CHLORHEXIDINE GLUCONATE- chlorhexidine gluconate rinse
Actavis Mid Atlantic LLC

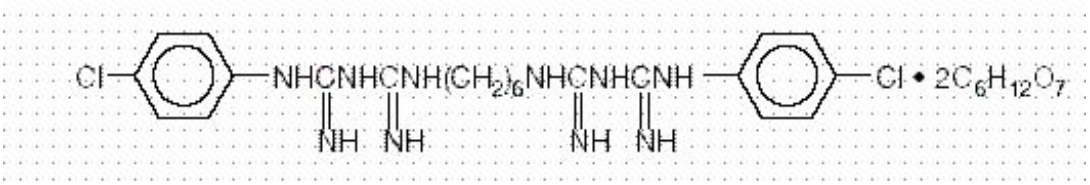
CHLORHEXIDINE GLUCONATE ORAL RINSE USP 0.12%

FORM NO. 0036
Rev. 10/06
VC2912

Rx Only

DESCRIPTION

This product is an oral rinse containing 0.12% chlorhexidine gluconate (1,1'-hexamethylene bis [5-(p-chlorophenyl) biguanide]di-D-gluconate) in a base containing water, 11.6% alcohol, glycerin, PEG-40 sorbitan diisostearate, peppermint oil, saccharin sodium, and FD&C Blue #1. The pH may be adjusted with hydrochloric acid or sodium hydroxide. The solution is near-neutral (pH range 5–7). Chlorhexidine gluconate is a salt of chlorhexidine and gluconic acid. Its molecular formula is $C_{22}H_{30}Cl_2N_{10}•2C_6H_{12}O_7$, molecular weight 897.77 and its structural formula is:



CLINICAL PHARMACOLOGY

Chlorhexidine gluconate provides antimicrobial activity during oral rinsing. The clinical significance of chlorhexidine gluconate's antimicrobial activities is not clear. Microbiological sampling of plaque has shown a general reduction of counts of certain assayed bacteria, both aerobic and anaerobic, ranging from 54–97% through six months' use.

Use of chlorhexidine gluconate oral rinse in a six-month clinical study did not result in any significant changes in bacterial resistance, overgrowth of potentially opportunistic organisms or other adverse changes in the oral microbial ecosystem. Three months after chlorhexidine gluconate use was discontinued, the number of bacteria in plaque had returned to baseline levels and resistance of plaque bacteria to chlorhexidine gluconate was equal to that at baseline.

Pharmacokinetics: Pharmacokinetic studies with 0.12% chlorhexidine gluconate oral rinse indicate approximately 30% of the active ingredient is retained in the oral cavity following rinsing. This retained drug is slowly released into the oral fluids. Studies conducted on human subjects and animals demonstrate chlorhexidine gluconate is poorly absorbed from the gastrointestinal tract. The mean plasma level of chlorhexidine gluconate reached a peak of 0.206 mcg/g in humans 30 minutes after they ingested a 300-mg dose of the drug. Detectable levels of chlorhexidine gluconate were not present in the plasma of these subjects 12 hours after the compound was administered. Excretion of chlorhexidine gluconate occurred primarily through the feces (~90%). Less than 1% of the chlorhexidine gluconate ingested by these subjects was excreted in the urine.

INDICATIONS AND USAGE

Chlorhexidine Gluconate Oral Rinse is indicated for use between dental visits as part of a professional program for the treatment of gingivitis as characterized by redness and swelling of the gingivae, including gingival bleeding upon probing. Chlorhexidine gluconate has not been tested among patients with acute necrotizing ulcerative gingivitis (ANUG). For patients having coexisting gingivitis and periodontitis, see PRECAUTIONS.

CONTRAINDICATIONS

This product should not be used by persons who are known to be hypersensitive to chlorhexidine gluconate or other formula ingredients.

WARNINGS

The effect of chlorhexidine gluconate on periodontitis has not been determined. An increase in supragingival calculus was noted in clinical testing in chlorhexidine gluconate oral rinse users compared with control users. It is not known if chlorhexidine gluconate use results in an increase in subgingival calculus. Calculus deposits should be removed by a dental prophylaxis at intervals not greater than six months.

Hypersensitivity and generalized allergic reactions have occurred. See CONTRAINDICATIONS.

PRECAUTIONS

General

1. For patients having coexisting gingivitis and periodontitis, the presence or absence of gingival inflammation following treatment with chlorhexidine gluconate should not be used as a major indicator of underlying periodontitis.

2. Chlorhexidine gluconate oral rinse can cause staining of oral surfaces, such as tooth surfaces, restorations, and the dorsum of the tongue. Not all patients will experience a visually significant increase in toothstaining. In clinical testing, 56% of chlorhexidine gluconate oral rinse users exhibited a measurable increase in facial anterior stain, compared to 35% of control users after six months; 15% of chlorhexidine gluconate users developed what was judged to be heavy stain, compared to 1% of control users after six months. Stain will be more pronounced in patients who have heavier accumulations of unremoved plaque.

Stain resulting from use of chlorhexidine gluconate oral rinse does not adversely affect health of the gingivae or other oral tissues. Stain can be removed from most tooth surfaces by conventional professional prophylactic techniques. Additional time may be required to complete the prophylaxis.

Discretion should be used when prescribing to patients with anterior facial restorations with rough surfaces or margins. If natural stain cannot be removed from these surfaces by a dental prophylaxis, patients should be excluded from chlorhexidine gluconate treatment if permanent discoloration is unacceptable. Stain in these areas may be difficult to remove by dental prophylaxis and on rare occasions may necessitate replacement of these restorations.

