Response to:

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Immunosuppressive therapy for kidney transplantation in adults (review of technology appraisal guidance 85)

Prepared by:

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08 May 2015

Response to the Assessment Report produced by Peninsula technology Assessment Group (PenTAG): Immunosuppressive therapy for kidney transplantation in adults (review of technology appraisal guidance 85)

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Any reference to the Assessment Report is referred to in the format: [page X, Section X.X]

Medicinal products:	Mycophenolate sodium Everolimus
Brand names:	Myfortic® Certican®
Manufacturer:	Novartis Pharmaceuticals UK Ltd
Date:	08 May 2015

Letter of response

Dear Sirs,

We would like to take this opportunity to thank the National Institute for Health and Care Excellence (NICE) and its Assessment Group (PenTAG) for the time and consideration they have devoted to this appraisal to date.

Upon reviewing the Assessment Report, Novartis Pharmaceuticals UK Ltd (Novartis) would like to comment on three areas, which we believe have resulted in the use of inappropriate parameter values, thereby leading to inaccurate assessments of Myfortic® (enteric-coated mycophenolate sodium; EC-MPS) and Certican® (everolimus; EVL):

1. The PenTAG model design and data inputs, specifically the utility values, where we have found variation compared with the Novartis model that affects incremental cost-effectiveness ratio (ICER) results
2. The treatment of population subgroups. We request that NICE reviews data, supplied in the original Novartis submission but not reviewed by PenTAG, which address subpopulations. These subpopulations include patients experiencing gastrointestinal (GI)-related adverse events with mycophenolate mofetil (MMF) and patients at high risk of cytomegalovirus (CMV) infection.
3. The systematic review inclusion/exclusion criteria and resulting study selection, which we believe has biased the data included against EC-MPS.

In addition, while revisiting the model for this analysis, the Novartis economic model was found to have an error, which we expected to have a significant impact on the outcome of the model. The calculations regarding the patients' status with a functioning graft were not functioning correctly, whereby a patient who had experienced graft loss and subsequent re-transplantation was not considered to have a functioning graft. This resulted in the patient unable to be at risk of graft loss after receiving a second transplant and the cost of further re-transplantation and dialysis was, therefore, not applied in our model. Other minor errors (including the calculation of the disutility and monthly maintenance cost of adverse events) were also identified. After these issues had been identified, they were corrected and the Novartis model re-run. Changes to the model and updated results are detailed in the accompanying document 'Corrections to the Novartis economic model'.

All regimens were associated with a large increase in overall costs, due to re-transplantation being correctly implemented in the model. The costs in the MMF arm increased the most,

due to the higher rate of graft loss (0.032 for EC-MPS, 0.092 for MMF), which was then associated with a higher rate of re-transplantation. This, in turn, led to lower incremental costs in the EVL analysis and EC-MPS becoming cost-saving in the EC-MPS comparison. For results tables, please see the accompanying document 'Corrections to the Novartis economic model'.

In the following sections of this response, where further exploratory results have been generated, the corrected Novartis model was used.

1. Differences between PenTAG and Novartis models

The cost-effectiveness conclusions presented by PenTAG vary greatly from those in the Novartis submission, which led us to review the PenTAG model in depth.

We identified the following key differences underlying the quality-adjusted life-year (QALY) and ICER discrepancies between the PenTAG and Novartis models:

- A network meta-analysis (NMA) was used to inform the key clinical inputs in the PenTAG model, while data from single studies were used in the Novartis model
- The PenTAG model implemented change in graft survival rate over time, and graft survival after one year linked to biopsy-proven acute rejection (BPAR), new-onset diabetes after transplant (NODAT) and renal function (estimated glomerular filtration rate; eGFR), while the Novartis model assumed a constant rate of graft loss over time and did not link graft survival to other clinical outcomes
- Inclusion of NODAT in the PenTAG model
- Different methods for estimating health state utility values between each model
- Different event and drug unit costs and resource use between each model.

Deterministic versus probabilistic analysis

PenTAG noted that the probabilistic sensitivity analysis (PSA) submitted by Novartis yielded substantially different results compared with the deterministic analysis. This indicates that the model has important non-linearities, and it might be more appropriate to use the probabilistic results for decision-making. The PenTAG model was also noted as having a difference between deterministic and probabilistic results. In particular, in the EC-MPS analysis, EC-MPS was associated with a positive number of incremental QALYs in the deterministic analysis and negative incremental QALYs in the probabilistic analysis. This indicates that there may also be non-linearities in the PenTAG model and that these may be

an intrinsic feature of modelling the renal transplant pathway. As such, we have also incorporated a probabilistic analysis in our revised analysis.

