between dose and plasma concentration is non-linear. Therefore, small increases in dosage in some patients may produce large increases in plasma concentration with acute toxic side effects. Similarly, a few missed doses or a small change in drug absorption may result in a marked change in plasma concentration.

Phenytoin is highly protein bound and extensively metabolised by the liver. Reduced dosage to prevent accumulation and toxicity may therefore be required in patients with impaired liver function.

Phenytoin Loading Dosage for Adults

By mouth, initially 3-4 mg/kg daily or 150mg -300mg daily (as a single dose or in 2 divided doses) increased gradually by no more than 50mg at a time (with plasma-phenytoin monitoring).

Phenytoin Maintenance Dose for Adults

The amount of phenytoin needed varies from one person to another. Most adults need between 200mg and 500mg a day either as a single or divided dose. Very occasionally higher doses are needed. Maintenance of treatment should be the lowest dose of anticonvulsant consistent with control of seizures. The most common daily dosage for phenytoin is 300mg daily.

Hepatic Impairment

Reduce dose to avoid toxicity

Side Effects

Symptoms of phenytoin toxicity include nystagmus, diplopia (double vision), slurred speech, ataxia, confusion and hyperglycaemia. At the first sign of acute toxicity, plasma levels are recommended. Dose reduction of phenytoin therapy is indicated if serum levels are
excessive; if symptoms persist, termination of therapy with phenytoin is recommended. For a full list of side effects, see current BNF or Summary of Product Characteristics.

**Interactions**

Herbal preparations containing St John's wort (*Hypericum perforatum*) should not be used while taking phenytoin due to the risk of decreased plasma concentrations and reduced clinical effects of phenytoin.

Phenytoin is an enzyme inducing medication, therefore there is the possibility that interacting medication may increase or decrease phenytoin levels or alternatively the effects of interacting medications may be enhanced or impaired.

For a list of medications that interact with Phenytoin see appendix 1 of current BNF.

**Monitoring**

Monitoring of plasma concentration improves dosage adjustment

Phenytoin doses greater than 500mg daily are unusual, however, there is a wide inter-patient variability in phenytoin serum levels with equivalent dosage, therefore, a wide range of doses are used.

*If patients are prescribed phenytoin levels higher than 300 mg daily, nursing staff should satisfy themselves that the phenytoin dosage has been prescribed in conjunction with appropriate serum level monitoring.*

**WARFARIN**

Warfarin belongs to a class of medicines called anticoagulants. Warfarin is used to prevent blood clots from forming. It may also be used to treat blood clots which have already formed. Some medical conditions increase the chances of blood clots forming. These are conditions such as heart-valve disease or certain types of heart rhythm problems. People with these types of conditions will often be prescribed warfarin to prevent clots from forming. People who have a history of blood clots forming may also be given warfarin even if there isn't a known illness that may be causing them.

**Warfarin Loading Dose for Adults:**

For patients who require rapid anticoagulation the usual starting dose is 5 to 10mg on the first day, with subsequent doses dependent upon the prothrombin time, reported as INR (international normalised ratio).

For patients who do not require rapid anticoagulation, a lower loading dose can be used over 3 to 4 weeks.

Warfarin doses may vary considerably between patients. **It is advised that any newly initiated therapy at doses greater than 5mg should be considered abnormal in the community. The dosage is likely to be less for the elderly.**
Side Effects

The main adverse effect is haemorrhage. Other reported side effects include nausea, vomiting, diarrhoea, jaundice, hepatic dysfunction, pancreatitis, pyrexia, alopecia, purpura, rash, "purple toes", skin necrosis. For a full list of side effects, see current BNF or Summary of Product Characteristics.

Interactions

For a list of medications that interact with warfarin see appendix 1 of current BNF. Please note the interactions for warfarin are listed under coumarins.

Monitoring

Checking the INR and adjusting the dose as appropriate is essential. In the early stages of treatment daily INRs should be taken. Eventually there may be longer intervals between INR monitoring of up to every 12 weeks. If a patient has new potentially interacting medication started or stopped, warfarin should be monitored more frequently.

Wirral University Teaching Hospital and other secondary care providers also will be complying with the NPSA alert recommendations.

INCIDENT REPORTING

Clinical incidents or near misses must be reported and a Trust Incident Form must be completed

EQUALITY ASSESSMENT

During the development of this protocol the Trust has considered the clinical needs of each protected characteristic (age, disability, gender, gender reassignment, pregnancy and maternity, race, religion or belief, sexual orientation). There is no evidence of exclusion of these named groups.

If staff become aware of any clinical exclusions that impact on the delivery of care a Trust Incident form would need to be completed and an appropriate action plan put in place.
REFERENCES

British National Formulary (BNF) [www.bnf.org](http://www.bnf.org)


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Status – New / Revised / Trust Change