Phenytoin/Fosphenytoin Administration Guidelines

Purpose:

The purpose of this issuance is to establish safe guidelines for administration of IV phenytoin and fosphenytoin using either intravenous push or intravenous infusion.

Guidance:

Intravenous phenytoin or fosphenytoin will be administered by the administration routes, at the infusion rates, in the concentrations, with the monitoring procedures described below.

Definitions:

Unless otherwise specified “IV Push” means the direct injection into a running intravenous line at or below the rate specified in these guidelines.

Intravenous infusion means a preparation of an appropriately diluted compatible solution for administration over a short period of time.

A central line is defined as a large bore catheter that is inserted into a central vessel whose distal tip resides in the superior vena cava and/or the subclavian, femoral vein, or cardiac chamber. The catheter may be a temporary or permanently tunneled catheter, which includes vascular venous access devices. Peripherally inserted central venous catheters (PICC) may also be included in this definition.

A peripheral line is defined as a temporary catheter residing in a peripheral vessel

Phenytoin

General Guidelines:

A. IV push is the preferred route of administration

B. If phenytoin is to be administered as an IV infusion the following criteria must be met:
   1. The patient is continuously observed by a nurse or physician (regardless of dose)
   2. For doses greater than 300 mg and/or infusion rates of 50 mg/min (pediatric: 1mg/kg/min) the patient is on a cardiac monitor with rate, rhythm, and blood pressure display.

      Note: If a patient is receiving intravenous phenytoin for status epilepticus, administration may begin prior to the arrival of monitoring.

   3. There is a 0.22 micron in-line IV filter in place as a final filter.
4. The infusion is completed within 2 hours of its preparation.

5. All tubing is flushed with normal saline, 30 mL, before and after infusion. The flush should be administered at a rate such that the residual phenytoin is infused at a rate no greater than that prescribed.

C. A nurse may administer phenytoin if:

1. Dose is 300 mg or less

2. For doses of greater than 300 mg and/or IV push at a rate of 50 mg/min the patient is on the above monitor (unless patient is in status epilepticus), the nurse is competent in ECG rhythm interpretation, and the patient’s physician is on the unit.

D. Assure patency of IV before, during and after administration of IV phenytoin. Patient should have acceptable IV access defined by one of the following: size at least as large as the antecubital fossa vein, 20 gauge or larger catheter size, or preexisting central line. If phenytoin is to be administered intravenously for greater than 48 hours a central line should be considered. In the absence of good venous access fosphenytoin should be considered as an alternative to phenytoin.

E. The drug is infused at a maximum rate of 50 mg/minute (pediatric: 1 mg/kg/min) for emergency situations. This rate is reduced to 25 mg/min or less (pediatric: 0.5 mg/kg/min or less up to a maximum rate of 25 mg/min) in the young (<7 years of age) and the elderly (>60 years of age) or patients at risk of cardiovascular toxicity, hypotensive, or experiencing infusion related pain. In nonemergency situations the drug should be infused at a maximal rate of 25 mg/min (pediatric: 0.5 mg/kg/min).

F. All patients should be observed continuously by a nurse or physician during the administration of IV phenytoin. The patient should be on a monitor with cardiac rate, ECG rhythm and blood pressure display when receiving more than 300 mg per dose or at a rate of 50 mg/min. Patients at high risk for vascular complications (burning, cording, local tissue damage, purple glove syndrome) are the young (<7 years of age). Patients at high risk for vascular complications and cardiovascular complications (hypotension, arrhythmias) are the elderly (>60 years of age).

Procedure for Administration of Phenytoin as IV Push

A. For doses of more than 300 mg and/or administration rates of 50 mg/min (pediatric: 1mg/kg/min) the patient should be on a cardiac monitor with rate, rhythm, and blood pressure display. Monitoring should be performed prior to administration, at 5 minutes, and at the end of the infusion.

