Integrated Impact Assessment Report for Clinical Commissioning Policies

Policy Reference Number	A02X05		
Policy Title	Chemosaturation for liver metastases from ocular melanomas		
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Section K - Activity Impact			
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)	
K1 Current Patient Population & Demography / Growth	K 1.1 What is the prevalence of the disease/condition?	K1.1 This policy proposes a **non-routine commissioning** position for chemosaturation for the treatment of liver metastases from ocular melanoma primary cancers. **Ocular melanoma (OM)** is a rare form of eye cancer that predominantly affects the uvea. In the UK, it is estimated that between 500 and 600 people are diagnosed with uveal melanoma each year. [i] For England, this represents **c.420-505** patients in 2014/15.[ii]	

	K1.2 What is the number of patients currently eligible for the treatment under the proposed policy?	K1.2 The number of patients **eligible for treatment** is a subset of the prevalent population; those with uveal melanoma with metastatic liver disease isolated predominantly to the liver. Of the 420-505 patients with uveal melanoma identified in K1.1, is it estimated that[iii]: • Between 30 and 50% (c. 125-250 patients) may suffer a recurrence of their cancer within 5-10 years of diagnosis associated with metastatic liver disease. • Of these around 70% (c. 90 to 175) may have metastasis isolated predominantly to the liver.[iv] • Of these patients, it is estimated that around **50-75** would be suitable for chemosaturation each year.[v]
	K1.3 What age group is the treatment indicated for?	K1.3 The treatment is indicated for adults (aged 18 years and over).
	K1.4 Describe the age distribution of the patient population taking up treatment?	K1.4 The average age of onset of uveal melanomas is estimated to be 55[vi] and the average age of a patient is estimated to be around 60[vii].
	K1.5 What is the current activity associated with currently routinely commissioned care for this group?	K1.5 For patients with OM liver metastases, there is no standard practice and the Metastatic Uveal Melanoma MDT reviews each patient on a case-by-case basis to determine next best course of intervention.[viii] The treatment for the patient will depend on the stage and location of the cancer, and how well the liver function is preserved.[ix]If metastases are detected early, there are interventions that potentially extend life expectancy and improve quality of life. These include[x]: • surgical resection; • thermal ablation;

		• systemic therapy; • selective internal radiation therapy (SIRT); and • transarterial chemoembolisation (TACE). Chemosaturation is currently used in some patients who are not amenable to treatments such as surgical resection and thermal ablation.[xi] It is estimated that around 22-23 patients received chemosaturation in 2014/15.[xii] [xiii] The remaining patients in the target population from K1.2 (who would be eligible for chemosaturation but do not currently receive currently it) are expected to receive either:[xiv] • systemic therapy[xv]; or • TACE, only to selected patients.[xvi]
	K1.6 What is the projected growth of the disease/condition prevalence (prior to applying the new policy) in 2, 5, and 10 years?	K1.6 Internationally, the incidence of uveal melanoma has remained stable over the last 30 years or so.[xvii] [xviii] Therefore, no future change to incidence of uveal melanoma is anticipated, and the population with uveal melanoma may grow in line with population growth and is estimated to be[xix]: • ~ 425 - 510 in 2016/17 (year 1) • ~ 430 - 515 in 2017/18 (year 2) • ~ 440 - 525 in 2018/19 (year 5)
	K1.7 What is the associated projected growth in activity (prior to applying the new policy) in 2,5 and 10 years	K1.7 Under a do-nothing scenario, the activity for chemosaturation is anticipated to grow in line with the population growth and is estimated to be broadly stable over the next five years at[xx]: • ~ 22-23 in 2016/17 (year 1)

		• ~ 22-23 in 2017/18 (year 2) • ~ 23-24 in 2020/21 (year 5)
	K1.8 How is the population currently distributed geographically?	K1.8 No evidence on the geographic distribution of ocular melanoma in the UK or England has been identified within this review.
K2 Future Patient Population & Demography	K2.1 Does the new policy: move to a non-routine commissioning position / substitute a currently routinely commissioned treatment / expand or restrict an existing treatment threshold / add an additional line / stage of treatment / other?	K2.1 This policy proposes a non-routine commissioning position.
	K2.2 Please describe any factors likely to affect growth in the patient population for this intervention (e.g. increased disease prevalence, increased survival)	K2.2 No factors have been identified in this review.
	K 2.3 Are there likely to be changes in geography/demography of the patient population and would this impact on activity/outcomes? If yes, provide details	K2.3 No changes have been identified.

