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Secundum Artem

Current & Practical Information for the Compounding Pharmacist

Topical Antibiotic Dosage Forms

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This month's topic is the preparation of topical antibiotic dosage forms. Pharmacists are seeing more prescriptions for topical antibiotics because of the occasional inadequacy of commercially available products and because many antibiotics first marketed before 1975 are no longer protected by patent and are readily available as nonsterile pyrogen free powder. These include clindamycin phosphate, gentamycin sulfate, polymyxin B sulfate, erythromycin, bacitracin, and nystatin. The nonsterile antibiotic powders are considerably less expensive than their sterile counterparts and the fact that they are not in solution means that one is not limited in concentration that can be obtained when compounding a topical dosage form.

Because antibiotics, as a drug class, appear to be less stable than other drug classes, the first thing one thinks about is stability. As a general rule water must be present in the dosage form for significant short term degradation to occur. If the antibiotic powder is incorporated into an oleaginous base such as white petrolatum or aquaphor (without the use of water) you can be virtually certain that the antibiotics will remain stable for the desired period of use (1 or 2 months, for example). If water is needed or you are using an emulsion base that contains water then you must do further research. One excellent empirical clue to antibiotic stability is to find out how the drug is supplied. For example, the injection forms of gentamycin sulfate and clindamycin phosphate are both supplied as aqueous solutions so that you can be reasonably assured that they are stable even in the presence of water. If you do not have any assurance that the drug in the topical dosage form you want to compound is stable one simple way to get further information is to call the Drug Information Service.

Stability and sterility are both primary concerns when compounding antibiotic wound irrigations. The simplest and most expensive way to prepare such solutions is to add the appropriate quantity of the commercially available injection to 500 or 1000 ml of 0.9% sodium chloride irrigation. If you frequently compound antibiotic irrigations considerable money can be saved by dissolving the non-sterile pyrogen free powder in sterile water for irrigation and passing the appropriate volume of the resulting solution through a sterilizing filter (0.2 micron pore size). The preparation of sterile irrigation solutions requires a thorough knowledge of aseptic compounding technique and access to a laminar flow hood.

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The University of Minnesota Department of Pharmaceutical Services is routinely preparing a wound irrigating solution developed by Dr. David Knighton's Laboratory.

It is much more economical to make it using the nonsterile powders provided that one has the necessary filtration equipment to sterilize the drugs.

The formula is: 0.1% gentamycin, 0.1% clindamycin and 0.05% polymyxin B in sterile water for irrigation. The solution may be prepared using the commercially available injectable form of each of the drugs. It is much more economical to make it using the nonsterile powders provided that one has the necessary filtration equipment to sterilize the drugs. The concentrations are expressed in terms of the base form of each drug so the appropriate calculations must be done to get the correct percentages. Such calculations can be confusing especially in the case of polymyxin B sulfate (PBS). The potency of each lot of all three drugs varies so that new calculations must be done each time you use a different lot of drug.

Because its potency is expressed in units instead of weight PBS concentration is the most confusing to calculate. We use the USP conversion of 10,000 units/mg to convert the potency of PBS from units to weight. For example, if you have a PBS powder with a potency of 7500 u/mg this will convert to 0.75 mg/mg. If you want to make a 2.5% solution (25 mg/ml) you must use 33 mg/ml of the powder

$$\left(\frac{25\,\text{mg/ml}}{0.75\,\text{mg/mg}} = 33.3\,\text{mg/ml}\right).$$

To prepare the above mentioned wound irrigating solution, we prepare three separate concentrated solutions from non-sterile pyrogen free powder: 10% gentamycin, 10% clindamycin and 5% polymyxin B solution, 5 ml of each of these solutions is separately added through a sterilizing filter to a 500 ml bottle of sterile water for irrigation.

As is customary in these formulations the overfill in the sterile water for irrigation and the volume added (15 ml) are ignored in calculating the final concentration. If the three concentrated solutions are mixed a precipitate will form.

LABEL EXAMPLE:

Clindamycin - Gentamycin - Polymyxin B
For Irrigation

Clindamycin	0.1%
Gentamycin	0.1%
Polymyxin B	0.05%
In Sterile Water For Irrigation	500 ml

Sterile Refrigerate
For External Use Only
Lot # Exp: 3 months

Unless data are available to justify a longer expiration date you should use the expiration dating recommended by manufacturers of the injectable forms of these drugs for their products. For maximum stability these solutions should be refrigerated. Refrigeration also slows the growth of micro-organisms should the solution be contaminated. If large batches of solution are prepared, sterility testing is a must.

Topical preparations for the treatment of acne must not exacerbate the patient's condition, i.e., must be noncomedogenic. Unfortunately, it is not possible to tell by examining the ingredients whether or not a formulation is comedogenic. An ingredient known to be comedogenic may not be when combined with other ingredients. The formulation must be tested to determine its comedogenicity. The net result is one must rely on manufacturer's claims in this regard.

Table 1 - Semisolid and Liquid Bases Known to be Noncomedogenic.

Eucerin
Moisturel
Vanicream
Vehicle N
Vehicle N Mild
Vehicle A

Vehicle-A

DESCRIPTION: Vehicle-A is a hydroalcoholic topical vehicle used for extemporaneous compounding. Vehicle-A will solubilize many dermatologic agents. Vehicle-A provides a system for topical application with a special filter/applicator top.

CONTENTS: Isopropyl Alcohol 68%, propylene glycol, purified water, glycerin, and laureth-4. Vehicle-A has a pH of 5.5.

PRECAUTIONS: Do not use near fire or flame due to alcohol content. FOR EXTERNAL USE ONLY. Avoid contact with eyes or eyelids. In case of contact with eyes, rinse eyes thoroughly with water and contact physician. Do not apply to open wound or irritated skin. Keep this and all medications out of the reach of children.