B. All tubing is flushed with normal saline, 30 ml, before administration of IV push phenytoin

C. Attach a 0.22 micron in-line particulate filter between IV catheter and IV tubing.
D. Administer IV push of phenytoin at a rate no greater than 50 mg/min (1 mg/kg/min for pediatric patients)

E. Patency should be checked frequently during the administration.

F. All tubing is flushed with normal saline, 30 ml, after completion of the IV push phenytoin. The flush should be administered at a rate such that the residual phenytoin is infused at a rate no greater than that prescribed.

Procedure for Administration of Phenytoin as IV Infusion

A. For doses of more than 300 mg and/or infusion rates of 50 mg/min (pediatric: 1mg/kg/min) the patient should be on a cardiac monitor with rate, rhythm, and blood pressure display.

B. Hang IV solution of normal saline (use Y-tubing if IV solution other than normal saline will be used after completion of phenytoin administration).

C. Attach a 0.22 micron in-line particulate filter between IV catheter and IV tubing.

D. Administer phenytoin at a maximum rate of 50 mg/min. CARDIAC AND RESPIRATORY ARREST CAN OCCUR WITH TOO RAPID ADMINISTRATION.

E. For doses greater than 300 mg and/or infusion rates of 50 mg/min (pediatrics: 1 mg/kg/min):
   1. Monitor baseline and every 10 minute heart rate, rhythm and blood pressure during administration.
   2. Monitor blood pressure and heart rate every 15 minutes for 1 hour after phenytoin administration is complete.

F. All tubing is flushed with normal saline, 30 ml, after completion of infusion. The flush should be administered at a rate such that the residual phenytoin is infused at a rate no greater than that prescribed.

G. Document and report any adverse experiences (changes in blood pressure or pulse; pain, burning, itching at infusion site) in medical record / CRIS.

Intravenous Infusion Formulation

The infusion should be completed within 2 hours of preparation.

Diluent: 0.9% NaCl

Final Concentration: Not > 6.7 mg/mL (preferably 5 mg/mL or less for peripheral administration; concentrations greater than 5 to 10 mg/mL may be associated with more frequent tissue damage, venous irritation and cardiovascular adverse events).
Suggested preparation: Do Not Refrigerate Admixture
Filtering when drawing up phenytoin from commercial vial is not necessary

<table>
<thead>
<tr>
<th>Phenytoin Dose</th>
<th>Minimum Volume (Peripheral Line)</th>
<th>Recommended Volume (Central Line)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 600 mg</td>
<td>250 ml 0.9% NaCl</td>
<td>100 ml 0.9% NaCl</td>
</tr>
<tr>
<td>301-600 mg</td>
<td>100 ml 0.9% NaCl</td>
<td>100 ml 0.9% NaCl</td>
</tr>
<tr>
<td>101-300 mg</td>
<td>50 ml 0.9% NaCl</td>
<td>50 ml 0.9% NaCl</td>
</tr>
<tr>
<td>100 mg or less</td>
<td>25 ml 0.9% NaCl</td>
<td>25 ml 0.9% NaCl</td>
</tr>
</tbody>
</table>

**Clearance of catheter occlusion**

Clogged IV tubing and/or peripheral catheters must be removed, discarded and replaced.

Whenever practical an indwelling catheter occluded due to phenytoin precipitation should be replaced to minimize the risk of microembolization of dislodged phenytoin precipitate. In circumstances where the physician elects clearance of the catheter occlusion over replacement the following procedure may be attempted.

**Agent:** Sodium Bicarbonate (NaHCO₃ 8.4%)

**Rationale:** Precipitation of phenytoin likely related to administration into an acidic solution (dextrose containing solution). Increasing the pH of the medium with sodium bicarbonate may allow for dissolution of the phenytoin precipitate and clearance of the catheter.

