Details of amendments made by the ERG to the manufacturer's decision model resubmitted to the NICE Single Technology Appraisal of Pemetrexed as maintenance therapy for NSCLC in April 2013 /updated August 2013

Amendments reported in Table 1 of ERG Addendum

1) *Recalculation of mean pemetrexed acquisition cost per cycle*

This amendment is activated by a binary switch variable (Mod_1) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'Resource!N47' with the following:

=IF(Mod_1=0,SUM(N45:N46),1481.37)

The mean cost per dose was obtained as follows:

For Males create a table of 100mg dose units equivalent to steps of 0.2m^2 BSA. Use a cumulative normal distribution function to calculate the proportion of patients who can be treated up to the maximum dose available in that step. Determine the number of 100mg and 500mg vials required to deliver the dose for that step. Use a SUMPRODUCT function to calculate the mean number of 100mg and 500mg vials required by Males, and multiple these by the vial unit costs to obtain the overall mean cost for Males. Note that a dose cap of 1000mg is applied on clinical advice. The same procedure is used for Females and then a weighted average cost for all patients is calculated using the balance between Males and Females in the population.

The BSA distribution parameters are derived from the Sacco survey data excluding adjuvant and neoadjuvant patients, as follows:

Males - mean 1.88568, standard deviation 0.17933

Females - mean 1.65503, standard deviation 0.17249

Males: Females ratio based on PARAMOUNT trial (313:226)

2) *Removal of inappropriate continuity correction applied to pemetrexed acquisition cost*s

This amendment is activated by a binary switch variable (Mod_2) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'Pem!DM11' with the following:

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=IF(Mod_2=0,AVERAGE(CW10,CW11),$D$4*BH10*PemCost
+$D$4*AVERAGE(BH10,BH11)*(propCTscans*pCTscans*cCTscan
+propconsults*pConsults*cConsult))
+IF(JMENcosts=1,AVERAGE(CX11,CX10)+AVERAGE(DD10,DD11))
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Copy this formula into cells 'Pem!DM12:DM366'

3) *Removal of differential use of second-line systemic therapies following disease progression*

The amendment is activated by a binary switch variable (Mod_3) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'Resource!N305' with the following:

=IF(Mod_3=0,IF(PSA=1,M305,F305),pBSCSyst)

Replace the formula in cell 'Resource!N306' with the following:

=IF(Mod_3=0,IF(PSA=1,M306,F306),pBSCSyst)

Replace the formula in cell 'Resource!F307' with the following:

=IF(Mod_3=0,F305/F304,1)

4) *Recalculation of mean docetaxel acquisition cost per cycle*

This amendment is activated by a 3-way switch variable (Mod_6) taking value 0 to use the original model logic, value 1 to apply the amendment using BNF prices and value 2 using eMIT prices.

Replace the formula in cell 'Resource!M376' with the following:

=CHOOSE(Mod_6+1,SUM(M373:M375),M375+800.06,M375+87.39)

The method of calculation is similar to that used for pemetrexed (see (1) above), with the following alterations:

- dosing steps are at 20mg intervals
- three vial sizes are used - 20mg, 80mg and 140mg
- the lowest generic BNF list prices are used (£154.61, £508.01 and £720.10 respectively)
- the best eMIT average contract prices are used (£11.13, £47.24 and £86.10 respectively)

5) *Re-estimation of monitoring costs*

This amendment is activated by a binary switch variable (Mod_11) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'Parameters!E163 with the following:

=IF(Mod_11=0,3%,100%)

Replace the formula in cell 'Resource!C163 with the following:

=IF(Mod_11=0, IF(CTscanNumber=1,1, IF(CTscanNumber=2,0.5, IF(CTscanNumber=3,0.25, IF(CTscanNumber=4,0.125, IF(CTscanNumber=5,0))))),0.25)

Replace the formula in cell 'Resource!C164 with the following:

=IF(Mod_11=0, IF(ConsVisitNumber=1,1, IF(ConsVisitNumber=2,0.5, IF(ConsVisitNumber=3,0.25, IF(ConsVisitNumber=4,0.125, IF(ConsVisitNumber=5,0))))),0.25)

6) *Re-estimation of terminal care costs*

This amendment is activated by a binary switch variable (Mod_12) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'JMEN_Resource!H45 with the following:

=IF(Mod_12=0,(E45/UKCPI_08)*UKCPI_11,3906.31)

This estimate is taken directly from an HTA report recently completed by the ERG for first-line chemotherapy for NSCLC, and encompasses costs of care for patients dying in hospital, in a hospice and at home, with all supportive community and voluntary services.