Model re-run

To explore the impact of the structural assumptions and data inputs between the two models, we re-ran the Novartis model for the EC-MPS comparison with various configurations of PenTAG data inputs.

The following changes were implemented in the Novartis model (see also the accompanying document 'Additional analyses'):

- Inclusion of NODAT, using the one-year rate from the NMA run by PenTAG and using the cost and disutility assumptions used by PenTAG
- Estimation of health state utility using the mechanism in the PenTAG model, where a baseline utility for each patient was estimated based on age and gender, with a disutility applied for functioning graft or dialysis
- The use of estimates from the PenTAG NMA for renal function, probability of BPAR and graft survival at one year
- Cost estimates and resource use as used by PenTAG (unit costs for haemodialysis, peritoneal dialysis and re-transplantation, and resource use and unit costs for drugs)
- Incorporation of graft survival over time, using the method reported by PenTAG, with graft survival modelled with a Weibull distribution, and using the rate parameters applied by PenTAG (which account for decreased graft survival due to BPAR, NODAT and poor renal function).

We adopted the methods used by PenTAG to estimate costs, the inclusion of NODAT and the estimates of effectiveness (graft survival, BPAR and renal function) provided by the NMA, and this resulted in an ICER of £27,327 for EC-MPS and of £100,459 for EVL. The results of the probabilistic analysis for these scenarios indicate that EC-MPS is associated with additional costs of £28,300 and 1.04 additional QALYs (with a resulting ICER of £27,241). EVL was associated with additional costs of £107,013 and 1.07 additional QALYs (with a resulting ICER of £100,446).

The accompanying document 'Additional analyses' details the amends to the model and associated results.

We found that:

- Imputing the costs (specifically, the unit costs and dosing assumptions for drugs, and the unit costs for BPAR, re-transplantation, haemodialysis and peritoneal dialysis) used by PenTAG in the Novartis model had a small impact on the total costs. The differences were largely observed in the drug costs, which were higher in the analysis with Novartis costs.
- Including the NMA in the Novartis model (with no other input or structural changes) resulted in a small reduction in total QALYs in both treatment arms, with similar incremental QALYs in each analysis (1.04 in the analysis with Novartis inputs and 1.03 in the analysis with one-year rates from the PenTAG NMA).
- The inclusion of NODAT in the analysis resulted in very little difference to the overall results of the model, with a small increase in overall costs and a small decrease in overall QALYs.

Due to the minor impact of these parameters, we agree with the PenTAG approach and have incorporated those parameters into our revised analysis.

In contrast, using the PenTAG method to estimate health state utilities had a large impact on the results of the analysis. The incremental QALYs were much smaller in the PenTAG model (0.11 incremental QALYs in the PenTAG analysis compared with 1.04 in the Novartis analysis), and using PenTAG utility values in the Novartis model also resulted in a smaller QALY difference (0.60 incremental QALYs) between the two arms.

The method used by PenTAG was to estimate a baseline utility based on age and gender, and then to apply a utility decrement for functioning graft, dialysis or NODAT. All the patients with a functioning graft were assumed to be at the same stage of disease; ie, the same utility value was assigned to all (as highlighted in our accompanying pro-forma response on the executable model [issue 2]). In contrast, the method used by Novartis linked kidney function (as measured by eGFR) to utility (Neri 2012). We believe that our method is more clinically justifiable, as it is a more granular approach, captures the wide variation in quality of life associated with a functioning graft and the long-term nephrotoxicity of calcineurin inhibitors (which can affect kidney function) and, thus, enables the model to be more sensitive to changes in the patient's health. Patients enter the model with a similar utility value in both models; however, the Novartis model observes a faster decline in utility, reflecting the deteriorating kidney function in patients with a functioning graft. The patients in the PenTAG model with a functioning graft have a very small utility decrement applied, so the natural decline in quality of life of these patients is more reflective of the general population.

