Addendum

Ledipasvir-sofosbuvir for treating chronic hepatitis C

Description of additional analyses undertaken by the ERG

Based on the issues identified during the pre-meeting teleconference and the recommendations of lead team, the following sets of additional analyses were undertaken:

1. Breakdown of the total costs
2. Use of higher starting age
3. No HRQoL increment with SVR
4. Using 12 week LDV/SOF+RBV for GT3 treatment-naïve non-cirrhotic patients

It should be noted that these additional analyses use the ERG-preferred base case analysis as a starting point. All analyses were undertaken using point estimates of parameters due to the excessive computation time and complexity associated with running the probabilistic version of the model. The ERG analyses report total costs and QALYs for LDV/SOF and each comparator to two decimal places. This may produce some rounding error in the calculation of ICERs.

ERG analysis 1: Breakdown of the total costs

Table 1 shows a breakdown of total costs in each analysis based on the company's model. It should be noted that the sum of treatment costs, monitoring costs, pharmacy costs and adverse event costs do not add up to total costs, due to the way the costs are calculated in the model.

Table 1: Breakdown of the total costs

(i) Genotype 1 treatment-naïve non-cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 12 weeks	£38,980.00	£2,222.66	£134.90	£0.21	£42,160.45
SMV+SOF	£57,380.94	£2,482.34	£422.62	£0.00	£61,415.79
SOF+PEG-IFN2a+RBV	£37,071.87	£2,210.51	£493.06	£101.09	£41,081.62
SMV+PEG-IFN2a+RBV	£27,429.07	£2,944.46	£1,054.53	£133.86	£33,316.62
TVR+PEG-IFN2a+RBV	£27,987.32	£3,054.32	£1,320.04	£221.92	£34,631.46
BOC+PEG-IFN2b+RBV	£26,720.99	£3,387.99	£2,073.93	£4.03	£35,002.22
PEG-IFN2a+RBV	£8,328.72	£3,347.80	£3,241.19	£209.75	£19,205.40
No treatment	£0.00	£116.40	£5,916.67	£0.00	£13,029.41
(ii) Genotype 1 treatment-naïve cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 24 weeks	£77,960.00	£2,659.99	£20,015.03	£0.21	£101,051.95
SMV+SOF	£57,380.94	£2,797.98	£20,852.69	£0.00	£81,484.72
SOF+PEG-IFN2a+RBV	£37,071.87	£2,404.45	£23,296.80	£101.09	£63,433.51
SMV+PEG-IFN2a+RBV	£27,429.07	£3,609.27	£27,195.21	£133.86	£59,097.68
BOC+PEG-IFN2b+RBV	£31,387.38	£4,923.13	£27,907.64	£4.03	£64,985.45
TVR+PEG-IFN2a+RBV	£27,987.32	£3,802.35	£28,526.52	£221.92	£61,326.36
PEG-IFN2a+RBV	£8,328.72	£4,425.57	£34,265.66	£209.75	£48,265.60
No treatment	£0.00	£356.26	£39,627.89	£0.00	£41,253.02
(iii) Genotype 4 treatment-naïve non-cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 12 weeks	£38,980.00	£2,222.66	£134.90	£0.21	£42,160.45
SMV+SOF	£57,380.94	£2,482.34	£422.62	£0.00	£61,415.79
SOF+PEG-IFN2a+RBV	£37,071.87	£2,210.51	£493.06	£101.09	£41,081.62
SMV+PEG-IFN2a+RBV	£27,429.07	£2,944.46	£1,054.53	£133.86	£33,316.62
PEG-IFN2a+RBV	£8,328.72	£3,347.80	£3,241.19	£209.75	£19,205.40
No treatment	£0.00	£116.40	£5,916.67	£0.00	£13,029.41
(iv) Genotype 4 treatment-naïve cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 24 weeks	£77,960.00	£2,659.99	£20,015.03	£0.21	£101,051.95
SMV+SOF	£57,380.94	£2,797.98	£20,852.69	£0.00	£81,484.72
SOF+PEG-IFN2a+RBV	£37,071.87	£2,404.45	£23,296.80	£101.09	£63,433.51
SMV+PEG-IFN2a+RBV	£27,429.07	£3,609.27	£27,195.21	£133.86	£59,097.68
PEG-IFN2a+RBV	£8,328.72	£4,425.57	£34,265.66	£209.75	£48,265.60
No treatment	£0.00	£356.26	£39,627.89	£0.00	£41,253.02
(v) Genotype 1/4 treatment-experienced non-cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 12 weeks	£38,980.00	£1,592.86	£346.08	£0.21	£41,978.77
SMV+SOF	£57,380.94	£1,852.54	£386.25	£0.00	£60,723.61

