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Pharmaceutical Service and Science
Extemporaneous Formulation

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Introduction

Compounding of pharmaceutical formulations remain as the core skill of pharmacists and this manual is produced to include well referenced recipes that are easy to prepare, use readily available ingredients, have the longest expiry date possible and when necessary, provide more than one strength of formulation to accommodate the unique needs of different groups of patients.
Efforts have been made to search for substantiated references in producing this manual of extemporaneous preparations.
Preparations included in the manual are for ingredients available commercially but not in the required dosage form for therapy and thus, necessitate extemporaneous preparations.
The use of this manual requires knowledge-based interpretation by healthcare professionals and is intended solely for use by pharmacists in healthcare facilities. All information contained in the manual has been provided with the sole intention that it be readily accessible for pharmacist's information and as a guide for preparing extemporaneous preparations that may be prescribed.

1.0 Objectives:

1.1 To standardize formulations of extemporaneous preparations and practice in healthcare facilities.

2.0 POLICY

2.1 **Change to policy**: no change
2.2 Always consider the use of commercially available products as far as possible.
2.3 If no suitable commercial product exists, consider a therapeutic alternative that is available in a suitable dosage form. This must be discussed with the physician.
2.4 Extemporaneous preparations should be done based on evidence-based references.
2.5 Always check for the suitability of the product/brand for extemporaneous preparations.
2.6 When no information is available, compound an oral medication by dispensing a tablet and/or capsule and directing the caregiver to mix just prior to administration.
2.7 Stability stated in this manual is applicable for shelf storage in the pharmacy without opening. Once opened, the stability will be calculated according to beyond use date. Maximum quantity of the extemporaneous preparations to be dispensed should not exceed 14 days.
2.8 Refrain assumptions on the therapeutic equivalence in the case of suggesting alternative agents as the possibilities and supporting data may be limited.
2.9 Techniques in compounding preparations and manipulations should always be in line with the standard Good Compounding Practice as delivering an accurate dose is paramount.
2.10 Staff and facilities are challenged to undertake intermittent competency assessments in order to achieve the standards requirement.
2.11 Documentation after each preparation should include details on the materials used, processes involved and the responsible personnel in charge.

3.0 CONSIDERATIONS FOR PREPARING EXTEMPORANEOUS COMPOUNDS

3.1 Pharmacy personnel are reminded not to empirically change flavoring or suspending agents because they can affect the pH and stability of the product and result in an unstable product.
3.2 Please consider ingredients in the formulations that require special precautions in neonates.
3.3 **Mixing of a compounded formulation should always be in line with the following principles:**
3.3.1 Ensure that all ingredients used are within the expiry date.
3.3.2 Ensure that all utensils are clean; including mortar and pestle, graduates, pill cutters and stirring rods.

3.3.3 Product should be labelled clearly and stored as recommended within the formula.
3.3.4 For solution or suspension products, emphasis on the importance of thorough shaking before administration.

3.4 If compounding a preparation using contents from an ampoule, remember to withdraw the solution (medication) from the ampoule using a filter needle to ensure no glass particles are incorporated into the compound.
3.5 Place tablet(s) within mortar and pestle to grind tablets to a fine powder. For film-coated tablets, it may be necessary to add a small quantity of diluents such as water, to soften the coating prior to grinding the tablets. This will ensure that the compound will not have an eggshell appearance from the film coating floating throughout the suspension. If you are using capsules, open the capsule and empty the powder into the mortar and discard the capsule shell.
3.6 Solutions will have a clearer appearance versus a compounded suspension.
3.7 Manipulations of the available dosage forms in order to fulfil the unusual practitioner's request may impose risks such as preparation and administration errors as well as unpredictable bioavailability, compatibility and stability profile.
3.8 Understand the roles of excipients in certain formulations and consider their risks over benefits limitation.
3.9 If distilled water is not available, water for injection can be used as a substitution, and vice versa.

