DESCRIPTION

Clindamycin hydrochloride is the hydrated hydrochloride salt of clindamycin. Clindamycin is a semisynthetic antibiotic produced by a 7β-chloro-substitution of the 7β-hydroxyl group of the parent compound lincomycin.

Clindamycin Hydrochloride Capsules, USP contain clindamycin hydrochloride equivalent to 150 mg or 300 mg of clindamycin.

Inactive ingredients: anhydrous lactose, magnesium stearate, starch (corn) and talc. The capsule shells are green colored shell for 150 mg capsules and yellow colored shell for 300 mg capsules.

The structural formula is represented below:

```
\begin{align*}
\text{CH}_3 & \quad \text{C} & \quad \text{OH} \\
\text{O} & \quad \text{N} & \quad \text{H} \\
\text{Cl} & \quad \text{H} & \quad \text{C} \quad \text{H}_3 \\
\text{OH} & \quad \text{O} & \quad \text{H} \\
\end{align*}
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M.W. 461.44

The chemical name for clindamycin hydrochloride is Methyl 7β-chloro-6-(1-methyl-trans-4-propyl-2-pyridylidene carboxamido)-1-thio-L-threo-β-D-galacto-octopyranoside monohydrochloride.

CLINICAL PHARMACOLOGY

Human Pharmacology

Absorption

Serum level studies with a 150 mg oral dose of clindamycin hydrochloride in 24 normal adult volunteers showed that clindamycin was rapidly absorbed after oral administration. An average peak serum level of 2.50 mcg/mL was reached in 40 minutes; serum levels averaged 1.51 mcg/mL at 3 hours and 0.70 mcg/mL at 6 hours. Absorption of an oral dose is virtually complete (90%) and the concomitant administration of food does not appreciably modify the serum concentrations; serum levels have been uniform and predictable from person to person and dose to dose. Serum level studies following multiple doses of clindamycin hydrochloride for up to 14 days show no evidence of accumulation or altered pattern of drug excretion. Dosages up to two grams of clindamycin per day for 14 days have been well tolerated by healthy volunteers, except that the incidence of gastrointestinal side effects is greater with the higher doses.

Distribution

Concentrations of clindamycin in the serum increased linearly with increased dose. Serum levels exceed the MIC (minimum inhibitory concentration) for most indicated organisms for at least six hours following administration of the usually recommended doses. Clindamycin is widely distributed in body fluids and tissues (including bones). No significant levels of clindamycin are attained in the cerebrospinal fluid, even in the presence of inflamed meninges.

Excretion

The average biological half-life is 2.4 hours. Approximately 10% of the bioavailability is excreted in the urine and 3.6% in the feces; the remainder is excreted as biliary metabolites.

Special Populations

Renal impairment

Serum half-life of clindamycin is increased slightly in patients with markedly reduced renal function. Hemodialysis and peritoneal dialysis are not effective in removing clindamycin from the serum.

Use in elderly

Pharmacokinetic studies in elderly volunteers (61 to 79 years) and younger adults (18 to 39 years) indicate that age alone does not alter clindamycin pharmacokinetics (clearance, elimination half-life, volume of distribution, and area under the concentration-time curve) after IV administration of clindamycin phosphate. After oral administration of clindamycin hydrochloride, elimination half-life is increased to approximately 5.5 hours (range 4.0 to 7.8 hours) in the elderly compared to 3.2 hours (range 2.1 to 4.2 hours) in younger adults. The extent of absorption, however, is not different between age groups and no dosage alteration is necessary for the elderly with normal hepatic function and normal (age-adjusted) renal function.

Microbiology

Clindamycin inhibits bacterial protein synthesis by binding to the 50S subunit of the ribosome. It has activity against Gram-positive aerobes and anaerobes and as well as some Gram-negative anaerobes. Clindamycin is bacteriostatic. Cross-resistance between clindamycin and lincomycin is complete. Antibacterial activity has been demonstrated between clindamycin and erythromycin. Clindamycin inducible resistance has been bacteriostatic. Cross-resistance between clindamycin and lincomycin is complete. Antagonism

At least 90% of the microorganisms listed below exhibit in vitro minimum inhibitory concentrations (MICs) less than or equal to the clindamycin susceptible MIC breakpoint for organisms of a similar type to those shown in Table 1. However, the efficacy of clindamycin in treating clinical infections due to these microorganisms has not been established in adequate and well-controlled clinical trials.

Gram-positive aerobes

- Staphylococcus aureus (methicillin-susceptible strains)
- Streptococcus pneumoniae (penicillin-susceptible strains)

Gram-positive anaerobes

- Peptostreptococcus micros
- Porphyromonas asaccharolytica

Table 1. Susceptibility Interpretive Criteria for Clindamycin

<table>
<thead>
<tr>
<th>Pathogen</th>
<th>Susceptibility Interpretive Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Minimum Inhibitory Concentration (MCI in mcg/mL)</td>
</tr>
<tr>
<td></td>
<td>≤</td>
</tr>
<tr>
<td>Staphylococcus spp.</td>
<td>≤0.06</td>
</tr>
<tr>
<td>Streptococcus pneumoniae and other Streptococci spp.</td>