	K2.4 What is the resulting expected net increase or decrease in the number of patients who will access the treatment per year in year 2, 5 and 10?	K2.4 The proposed policy establishes a 'not routinely commissioned' proposal for the relevant population (the specific cohort set out in K1.2). The number of patients who fall outside of the cohort covered by the proposed policy, or for whom exceptionality might be demonstrated is likely to be very small. As such there is expected to be a **net decrease** in the number of patients accessing the treatment each year. As activity is expected to be zero in future years, the decrease in activity is equal to the estimated future activity in the 'do nothing' case, as identified in K1.7: • ~ 22-23 in 2016/17 (year 1) • ~ 22-23 in 2017/18 (year 2) • ~ 23-24 in 2020/21 (year 5) For these patients[xxi]: • ~ 8-10 are expected to receive TACE; and • ~ 13-14 patients are expected to receive systemic therapy (chemotherapy either with or without immunotherapy). The activity for these patients further along the pathway could be different when compared to the 'do-nothing'. This may be dependent on two factors[xxii]: i. The comparative response rate of the treatments. If the response rate of chemosaturation is greater than that of the comparative treatments, then more patients may require further line treatments such as systemic therapy and palliative care when compared to the 'do-nothing'. ii. How much each treatment increases the length of survival. However given the uncertainty in treatment options and outcomes, there is limited evidence to quantify the impacts in the subsequent stages of the pathway.

K3 Activity	K3.1 What is the current annual activity for the target population covered under the new policy? Please provide details in accompanying excel sheet	K3.1 Current annual activity is identified in K1.5.
	K3.2 What will be the new activity should the new / revised policy be implemented in the target population? Please provide details in accompanying excel sheet	K3.2 Future chemosaturation activity for the target population is expected to be zero in future years given a non-routinely commissioned position. As identified in K2.4, instead these patients are expected to receive either TACE or systemic therapy.
	K3.3 What will be the comparative activity for the 'Next Best Alternative' or 'Do Nothing' comparator if policy is not adopted? Please details in accompanying excel sheet	K3.3 The activity under the 'Do Nothing' is as described in K1.7.
K4 Existing Patient Pathway	K4.1 If there is a relevant currently routinely commissioned treatment, what is the current patient pathway? Describe or include a figure to outline associated activity	K4.1 – K4.2 Once liver metastasis are confirmed the patient will be referred to a specialist metastatic uveal melanoma multi-disciplinary team (MDT). The MDT is comprised of interventional radiologists, oncologists, HPB surgeons, cancer nurse specialists, anaesthetists and occasionally pathologists. This MDT receives referrals from ophthalmology oncologists, medical oncologists and hepatobiliary MDTs and is responsible for deciding, with the patient, the best management approach. The MDT may undertake further imaging including PET CT scanning and cardiopulmonary exercise tolerance testing although these are occasionally undertaken by the referring team. After full assessment of the patient, the MDT will consider whether surgical resection, thermal ablative therapy, systemic chemotherapy, SIRT, immunotherapy or chemosaturation is the most suitable. For liver only (intrahepatic) metastases,

		surgical resection or thermal ablative therapy would be the preferred treatment options, as these would result in tumour removal. However there are estimated to be less than 10% of patients who would be suitable for these interventions. The MDT will be required to decide if chemosaturation represents the best opportunity for prolonging life and improving quality of life. Patients with significant cardiac history, respiratory disease, brain metastases, abnormal liver anatomy or high risk of bleeding elsewhere will be unable to undergo chemosaturation, as determined by the MDT. Patients with extrahepatic metastasis may require a systemic therapy as first-line, either as immunotherapy or systemic chemotherapy.
	K4.2. What are the current treatment access criteria?	
	K4.3 What are the current treatment stopping points?	K4.3 Metastases from ocular melanoma is a palliative condition and therefore all patients will require palliative, and eventually end of life care. Current stopping points from active treatment (to palliative care) are: (1) Following surgical or thermal ablative therapy (2) Following systemic chemotherapy
K5 Comparator (next best alternative treatment) Patient Pathway	K5.1 If there is a 'next best' alternative routinely commissioned treatment what is the current patient pathway? Describe or include a figure to outline associated activity.	K5.1 – K5.2 as K4.1-4.2
	K5.2 Where there are different stopping points on the pathway please indicate how many patients	

