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REVIEW OF DOSAGE AND EFFECTS ON METAXALONE

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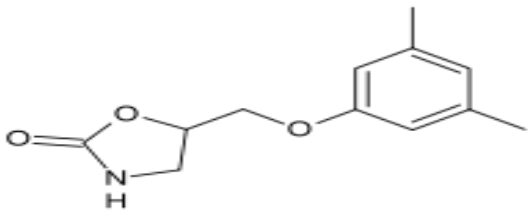
INTRODUCTION

Metaxalone (marketed by King Pharmaceuticals under the brand name **Skelaxin**) is a muscle relaxant used to relax muscles and relieve pain caused by strains, sprains, and other musculoskeletal conditions. Its exact mechanism of action is not known, but it may be due to general central nervous systemdepression. It is considered to be a moderately strong muscle relaxant, with relatively low incidence of side effects. Skelaxin is available in an 800 mg scored tablet. Possible side effects include nausea, vomiting, drowsiness and CNS side effects, such as dizziness, headache and irritability.

1. The metabolism of metaxalone involves the liver cytochrome P450 system. Based on the information in the labeling, patients receiving metaxalone therapy and physicians prescribing metaxalone are directed to take precaution when coadministering it with other medications involving the P450 system.[1][2]
2. Because of potential for side effects, this drug is considered high risk in the elderly. As of 2015 the cost for a typical month of medication in the United States is 100 to 200 USD.[3]

Table 3.1: Metaxalone

Description	**White crystalline powder**
Structure	
Chemical name	5-[(3,5-dimethyl phenoxy)methyl]-1,3 oxazolidin-2-one
Molecular Formula	$C_{12}H_{15}NO_3$
Molecular weight	221.25
Therapeutic Category	Skeletal muscle relaxant
Melting point	121°C
Log P	2.42
P^{ka}	6.5
BCS Classification	Class II
Solubility	Freely soluble in chloroform& Di-Chloro methane Soluble in methanol and 96%ethanol Practically insoluble ether & water
Mechanism of Action	Mechanism of action has not been established, but may be due to general CNS depression. It has no direct action on the contractile mechanism of striated muscle, the motor end plate or the nerve fibre

Pharmacokinetics

Absorption

The absorption of metaxalone from immediate release tablets is slow, erratic and unpredictable. Peak plasma concentration is usually attained 3 hours after oral dosing. Absolute bio availability is not known. The AUC and C_{max} of 800 mg tablets are more than 400mg tablets and T_{max} is low.

Food-Drug interactions

Metaxalone is a poorly soluble drug, but the solubility can be increased by administering with the fatty food. Food contains lipids& bile salts and enzymes induced in the stomach act as Solubilizer. So that drug dissolves more and bio availability increases.

Distribution

The mean volume of distribution of Metaxalone generally ranges from 750 to 800L after administration of 800mg dose, indicating widespread distribution into body tissues. Metaxalone reaches its peak levels in skin tissues and in blister fluid of healthy subjects at approximately 3hrs after dosing.

Metabolism

Metaxalone is metabolized in the liver. Cytochrome P450 was identified as major enzyme responsible for it.

Excretion

Metaxalone is excreted largely as unchanged drug in the urine. The mean terminal plasma elimination half-life of Metaxalone ranges from approximately 6 to 10hrs following administration of 3 to 4 times per day. The mean apparent total body clearance and renal clearance range from approximately 46 to 95mL/min and 56 to 115mL/min, respectively. Renal clearance in excess of the glomerular filtration rate suggests that tubular secretion of Metaxalone occurs in addition to its glomerular filtration.

Adverse Effects

- CNS- Drowsiness, Head ache and Irritability.
- Hepatic- Jaundice
- Digestive system- Nausea, Vomiting &GIT upset.
- Metaxalone over doses significantly cause death.

Uses

- Skeletal muscle relaxant
- Relieves pain caused by strains & sprains
- Analgesic

Dosage

The usual dose of Metaxalone Tablets is 800 mg administered orally 3 to 4 times per day.

Drug interactions

Metaxalone enhances the effects of alcohols, barbiturates and other CNS depressants.

Precautions

Metaxalone should not be administered with other CNS depressants.

Marketed formulations

SKELAXIN- King Pharmaceutical, USA.
ZORANE- Novartis Ltd.

EXCIPIENT PROFILE

ALGINIC ACID

Synonyms

Protacid; Acidic alginicum; E400; Kelacid; L-gluco-Dmannoglycuronan; Polymannuronic acid; Satiagine H8.

Structural formulae

The PhEur 6.3 describes alginic acid as a mixture of poly uronic acids $[(C_6H_8O_6)_n]$ composed of residues of D-mannuronic acid and L-glucoronic acid, and obtained mainly from algae belonging to the Phaeophyceae. A small proportion of carboxylic group may be neutralized.