Based on our in-depth review of the PenTAG economic model, we have made a number of amendments to the Novartis analysis: the use of the NMA to inform clinical inputs at one year (rate of graft survival, rate of BPAR and renal function), the inclusion of NODAT, and the methods used by PenTAG to estimate drug costs and unit costs for dialysis and re-transplantation. We do, however, maintain that the method used by Novartis linking kidney function (as measured by eGFR) to utility is more clinically justifiable in this patient population than the approach used by PenTAG. We propose that PenTAG amend their model to link kidney function to utility.

2. Subpopulation considerations

The PenTAG assessment has not considered the use of EC-MPS or EVL in specific subpopulations **[page 550, Section 8.2.2]**.

EC-MPS

We are of the opinion that some data excluded from the PenTAG systematic review demonstrate that EC-MPS is of benefit to subpopulations, especially in a second-line setting for patients experiencing intolerable GI-related adverse events. A core aspect of successful renal transplantation is adherence to maintenance therapy (Pelletier 2003, Knoll 2003, Tierce 2005) and, thus, avoidance of mycophenolic acid (MPA) dose reduction due to tolerability issues, such as GI-related adverse events, is desirable. A large-scale analysis of data from the United States Renal Data System aimed to assess the association between MMF dose reductions and discontinuations following GI complications and graft survival (Bunnapradist 2006). The study found that compared with no MMF dose reductions or discontinuations, a higher risk of graft failure was associated with a dose reduction of less than 50% (hazard ratio 1.637) and dose reduction of more than 50% (hazard ratio 2.364).

We propose that data selection and interpretation led to bias against EC-MPS, as GI-related adverse events rates are different with EC-MPS and MMF. Studies such as myVIDA (Ortega 2011), MORE (Langone 2013, Chan 2013) and myQoL (Shetata 2009), which were excluded from the PenTAG report but included in the Novartis submission, contain data supporting use in this population. MyQoL found that renal transplant patients receiving reduced-dose MMF due to GI-related adverse events can tolerate a significant increase in MPA dose after conversion to EC-MPS. Patient-reported GI outcomes with higher doses of EC-MPS were at least as good as in reduced-dose MMF-treated controls. MyVIDA found that the incidence of GI complications was significantly lower in the EC-MPS group and the

GI quality of life index was significantly higher. We believe that, with the inclusion of these data, the GI benefits of EC-MPS can be recognised and need not be considered speculative **[page 550, Section 8.2.2]**.

In support of this point, we have re-run the Novartis model with PenTAG inputs and using a subpopulation of patients taking EC-MPS as a second-line therapy after failure of MMF due to GI-related adverse events; results of this analysis are provided in the accompanying document 'Additional analyses' for illustrative purposes.

Both the myQOL and myVIDA studies had relatively short follow-up periods (12 weeks) and the primary endpoint was the proportion of patients receiving a higher MPA dose at Week 12 than at randomisation. As such, very few events of interest occurred within the trial (one acute rejection in each study and no graft loss).

To assess the potential cost-effectiveness of EC-MPS in this patient subgroup, we conducted further illustrative analyses. We compared a group of patients who have previously experience GI-related side effects, who have either remained of MMF or have switched to an equimolar dose of EC-MPS. To estimate the graft survival rates in the MMF arm, the rates of graft loss in that arm were adjusted using the ratio reported by Bunnapradist 2006. Since the proportion of patients receiving either of these two levels of dose reduction is not known, a conservative approach was taken in selecting the adjustment factor and we used the adjustment factor for patients with a dose reduction of less than 50 (1.637).

The rate of graft loss for MMF in the Novartis model is relatively high compared with the rate of graft loss in the PenTAG NMA, and so the Novartis model with both sets of inputs was run to provide an illustrative comparison. The Novartis model used data from Vitko 2004 to estimate the rate of graft loss at one year for MMF patients. MMF patients in this study were reported as receiving a 2 g daily dose; whether patients received a reduced dose throughout the study was not reported. The PenTAG clinical inputs were based on the NMA. It is likely that both groups include some degree of dose reduction already, but the full extent is not known.

We have also run an additional demonstrative analysis in this subpopulation, for which no significant difference in graft survival between EC-MPS and MMF in the general renal transplant population was assumed.

