Evidence

Doxycycline is a tetracycline antibiotic and tauroursodeoxycholic acid (TUDCA) is a bile acid. The combination of doxycycline and TUDCA has a synergistic effect in mouse models and seems to inhibit TTR amyloid formation and promote resorption of TTR amyloid.

There has been one Phase II trial for doxycycline 100mg bd and tauroursodeoxycholic acid. This trial had 40 subjects. n=13 had wtTTR and the rest had inherited TTR. N=4 discontinued treatment due to doxycycline related GIT side effects and n=1 for rash. N=24 patients completed 12 months of treatment. Stable neuropathy was observed in 6/13 evaluable patients. 18/24 evaluable patients had stable NTproBNP.

The main and common side effect is gastric irritation secondary to doxycycline. Doxycycline may also cause significant photosensitivity skin reactions. Tauroursodeoxycholic acid is well tolerated but there are occasional reports of mild gastrointestinal side effects.

Cost and funding

Tauroursodeoxycholic acid is not Medicare rebated. The cost is dependent on the importer and distributor and is approximately $36 (+GST) for 20 capsules as of April 2019. The cost of a month's supply of 100 capsules is $112. This cost does not include pharmacy handling and dispensing fees or GST and can amount to $200-250 per month.

PBS funding can be obtained for certain indications for Doxycycline.

Administrative requirements

1. TGA SAS Category B approval
2. Patient consent for SAS drug prescription
3. Script
   Doxycycline 100mg po bd, x56 and repeats (PBS funding can be obtained for certain indications. Ring 1800 888 333 for authorisation of increased quantity).

   Tauroursodeoxycholic acid 250mg po tds

Monitoring

We suggest monitor with a TTE every 6-12 months and NTproBNP every 3-6 months to determine if there is stabilisation or slowing of deterioration of cardiac parameters. This therapy is prescribed so long as it appears to be slowing or stalling progression and no significant toxicity. Given the slowly progressive nature of the disease this may be hard to determine.

References