Functional category

Stabilizing agent; suspending agent; tablet binder; tablet disintegrant; viscosity- increasing agent.

Description

Tasteless, practically odorless, white to yellowish-white, fibrous powder.

Stability and storage

It hydrolyzes slowly at warm temperatures producing a material with a lower molecular weight and lower dispersion viscosity. Alginic acid dispersions are susceptible to microbial spoilage on storage, which may result in some depolymerization and hence a decrease in viscosity. Dispersions can be preserved with anti microbial agents such as benzoic acid, sodium benzoate, sorbic acid, etc. Alginic acid should be stored in a well-closed container in a cool and dry place.

Safety

Alginic acid is widely used in food products, topical and oral pharmaceutical formulations. It is generally regarded as a nontoxic and non irritant material, although excessive oral consumption may be harmful. Inhalation of alginate dust may be irritant and has been associated with industrially related asthma.

Applications

In Oral & topical formulations- as a binder and disintegrating agent at a concentration of 1-5% w/w. It is widely used as a thickening and suspending agent in a variety of pastes, creams and gels. Therapeutically it is an antacid.

AMMONIUM CALCIUM ALGINATE

Proprietary names
None adopted.

Synonyms
Keltose; Alginic acid; Ammonium salt; Ammonium poly mannurate; E404.

Empirical formula
($C6H11NO6)_n$

Functional category
Diluent; stabilizing agent and thickening agent.

Description
Occurs as white to yellowish brown filamentous, grainy, granular or powder form.

Stability and storage
Ammonium alginate is a hygroscopic material, although it is stable if stored at low relative humidities and cool temperatures.

Safety
Ammonium alginate is widely used in cosmetics and food products and also in pharmaceutical formulations such as tablets. It is generally regarded as a non toxic and non irritant material, although excessive oral consumption may be harmful.

Applications
It is mainly used as food stabilizer, thickener and emulsifier.

CORN STARCH

Synonyms
Amylum; C*PharmGel; Eurylon; fecule; amidion; Hylon.

Functional category
Tablets and capsules- diluent, disintegrant, binder and thickening agent.

Empirical formula and molecular weight
($C_6H_{20}O_5)_n$ where n= 300-1000.

Starch consists of linear amylase and branched amylopectin, two polysaccharides based on α-(D) glucose. Both polymers are organized in a semi crystalline structure and in the starch granule, amylopectin forms the crystalline portion. The exact structure of starch is not yet fully understood.

Description
Starch occurs as an odorless and tasteless, fine, white to off-white powder.

Solubility
Practically insoluble in cold ethanol (96%) and in cold water. Starch swells instantaneously in water by about 5-10% at 37°c. Starch becomes soluble in hot water at temperatures above the gelatinization temperature.

Stability and storage
Dry starch is stable if protected from high humidity. Starch is considered to be chemically and microbiologically inert under normal storage conditions. Starch solutions and pasts are physically unstable and are readily metabolized by the micro organisms, they should be therefore be freshly prepared when used for wet granulations. Starch should be stored in an airtight container in a cool and dry place.

Safety
Starch is an edible food substance, considered a food ingredient and not a food additive. It is generally regarded as a non-toxic and non irritant material. Therefore it is widely used in pharmaceutical formulations.

Applications
Starch is a versatile excipient used primarily in oral solid-dosage formulations where it is used as a binder, diluent and disintegrant. In tablet formulations starch is used at a concentration of 3-20%w/w as a binder for wet granulation and as a disintegrant at a concentration of 3-25% used.

MAGNESIUM STEARATE

Synonyms
Dibasic magnesium stearate, Stearic acid.

Empirical formulae
The USP32-NF27 describes magnesium stearate as a compound of magnesium with a mixture of solid organic acids that consists chiefly of variable proportions of magnesium stearate and magnesium palmitate obtained from sources of vegetable or animal origin.

Functional category
Tablet and capsule lubricant.

Description
Very fine, light weight, precipitated or milled impalpable powder of low bulk density having a faint odor of stearic acid and a characteristic taste.

Incompatibilities
Incompatible with strong acids, alkalis and iron salts. Avoid mixing with strong oxidizing materials. It cannot be used in products containing aspirin, some vitamins and most alkaloidal salts.

Stability and storage
It is stable and should be stored in a well closed container in a cool and dark place.

Handling precautions
Eye protection and gloves are recommended. Excessive inhalation of magnesium stearate dust causes respiratory problems.

Applications
It is widely used in cosmetics, foods and pharmaceutical formulations. It is primarily used as a lubricant in capsules and tablets manufacturing at a concentration between 0.25 and 5.0% w/w.

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