Since the clinical inputs in the original Novartis model were based on a mixed patient population, in terms of the MMF dose received, the true value of the ICER is likely to lie somewhere between that of the original analysis and the analysis with the adjusted MMF rate. Based on these illustrations, we request that NICE considers a re-analysis to further review the treatment options for this particular subpopulation.

EVL

The PenTAG assessment has not considered the use of EVL in specific subpopulations **[page 550, Section 8.2.2]**. The Novartis systematic review demonstrates that the addition of EVL to a ciclosporin-based regimen allows for reduction in ciclosporin dose while demonstrating a lower risk of developing CMV infection compared with MMF and standard-dose ciclosporin, with no significant differences in efficacy and other safety parameters. This is of significance because CMV disease is associated with inferior long-term patient and graft survival (Hartmann 2006, Tedesco-Silva 2013).

The published NICE scope makes provision for the analysis of interventions in 'people at high risk of complications from immunosuppression'. In our view, EVL patients considered by their physician to be at high risk from CMV infection (eg, donor+/recipient patients, patients with recurrent CMV infection, patients experiencing CMV infection despite prophylaxis, ATG induction immunosuppression) should be considered a specific subgroup in which EVL use is supported based on the following data:

In the randomised study, B201, CMV infection was significantly less likely at 36 months in both EVL groups than in the MMF group (5.7% and 8.1% in the EVL 1.5 mg/day and 3 mg/day groups versus 19.9% in the MMF group; p=0.0001) (Vitko 2005). Another randomised trial compared the effect of EVL with that of MMF plus reduced-dose tacrolimus on the incidence of CMV infection in renal transplant recipients for 12 months. Preliminary data up to 239 days indicate that patients receiving EVL are at lower risk of developing CMV infection compared with those receiving MMF, with no significant differences in efficacy and other safety parameters (Tedesco-Silva 2013).

Novartis, therefore, requests that NICE should consider the use of EVL in patients at high risk from CMV infection, because CMV disease is associated with inferior long-term patient and graft survival.

3. Systematic review inclusion/exclusion criteria and study selection

As described within the Assessment Report **[page 81, Section 4.1.3.1]**, only randomised controlled trials (RCTs) or systematic reviews of RCTs were included as part of the study selection process to assess clinical effectiveness. While Novartis appreciates that this is a standard and well-recognised approach undertaken for systematic reviews in the context of a health technology assessment (HTA), by only including RCTs the evidence appraised does not provide the complete, long-term, real-world evidence (RWE) database available (eg, open-label extension studies, conversion studies, registry data, etc). Differences between EC-MPS and MMF, such as incidence of adverse events and effect on quality of life, are more likely to be evident in RWE, as such studies are designed to capture these outcomes. Indeed, it is becoming more widely recognised that RCTs are not the only evidence base for decision-making – assessing the value of a drug or technology also requires an understanding of its impact on current management in a practical, real-life setting (Annemans 2007).

We propose that the exclusion of key studies from the PenTAG systematic review and exclusion of data from these key studies in the NMA has impacted clinical and cost-effectiveness outputs when EC-MPS is considered in the full renal transplant population. Table 140 from the PenTAG report **[page 313, Section 4.5.4]** lists the studies included in the Novartis submission and states whether they were included or excluded from the PenTAG report. Many have been excluded, some of which we consider should be included, as they present valuable data that support key differences between MMF and EC-MPS. These studies and Novartis' rationale for inclusion are listed in the Appendix. We request more clarity around exclusion decisions for these studies.

Conclusions

In conclusion, Novartis recognises the majority of inputs used in the PenTAG model: the use of the NMA to inform clinical inputs at one year (rate of graft survival, rate of BPAR and renal function), the inclusion of NODAT, and the methods used by PenTAG to estimate drug costs and unit costs for dialysis and re-transplantation. We do, however, maintain that PenTAG should adopt the method used by Novartis linking kidney function (as measured by eGFR) to utility, as this is more clinically justifiable. We also request that PenTAG revises their model to correct certain errors identified in the accompanying pro-forma response on the executable model.

Novartis requests that NICE considers certain subpopulations of patients in their review, specifically those with GI-related adverse events due to intolerance to MMF and the high-risk CMV-positive population. These are important groups of patients that, with the right treatments, can benefit from appropriate, full-dose immunosuppression to ensure the highest chances of long-term patient and graft survival.