	out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	
K6 New Patient Pathway	K6.1 Describe or include a figure to outline associated activity with the patient pathway for the proposed new policy	K6.1 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K6.2 Where there are different stopping points on the pathway please indicate how many patients out of the number starting the pathway would be expected to finish at each point (e.g. expected number dropping out due to side effects of drug, or number who don't continue to treatment after having test to determine likely success). If possible please indicate likely outcome for patient at each stopping point.	K6.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
K7 Treatment Setting	K7.1 How is this treatment delivered to the patient?	K7.1 Chemosaturation therapy may be performed in an interventional radiology department and patients may stay in a level 2[xxiii] or level 3[xxiv] care unit for one night, with a subsequent 1 or 2 night stay on the ward.[xxv]

	○ Acute Trust: Inpatient/Daycase/ Outpatient ○ Mental Health Provider: Inpatient/Outpatient ○ Community setting ○ Homecare delivery K7.2 Is there likely to be a change in delivery setting or capacity requirements, if so what? *e.g. service capacity*	K7.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
K8 Coding	K8.1 In which datasets (e.g. SUS/central data collections etc.) will activity related to the new patient pathway be recorded? K8.2 How will this activity related to the new patient pathway be identified?(e.g. ICD10 codes/procedure codes)	K8.1 Not applicable as chemosaturation is proposed to be not routinely commissioned. K8.2 Not applicable chemosaturation is proposed to be not routinely commissioned.
K9 Monitoring	K9.1 Do any new or revised requirements need to be included in the NHS Standard Contract Information Schedule?	K9.1 Not applicable as chemosaturation is proposed to be not routinely commissioned.

	K9.2 If this treatment is a drug, what pharmacy monitoring is required?	K9.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K9.3 What analytical information /monitoring/ reporting is required?	K9.3 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K9.4 What contract monitoring is required by supplier managers? What changes need to be in place?	K9.4 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K9.5 Is there inked information required to complete quality dashboards and if so is it being incorporated into routine performance monitoring?	K9.5 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K9.6 Are there any directly applicable NICE quality standards that need to be monitored in association with the new policy?	K9.6 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	K9.7 Do you anticipate using Blueteq or other equivalent system to guide access to treatment? If	K9.7 Not applicable as chemosaturation is proposed to be not routinely commissioned.

	so, please outline. *See also linked question in M1 below*	
Section L - Service Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)
L1 Service Organisation	L1.1 How is this service currently organised? (i.e. tertiary centres, networked provision)	L1.1 Two metastatic uveal melanoma MDTs exist in tertiary centres nationwide. These MDTs are currently responsible for deciding the most appropriate next treatment step on a case-by-case basis.
	L1.2 How will the proposed policy change the way the commissioned service is organised?	L1.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
L2 Geography & Access	L2.1 Where do current referrals come from?	L2.1 Referrals typically come from ophthalmologists, hepatobiliary MDTs and oncology MDTs.
	L2.2 Will the new policy change / restrict / expand the sources of referral?	L2.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L2.3 Is the new policy likely to improve equity of access	L2.3 As chemosaturation is not being routinely commissioned; equity of access will remain unchanged.
	L2.4 Is the new policy likely to improve equality of access /	L2.4 As chemosaturation is not being routinely commissioned; equality of access will

	outcomes?	remain unchanged.
L3 Implementation	L3.1 Is there a lead in time required prior to implementation and if so when could implementation be achieved if the policy is agreed?	L3.1 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.2 Is there a change in provider physical infrastructure required?	L3.2 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.3 Is there a change in provider staffing required?	L3.3 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.4 Are there new clinical dependency / adjacency requirements that would need to be in place?	L3.4 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.5 Are there changes in the support services that need to be in place?	L3.5 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.6 Is there a change in provider / inter-provider governance required? (e.g. ODN arrangements	L3.6 Not applicable as chemosaturation is proposed to be not routinely commissioned.