**Technique:**
1. Withdraw 3 mL of sodium bicarbonate (NaHCO₃ 8.4%) into a 5 mL syringe.
2. Aspirate tubing with empty syringe.
3. Clamp tubing.
4. Exchange empty syringe with syringe containing sodium bicarbonate and instill solution.
5. Using a new sodium bicarbonate filled syringe repeat the procedure every 15 minutes for 1 hour, then every 30 minutes for 2 hours. If after 2 hours the catheter is uncleared consider replacing clogged catheter.

**Extravasation**

Should extravasation occur:
1. Discontinue the infusion immediately
2. Elevate affected limb

3. Apply dry heat (approximately 37°C)

4. Contact patient’s physician immediately

5. Document and report occurrence in medical record / CRIS

**Fosphenytoin**

1. **Indications for Use**
   
   A. Requirement of phenytoin loading dose in patient with unacceptable IV access defined by one of the following: size at smaller than the antecubital fossa vein, less than 20 gauge catheter size, or absence of preexisting central line.

   B. No venous access.

   C. Patients with unstable hemodynamics who would be unable to tolerate the cardiovascular adverse effects of intravenous phenytoin.

2. **Dosing and Administration**
   
   A. Ordering fosphenytoin: fosphenytoin should be ordered as mg of phenytoin equivalents (PE). A 1500 mg vial of fosphenytoin provides 1000 mg of phenytoin equivalents.

   B. Determine dose/diluent/administration rate based on attached table and indication for use

      i. Loading dose Status Epilepticus

      ii. Treatment or prophylaxis of seizures

      iii. Maintenance doses

3. **Guidelines for monitoring**
   
   A. For IV loading doses greater than 300 mg PE and/or infusion rates greater than 25 mg PE/min:

      i. Monitor baseline and every 10 minute heart rate, rhythm and blood pressure during administration.

      ii. Monitor blood pressure and heart rate every 15 minutes for 1/2 hour after fosphenytoin administration is complete
B. Phenytoin concentrations should not be determined until at least 2 hours following completion of the intravenous infusion. Results may be falsely increased in patients with renal insufficiency.