4.0 STANDARD LABEL DESIGN & WORKSHEET REQUIREMENTS FOR EXTEMPORANEOUS PREPARATIONS

4.1 The proposed label for extemporaneous preparations must have the information as shown below:

4.1.1 Details of Hospital
4.1.2 Details of Patient
4.1.3 Expiry Date
4.1.4 Drug's Name with Strength
4.1.5 Administration Instructions

4.2 The worksheet of the product should contain the following details:

4.2.1 Patient's name
4.2.2 ID number
4.2.3 Prescription number
4.2.4 Date of preparation
4.2.5 Name of drug
4.2.6 Dose
4.2.7 Total volume of the bottle

5.0 CHEMICALS AND EQUIPMENTS:

5.1 CHEMICALS:

5.1.1 **SUSPENDING VEHICLE:**

5.1.1.1 It a suspending vehicle used to simplify the process involved in the extemporaneous compounding of oral suspensions.

5.1.2 **Ingredients:**

5.1.2.1 Water

5.1.2.2 Microcrystalline cellulose

5.1.2.2.1 act as suspending agents in water, producing thixotropic structured vehicles.

5.1.2.2.2 (Remington Essentials of Pharmaceutics First edition published 2013, pg. 369)

5.1.2.3 **Sodium carboxy methyl cellulose**

5.1.2.3.1 USP 31 (Carboxy methylcellulose Sodium).

5.1.2.3.2 A white to cream colored, hygroscopic powder or granules. It contains not less than 6.5% and not more than 9.5% of sodium, calculated on the dried basis.

5.1.2.3.3 Easily dispersed in water to form colloidal solutions; insoluble in alcohol, in ether, and in most other organic solvents.

5.1.2.3.4 pH of a 1% solution in water is between 6.5 and 8.5.
Store in airtight containers.
(Martindale the complete drug reference Thirty-sixth edition pg.

N.B: Uses and Administration Powdered cellulose and microcrystalline cellulose are used in pharmaceutical manufacturing as tablet binders and disintegrates and as capsule and tablet diluents. These two forms of cellulose are also used in the food industry.
Dispersible cellulose (which also contains some carmellose sodium) forms a thixotropic gel with water and is used pharmaceutically as a suspending and thickening agent.
(Martindale the complete drug reference Thirty-sixth edition pg. 2143)

2142)

5.1.2.4 **Xanthan gum**

5.1.2.4.1 Ph. Eur. 6.2 (Xanthan Gum). A gum produced by fermentation of a carbohydrate with Xanthomas campestris and purified. It is the sodium, potassium, or calcium salt of a high-molecular weight polysaccharide containing D-glucose, mannose, and glucuronic acid.
It also contains not less than 1.5% of pyruvic acid, calculated with reference to the dried substance. A white or yellowish-white, free-flowing powder.

5.1.2.4.2 Soluble in water giving a highly viscous solution; practically insoluble in organic solvents.

5.1.2.4.3 A 1% solution in water has a pH of 6.0 to 8.0.

5.1.2.4.4 (Martindale the complete drug reference Thirty-sixth edition pg. 2142) Uses

5.1.2.4.5 Xanthan gum is used in pharmaceutical manufacturing as a suspending, stabilizing, thickening, and emulsifying agent. It is also used similarly in the food industry.

5.1.2.4.6 Suspensions of crushed tablets or insoluble powders made with xanthan gum were reported to be preferable to those made with tragacanth.