	/ prime contractor)	
	L3.7 Is there likely to be either an increase or decrease in the number of commissioned providers?	L3.7 Not applicable as chemosaturation is proposed to be not routinely commissioned.
	L3.8 How will the revised provision be secured by NHS England as the responsible commissioner? (e.g. publication and notification of new policy, competitive selection process to secure revised provider configuration)	L3.8 Not applicable as chemosaturation is proposed to be not routinely commissioned.
L4 Collaborative Commissioning	L4.1 Is this service currently subject to or planned for collaborative commissioning arrangements? (e.g. future CCG lead, devolved commissioning arrangements)	L4.1 Not applicable as chemosaturation is proposed to be not routinely commissioned.
Section M - Finance Impact		
Theme	**Questions**	**Comments** (Include source of information and details of assumptions made and any issues with the data)

M1 Tariff	M1.1 Is this treatment paid under a national prices*, and if so which?	M1.1 There is no specific tariff or NHS funding stream for chemosaturation and it is expected that current activity may be funded using the tariff price used for TACE (as a proxy) as well as through unbundled codes for ICU bed days.[xxvi] The **cost per cycle of chemosaturation** is estimated to be in the region of **£22,000 to £23,000** including the device, radiology and inpatient costs. This is expected to break down as[xxvii]: • ~ £4,000 for the bypass; • ~ £5,000 for the procedure (this is recorded under the same as tariff as TACE)[xxviii]; • ~ £2,000 for ICU bed days; and • ~ £11,000 - £12,000 for the device.
	M1.2 Is this treatment excluded from national prices	M1.2 Please refer to M1.1.
	M1.3 Is this covered under a local price arrangements (if so state range), and if so are you confident that the costs are not also attributable to other clinical services?	M1.3 The device would be excluded from national prices and the price would be agreed locally; with a full price of c. £11,000 - £12,000.[xxix]
	M1.4 If a new price has been proposed how has this been derived / tested? How will we ensure that associated activity is not additionally / double charged through existing routes?	M1.4 Not applicable.

	M1.5 is VAT payable (Y/N) and if so has it been included in the costings?	M1.5 VAT would be recoverable under certain specific conditions[xxx]. It is assumed here that VAT would not be recoverable.
	M1.6 Do you envisage a prior approval / funding authorisation being required to support implementation of the new policy?	M1.6 Not applicable.
M2 Average Cost per Patient	M2.1 What is the revenue cost per patient in year 1?	M2.1 With a non-routine commissioning position, the cost per patient for chemosaturation under the policy would be nil. For reference, the cost per patient for chemosaturation would typically comprise[xxxi]: **1. Pre assessment.** Prior to the procedure patients may require: a. A CT scan of the chest or abdomen, at an estimated cost of between c. £85 and £150.[xxxii] b. An MRI scan of the liver, at an estimated cost of between c. £150 and £330.[xxxiii] c. A CT scan of the brain, at an estimated cost of between c. £85 and £150[xxxiv] d. In some cases an angiogram would be required, at an estimated cost c. £2,225.[xxxv] [xxxvi] Total pre-assessment costs could therefore range between £320 and £2,850. **2. Chemosaturation.** As identified in M1.1, the cost per cycle of chemosaturation is in the region of £22,000 to £23,000. On average, patients would complete between 1 and 3 cycles of chemosaturation, with a median of 2[xxxvii]. This would therefore cost between £22,000 and £69,000 per patient, with a **median cost of £45,500.** **3. Follow-up**. Following chemosaturation, a patient would be expected to be

		closely followed up every 3 months for the first 6 to 12 months, where they may receive an MRI or CT scan. Patients would previously have been seen either once or twice a year.[xxxviii] This could cost between £170 and £1,315 per year.[xxxix] For a patient receiving chemosaturation, the cost in year 1, excluding further treatments, could therefore range between c. **£22k and £73k, with a mid-estimate of c. £48k.**[xl] However, as chemosaturation is proposed to be not routinely commissioned, these patients would be expected to receive either TACE or systemic therapy, as described in K2.4. For **TACE**, the cost per patient would typically comprise: 1. **Pre assessment.** Prior to the procedure, patients may require: a. A CT scan of the chest or abdomen, at an estimated cost of between c. £85 and £150.[xli] b. An MRI scan of the liver, at an estimated cost of between c. £150 and £330.[xlii] Total pre-assessment costs could therefore range between £235 and £480. 2. **TACE**, which has an estimated cost per cycle of **c. £5,000**.[xliii] [xliv] The number of cycles typically ranges between 2 and 4, with a median of 3[xlv], resulting in estimated per patient costs ranging between £10,000 and £20,000, with a **median of £15,000**. *Unlike for chemosaturation, no bypass or ITU bed days would be required and it is expected that there would be an increased likelihood of adverse impacts in the form of increased pain and readmissions when compared to chemosaturation.*[xlvi][xlvii] 3. **Follow-up.** As with chemosaturation, a patient would be expected to be closely followed up every 3 months for the first 6 to 12 months, where they may receive an MRI or CT scan. Patients would previously have been seen either once or twice a year.[xlviii] This could cost between £170 and £1,315 per