<td>≤0.25</td>
</tr>
<tr>
<td>Anaerobic Bacteria</td>
<td>≤2</td>
</tr>
</tbody>
</table>

A report of “Susceptible” indicates that the pathogen is likely to be inhibited if the antimicrobial compound in the blood reaches the concentrations usually achievable. A report of “Intermediate” indicates that the result should be considered equivocal, and, if the microorganism is not fully susceptible to alternative, clinically feasible drugs, the test should be repeated. This category implies possible clinical applicability in body sites where the drug is physiologically concentrated or in situations where high dosage of drug can be used. This category also provides a buffer that prevents small, uncontrolled technical factors from causing major discrepancies in interpretation.

Quality Control

Standardized susceptibility test procedures require the use of laboratory controls to monitor and ensure the accuracy and precision of the supplies and reagents used in the assay, and the techniques of the individuals performing the test.1,2,4 Standard clindamycin powder should provide the MIC ranges in Table 2. For the disk diffusion technique using the 2 mcg clindamycin disk the criteria provided in Table 2 should be achieved.

Table 2. Acceptable Quality Control Ranges for Clindamycin to be Used in Validation of Susceptibility Test Results

<table>
<thead>
<tr>
<th>QC Strain</th>
<th>Minimum Inhibitory Concentration Range (mcg/mL)</th>
<th>Disk Diffusion Range (Zone Diameter in mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Staphylococcus aureus</td>
<td>0.06 to 0.25</td>
<td>NA</td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>≤0.5</td>
<td>24 to 30</td>
</tr>
<tr>
<td>Streptococcus pyogenes</td>
<td>≤0.03 to 0.12</td>
<td>18 to 26</td>
</tr>
<tr>
<td>Anaerobic Pathogens</td>
<td>≤0.06 to 0.25</td>
<td>NA</td>
</tr>
<tr>
<td>Anaerobes</td>
<td>≤0.06</td>
<td>2 to 8</td>
</tr>
<tr>
<td>Clostridium perfringens</td>
<td>≤0.06</td>
<td>2 to 8</td>
</tr>
<tr>
<td>Clostridium difficile</td>
<td>≤0.06</td>
<td>2 to 8</td>
</tr>
<tr>
<td>Clostridium tetani</td>
<td>≤0.06</td>
<td>2 to 8</td>
</tr>
</tbody>
</table>

Outsert Orientation: Head to Head - Front

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2. Barcode(s) provided on this proof is (are) for purposes of indicating encodcation only and not to be used for grading according to ANSI standards, as applicable.
INDICATIONS AND USAGE

Clindamycin is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Pregnancy: Teratogenic effects

Pregnancy Category B

In clinical trials with pregnant women, the systemic administration of clindamycin during the second and third trimesters of pregnancy did not show an increased risk of fetal harm. Clindamycin should be used during the first trimester of pregnancy only if clearly needed. There are no adequate and well-controlled studies in pregnant women during the first trimester of pregnancy. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.

Nursing Mothers

Clindamycin has been reported to appear in breast milk in the range of 0.7 to 3.8 mcg/ml. Because of the potential for serious adverse reactions in nursing infants, clindamycin should not be taken by nursing mothers.

Drug Interactions

During prolonged therapy, periodic liver and kidney function tests and blood counts should be performed.

Diarrhea is a common problem caused by antibiotics which usually ends when the antibiotic is discontinued. It is important to encourage the patient to report diarrhea to the physician even if it occurs after therapy is stopped.

Fertility studies in rats treated orally with up to 300 mg/kg/day (approximately 1.6 times the highest recommended adult human dose based on mg/m²) revealed no evidence of teratogenicity.

Pharmacodynamics

Clindamycin is a synthetic analogue of a naturally occurring clavulanate that is present in many species of Clostridium and other gram-positive bacteria.

Chemistry

Clindamycin hydrochloride is contraindicated in individuals with a history of hypersensitivity to preparations containing clindamycin or lincomycin.

INDICATIONS AND USES

Clindamycin hydrochloride is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Staphylococci:

Serious skin infections (such as Toxic Epidermal Necrolysis, erythema multiforme, some resembling Stevens-Johnson syndrome, and anaphylactoid reactions). Esophageal ulcer has been reported.

Streptococci:

More severe infections (such as endocarditis and complications of meningitis). Pneumococcal infections may occur during or after antibacterial treatment (see WARNINGS). Esophagitis ulcer has been reported.

Serratia spp. and other Enterobacteriaceae:

Infections caused by these organisms are usually resistant to most antibiotics and require treatment with agents other than clindamycin.

Therapy for Bacterial Endocarditis:

Infections caused by susceptible organisms should be treated for at least 10 days.

For Therapy in Pregnant Women:

Clindamycin hydrochloride is indicated in the treatment of serious infections caused by susceptible anaerobic bacteria.

Dosage and Administration

No significant differences were observed in the clinical efficacy of clindamycin hydrochloride when it was administered by the oral, intramuscular, subcutaneous, or intravenous routes.