SOF+PEG-IFN2a+RBV	£37,071.87	£1,580.71	£1,405.96	£101.09	£42,386.90
SMV+PEG-IFN2a+RBV	£32,289.02	£3,193.56	£1,222.23	£133.86	£38,729.70
TVR+PEG-IFN2a+RBV	£29,612.42	£2,898.56	£1,458.96	£305.85	£36,459.92
BOC+PEG-IFN2b+RBV	£32,200.42	£3,052.59	£1,857.90	£178.43	£39,911.38
PEG-IFN2a+RBV	£6,570.89	£2,342.36	£4,355.35	£253.28	£18,984.11
No treatment	£0.00	£116.40	£5,407.55	£0.00	£12,159.72
(vi) Genotype 1/4 treatment-experienced cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF 24 weeks	£77,960.00	£1,837.89	£19,045.56	£0.21	£99,222.17
SMV+SOF	£57,380.94	£1,975.88	£19,980.23	£0.00	£79,754.31
SOF+PEG-IFN2a+RBV	£37,071.87	£1,582.35	£23,860.01	£101.09	£63,193.43
SMV+PEG-IFN2a+RBV	£32,289.02	£4,269.65	£24,735.23	£133.86	£62,045.65
TVR+PEG-IFN2a+RBV	£29,612.42	£3,798.82	£28,822.27	£305.85	£63,324.53
BOC+PEG-IFN2b+RBV	£32,200.42	£3,986.36	£31,167.10	£178.43	£68,413.45
PEG-IFN2a+RBV	£6,570.89	£2,927.91	£36,585.24	£253.28	£47,441.22
No treatment	£0.00	£356.26	£39,085.18	£0.00	£40,650.80
(vii) Genotype 3 treatment-naïve non-cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF+RBV 24 weeks	£80,179.85	£2,466.01	£0.00	£6.27	£83,330.76
PEG-IFN2a+RBV	£3,907.31	£2,716.28	£2,312.13	£82.87	£11,359.86
No treatment	£0.00	£116.40	£8,132.21	£0.00	£14,928.01
(viii) Genotype 3 treatment-naïve cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF+RBV 24 weeks	£80,179.85	£2,659.99	£19,408.44	£6.27	£102,644.92
SOF+RBV	£72,067.61	£2,653.80	£20,772.92	£0.16	£95,947.03
SOF+PEG-IFN2a+RBV	£37,585.67	£2,416.64	£22,778.35	£101.09	£63,418.53
No treatment	£0.00	£356.26	£39,627.89	£0.00	£41,253.02
(ix) Genotype 3 treatment-experienced IFN-ineligible non-cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF+RBV 24 weeks	£80,179.85	£1,836.21	£799.75	£6.27	£84,108.64
SOF+RBV	£72,067.61	£1,830.05	£957.76	£0.16	£76,209.40
No treatment	£0.00	£116.40	£7,464.37	£0.00	£13,935.71
(x) Genotype 3 treatment-experienced IFN-ineligible cirrhotic					
Option	Treatment costs	Monitoring costs	Pharmacy costs	Adverse event costs	Total costs
LDV/SOF+RBV 24 weeks	£80,179.85	£1,837.89	£23,186.66	£6.27	£105,760.87
SOF+RBV	£72,067.61	£1,831.70	£26,519.70	£0.16	£101,108.73
No treatment	£0.00	£356.26	£39,085.18	£0.00	£40,650.80

* pharmacy costs are health state costs (i.e costs associated with disease progression)

ERG analysis 2: Use of higher starting age

The starting population in the company's model is 40 for treatment naïve patients and 45 for treatment experienced patients. Table 2 presents an exploratory analysis using higher starting ages of 50 years for the treatment-naïve population and 55 years for the treatment-experienced population.