		year.[xlix] The total cost per patient for TACE could therefore be in the region of **£10k and £22k, with a median of £16k.**[l] For **systemic therapy**, patients could receive either: 1. Systemic chemotherapy, with an estimated cost of **c. £4k**[li]; or **2.** Systemic chemotherapy with immunotherapy, with an estimated per patient cost of c. **£35k - £79k**.[lii] The total cost per patient for systemic therapy could therefore range between **c. £4k** and **£79k**. Were 50% of patients to receive each option, a mid-cost estimate could be c. **£30k.**
	M2.2 What is the revenue cost per patient in future years (including follow up)?	M2.2 Following the first year of treatment, patients may receive an MRI scan every 4 months. The number of subsequent MRI scans, and more generally the cost of care in future years, is dependent on the length of survival in each patient, and is likely to vary greatly across the patient group.[liii]
M3 Overall Cost Impact of this Policy to NHS England	M3.1 Indicate whether this is cost saving, neutral, or cost pressure to NHS England	M3.1 The policy is to **not routinely commission** this treatment. The 22-23 net decrease in patients receiving chemosaturation each year identified in K2.4 would lead to an estimated **annual cost saving to NHS England** in the region of **£1.1m**.[liv] The reduced use of chemosaturation would lead to an increase in comparator activity as outlined in K2.4. This could offset the cost saving by c. **£0.5 - £0.6m** annually.[lv] The net financial **saving** could therefore be in the region of **£0.5m annually**[lvi]**.** Following these treatment options, further costs could be incurred. As described in K2.4, the full cost impact would therefore depend on how activity differs in later stages of the pathway for patients who would have received chemosaturation in the

		'do nothing' who now would receive TACE or systemic chemotherapy. Given the uncertainty in the subsequent treatment options and also in outcomes (including mortality) it has not been possible to quantify this. Please refer to M6.1.
	M3.2 Where this has not been identified, set out the reasons why this cannot be measured	M3.2 Please refer to M6.1.
M4 Overall cost impact of this policy to the NHS as a whole	M4.1 Indicate whether this is cost saving, neutral, or cost saving for other parts of the NHS (e.g. providers, CCGs)	M4.1 This is expected to be cost neutral to other parts of the NHS.
	M4.2 Indicate whether this is cost saving, neutral, or cost pressure to the NHS as a whole	M4.2 As discussed in M3.1, there is expected to be a **direct cost saving** to the NHS as a whole of c. £0.5m per year.
	M4.3 Where this has not been identified, set out the reasons why this cannot be measured	M4.3 Please refer to M6.1.
	M4.4 Are there likely to be any costs or savings for non NHS commissioners / public sector funders?	M4.4 None expected.
M5 Funding	M5.1 Where a cost pressure is indicated, state known source of	M5.1 Not applicable.

	funds for investment, where identified *e.g. decommissioning less clinically or cost-effective services*	

M6 Financial Risks Associated with Implementing this Policy	M6.1 What are the material financial risks to implementing this policy?	M6.1. As discussed in K2.4, patients who no longer receive chemosaturation under the policy would be expected to instead receive systemic chemotherapy (either with or without immunotherapy).
		
		Depending on the outcomes from these treatments, patients could incur future costs further down the pathway. Given the uncertainty around how patients would be treated in future in the 'do-nothing' and with the policy and their comparative outcomes, this has not been quantified.
		