We understand that RWE is currently only rarely considered in HTA processes. However, in this particular disease area, where products have been licensed and in general clinical use for many years, data from outside classical RCTs, such as open-label extension trials, add valuable insights. Novartis calls on NICE to widen the data set being considered to include non-RCT evidence that provides relevant efficacy, safety and patient outcome endpoints.

We welcome continued dialogue with NICE on this technology appraisal.

Yours faithfully,

[redacted]

Novartis Pharmaceuticals UK Limited

References

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Hartmann A, Sagedal S, Hjelmesaeth J. The natural course of cytomegalovirus infection and disease in renal transplant recipients. *Transplantation* 2006; **82**(Suppl): S15– S17.

Knoll GA, MacDonald I, Khan A, Van Walraven C. Mycophenolate mofetil dose reduction and the risk of acute rejection after renal transplantation. *J Am Soc Nephrol.* 2003; **14**(9): 2381-2386.

Langone A, Doria C, Greenstein S *et al.* Does reduction in mycophenolic acid dose compromise efficacy regardless of tacrolimus exposure level? An analysis of prospective data from the Mycophenolic Renal Transplant (MORE) Registry. *Clin Transplant* 2013; **27:** 15-24.

Neri L, McEwan P, Sennfalt K *et al.* Characterizing the relationship between health utility and renal function after kidney transplantation in UK and US: A cross-sectional study. *Health Qual Life Outcomes* 2012; **10:** 139.

Ortega F, Sanchez-Fructuoso A, Cruzado JM *et al*. Gastrointestinal quality of life improvement of renal transplant recipients converted from mycophenolate mofetil to enteric-coated mycophenolate sodium drugs or agents: mycophenolate mofetil and enteric-coated mycophenolate sodium. *Transplantation* 2011; **92:** 426-432.

Pelletier RP, Akin B, Henry ML *et al*. The impact of mycophenolate mofetil dosing patterns on clinical outcome after renal transplantation. *Clin Transplant* 2003; **17**(3): 200-205.

Shehata M, Bhandari S, Venkat-Raman G *et al.* Effect of conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium on maximum tolerated dose and gastrointestinal symptoms following kidney transplantation. *Transpl Int* 2009; **22:** 821-830.

Tedesco-Silva H, Cibrik D, Johnston T *et al*. Everolimus plus reduced-exposure CsA versus mycophenolic acid plus standard-exposure CsA in renal-transplant recipients. *Am J Transplant* 2010; **10:** 1401-1413.

Tedesco-Silva H, Sandes-Freitas T, Felipe C *et al.* A prospective randomised trial aimed to reduce the incidence of cytomegalovirus (CMV) infection in Kidney Transplant (KT) recipients. *Transplant International* 2013; **26**(Suppl. 2): abstract BO296.

Tierce JC, Porterfield-Baxa J, Petrilla AA *et al*. Impact of mycophenolate mofetil (MMF)-related gastrointestinal complications and MMF dose alterations on transplant outcomes and healthcare costs in renal transplant recipients. *Clin Transplant.* 2005; **19**(6): 779-784.

Vitko S, Margreiter R, Weimar W *et al*. Everolimus (Certican) 12-month safety and efficacy versus mycophenolate mofetil in de novo renal transplant recipients. *Transplantation* 2004; **78:** 1532-1540.

Vitko S, Margreiter R, Weimer W *et al*. Three-Year Efficacy and Safety Results from a Study of Everolimus Versus Mycophenolate Mofetil in de novo Renal Transplant Patients. *Am J Transplant* 2005; **5:** 2521–2530.

Appendix: Studies included in the Novartis systematic review featuring in PenTAG's exclusion list (primary study report in black)