Table 2: Central estimates of cost-effectiveness using higher starting age

(i) Genotype 1 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	15.03	£42,179.77	0.40	£8,711.15	£21,778
SMV+SOF	14.92	£61,477.87	-	-	dominated
SOF+PEG-IFN2a+RBV	14.86	£41,154.17	-	-	ext dom
SMV+PEG-IFN2a+RBV	14.63	£33,468.62	0.87	£13,811.58	£15,875
TVR+PEG-IFN2a+RBV	14.50	£34,820.22	-	-	dominated
BOC+PEG-IFN2b+RBV	14.22	£35,293.78	-	-	dominated
PEG-IFN2a+RBV	13.76	£19,657.04	0.95	£5,749.14	£6,052
No treatment	12.81	£13,907.90	-	-	-
(ii) Genotype 1 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	9.18	£98,999.46	0.17	£19,544.01	£114,965
SMV+SOF	9.01	£79,455.45	0.53	£17,983.47	£33,931
SOF+PEG-IFN2a+RBV	8.48	£61,471.98	2.27	£14,880.83	£6,555
SMV+PEG-IFN2a+RBV	7.66	£57,240.97	-	-	ext dom
BOC+PEG-IFN2b+RBV	7.51	£63,143.37	-	-	dominated
TVR+PEG-IFN2a+RBV	7.38	£59,504.69	-	-	ext dom
PEG-IFN2a+RBV	6.21	£46,591.15	1.11	£6,846.99	£6,168
No treatment	5.10	£39,744.16	-	-	-
(iii) Genotype 4 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	15.03	£42,179.77	0.40	£8,711.15	£21,778
SMV+SOF	14.92	£61,477.87	-	-	dominated
SOF+PEG-IFN2a+RBV	14.86	£41,154.17	-	-	ext dom
SMV+PEG-IFN2a+RBV	14.63	£33,468.62	0.87	£13,811.58	£15,875
PEG-IFN2a+RBV	13.76	£19,657.04	0.95	£5,749.14	£6,052
No treatment	12.81	£13,907.90	-	-	-
(iv) Genotype 4 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	9.18	£98,999.46	0.17	£19,544.01	£114,965
SMV+SOF	9.01	£79,455.45	0.53	£17,983.47	£33,931
SOF+PEG-IFN2a+RBV	8.48	£61,471.98	2.27	£14,880.83	£6,555
SMV+PEG-IFN2a+RBV	7.66	£57,240.97	-	-	ext dom
PEG-IFN2a+RBV	6.21	£46,591.15	1.11	£6,846.99	£6,168
No treatment	5.10	£39,744.16	-	-	-
(v) Genotype 1/4 treatment-experienced non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	13.67	£41,997.83	1.77	£29,521.91	£16,679
SMV+SOF	13.66	£60,745.02	-	-	dominated
SOF+PEG-IFN2a+RBV	13.27	£42,468.18	-	-	dominated
SMV+PEG-IFN2a+RBV	13.26	£38,782.65	-	-	ext dom
TVR+PEG-IFN2a+RBV	13.21	£36,527.97	-	-	ext dom

