New drugs

Retapamulin

Approved indication: skin infections
Altargo (GlaxoSmithKline)
tubes containing 1% ointment
Australian Medicines Handbook section 8.4.3

Retapamulin is a topical pleuromutilin antibiotic. It is indicated for impetigo and mild secondary skin infections arising from lacerations, abrasions, sutured wounds, psoriasis or dermatitis. These infections are mainly caused by Staphylococcus aureus, but can also be due to Streptococcus pyogenes.

In vitro, retapamulin is bacteriostatic against S. aureus and S. pyogenes. It is thought to act by inhibiting protein synthesis through the 50S bacterial ribosomal unit. From in vitro studies, the likelihood of S. aureus and S. pyogenes becoming resistant to retapamulin is predicted to be low.

The recommended dose is a thin layer of ointment, twice a day for five days. Systemic exposure following application to intact skin is generally very low. However, detectable concentrations were observed in 69% of babies aged 2−9 months. Retapamulin is therefore contraindicated in babies under nine months. As this drug is metabolised by cytochrome P450 (CYP) 3A4, inhibitors of this enzyme (e.g. ketoconazole) may increase retapamulin exposure in children under two years.

The efficacy of retapamulin 1% ointment in patients aged nine months and older has been studied in several phase III trials (see Table).

Impetigo

There have been two comparative trials of retapamulin for impetigo – one with a placebo and the other with sodium fusidate ointment 2% (3 times daily for 7 days). The median age of the participants was 7−9 years and most of them had only one impetigo lesion. Clinical success was defined as drying up (without crusts) or resolution of the lesion, or an improvement such that no further treatment was needed. The efficacy of retapamulin was significantly better than placebo and was non-inferior to sodium fusidate (see Table).

Infected wounds

Retapamulin has also been compared to a 10-day course of oral cephalexin 500 mg (twice a day) in people with secondarily infected wounds caused by trauma. Two identical trials enrolled participants who had wounds less than 10 cm long with no more than 2 cm of surrounding erythema. Response to treatment was scored using a skin infection rating scale which

### Table: Efficacy of topical retapamulin 1% for superficial skin infections in phase III trials

<table>
<thead>
<tr>
<th>Indication</th>
<th>Trial</th>
<th>Treatment†</th>
<th>Number of patients</th>
<th>Clinical success rates§</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impetigo</td>
<td>Koning¹</td>
<td>retapamulin</td>
<td>139</td>
<td>85.6%</td>
</tr>
<tr>
<td></td>
<td>placebo</td>
<td>71</td>
<td></td>
<td>52.1%</td>
</tr>
<tr>
<td></td>
<td>Oranje²</td>
<td>retapamulin</td>
<td>345</td>
<td>94.8%</td>
</tr>
<tr>
<td></td>
<td>sodium fusidate</td>
<td>172</td>
<td></td>
<td>90.1%</td>
</tr>
<tr>
<td>Secondarily-infected wounds</td>
<td>Free¹</td>
<td>retapamulin</td>
<td>1268</td>
<td>86.3%</td>
</tr>
<tr>
<td></td>
<td>oral cephalaxin</td>
<td>636</td>
<td></td>
<td>85.7%</td>
</tr>
<tr>
<td></td>
<td>Tomayko³</td>
<td>retapamulin</td>
<td>246</td>
<td>74.8%</td>
</tr>
<tr>
<td></td>
<td>placebo</td>
<td>113</td>
<td></td>
<td>66.4%</td>
</tr>
<tr>
<td>Secondarily-infected dermatoses</td>
<td>Parish⁵</td>
<td>retapamulin</td>
<td>363</td>
<td>82.9%</td>
</tr>
<tr>
<td></td>
<td>oral cephalaxin</td>
<td>183</td>
<td></td>
<td>86.3%</td>
</tr>
</tbody>
</table>

† retapamulin ointment was applied twice a day for 5 days, sodium fusidate ointment was applied 3 times a day for 7 days, oral cephalaxin 500 mg was given twice a day for 10 days
§ clinical success was reported in the intention-to-treat population and defined as resolution or improvement in signs and symptoms such that no further treatment was needed at the end of the study period
assessed exudates, crusting, inflammation, tissue warmth, oedema, itching and pain. The efficacy of retapamulin appeared to be non-inferior to oral cephalaxin, with most patients requiring no further treatment at the end of the study period (see Table). In another trial, retapamulin did not reach statistically significant superiority over placebo for people with secondarily infected wounds. This was presumably because clinical success rates were quite high in the placebo arm (see Table).  

**Infected dermatoses**  
A single trial investigated retapamulin for secondary infections arising from psoriasis or dermatitis (atopic or allergic). The ointment was found to have comparable efficacy to oral cephalaxin 500 mg twice a day for 10 days (see Table).  

**MRSA infections**  
Evidence that retapamulin is effective against infections caused by methicillin-resistant *S. aureus* (MRSA) is limited. In one of the studies of secondarily infected wounds, clinical success rates were lower for MRSA infections than for methicillin-sensitive *S. aureus* infections – 68.6% (35/51) versus 92.2% (330/358). In an unpublished study of people with impetigo or secondarily infected wounds caused by MRSA, clinical success rates were significantly lower with retapamulin than with oral linezolid (63.9% vs 90.6%).  

**Safety and precautions**  
Application site reactions were the most frequently reported adverse events with retapamulin and included irritation, pruritus, paraesthesia and pain. In most of the trials, these were reported by less than 2% of people. In comparative trials with oral cephalaxin, diarrhoea was less common with retapamulin than with oral cephalaxin (1.6% vs 2.7%). Retapamulin should not be used to treat abscesses or cellulitis and should not be applied to mucosal membranes or eyes. When prescribing antibiotics for skin infections, geographical variations in antibiotic susceptibility should be considered. If a patient is not responding to retapamulin, they may need to be switched to the appropriate systemic therapy.  

**Conclusion**  
Retapamulin ointment is better than placebo for impetigo, however, it has not been compared to mupirocin ointment. Retapamulin may be a preferable alternative to oral antibiotic therapy for mild secondary skin infections. Clinical evidence does not support the use of this drug for MRSA infections.  

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**REFERENCES**  

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