CONTRAINDICATIONS: Vehicle-A is contraindicated in persons who have shown hypersensitivity to any of the listed ingredients.

COMPOUNDING INSTRUCTIONS:

1. Remove the cap from the bottle.
2. Add the measured quantity of active ingredient to Vehicle-A, cap and shake vigorously until active ingredient is dissolved.
3. Push applicator firmly into bottle using the white overcap as a holder. Screw cap down to seat applicator.

FORMULATION GUIDE
(VEHICLE-A 60 ml)

PREPARATION OF COMMON ACTIVE INGREDIENTS IN VEHICLE-A

Clindamycin Phosphate

1. Calculate amount of clindamycin phosphate to yield a 1% solution.
2. Dissolve clindamycin phosphate in approximately 5 ml of purified water.
3. Add solubilized clindamycin phosphate to 60 ml of Vehicle-A, cap, and shake well.

Erythromycin

1. Calculate amount of erythromycin base powder to yield desired concentration (usually 2%).
2. Add measured amount of erythromycin powder directly into Vechicle-A, cap, and shake well.

Minoxidil

1. Calculate amount of minoxidil to yield desired concentration (2% - 5%).
2. Add measured amount of minoxidil directly to Vehicle-A, cap, and shake well. Higher concentrations (3% - 5%) may require moderate heating to solubilize drug.

Market Your Compounding Practice

Assume you have decided to start or expand your compounding practice. How do you determine what compounded formulations or services you need to provide?

One suggested answer is to use market segmentation or grouping. Market grouping allows one to identify distinct groups that have common needs and benefits that will respond similarly to specific tangible marketing actions. These actions may involve separate products, price, place, or promotion strategies — the four P's.

Numerous variables may be used to segment patient and customer markets. Some examples of demographic customer characteristics are: age, sex, family size, disease state, stage of family life, ages of children, income, occupation, education, and race. A useful framework to relate market groupings to products or services offered is a market-product grid.

A straight forward approach to grouping, targeting, and reaching a market involved five steps: (1) group patients into segments according to characteristics such as their needs, (2) group the products offered or marketing actions into meaningful categories, (3) develop a market-product grid that relates potential sales of product lines to the segments, (4) select the target segments for emphasis, and (5) take marketing action to reach those target segments.

The acid test for the usefulness of the segmentation process is whether it leads to tangible market actions.

How do you determine what compounded formulations or services you need to provide?

PRODUCT				
MARKET Age-Years	**Suspensions**	**Suppositories**	**Topicals**	**Cosmetic**
Infant-11	L	L	M	S
12-17	M	M	L	M
18-24	S	S	L	L
25-49	S	M	M	L
50-over	L	L	M	M

KEY: L, Large Market; M, Medium Market; S, Small Market.

Market-product grid showing size of markets for selected compounded formulations for five different age segments of patients.

Compounders Corner:

QUESTIONS, ANSWERS, AND UP-TO-DATE INFORMATION ABOUT EXTEMPORANEOUS COMPOUNDING

Question:

What is the best way to prepare steroid topical creams and ointments in strengths that are not commercially available?

Answer:

Corticosteroid topical preparations can often be prepared using commercially available finished products as the source of the active ingredient. The simple dilution of a corticosteroid cream or ointment may present a problem of incompatibility of bases. In general an oleaginous base can be mixed with another oleaginous base or a water-in-oil emulsion based cream. Creams of the same emulsion type may usually be mixed without any problem. Mixing oleaginous bases with oil-in-water emulsion based creams or mixing creams of opposite emulsion type may result in a rather inelegant finished product. Eucerin and Aristocort Cream are not compatable. If Aristocort is your only source of triamcinolone acetonide a marginally dispensable product can be compounded by replacing 10% of the Eucerin with Aquaphor.

Steroid topical creams and ointments in strengths not commercially available can also be prepared using USP powders and a comparable topical base. A frequent problem with compounding corticosteroid based creams and ointments is achieving a smooth, lump-free finished product. For small quantities it is best to first mix a portion of the base with the powder into a thick paste. Higher shear forces can be generated in a viscous system resulting in more efficient elimination of lumps. The thick paste can then be diluted out with the remaining base. If the finished product is unacceptably lumpy it is usually easier (and cheaper) to start over than it is to triturate out the lumps.

Question:

Some of the doctors I work with are concerned about the cost and presence of metabisulfate in commercially available 5-ASA rectal suspension enemas. Can you suggest different formulas that avoid these problems?

Answer:

Suggested Formula For 5-ASA (5-Amino Salicyclic Acid) Enema 60 ml.

Formula # 1

5-ASA	1.2g	3.0g	4.0g
Methylcellulose Gel 2%	30 ml	30 ml	30 ml
Distilled Water, qs ad	60 ml	60 ml	60 ml

**Ascorbic Acid, USP, 100 mg. per 60 ml may be added to prevent discoloring

Formula # 2

5-ASA	1.2g	3.0g	4.0g
Propylene Glycol	10 ml	10 ml	10 ml
Methylcellulose 2%			
Distilled Water, qs ad	60 ml	60 ml	60 ml

Formula # 3

5-ASA	1.2g	3.0g	4.0g
Vehicle-S, qs ad	60 ml	60 ml	60 ml

Suggested Compounding Procedure

1. Weigh out 5-ASA and place in glass mortar.
2. Add Ascorbic Acid and triturate.
3. Add Methylcellulose Gel (previously prepared) or Vehicle-S in divided portions (geometric) to form smooth lump free dispersion.
4. Add water as needed to "qs" in divided portions until all is incorporated.
5. Refrigerate. Dispense with expiration date and instructions to patient.

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