Additional information on special populations

1. **Elderly patients**: The pharmacokinetics of moxifloxacin in elderly patients differ from those in younger adults. The elderly may have reduced renal function and a higher incidence of other conditions that may affect drug clearance. The dosage of moxifloxacin should be adjusted in elderly patients as required.

2. **Children and adolescents**: The safety and efficacy of moxifloxacin in children and adolescents have not been established. The use of moxifloxacin in children is not recommended.

3. **Liver cirrhosis**: In patients with liver cirrhosis as pre-existing QT prolongation in these patients cannot be excluded. No interaction during concomitant treatment with warfarin on prothrombin time (PT) was observed in studies in patients with liver cirrhosis.

4. **Hepatic impairment**: Moxifloxacin dose should be reduced in patients with moderate to severe hepatic impairment. In these patient populations, moxifloxacin and/or concomitant drugs may increase the risk of proarrhythmic events.

5. **Hypothyroidism**: In patients with hypothyroidism, the QT interval may be prolonged. Moxifloxacin should be used with caution as an additive effect of moxifloxacin on the QT interval may occur in patients with hypothyroidism. Special caution is required in patients with pre-existing QT prolongation.

6. **Myasthenia gravis**: Moxifloxacin use in patients with myasthenia gravis should be avoided. The use of moxifloxacin in patients with myasthenia gravis may result in serious exacerbation of symptoms.

7. **Irradiation**: Moxifloxacin use in patients who have received a history of irradiation may increase the risk of proarrhythmic events.

8. **Cardiac arrhythmias**: Moxifloxacin should be used with caution in patients with a history of cardiac arrhythmias. Special caution should be taken in patients with a history of cardiac arrhythmias.

9. **Congestive heart failure**: Moxifloxacin should be used with caution in patients with congestive heart failure. The use of moxifloxacin in patients with congestive heart failure may increase the risk of proarrhythmic events.

10. **Drug interactions**: Moxifloxacin may interact with a variety of medications that prolong the QT interval. Special caution is required in patients who are taking medications that prolong the QT interval.

11. **CNS disorders**: Moxifloxacin may cause CNS disorders such as agitation, confusion, dizziness, and tinnitus. Special caution is required in patients with a history of CNS disorders.

12. **Depression**: Moxifloxacin use in patients with a history of depression may increase the risk of suicidal ideation or behavior. Special caution is required in patients with a history of depression.

13. **Hepatic function**: Moxifloxacin is eliminated primarily through the liver. Special caution is required in patients with impaired hepatic function.

14. **Renal function**: Moxifloxacin is predominantly renally excreted. Special caution is required in patients with impaired renal function.

15. **Pregnancy and lactation**: Moxifloxacin should be used with caution in pregnant and lactating women. Special caution is required in pregnant and lactating women.

16. **Pediatric use**: Moxifloxacin use in pediatric patients is not recommended. Special caution is required in pediatric patients.

17. **Geriatric use**: Moxifloxacin use in elderly patients is not recommended. Special caution is required in elderly patients.

18. **Hypothyroidism**: Moxifloxacin use in patients with hypothyroidism is not recommended. Special caution is required in patients with hypothyroidism.

19. **Hepatic impairment**: Moxifloxacin use in patients with hepatic impairment is not recommended. Special caution is required in patients with hepatic impairment.

20. **Lung conditions**: Moxifloxacin use in patients with lung conditions is not recommended. Special caution is required in patients with lung conditions.

21. **Lactation**: Moxifloxacin use in lactating women is not recommended. Special caution is required in lactating women.

22. **Geriatric use**: Moxifloxacin use in geriatric patients is not recommended. Special caution is required in geriatric patients.

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Avelox is not recommended for the treatment of methicillin resistant S. aureus (MRSA) infections. In **Clinical efficacy has been demonstrated for susceptible isolates and approved clinical indications**. In vitro Susceptibility Data

In vitro studies have demonstrated that resistance to Moxifloxacin develops slowly by multiple step mutations. A very low frequency of resistance was demonstrated (10⁻¹⁰⁻¹²). Serial exposure of strains to sub-MIC concentrations of moxifloxacin showed only a small increase in MIC values.

Cross resistance among quinolones has been observed. However, some gram-positive and anaerobic organisms resistant to other quinolones are susceptible to moxifloxacin.

Effect on the intestinal flora in humans

In two volunteer studies, the following changes in the intestinal flora were seen following oral dosing with Moxifloxacin. E. coli, Bifidobacterium, Enterococci, and Clostridia spp. were reduced, whereas the anaerobes Bifidobacterium, Escherichia, and Peptostreptococci, Bacteroides thetaiotaomicron, were increased. These changes returned to normal within two weeks. Clostridium difficile infection was not found.

**In vitro Susceptibility Data**

The following table provides the respective PK/PD surrogate for intravenous and oral administration of 400 mg moxifloxacin calculated from single dose data.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Intravenous</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>AUC</td>
<td>0.15 µg/L</td>
<td>0.13 µg/L</td>
</tr>
<tr>
<td>Cmax</td>
<td>15.5 mg/L</td>
<td>16.0 mg/L</td>
</tr>
<tr>
<td>t1/2</td>
<td>75.7 h</td>
<td>99.4 h</td>
</tr>
</tbody>
</table>

**Pharmacokinetic Properties**

Moxifloxacin is absorbed rapidly and almost completely. The absolute bioavailability amounts to approx. 90%. Following oral administration moxifloxacin is absorbed rapidly and almost completely. The absolute bioavailability amounts to approx. 90%. Approximately 95% of the drug is bound to plasma proteins. Moxifloxacin is not appreciably metabolized in vivo, [α]-hydroxylation being the only minor route of metabolism identified. The nor-moxifloxacin metabolite is rapidly cleared and is not pharmacologically active.

**The MIC for effective control for reference for age dilution testing**

<table>
<thead>
<tr>
<th>Concentration (mg/L)</th>
<th>S</th>
<th>I</th>
<th>R</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.25</td>
<td>≤ 2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1.0</td>
<td>≤ 2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2.0</td>
<td>≤ 2.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>≥ 8.0</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Pharmacokinetic Properties**

Moxifloxacin is distributed very rapidly to extra vascular spaces. Exposure to drug in terms parameter (Cmax/MIC90) is high with a volume of distribution at steady state (Vss) of 4.4 mg/l were observed at the end of a 1h infusion. AUC/MIC is most predictive for antimicrobial efficacy of quinolones, this effect is maximized at a Cmax of 10 µg/ml. Administration of moxifloxacin to healthy volunteers and patients resulted in a Cmax/MIC90 of 4.1 mg/L were reached in the plasma at the end of infusion which corresponds to a mean increase of approx. 26% to the oral application. Exposure to drug in terms of AUC at a value of approximately 39 µg/mL is only slightly higher compared to the exposure after oral administration (35 µg/mL) as an absolute bioavailability of approximately 99%.

Following multiple intravenous dosing (3 infusion, peak and trough plasma concentrations at steady state (400 mg) were observed between 1.4 ± 0.9 mg/L (0.6 mg/L) and 3.8 mg/L (1.9 mg/L) respectively for the exposure within the dose interval is approximately 30 % higher than after the first dose. In patients mean steady state concentrations of 4.4 mg/L were observed at the end of a 1h infusion.

**Distribution**

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