5.1.2.4.7 (Anonymous. "Extremely useful" new suspending agent. Pharm J 1986; 237: 665)

5.1.2.5 **Sodium phosphate dibasic**

5.1.2.5.1 USP 31 (Dibasic Sodium Phosphate).

5.1.2.5.2 It is dried, or contains one, two, seven, or twelve molecules of water of hydration.

5.1.2.5.3 The dried substance is a white powder that readily absorbs moisture.

5.1.2.5.4 It is soluble 1 in 8 of water; insoluble in alcohol.

5.1.2.5.5 The heptahydrate is a colorless or white, granular or caked salt that effloresces in warm, dry air.

5.1.2.5.6 It is freely soluble in water; very slightly soluble in alcohol.

5.1.2.5.7 Its solutions are alkaline to phenolphthalein, a 0.1M solution having
a pH of about 9.

5.1.2.5.8 Store all forms in airtight containers.

5.1.2.6 **Methyl paraben**

5.1.2.6.1 [Code of Federal Regulations]

5.1.2.6.2 [Title 21, Volume 3]

5.1.2.6.3 [Revised as of April 1, 2017]

5.1.2.6.4 PART 184 -- DIRECT FOOD SUBSTANCES AFFIRMED AS GENERALLY RECOGNIZED AS SAFE

5.1.2.6.5 Subpart B--Listing of Specific Substances Affirmed as GRAS

5.1.2.6.6 Sec. 184.1490 Methyl paraben.

5.1.2.6.7 The ingredient is used as an antimicrobial agent.

5.1.2.7 **Potassium sorbate**

5.1.2.7.1 [Code of Federal Regulations]

5.1.2.7.2 [Title 21, Volume 3]

5.1.2.7.3 [Revised as of April 1, 2017]

5.1.2.7.4 [CITE: 21CFR182.3640]

5.1.2.7.5 PART 182 -- SUBSTANCES GENERALLY RECOGNIZED AS SAFE

5.1.2.7.6 Subpart D--Chemical Preservatives

5.1.2.7.7 Sec. 182.3640 Potassium sorbate.

5.1.3 **Flavored syrup vehicle:**

5.1.3.1 **Syrup vehicle used to simplify the process of flavoring and sweetening extemporaneous compounded oral preparations**.

5.1.3.1.1 Sucrose Used for syrup formation

5.1.3.1.2 Glycerin is a clear, syrupy liquid with a sweet taste and is miscible with water and alcohol.

5.1.3.1.3 glycerin is used mainly as a solvent.

5.1.3.1.4 In oral solutions, glycerin is used as a solvent, sweetening agent, antimicrobial preservative, and viscosity-increasing agent.

5.1.3.1.5 (Michael M. Crowley, PhD Chapters 24 Solutions, Emulsions, Suspensions, and Extracts, Remington Essentials of Pharmaceutics First edition published 2013 pg. 437)

5.1.3.1.6 Citric acid Description: A white, granular to fine crystalline powder; odorless; strongly acid taste Properties: 1 g in 0.5 mL water, 2 mL alcohol; density 1.5 g/cc Uses: As an acidifier, antioxidant, buffering agent, and sialagogue.

5.1.3.1.7 (William J. Reilly Jr., MBA: Chapter 36 Pharmaceutical Excipients, Remington Essentials of Pharmaceutics pg.690)

5.1.3.1.8 disodium hydrogen phosphate USP 31 (Dibasic Sodium Phosphate).

5.1.3.1.9 It is dried, or contains one, two, seven, or twelve molecules of water of hydration.

5.1.3.1.10 The dried substance is a white powder that readily absorbs moisture. It is soluble 1 in 8 of water; insoluble in alcohol.

