**Annex 7**

**Medication Preparation, Storage and Handling**

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**Storage and Handling**

Follow instructions for medications/vaccinations per package inserts.

**Pediatric Dispensing**

**Ciprofloxacin, Doxycycline and Amoxicillin Suspensions**

The Strategic National Stockpile has limited amounts of oral suspensions of ciprofloxacin, doxycycline, and amoxicillin in managed inventory. This is due to the:

* High cost,
* Relatively short shelf life,
* Limited use in the private sector (thus making it difficult to rotate), and
* Difficulty in predicting the numbers of people who might need these drugs.

**Suspensions will need to be mixed at the POD site**. Pharmacists will need to oversee the performance of this task; creating the suspensions centrally in the POD will minimize the number of pharmacists that will be needed. In addition, this procedure should occur at the POD in an area, separate from dispensing, where there is easy access to water.

Consider the amount of effort and staff that are needed to produce oral suspensions and plan accordingly. All pharmacists learn how to compound drugs, but few do it frequently enough to be proficient. However, every community has a small number of pharmacies that specialize in compounding. A pharmacist that specializes in compounding can be located by calling your local pharmacies or contacting the State Board of Pharmacy. Establishing MOUs would be beneficial to all parties.

**Weighing Children**

Young children cannot take the same regimen as larger children and adults. The regimen they need will depend on their age and weight, but weighing a child will take time and reduce throughput. Decide whether to physically weigh children or use an average weight chart based on age and height. The CDC provides these charts, and can be located at: <http://www.cdc.gov/nchs/data/nhanes/growthcharts/set1/all.pdf>.

Another source to calculate dosage would be with the use of the “Broselow Pediatric Emergency Tape” information can be found at: <http://www.armstrongmedical.com/ami/item.cfm?sction=3&sbsection=14&itemid=755>

**Compounding Ciprofloxin and Doxycycline Tablets**

An alternative to suspensions is to convert ciprofloxacin and doxycycline tablets into oral suspensions. You can find information about this process at the Food and Drug Administration’s website <http://www.fda.gov/cder/drug/infopage/penG_doxy/doxycyclinePeds.htm>

1. Compounding Ciprofloxacin Oral Suspension

The instructions below produce 100 ml of 50 mg/ml ciprofloxacin hydrochloride oral suspension. If the mortar and pestle allow, it is possible to double or triple ingredient quantities to triturate sufficient tablets. Typically, however, the size of the mortar and pestle will limit the number of tablets that can be crushed, wet, and suspended at one time. Mechanized equipment can speed the process and becomes increasingly important if large quantities are needed.

The instructions below use 500 mg Bayer brand ciprofloxacin (Cipro) tablets, which are in the SNS inventory. This tablet contains 500 mg of the active drug component. These instructions do not require sieving, although the tablet contains a thin film coating.

**Ingredients**

The following ingredients prepare 100 ml of ciprofloxacin hydrochloride oral suspension in strength of 50 mg/ml:

* Active ingredient: 10 Bayer Cipro 500 mg tablets
* Wetting agent: distilled water
* Suspending agent: Ora-Plus (Paddock Laboratories), 50 ml
* Vehicle: Ora-Sweet (Paddock Laboratories), to fill to (q.s.) to final volume (100 ml).

**Directions**

**a. Triturate tablets in a mortar with pestle**

Finely grind tablets with a ceramic or Wedgwood mortar and pestle. The finer the powder, the better the suspension. The resultant powder should be uniform in color and particle size.

**b. Wet powder with distilled water (CRITICAL STEP)**

Wet the powder mass with a minimal amount of water to form a thick viscous paste. A common mistake in compounding suspensions is to use too much wetting agent. Add water gradually to ensure minimal use and a thick paste. The mass should be smooth and uniform with no lumps when you are done.