		Future stages of the pathway could include[lvii]:
		
		• No treatment where there has been a good response;
		• Palliative care where they do not respond;
		• Where patients do not achieve remission and the cancer returns, options could include:
		  • Surgical intervention targeting the liver metastases;
		  • Immunotherapy; or
		  • Palliative care.

	M6.2 Can these be mitigated, if so how?	M6.2 N/A
	M6.3 What scenarios (differential assumptions) have been explicitly tested to generate best case, worst case and most likely total	M6.3 The costs set out in M3.1 is based on the scenarios developed around the number of patients and the per patient costs.

	cost scenarios?	The cost saving of c. £1.1m is based on:
		• 22-23 patients no longer receiving chemosaturation at a cost of c. £48k per patient.
		
		This could range between c. £0.5m and £1.7m when using the low and high per patient estimates in M2.1.
		
		The cost pressure from an increase in comparator activity of c. £0.5m - £0.6m is based on:
		
		• 8-10 patients receiving TACE at a cost of c. £16k per patient; and
		• 13-14 patients receiving systemic therapy, where:
		  • 50% receive systemic chemotherapy at a cost of c. £4k per patient; and
		  • 50% receive systemic chemotherapy and immunotherapy at a cost of c. £57k per patient.
		
		This could range between c.£0.4 - £0.8m when using the low and high per patient estimates in M2.1.

M7 Value for Money	M7.1 What evidence is available that the treatment is cost effective? *e.g. NICE appraisal, clinical trials or peer reviewed literature* M7.2 What issues or risks are associated with this assessment? *e.g. quality or availability of evidence*	M7.1 No evidence demonstrated M7.2 No evidence demonstrated
M8 Cost Profile	M8.1 Are there non-recurrent capital or revenue costs	M8.1 Not applicable.

	associated with this policy? *e.g. Transitional costs, periodical costs* M8.2 If so, confirm the source of funds to meet these costs	 M8.2 Not applicable.

[i] Macmillan.org.uk, (2016). Ocular melanoma (melanoma of the eye) - Cancer Information - Macmillan Cancer Support. [online] Available at: http://www.macmillan.org.uk/Cancerinformation/Cancertypes/Eye/Melanomaoftheeye.aspx [Accessed 4 Jan. 2016].

[ii] This accounts for the population of England in the UK as a whole (84% of the 500-600). ONS (2015) Population estimates for England and the UK.

[iii] Policy proposition

[iv] Ocular Melanoma Foundation (2015).

[v] Patients may be suitable for chemosaturation provided that they are reasonably fit and have more than a 60% burden of liver disease (i.e. the cancer is taking up over 60% of the liver). Alternatively, patients may be unsuitable if they have significant cardiac or respiratory disease, brain metastasis (as high risk of bleeding during procedure), an abnormal liver anatomy (that would not allow the catheter to pass through), clotting disorders) that increase risk of bleeding). Based on discussions with the policy working group.

[vi] Graell, A., Caminal, JM., Masuet, C., Arias, L., Rubio, M., Pujol, O., Arruqa, J. (2007). Age distribution of uveal melanoma and its relationship to survival. Arch Soc Esp Oftalmol. 2007 Jun;82(6):343-7. [Online] Available at: http://www.ncbi.nlm.nih.gov/pubmed/17573643

[vii] Based on: Singh, A., Sisley, K., Xu, Y., Li, J., Faber, P., Plummer, S., Mudhar, H., Rennie, I., Kessler, P., Casey, G. and Williams, B. (2007). Reduced expression of autotaxin predicts survival in uveal melanoma. British Journal of Ophthalmology, 91(10), pp.1385-1392.

[viii] Based on discussion with the policy working group

[ix] NICE Guidance. (2013). Chemosaturation via percutaneous hepaticartery perfusion and hepatic vein isolation for primary or metastatic liver cancer (IPG488).

[x] Policy proposition

[xi] Based on discussions with the policy working group.

[xii] Based on discussions with the policy working group.

[xiii] Currently patients are recommended chemosaturation by NICE only within the context of research. Based on discussions with the policy working group.

[xiv] NICE IP 1062 [IPG488]. IP overview: Chemosaturation via percutaneous hepatic artery perfusion and hepatic vein isolation for primary or metastatic cancer of the liver. [online] Available at: http://www.nice.org.uk/guidance/ipg488/evidence/chemosaturation-via-percutaneous-hepatic-artery-perfusion-and-hepatic-vein-isolation-for-primary-or-metastatic-liver-cancer-overview2 [Accessed 4 Jan. 2016].

