



Everolimus

Formulary Management Expert Committee Responses to Questions From the Drug Programs

Table 1: Response Summary

Drug program implementation questions	Clinical expert response	FMEC response
Special implementation issues		
<p>Given the limited data on the pediatric population with TSC-associated renal AML, would patients aged younger than 18 years with TSC-associated renal AML be considered for treatment with everolimus?</p>	<p>Patients aged younger than 18 years who have AMLs and meet the criteria for treatment, by virtue of size, vascularity, rate of growth, multiplicity, and so forth should be considered for treatment with everolimus. The indirect evidence available from trials in this age group with TSC, which primarily target SEGA, have shown the drug to be safe, have informed the pharmacokinetics and dosing in this group, and have demonstrated the expected biological effect on these lesions on renal AMLs.</p>	<p>FMEC defers to the clinical experts' opinion.</p>
<p>How can the FMEC recommendation for everolimus, if funded for TSC-associated renal AML, address the benefit of the drug in other manifestations of TSC without reviewing evidence on these benefits?</p>	<p>Dysregulated mTOR is at the heart of all manifestations of TSC. The clinical experts commented that it is fair to say that AML treatments that are specifically targeting just those lesions (i.e., surgery or ablation) are not targeting other lesions in the kidneys, heart, brain, or lungs, which are favourably impacted by mTOR inhibition. Whether or not the drugs favourably impact all aspects of TSC is beyond the scope of this review. Saying that treating renal AMLs with mTOR inhibition is having potentially favourable off-target effects is reasonable according to the clinical experts, but they reported that making a statement that it would definitely have favourable effects in all patients for all manifestations would be an overreach.</p>	<p>FMEC's recommendation was based on a review of the benefit of everolimus on renal AML. FMEC acknowledged that there will potentially be benefit for other manifestations of TSC, but that data were not reviewed and are not part of the current recommendation.</p>

AML = angiomyolipoma; FMEC = Formulary Management Expert Committee; mTOR = mammalian target of rapamycin; SEGA = subependymal giant cell astrocytoma; TSC = tuberous sclerosis complex.