Nifurtimox, Tablet 30 mg 120 mg 250 mg

WHO Model Formulary information

Acute American trypanosomiasis (Chagas disease). At present the only therapeutic agents of value are benznidazole and nifurtimox. Both suppress parasitaemia and are efficacious during the early stages of infection. Studies are in progress to determine whether benznidazole and nifurtimox have any influence on the later manifestations of the disease. Symptomatic treatment may be necessary in advanced cases.

WHO Essential Medicines Library. Rationale for inclusion

Date added to complementary list: 1977.
Moved to core list: 1988.
Antiprotozoal drug for adults and children.
Specific expertise, diagnostic precision, individualization of dosage or special equipment required for proper use.
Cochrane review: Trypanocidal drugs for late stage, symptomatic Chagas disease (Trypanosoma cruzi infection).

Evidence

Cochrane reviews:

Description of results:
The only RCT, identified by the Cochrane review, involving 77 participants with chronic Chagas disease, found, that parasitologic cure was achieved in patients who received either Benznidazole (n=26) or Nifurtimox (n=27), 98% and 90% respectively. People treated with placebo (n=24) had a 66% parasitologic cure rate (P > 0.05).

Reviewers’ conclusion:
There is insufficient evidence to support the efficacy of nitrofurans or imidazolic drugs as recommended treatment in CCC (chronic Chagas cardiomyopathy) and chronic T. cruzi infections, specifically if overt heart disease is present.


Trypanocidal medicines for chronic asymptomatic T. cruzi infection have been tested in few, small size RCTs which were designed to assess parasitic-related, but not clinical outcomes. The data show that the potential of trypanocidal therapy to prevent Chagas' disease among asymptomatic, chronically infected subjects is promising, but clinical outcomes have not been evaluated. See table:
<table>
<thead>
<tr>
<th>Comparison</th>
<th>Participants</th>
<th>Study</th>
<th>Outcome</th>
<th>RR [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nitrosamine derivatives vs placebo</td>
<td>Adults (Brazil) - 53 vs 24</td>
<td>Coura, 1997</td>
<td>Negative xenodiagnosis</td>
<td>19.47 [2.85, 133.23]</td>
</tr>
<tr>
<td>nifurtimox vs placebo</td>
<td>Adults (Brazil) - 27 vs 24</td>
<td>Coura, 1997</td>
<td>Negative xenodiagnosis</td>
<td>16.19 [2.34, 111.78]</td>
</tr>
<tr>
<td>Active treatment vs placebo</td>
<td>benznidazole 7.5 mg/k/d (8 wk) vs Placebo</td>
<td>School children, Brazil, 64 vs 65</td>
<td>Andrade, 1996</td>
<td>Reduction of antibody titres (Indirect immunofluorescence)</td>
</tr>
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<td></td>
<td>allpurinol 300mg TID (8wk) vs Placebo</td>
<td>Adults, Bolivia, 20 vs 20</td>
<td>Gianella, 1997</td>
<td>Reduction of antibody titres (Indirect immunofluorescence)</td>
</tr>
<tr>
<td></td>
<td>benznidazole (n=55) 5 mg/k/d (8wk) vs Placebo</td>
<td>School children, Argentina, 44 vs 44</td>
<td>Sosa-Estani, 1998</td>
<td>Reduction of antibody titres (Indirect immunofluorescence)</td>
</tr>
</tbody>
</table>

**Secretariat’s conclusion**

The existing sparse evidence from a Cochrane systematic review (Villar 2002) suggests that trypanocidal therapy, particularly nitroimidazolic derivatives given to asymptomatic children or adults with positive xenodiagnosis (chronic asymptomatic Trypanosoma cruzi infection) improve parasite-related outcomes. No data for clinical outcomes are available. In late stage symptomatic Chagas disease parasitologic cure rates were found to be similar with nifurmitox treatment and placebo without benefits for clinical symptoms, as evidenced by the only RCT (Rodriguez Coura) identified by a Cochrane review (Reyes 2005).

In view of the major public health importance of Chagas disease the Committee is requested to consider retaining nifurtimox on the Model List.

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