Lesinurad in combination with a xanthine oxidase inhibitor

for chronic hyperuricaemia in gout

The ERG response to factual error issue 3 has been updated as detailed below.

Factual error issue 3: Common discontinuation for adjunctive lesinurad and allopurinol not fully implemented

Description of problem	Description of proposed amendment	Justification for amendment	ERG response
Section 6 (p119) Scenario 2 in Table 49 specifies a common discontinuation rate for all treatments. However, the first line allopurinol rates used after lesinurad patients revert to first line were not modified on the Fline AEs sheet.	Rerun analyses of scenario 2 and any combined scenarios which include scenario 2 and change the results in Table 49 appropriately.	Appropriately changing to the same discontinuation rate for allopurinol after reverting from lesinurad+allopurinol produces an ICER for scenario 2 of £17,916 instead of the £18,000 reported in Table 49.. Analyses of combinations including scenario 2 also produce ICERs that are too high due to the existing error.	We agree Table 49 updated

The ERG has updated Table 49 (to replace that seen on ERG report p116) and subsequent paragraph of text on p116-7 as follows:

Table 1: ERG re-estimation of cost-effectiveness

	ΔC	ΔQALY	ΔC/QALY	Ratio[+]
CS base case model	£2,848	0.173	£16,468	
ERG Models				
1. Average age of 2nd line treatment (Male 66.1y; Female 73.7y)	£2,193	0.112	£19,537	1.19
2. Common discontinuation rate for adjunctive lesinurad and allopurinol (trial-based)	£2,620	0.146	£17,916	1.09
3. Resolution of tophi (trial-based extrapolation)	£2,862	0.065	£43,790	2.66
4. Gout-related mortality SMRs (UK-based rates and conservative tophi HR)	£2,970	0.114	£26,036	1.58
5. Second line treatment efficacy	£2,848	0.147	£19,312	1.17

(sUA levels matching primary outcome)				
Combined (1-5)	£2,270	0.015	£152,820	9.28

+ Ratio of ERG model to CS base case model

The most important assumption in the company model concerns the resolution of tophi by serum urate level. To the extent that tophi resolves more quickly with lower serum urate, adjunctive lesinurad achieves mortality and quality of life gains. The second key parameter is the size of gains in mortality of tophi over and above non-tophi gout. Setting aside the trial evidence which does not find a relationship with tophi resolution and serum urate level at one year, the company model uses epidemiological findings and assumptions of attribution to arrive at the base case value. The ERG have attempted a balanced interpretation of the epidemiological literature, exploring current uncertainties about the value of adjunctive lesinurad in second line treatment of gout patients, in the absence of robust long term evidence. However, a difference of approach lies in the base case model assuming 100% of epidemiological differences are achievable by modifying risk factors, while the ERG has assumed 50%: for a discussion of this issue, see 5.2.5.1. Taking all of the ERG assessments together the ERG re-estimates the base case to be £152,820/QALY. The PSA gives £171,301/QALY (95%CI: 61,644 to ∞) and CEAC (see Figure 17), indicates p=0% probability of cost effectiveness at the NICE £20,000/QALY and £30,000/QALY thresholds (using ERG estimation of model replicates, see 5.2.8.1 for an explanation).