7) Include cost of blood products

This amendment is activated by a binary switch variable (Mod_4) with value 1 to apply the amendment and value 0 to use the original model logic.

Replace the formula in cell 'Resource!F293 with the following:

=IF(Mod_4=0,58,58+125)

NB - this modification only alters the ICER if PARAMOUNT resource use is employed (see amendment 9 below)

<u>Amendments reported in Table 2 of ERG Addendum</u>

8) *Use of the Nafees EQ-5D model to determine utility values*

This amendment is applied by setting range 'QoLdata' to value 4 on worksheet ‘Parameters’.

9) *PARAMOUNT resource use*

To change from JMEN to PARAMOUNT resource use enter “1” in Cell ‘Parameters!E100’. To revert to JMEN resource use enter “2”.

10) *Substitution of ERG long-term model OS projections*

This amendment is activated by a switch variable (Mod_13) with value 0 to use the original model logic, value 1 to apply the ERG original amendment and value 2 to apply the ERG revised amendment using a common survival proportion for starting projection in both model arms.

The modification to the <u>BSC worksheet</u> requires the following changes:

- Set Cell AZ7 to " =0.00176541033416705 * 21 (This is the exponential risk parameter for a 21-day cycle)

- Set Cell AZ10 to "= AN10", then copy this formula to the range AZ11:AZ27

- Set Cell AZ28 to “= CHOOSE(Mod_13+1, AN28, 0.442052576677688, AN28)”

- Set Cell AZ29 to " =IF(Mod_13=1,AZ28*EXP(-AZ7),AN29)" and copy this formula to range AZ30:AZ32

- Set Cell AZ33 to “=AZ32*EXP(-AZ7)” and copy this formula to range AZ34:AZ366

Replace the formula in cell AW11 as follows:

=IF(Mod_13=0, IF(Cycles<=IF(D4=0,KMstopOSBSC,KMstopOSPem), 1-AN11/AN10, IF(OSModel=1, AQ11, IF(OSModel=2,AR11 ,IF(OSModel=3,AS11 ,IF(OSModel=4,AT11, IF(OSModel=5,AU11,AV11)))))), 1-AX11/AX10)

Replace the formula in cell AX11 as follows:

=IF(Mod_13=0,(1-AW11)*AX10,AZ11)

Copy the range AW11:AX11, and paste the formulae to the range AW12:AX366

The modification to the <u>Pem worksheet</u> requires similar changes:

- Set Cell AY7 to value 8 (time when original projection begins)

- Set Cell AZ7 to "=0.00170103676595399 * 21

- Set Cell AZ10 to "= AN10", then copy this formula to the range AZ11:AZ16

- Set Cell AZ17 to “=CHOOSE(Mod_13+1,AN17,0.8453,AN17)”

- Set Cell AZ18 to " =IF(Mod_13<2,IF(F18<AY7,AN18,AZ17*EXP(-AZ7)),AN18)" and copy this formula to range AZ19:AZ39

- Set Cell AZ40 to “=IF(F40<AY7,AN40,AZ39*EXP(-AZ7))” and copy this formula to range AZ41:AZ366

Replace the formula in cell AW11 as follows:

=IF(Mod_13=0, IF(Cycles<=IF(D4=0,KMstopOSBSC,KMstopOSPem), 1-AN11/AN10, IF(OSModel=1, AQ11, IF(OSModel=2,AR11, IF(OSModel=3,AS11, IF(OSModel=4,AT11, IF(OSModel=5,AU11,AV11)))))), 1-AZ11/AZ10)

Replace the formula in cell AX11 as follows:

=IF(Mod_13=0,(1-AW11)*AX10,AZ11)

Copy the range AW11:AX11, and paste the formulae to the range AW12:AX366