Trial identifier	Reference	Data supporting differences between MMF and EC-MPS
B302	Budde K *et al*. Enteric-coated mycophenolate sodium can be safely administered in maintenance renal transplant patients: results of a 1-year study. *American Journal of Transplantation* 2003; **4:** 237-243. Budde K *et al*. Safety and efficacy after conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium: results of a 1-year extension study. *Transplant Proc* 2005; **37:** 912-915. Budde K *et al*. Long-term safety and efficacy after conversion of maintenance renal transplant recipients from mycophenolate mofetil (MMF) to enteric-coated mycophenolate sodium (EC-MPA, myfortic). *Clin Nephrol* 2006; **66:** 103-111.	The reason for exclusion of this study from the PenTAG systematic review was stated as 'intervention' **[page 313, Section 4.5.4]**. We would appreciate clarity on this point, as the interventions used in this study (MMF and EC-MPS) are both listed as included therapies **[page 81, Section 4.1.3.3]**. B302 (Budde 2003) is an RCT, supported by two open-label extension/conversion studies, which provides valuable data supporting the adverse event profile of EC-MPS. Results at three months showed overall similarity of the side effect profile for EC-MPS and MMF. While incidence of all infections with EC-MPS was similar to MMF, for serious adverse events (23.3 versus 30.1%; p=ns) and serious infections (8.8% versus 16.0%; $p<0.05$), the profile was in favour of EC-MPS. Budde 2003 also reports a consistent (p=NS) reduction in BPAR, graft loss and death over 12 months compared with MMF. By excluding this study, these data are not captured in the PenTAG analysis. Although the conversions studies (Budde 2005, Budde 2006) do not fall within PenTAG's inclusion criteria, such studies provide valuable long-term data regarding patient follow-up, including graft and patient survival data, especially when modelling a disease with a long-term horizon such as end-stage renal failure (ESRF).
MORE	Langone *et al*. Does reduction in mycophenolic acid dose compromise efficacy regardless of tacrolimus exposure level? An analysis of prospective data from the Mycophenolic Renal Transplant (MORE) Registry. *Clin Transplant* 2013; **27**: 15-24. Chan *et al*. Mycophenolic acid (MPA) dosing: Effect on efficacy to 4 years after kidney transplantation in the mycophenolic acid observational renal transplant (MORE) study. *Am J Transplant* 2013; **13**: 337.	This is an observational registry study and, therefore, outside PenTAG's inclusion criteria with respect to study designs. However, such studies provide valuable long-term data regarding patient follow-up, including graft and patient survival data, especially when modelling a disease with a long-term horizon such as ESRF.

Ortega 2011 (myVIDA)	Ortega F *et al*. Gastrointestinal quality of life improvement of renal transplant recipients converted from mycophenolate mofetil to enteric-coated mycophenolate sodium drugs or agents: mycophenolate mofetil and enteric-coated mycophenolate sodium. *Transplantation* 2011; **92:** 426-432.	The reason for exclusion of this study from the PenTAG systematic review was stated as 'study design' **[page 313, Section 4.5.4]**. We would appreciate clarity on this point, as Ortega 2011 is an RCT. We suspect that the driver for exclusion was actually 'outcomes' as the primary endpoint for this study was specific GI health-related quality of life (total GIQLI score) and GI adverse events were not included in the list of adverse event outcomes included by PenTAG, although health-related quality of life outcomes were **[page 83, Section 4.1.3.5]**. Incidence of certain adverse events is a key differentiator between MMF and EC-MPS and excluding studies that investigate this endpoint results in an incomplete view of the available therapy options. Ortega 2011 showed that a better GI tolerability was observed in EC-MPS patients, as displayed by the lower incidence (67.8% EC-MPS versus 87% MMF; p=0.015; see Table 4.3 in the submission) and intensity of GI AEs. GI AEs were severe in 9.3% of patients on MMF and 3.39% on EC-MPS.
Shehata 2009 (myQoL)	Shehata *et al*. Effect of conversion from mycophenolate mofetil to enteric-coated mycophenolate sodium on maximum tolerated dose and gastrointestinal symptoms following kidney transplantation. *Transpl Int* 2009; **22**: 821-830.	The reason for exclusion of this study from the PenTAG systematic review was stated as 'study design' **[page 313, Section 4.5.4]**. We would appreciate clarity on this point, as Shehata 2009 is an RCT. We suspect that the driver for exclusion was actually 'outcomes' as the primary endpoint for this study was the proportion of patients receiving a higher MPA dose at Week 12 than at randomisation, which was not included in the list of outcomes included by PenTAG **[page 82, Section 4.1.3.5]**. Shehata 2009 showed that the proportion of patients receiving the maximum recommended dose at the end of the study was 50% (34/68) in the EC-MPS arm compared with 26.2% (16/61) in the MMF arm (p=0.007), a difference of 23.8% (95% CI 7.6–40.0). These data are especially relevant to economic modelling in this disease as adherence to full-dose maintenance therapy will impact patient outcomes.