**c. Add 50 ml of Ora-Plus in geometric dilution**

Add Ora-Plus to the paste in ever-increasing amounts, working in each addition until there is a uniform mix. The volume of the first addition of Ora-Plus should be similar to that of the Cipro/water paste. Geometric dilution means that each addition of Ora-Plus should approximately equal the volume of mixture in the mortar until you add all 50 ml.

CDC recommends using Ora-Plus as the suspending agent because its physical characteristics make it easer to achieve proper volume than with some other suspending agents. Veegum is a viable alternative to Ora-Plus for this recipe. Other agents may work in an emergency after trial and error. Carefully inspect the resultant product for desired physical characteristics.

**d.** **Q.S. to 100 ml with Ora-Sweet**

Transfer the mixture from Step C into the final container and use Ora-Sweet as the vehicle to wash out the mortar. Add Ora-Sweet in portions to the empty mortar to lift any drug mixture that sticks to the mortar’s walls. Gradually add the washes to the final container. Top off the final container with Ora-Sweet to the desired volume and shake well. It is helpful to use a container that is slightly larger than the final desired volume for this step to allow for even dispersion after vigorous shaking.

CDC recommends Ora-Sweet in this step. It is a berry-flavored vehicle that masks the bitter taste of drugs. It is compatible with Ora-Plus; the same manufacturer makes both.

It may be more convenient to compound a volume that intentionally exceeds the desired dispensing volume because when the final volume is poured directly from the mortar to the dispensing container some mixture will stick to the mortar walls.

Alternatives to Ora-Sweet are cherry syrup, USP; sorbitol 70%; and simple syrup, USP. Cherry syrup, USP, is a good substitute because it effectively masks drug taste. If you use sorbitol or simple syrup, USP, you need to add a flavoring agent because their sweetness alone does not mask drug taste.

To achieve the proper final volume, you need to include the volume of the flavoring agent. A 3- to 4-ml addition of cherry flavor, USP (not the same as syrup), should be sufficient.

Taste the final product to confirm its sweetness. If it is unpleasant, make adjustments. Flavoring is very important to achieve patient compliance. Not all flavorings mask the taste of drugs equally. Cherry and berry flavors usually work well at hiding bitter drug taste, as does unsweetened Kool-Aid powder. Add small amounts of the flavoring until you mask the drug’s bitterness.

The bitterness of ciprofloxacin suspension made from tablets makes it a particular challenge. Several compounding pharmacists stated it is very difficult to mask its bitter taste. In addition, it was indicated that the flavorings suggested above might not be acceptable to all patients. Further suggestions are to try to give patients a dose dab of Hershey’s syrup (assuming no chocolate allergy) before and after administering the suspension. This is common practice in children’s hospitals. Suggestions are that the dispensing pharmacist witnesses the administration of the first dose to ensure compliance.

**e. Label the container**

Label the container as follows:

* Do not freeze; store in refrigerator.
* Preparation is stable for 2 months in refrigerator.
* Shake well before use.

**Mark filling levels (based on patient weight) on the reusable calibrated oral dosing syringes in the SNS inventory and use them to dispense this suspension.**

2. Compounding Doxycycline Hyclate Oral Suspension

The instructions below produce 60 ml of doxycycline hyclate oral suspension in strength of 10 mg/ml. Using a mortar and pestle, double or triple ingredient quantities if able to triturate sufficient tablets. Typically, however, the size of the mortar and pestle will limit the number of tablets that can be crushed, wet, and suspended at one time. Mechanized equipment can speed the process and becomes increasingly important if large quantities are needed.

The instructions below use Zenith-Goldline and Schein brands of doxycycline tablet, which are in the SNS inventory. These brands do not contain excessive film coatings or other formulation characteristics that require additional preparation steps (e.g., sieving), which may not be true for other brands of doxycycline tablet. Note that a 100-mg doxycycline hyclate tablet contains 100 mg of doxycycline. Thus, complicated adjustments are not necessary to compensate for the hyclate portion in the tablet to deliver 100% of the active drug component.