### Fosphenytoin Dilution Guidelines

<table>
<thead>
<tr>
<th>Weight (Kg)</th>
<th>Loading Dose Status</th>
<th>Diluent/Volume</th>
<th>Treatment or Prophylaxis of Seizures</th>
<th>Diluent/Volume</th>
<th>Total Daily Maintenance Dose 4-6 mg PE/kg (ml/dose)</th>
<th>Diluent/Volume</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>375-500 mg PE (7.5-10 ml)</td>
<td>NS or D5W 50 ml</td>
<td>250-500 mg PE (5-10 ml)</td>
<td>NS or D5W 50 ml</td>
<td>100-150 mg PE (2-3 ml)</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td>30</td>
<td>450-600 mg PE (9-12 ml)</td>
<td>NS or D5W 50 ml</td>
<td>300-600 mg PE (6-12 ml)</td>
<td>NS or D5W 50 ml</td>
<td>120-180 mg PE (2.4-3.6 ml)</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td>35</td>
<td>525-700 mg PE (10.5-14 ml)</td>
<td>NS or D5W 50 ml</td>
<td>350-700 mg PE (7-14 ml)</td>
<td>NS or D5W 50 ml</td>
<td>140-210 mg PE (2.8-4.2 ml)</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td>40</td>
<td>600-800 mg PE (12-16 ml)</td>
<td>NS or D5W 50 ml</td>
<td>400-800 mg PE (8-16 ml)</td>
<td>NS or D5W 50 ml</td>
<td>160-240 mg PE (3.2-4.8 ml)</td>
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<tr>
<td>45</td>
<td>675-900 mg PE (13.5-18 ml)</td>
<td>NS or D5W 50 ml</td>
<td>450-900 mg PE (9-18 ml)</td>
<td>NS or D5W 50 ml</td>
<td>180-270 mg PE (3.6-5.4 ml)</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td>50</td>
<td>750-1000 mg PE (15-20 ml)</td>
<td>NS or D5W 50 ml</td>
<td>500-1000 mg PE (10-20 ml)</td>
<td>NS or D5W 50 ml</td>
<td>200-300 mg PE (4-6 ml)</td>
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<tr>
<td>55</td>
<td>825-1100 mg PE (16.5-22 ml)</td>
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<td>550--1100 mg PE (11-22 ml)</td>
<td>NS or D5W 50 ml</td>
<td>220-330 mg PE (4.4-6.6 ml)</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td>Weight (Kg)</td>
<td>Loading Dose Status</td>
<td>Epilepticus 15-20 mg PE/kg (ml/dose)</td>
<td>Diluent/Volume</td>
<td>Treatment or Prophylaxis of Seizures 10-20 mg PE/kg (ml/dose)</td>
<td>Diluent/Volume</td>
<td>Total Daily Maintenance Dose 4-6 mg PE/kg (ml/dose)</td>
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<tr>
<td>60</td>
<td>900-1200 mg PE</td>
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<td>600-1200 mg PE</td>
<td>NS or D5W 50 ml</td>
<td>240-360 mg PE</td>
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<td></td>
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<td>(18-24 ml)</td>
<td>(12-24 ml)</td>
<td>(4.8-7.2 ml)</td>
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<tr>
<td>65</td>
<td>975-1300 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>650-1300 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>260-390 mg PE</td>
<td>NS or D5W 50 ml</td>
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<td>(19.5-26 ml)</td>
<td>(13-26 ml)</td>
<td>(5.2-7.8 ml)</td>
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<tr>
<td>70</td>
<td>1050-1400 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>700-1400 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>280-420 mg PE</td>
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<td>(5.6-8.4 ml)</td>
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<td>750-1500 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>300-450 mg PE</td>
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<td>(22.5-30 ml)</td>
<td>(15-30 ml)</td>
<td>(6-9 ml)</td>
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<td>80</td>
<td>1200-1600 mg PE</td>
<td>NS or D5W 100 ml</td>
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<td>NS or D5W 100 ml</td>
<td>320-480 mg PE</td>
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<td></td>
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<td>(6.4-9.6 ml)</td>
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<td>85</td>
<td>1275-1700 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>850-1700 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>340-510 mg PE</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td></td>
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<td>(25.5-34 ml)</td>
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<td>(6.8-10.2 ml)</td>
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<td>90</td>
<td>1350-1800 mg PE</td>
<td>NS or D5W 100 ml</td>
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<td>NS or D5W 100 ml</td>
<td>360-540 mg PE</td>
<td>NS or D5W 50 ml</td>
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<tr>
<td></td>
<td></td>
<td>(27-36 ml)</td>
<td>(18-36 ml)</td>
<td>(7.2-10.8 ml)</td>
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<tr>
<td>95</td>
<td>1425-1900 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>950-1900 mg PE</td>
<td>NS or D5W 100 ml</td>
<td>380-570 mg PE</td>
<td>NS or D5W 50 ml</td>
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<td></td>
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<td>(28.5-38 ml)</td>
<td>(19-38 ml)</td>
<td>(7.6-11.4 ml)</td>
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<td></td>
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<td>(30-40 ml)</td>
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<td>(8-12 ml)</td>
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</table>
Each 1 ml contains: Fosphenytoin 75 mg equivalent to Phenytoin 50 mg; Loading doses for the treatment of status epilepticus should be infused at a rate of 150 mg PE/min with continuous cardiac monitoring. Prophylactic loading doses should be infused at a rate of 100 mg PE/min with continuous cardiac monitoring. Doses greater than 300mg PE and/or infusion rates of greater than 25mg PE/min must be accompanied by cardiac monitoring.

Calculating infusion rate:

\[
\text{Infusion rate (mL/hr)} = \frac{\text{fosphenytoin volume (mL)} + \text{diluent volume (mL)} \times \text{infusion rate (mg PE/min)}}{\text{fosphenytoin dose (mg PE)}} \times \frac{60 \text{ min}}{1 \text{ hr}}
\]

References


