GALENIC VALIDATION OF A DEXAMETHASONE 0.01% MOUTHWASH SOLUTION TO PREVENT EVEROLIMUS RELATED STOMATITIS

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BACKGORUND AND IMPORTANCE

Stomatitis is a common adverse drug reaction of the mTOR inhibitor everolimus. HS Rugo et al (2016) reported that dexamethasone mouthwash solution prevents stomatitis grade ≥ 2 in patients with everolimus treatment for hormone receptor-positive and HER2-negative metastatic breast cancer.

No commercial presentation is available in our country.

AIM AND OBJECTIVE

Development of an oral solution of dexamethasone 0.1% for mouth washing, committed to these patients, based on others still marketed.

MATHERIALS AND METHODS

Proposal of two formulations, based on the one described on US Pharmacopeia.

Source of dexamethasone water soluble salt (phosphate). Commercially available dexamethasone 4mg/mL injectable solution (Kern Pharma ®)

Study of basic pharmaceutical properties for 30 days: organoleptic characteristics and pH

Composition of solutions implicated in the whole process are shown in table 1.

RESULTS

Transparent, homogenous solution free of visible and rare particles

Physicochemical stability guaranteed: support on pre-existing formulations to develop ours.

- Organoleptic characteristics (cleanness, colour, odour, flavour) constant
- pH stable = 3-5

Microbiologic period of validity assignment according to *Risk matrix from Good Manufacture Practices of Spanish Hospital Pharmacy Society*.

30 days in closed bottle and 30 days after opening under refrigeration.

Final choice:

Formula without EDTA

Table 1. Solutions involved in this work and their components

Imitate this	*Starting material*	*Our proposals*	
Dexamethasone USP oral solution	Dexamethasone 4mg/mL injectable ampule	Dexamethasone 0.1% without added EDTA	Dexamethasone 0.1% with added EDTA
Dexamethasone	Dexamethasone sodium phosphate	Dexamethasone sodium phosphate [10mg[1]]	Dexamethasone sodium phosphate [10mg[1]]
Glycerin	-	-	-
Propylen glycol	-	-	-
Methylparaben	-	Preservative water[2] [qs 100 mL]	Preservative water[2] [qs 100 mL]
Propylparaben	-		
Flavoring	-	-	-
Sorbitol	-	-	-
Citric acid	Sodium citrate and sodium hydroxide	Citric acid 25% sol [qs pH 3-5]	Citric acid 25% sol [qs pH 3-5]
Sodium edetate	Sodium edetate	-	Sodium edetate [10mg]
Water	Water for injectable preparations	2	2
pH 3-5	pH 7-8,5	pH 4,3-4,8 [Refrigerated]	pH 4,4-4,6 [Refrigerated]

qs. *Quantum sufficit*.

[1] From 2,5 mL of dexamethasone 4mg/mL injectable ampule

[2] Preservative water contains methylparaben (9%) and propylparaben (2,2%)

CONCLUSION AND RELEVANCE

- Formulation simple to prepare
- Can be used in other hospitals
- Coverage of therapeutic lagoon

https://www.eahp.eu/25-3PC-040

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Background bibliography. Hope S Rugo et al. Lancet Oncol. 2017 May;18(5):654-662.