**Ingredients**

The ingredients below prepare doxycycline hyclate oral suspension, 10 mg/ml, 60 ml:

* Active ingredient: 6 doxycycline hyclate tablets
* Wetting agent: glycerin, USP, 1 ml
* Suspending agent: Ora-Plus (Paddock Laboratories), 30 ml
* Vehicle: Ora-Sweet (Paddock Laboratories), to q.s. to final volume (60 ml).

To provide flexibility, some alternatives to the wetting agent are mentioned as well as suspending agent and vehicle in the directions.

**Directions**

**a. Triturate tablets in a mortar with pestle**

Finely grind tablets with a ceramic or Wedgwood mortar and pestle. The finer the powder, the better the suspension. The resultant powder should be uniform in color and particle size.

**b. Wet powder with 1 ml glycerin (CRITICAL STEP)**

Wet the powder mass with minimal amounts of glycerin to form a thick viscous paste (the full 1 ml may be needed). Adding too much wetting agent is a common mistake in compounding suspensions. Add glycerin gradually to ensure minimal use and a thick paste. The mass should be smooth and uniform with no lumps when done.

If glycerin, USP, is not available, ethanol, docusate sodium liquid or Ora-Plus may be used as a wetting agent. Ora-Plus is primarily a suspending agent but can be used as a wetting agent. Whichever wetting agent used, make sure a smooth, uniform, thick paste is produced.

**c. Add 30 ml Ora-Plus in geometric dilution**

Add Ora-Plus to the paste in ever-increasing amounts, working in each addition until a uniform mix is formed. The volume of the first addition of Ora-Plus should be similar to that of the doxy/glycerin paste. Geometric dilution means that each addition of Ora-Plus should approximately equal the volume of mixture in the mortar until you add all 30 ml.

CDC suggests you use Ora-Plus as your suspending agent because it’s physical characteristics make it easer to achieve proper volume than some suspending agents. Scrip-Tech suggests no alternatives to Ora-Plus for this recipe; therefore, no alternatives are recommend. Other agents may work in an emergency after trial and error. Make sure to carefully inspect the resultant product for desired physical characteristics.

**d. Q.S. to 60 ml with Ora-Sweet**

Transfer the mixture from Step C into the final container and use Ora-Sweet as the vehicle to wash out the mortar. Add Ora-Sweet in portions to the empty mortar to lift any drug mixture that sticks to the mortar’s walls. Gradually add the washes to the final container. Top off the final container with Ora-Sweet to the desired volume and shake well. It is helpful to use a container that is slightly larger than the final desired volume for this step to allow for even dispersion after vigorous shaking.

Ora-Sweet is recommended in this step. It is a berry-flavored vehicle that masks the bitter taste of drugs. It is compatible with Ora-Plus; the same manufacturer makes both.

It may be more convenient to compound a volume that intentionally exceeds the desired dispensing volume so that when the final volume can be poured from the mortar to the dispensing container even though some mixture will stick to the mortar walls.

Alternatives to Ora-Sweet are cherry syrup, USP; sorbitol 70%; and simple syrup, USP. Cherry syrup, USP, is a good substitute because it effectively masks drug taste. If sorbitol or simple syrup, USP, is used, add a flavoring agent because their sweetness alone does not mask drug taste.

To achieve the proper final volume, include the volume of the flavoring agent. A 2-ml addition of cherry flavor, USP (not the same as syrup), should be sufficient.

Taste the final product to confirm its sweetness. If it is unpleasant, make adjustments. Flavoring is very important to achieve patient compliance. Not all flavorings mask the taste of drugs equally. Cherry and berry flavors work especially well at hiding bitter drug taste. Unsweetened Kool-Aid powder also works well as a flavoring agent. Add small amounts of it until you mask the drug’s bitterness.

**e. Label the container**

Label the container as follows:

* Do not freeze; store in refrigerator.
* Preparation is stable for 2 months in refrigerator.
* Shake well before use.

It is also suggested to mark filling levels (based on patient weight) on the reusable calibrated oral dosing syringes in the SNS and use them to dispense this suspension.