BOC+PEG-IFN2b+RBV	13.08	£39,995.14	-	-	dominated
PEG-IFN2a+RBV	12.21	£19,202.69	-	-	ext dom
No treatment	11.90	£12,475.92	-	-	-
(vi) Genotype 1/4 treatment-experienced cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	8.60	£96,741.49	0.17	£19,455.10	£114,442
SMV+SOF	8.43	£77,286.39	0.72	£16,507.89	£22,928
SOF+PEG-IFN2a+RBV	7.71	£60,778.50	2.73	£22,334.67	£8,181
SMV+PEG-IFN2a+RBV	7.49	£59,629.20	-	-	ext dom
TVR+PEG-IFN2a+RBV	6.82	£60,957.41	-	-	dominated
BOC+PEG-IFN2b+RBV	6.42	£66,069.18	-	-	dominated
PEG-IFN2a+RBV	5.44	£45,172.23	-	-	ext dom
No treatment	4.98	£38,443.83	-	-	-
(vii) Genotype 3 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	15.07	£83,330.04	0.86	£71,502.36	£83,142
PEG-IFN2a+RBV	14.21	£11,827.68	-	-	-
No treatment	12.20	£16,600.60	-	-	dominated
(viii) Genotype 3 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	9.30	£100,575.61	0.71	£39,132.98	£55,117
SOF+RBV	9.01	£93,916.61	-	-	ext dom
SOF+PEG-IFN2a+RBV	8.59	£61,442.63	3.49	£21,698.47	£2,526
No treatment	5.10	£39,744.16	-	-	-
(ix) Genotype 3 treatment-experienced IFN-ineligible non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	13.53	£84,212.49	0.06	£7,882.19	£131,370
SOF+RBV	13.47	£76,330.30	2.07	£61,414.73	£29,669
No treatment	11.40	£14,915.57	-	-	-
(x) Genotype 3 treatment-experienced IFN-ineligible cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	7.85	£103,336.75	2.87	£64,892.92	£22,611
SOF+RBV	7.25	£98,722.93	-	-	ext dom
No treatment	4.98	£38,443.83	-	-	-

Inc. – incremental; ICER – incremental cost-effectiveness ratio; ext dom – extended dominance; IFN – interferon

ERG analysis 3: No HRQoL increment with SVR

The HRQoL gain associated with achieving SVR (0.04) in the company's model was derived using the US EQ-5D tariff (Vera-Llonch et al, 2013). Table 3 presents an exploratory analysis was undertaken using no HRQoL improvement due to SVR.

Table 3: Central estimates of cost-effectiveness using no HRQoL increment with SVR

(i) Genotype 1 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	16.34	£42,160.45	0.24	£8,843.83	£36,849
SMV+SOF	16.28	£61,415.79	-	-	dominated
SOF+PEG-IFN2a+RBV	16.24	£41,081.62	-	-	ext dom
SMV+PEG-IFN2a+RBV	16.10	£33,316.62	0.51	£14,111.22	£27,669
TVR+PEG-IFN2a+RBV	16.03	£34,631.46	-	-	dominated
BOC+PEG-IFN2b+RBV	15.86	£35,002.22	-	-	dominated
PEG-IFN2a+RBV	15.59	£19,205.40	0.52	£6,175.99	£11,877
No treatment	15.07	£13,029.41	-	-	-
(ii) Genotype 1 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	9.44	£101,051.95	0.18	£19,567.23	£108,707
SMV+SOF	9.26	£81,484.72	0.54	£18,051.21	£33,428
SOF+PEG-IFN2a+RBV	8.72	£63,433.51	2.33	£15,167.91	£6,510
SMV+PEG-IFN2a+RBV	7.88	£59,097.68	-	-	ext dom
BOC+PEG-IFN2b+RBV	7.73	£64,985.45	-	-	dominated
TVR+PEG-IFN2a+RBV	7.60	£61,326.36	-	-	ext dom
PEG-IFN2a+RBV	6.39	£48,265.60	1.14	£7,012.58	£6,151
No treatment	5.25	£41,253.02	-	-	-
(iii) Genotype 4 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	16.34	£42,160.45	0.24	£8,843.83	£36,849
SMV+SOF	16.28	£61,415.79	-	-	dominated
SOF+PEG-IFN2a+RBV	16.24	£41,081.62	-	-	ext dom
SMV+PEG-IFN2a+RBV	16.10	£33,316.62	0.51	£14,111.22	£27,669
PEG-IFN2a+RBV	15.59	£19,205.40	0.52	£6,175.99	£11,877
No treatment	15.07	£13,029.41	-	-	-
(iv) Genotype 4 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	9.44	£101,051.95	0.18	£19,567.23	£108,707
SMV+SOF	9.26	£81,484.72	0.54	£18,051.21	£33,428
SOF+PEG-IFN2a+RBV	8.72	£63,433.51	2.33	£15,167.91	£6,510
SMV+PEG-IFN2a+RBV	7.88	£59,097.68	-	-	ext dom
PEG-IFN2a+RBV	6.39	£48,265.60	1.14	£7,012.58	£6,151
No treatment	5.25	£41,253.02	-	-	-
(v) Genotype 1/4 treatment-experienced non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 12 weeks	15.34	£41,978.77	1.03	£29,819.05	£28,951
SMV+SOF	15.33	£60,723.61	-	-	dominated
SOF+PEG-IFN2a+RBV	15.10	£42,386.90	-	-	dominated
SMV+PEG-IFN2a+RBV	15.07	£38,729.70	-	-	ext dom
TVR+PEG-IFN2a+RBV	15.04	£36,459.92	-	-	ext dom