5.1.3.1.11 The heptahydrate is a colorless or white, granular or caked salt that effloresces in warm, dry air.

5.1.3.1.12 It is freely soluble in water; very slightly soluble in alcohol.

5.1.3.1.13 Its solutions are alkaline to phenolphthalein, a 0.1M solution having a pH of about 9.

5.1.3.1.14 Store all forms in airtight containers.

5.1.3.1.15 Potassium sorbate

5.1.3.1.16 Methyl paraben sodium

5.1.4 **Sugar free flavored vehicle:**

5.1.4.1 saccharin sodium

5.1.4.2 glycerin

5.1.4.3 xanthan gum

5.1.4.4 methyl paraben

5.1.4.5 propyl paraben

5.1.4.6 potassium sorbate

5.1.4.7 flavoring agent

5.1.4.8 citric acid

5.1.4.9 sodium citrate

5.1.4.10 water

5.2 EQUIPMENTS:

5.2.1 Balances; electronic, minimum sensitivity of 1 mg and 10 mg.

5.2.2 Beakers 50-1000 ml glass.

5.2.3 Beaker hot stand.

5.2.4 Bottles; glass.

5.2.5 Capsule filling equipment.

5.2.6 Coffee grinder.

5.2.7 Cylinders glass.

5.2.8 Droppers.

5.2.9 Fume cupboards.

5.2.10 Heater.

5.2.11 Mixer.
5.2.12 Mortars.
5.2.13 Magnetic stirrer.
5.2.14 PH meter.
5.2.15 Pipette bulbs.
5.2.16 Thermometers.
5.2.17 Water system.

6.0 Topical preparations

6.1 ZnO 15% in aqueous cream base
6.2 Anti-lice hair serum:
6.3 Salicylic acid 10 % + urea 10 % in ointment base:
6.4 Salicylic acid 5 % + urea 10 % in ointment base:
6.5 Bergamot paint 10% in alcohol base:
6.6 Sulfur ointment 5%:
6.7 Phenol 1% + resorcinol 2 % + sulfur 3% in calamine lotion base:

Formulary of extemporaneous preparations

7.0 Compounding monograph:

Drug name	Concentration	Vehicle used for preparation
Acetazolamide	25 mg/ml	Suspending vehicle / sweeting vehicle
Amlodipine	1 mg/ml	Suspending vehicle / sweeting vehicle
Amitriptyline	1 mg/ml	Simple syrup
Aprepitant	20 mg/ml	Suspending vehicle / sweeting vehicle
Atenolol	2 mg/ml	Sugar free sweeting vehicle
Captopril	1 mg/ml	Simple syrup
Carvedilol	0.5 mg/ml	Suspending vehicle / sweeting vehicle
Ciprofloxacin	50 mg/ml	Suspending vehicle / sweeting vehicle
Cyclophosphamide	10 mg/ml	Saline/ suspending vehicle
Gabapentin	100 mg/ml	Suspending vehicle / sweeting vehicle
GTN	0.2% w/w	Vaseline
Hydrocortisone	50 mg/ml	Suspending vehicle / sweeting vehicle
Hydroxyurea	100 mg/ml	Distilled water/ cherry syrup
KMnO4	1/8000	Distilled water
Lamotrigine	1 mg/ml	Suspending vehicle / sweeting vehicle

Levofloxacin	50 mg/ml	Strawberry syrup/ suspending vehicle
6 mercaptopurine	25 mg/ml	SWFI / simple syrup / cherry syrup
Methyldopa	50 mg/ml	Simple syrup
Nifedipine	1 mg/ml	Suspending vehicle / sweeting vehicle
Omeprazole	2 mg/ml	Sodium bicarbonate 8.4 w/v
Oseltamivir	6 mg/ml	Simple syrup
Propranolol	1 mg/ml	Simple syrup + citric acid
Temozolomide	10 mg/ml	Suspending vehicle / sweeting vehicle + pk30
Thalidomide	20 mg/ml	Suspending vehicle / sweeting vehicle
Sevelamer	50 mg/ml	Simple syrup
Sorafenib	35 mg capsule	Corn starch
Sunitinib	10 mg/ml	Suspending vehicle / sweeting vehicle
Ursodeoxycholic acid	30 mg/ml	Simple syrup
Valganciclovir	60 mg/ml	Suspending vehicle / sweeting vehicle
Zonisamide	10 mg/ml	Suspending vehicle / sweeting vehicle

8.0 References:

8.1 JCI standards 7th edition – MMU Chapter. (MMU.5.2)
8.2 JCI standard 7th addition
8.3 ASHP guidelines
8.4 GAHAR standards.MMS.14, 15 and 16