Additional notes for PTAC

PTAC minutes from May 2013 state:

“6.2 The Committee recommended that dexrazoxane be funded for paediatric cancer patients participating in a randomised clinical trial.”

The interpretation of these minutes is difficult. Firstly it implies that if a patient is enrolled in a non-randomised trial (including single arm phase II) including dexrazoxane that it is not funded. An example of is the International Childhood Liver Tumours Strategy Group study SIOP-IV. It is also not clear whether dexrazoxane is funded in situations where a patient is enrolled on a randomised trial where dexrazoxane is recommended or allowed without being mandated.

The minutes further state:

6.7 The Committee considered that there is no evidence that the use of dexrazoxane increases life expectancy. Members noted that neither the van Dalen Cochrane review nor the Lipshultz study reported a difference in either overall survival or progression-free survival. Members also noted that the POG-9404 study is not fully available and so overall survival data is not yet published, but that 10-year event-free survival is worse in the dexrazoxane group.

As noted in the NCCN document, POG-9404 has now been published and demonstrates no impairment in 5 year event free survival in the dexrazoxane group and no additive toxicity. LV function measures are statistically significantly worse in the group who did not receive dexrazoxane.

The expectation is that data showing better overall survival in dexrazoxane cohorts may be many decades in the future as death from cardiac failure is a rare and late event. Surrogate measures of efficacy such as LV functional measures and troponin release can reasonably be assumed to be representative of later dysfunction, despite not being a hard endpoint in themselves.

The minutes further state:

6.14 The Committee made a recommendation for dexrazoxane to be funded for paediatric patients enrolled in oncology trials, despite considering dexrazoxane itself to have no clear benefit and some evidence of harm. Members stressed that the positive recommendation was based on providing young patients with access to US-run, international collaborative clinical trials, and that health gains are expected to be achieved by participating in the trial itself rather than from the effects of dexrazoxane.”

With multiple further publications on efficacy and safety since this time and consensus among the National Childhood Cancer Network on the use of dexrazoxane in paediatric patients this recommendation requires revisiting.

Absolute cost of the drug per year is able to be estimated. Cost per 500mg vial is currently $640.26. Estimated average cost per patient is approximately $5500 (using surface area 1.2m² and cumulative anthracycline dose 350mg/m²) although there will be considerable variation between patients. Children with the following diagnoses are most likely to fall within the NCCN guidelines for use of dexrazoxane:

- Acute myeloid leukaemia (not including Down syndrome)
- Osteosarcoma
- Ewing sarcoma
- Hepatoblastoma (high risk only)
- Subset of rhabdomyosarcoma, nephroblastoma

This is likely to represent 8-10% of new diagnoses. With around 160 new diagnoses per year across the country this accounts for perhaps 15 patients per year receiving dexrazoxane at a cost of around $80,000 per year. Use and costs of dexrazoxane can be tracked over time.

Cost of congestive heart failure from diagnosis to death is estimated at US$110,000 (NADS$160,000) per patient in an adult population (Dunlay SM, Shah ND, Shi Q et al. Lifetime Costs of Medical Care After Heart Failure Diagnosis. Circ Cardiovasc Qual Outcomes. 2011 Jan 1;4(1):68-75). Due to diagnosis much earlier in life and consideration of cardiac transplantation for many childhood cancer survivors with heart failure, the cost is likely to be much higher in this cohort. Even if this is not the case, and ignoring social, personal and indirect costs, if 1 case of congestive heart failure is prevented for every 30 children treated with dexrazoxane then there has been a net monetary gain to the health system. This also ignores pericardial disease and valvular disease which are also more common after anthracycline exposure.