BOC+PEG-IFN2b+RBV	14.97	£39,911.38	-	-	dominated
PEG-IFN2a+RBV	14.47	£18,984.11	-	-	ext dom
No treatment	14.31	£12,159.72	-	-	-
(vi) Genotype 1/4 treatment-experienced cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF 24 weeks	9.08	£99,222.17	0.18	£19,467.86	£108,155
SMV+SOF	8.90	£79,754.31	0.77	£16,560.88	£21,508
SOF+PEG-IFN2a+RBV	8.13	£63,193.43	2.94	£22,542.63	£7,668
SMV+PEG-IFN2a+RBV	7.90	£62,045.65	-	-	ext dom
TVR+PEG-IFN2a+RBV	7.17	£63,324.53	-	-	dominated
BOC+PEG-IFN2b+RBV	6.73	£68,413.45	-	-	dominated
PEG-IFN2a+RBV	5.68	£47,441.22	-	-	ext dom
No treatment	5.19	£40,650.80	-	-	-
(vii) Genotype 3 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	16.36	£83,330.76	0.55	£71,970.90	£130,856
PEG-IFN2a+RBV	15.81	£11,359.86	-	-	-
No treatment	14.57	£14,928.01	-	-	dominated
(viii) Genotype 3 treatment-naïve cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	9.56	£102,644.92	0.73	£39,226.39	£53,735
SOF+RBV	9.27	£95,947.03	-	-	ext dom
SOF+PEG-IFN2a+RBV	8.83	£63,418.53	3.58	£22,165.51	£2,510
No treatment	5.25	£41,253.02	-	-	-
(ix) Genotype 3 treatment-experienced IFN-ineligible non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	15.24	£84,108.64	0.04	£7,899.24	£197,481
SOF+RBV	15.20	£76,209.40	1.32	£62,273.69	£47,177
No treatment	13.88	£13,935.71	-	-	-
(x) Genotype 3 treatment-experienced IFN-ineligible cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 24 weeks	8.27	£105,760.87	3.08	£65,110.07	£21,140
SOF+RBV	7.63	£101,108.73	-	-	ext dom
No treatment	5.19	£40,650.80	-	-	-

Inc. – incremental; ICER – incremental cost-effectiveness ratio; ext dom – extended dominance; IFN – interferon

ERG analysis 4: 12-week treatment duration for LDV/SOF+RBV in GT3 treatment naïve non-cirrhotic population

Table 4 presents the central estimates of cost-effectiveness results of an analysis in which includes a 12-week treatment duration is assumed for LDV/SOF+RBV in the GT3 treatment-naïve non-cirrhotic population.

Table 4: Central estimates of cost-effectiveness in GT3 treatment naïve non-cirrhotic population using 12-week treatment duration for LDV/SOF+RBV

Genotype 3 treatment-naïve non-cirrhotic					
Option	QALYs	Costs	Inc. QALYs	Inc. costs	ICER
LDV/SOF+RBV 12 weeks	17.24	£42,997.49	0.81	£31,637.63	**£39,277**
PEG-IFN2a+RBV	16.43	£11,359.86	-	-	-
No treatment	14.57	£14,928.01	-	-	dominated