3. Some patients may experience an alteration in taste perception while undergoing treatment with chlorhexidine gluconate oral rinse. Rare instances of permanent taste alteration following use of chlorhexidine gluconate oral rinse have been reported via postmarketing surveillance.

Pregnancy

Teratogenic Effects

Pregnancy category B. Reproduction studies have been performed in rats and rabbits at chlorhexidine gluconate doses up to 300 mg/kg/day and 40 mg/kg/day, respectively, and have not revealed evidence of

harm to the fetus. However, adequate and well-controlled studies in pregnant women have not been done. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when chlorhexidine gluconate is administered to a nursing woman.

In parturition and lactation studies with rats, no evidence of impaired parturition or of toxic effects to suckling pups was observed when chlorhexidine gluconate was administered to dams at doses up to 100 mg/kg/day.

Pediatric Use

Clinical effectiveness and safety of chlorhexidine gluconate have not been established for pediatric patients under the age of 18.

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a drinking water study in rats, carcinogenic effects were not observed at doses up to 38 mg/kg/day. Mutagenic effects were not observed in two mammalian *in vivo* mutagenesis studies with chlorhexidine gluconate. The highest doses of chlorhexidine used in a mouse dominant-lethal assay and a hamster cytogenetics test were 1000 mg/kg/day and 250 mg/kg/day, respectively. No evidence of impaired fertility was observed in rats at doses up to 100 mg/kg/day.

ADVERSE REACTIONS

The most common side effects associated with chlorhexidine gluconate oral rinses are (1) an increase in staining of teeth and other oral surfaces, (2) an increase in calculus formation, and (3) an alteration in taste perception; see WARNINGS and PRECAUTIONS. Oral irritation and local allergy-type symptoms have been spontaneously reported as side effects associated with the use of chlorhexidine gluconate rinse. The following oral mucosal side effects were reported during placebo-controlled adult clinical trials: aphthous ulcer, grossly obvious gingivitis, trauma, ulceration, erythema, desquamation, coated tongue, keratinization, geographic tongue, mucocele, and short frenum. Each occurred at a frequency of less than 1.0%.

Among postmarketing reports, the most frequently reported oral mucosal symptoms associated with chlorhexidine gluconate are stomatitis, gingivitis, glossitis, ulcer, dry mouth, hypesthesia, glossal edema, and paresthesia.

Minor irritation and superficial desquamation of the oral mucosa have been noted in patients using chlorhexidine gluconate oral rinse.

There have been cases of parotid gland swelling and inflammation of the salivary glands (sialadenitis) reported in patients using chlorhexidine gluconate oral rinse.

OVERDOSAGE

Ingestion of 1 or 2 ounces of chlorhexidine gluconate oral rinse by a small child (~10 kg body weight) might result in gastric distress, including nausea, or signs of alcohol intoxication. Medical attention should be sought if more than 4 ounces of chlorhexidine gluconate oral rinse is ingested by a small child or if signs of alcohol intoxication develop.

DOSAGE AND ADMINISTRATION

Chlorhexidine Gluconate Oral Rinse therapy should be initiated directly following a dental prophylaxis.

Patients using chlorhexidine gluconate should be reevaluated and given a thorough prophylaxis at intervals no longer than six months.

Recommended use is twice daily oral rinsing for 30 seconds, morning and evening after toothbrushing. Usual dosage is ½ fl. oz. (marked in cup) of undiluted chlorhexidine gluconate oral rinse. Patients should be instructed to not rinse with water, or other mouthwashes, brush teeth, or eat immediately after using chlorhexidine gluconate oral rinse. Chlorhexidine Gluconate Oral Rinse is not intended for ingestion and should be expectorated after rinsing.

HOW SUPPLIED

Chlorhexidine Gluconate Oral Rinse 0.12% is supplied as a blue liquid in child-resistant bottles of one pint (473 mL), individually cartoned with a dosage cup.

Store at controlled room temperature 15°-30°C (59°-86°F).

Dispense in original container or in amber glass bottles.

Manufactured by:
Actavis MidAtlantic LLC
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Baltimore, MD 21244 USA

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CHLORHEXIDINE GLUCONATE

chlorhexidine gluconate rinse

Product Information			
Product Type	HUMAN PRESCRIPTION DRUG	**Item Code (Source)**	NDC:0472-0036
Route of Administration	ORAL		

Active Ingredient/Active Moiety		
Ingredient Name	**Basis of Strength**	**Strength**
Chlorhexidine Gluconate (UNII: MOR84MUD8E) (Chlorhexidine - UNII:R4KO0DY52L)		0.12 mg in 1 mL

Inactive Ingredients	
Ingredient Name	**Strength**
glycerin (UNII: PDC6A3C0OX)	
PEG-40 sorbitan diisostearate ()	
peppermint oil (UNII: AV092KU4JH)	
saccharin sodium (UNII: SB8ZUX40TY)	
FD&C Blue #1 ()	
hydrochloric acid (UNII: QTT17582CB)	
sodium hydroxide (UNII: 55X04QC32I)	

Packaging

#	Item Code	Package Description	Marketing Start Date	Marketing End Date
1	NDC:0472-0036-16	1 in 1 CARTON		
1		473 mL in 1 BOTTLE		

Labeler - Actavis Mid Atlantic LLC

Revised: 2/2009 Actavis Mid Atlantic LLC