[xv] Dacarbazine is the conventional first line chemotherapeutic agent used to treat liver metastases secondary to ocular melanoma. However, only < 5% of patients respond to systemic chemotherapy as it is usually not tolerated. (Source: Policy Proposition)

[xvi] Based on discussions with the policy working group

[xvii] Jovanovic et al. (2013). Ocular melanoma: an overview of the current status. Int J Clin Exp Pathol. 2013; 6(7): 1230–1244. [Online] Available at: http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3693189/

[xviii] Although the incidence of conjunctival melanoma is increasing (Jovanovic et al, 2013), it is not associated with metastasis and has not therefore been included in the disease incidence projection.

[xix] Population growth figures are derived for over 18s from ONS (2012) population projections.

[xx] Demographic growth projections are derived from ONS (2012) population projections for adults.

[xxi] Based on discussions with the policy working group.

[xxii] Based on discussions with the policy working group.

[xxiii] High Dependency Unit

[xxiv] Intensive Care Unit

[xxv] Based on discussions with the policy working group.

[xxvi] Based on discussions with the policy working group.

[xxvii] Based on discussions with the policy working group

[xxviii] Based on HRG code: RC31Z (IR Procedures - Hepatobiliary – Major), RC32Z (IR Procedures - Hepatobiliary – Intermediate) and RC33Z (IR Procedures - Hepatobiliary – Minor) from the 2014/15 national tariff. The spell tariff is £4,568, or c. £4,945 with a includes a market forces factor (MFF) uplift of 10%, and an efficiency factor of -3.5% and inflation rate of 1.9% for 2015/16 prices.

[xxix] Based on discussions with the policy working group.

[xxx] Please refer to Section 3.2 of VAT Notice 701/557 (https://www.gov.uk/government/publications/vat-notice-70157-health-professionals-and-pharmaceutical-products/vat-notice-70157-health-professionals-and-pharmaceutical-products)

[xxxi] Based on discussions with the policy working group.

[xxxii] The tariffs for CT scans vary dependent on the number of areas and whether the scan is with or without contrast. This is from the 2014/15 national tariff and includes a market forces factor (MFF) uplift of 10%, In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xxxiii] The tariffs for MRI scans vary dependent on the number of areas and whether the scan is with or without contrast. This is from the 2014/15 national tariff and includes a market forces factor (MFF) uplift of 10%, In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xxxiv] The tariffs for CT scans vary dependent on the number of areas and whether the scan is with or without contrast. This includes a market forces factor (MFF) uplift of 10%, In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xxxv] This applies a market forces factor (MFF) uplift of 10% to the tariff in 2014/15 of £2,021. In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xxxvi] NHS UCL Hospitals. Provider to provider services 2014/15 Tariff. [Online] available at: https://www.uclh.nhs.uk/aboutus/wwd/Documents/Provider%20to%20Provider%20Tariff%202014-15.pdf [Accessed 12 Jan. 2016]

[xxxvii] Based on discussions with the policy working group. It is estimated that c.20% of patients would receive 1 cycle, whereas c.80% would receive a second cycle.

[xxxviii] Based on discussions with the policy working group

[xxxix] The lower bound assumes each patient receives two CT scans at a cost of £77 each. The upper bound assumes four MRI scans at a cost of £330 each.

[xl] Please note that figures are rounded to the nearest £1,000.

[xli] The tariffs for CT scans vary dependent on the number of areas and whether the scan is with or without contrast. This is from the 2014/15 national tariff and includes a market forces factor (MFF) uplift of 10%, In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xlii] The tariffs for MRI scans vary dependent on the number of areas and whether the scan is with or without contrast. This is from the 2014/15 national tariff and includes a market forces factor (MFF) uplift of 10%, In 2015/16, an efficiency factor of -3.5% and inflation rate of 1.9% are applied to all costs paid via tariff.

[xliii] Based on HRG code: RC31Z (IR Procedures - Hepatobiliary – Major), RC32Z (IR Procedures - Hepatobiliary – Intermediate) and RC33Z (IR Procedures - Hepatobiliary – Minor) from the 2014/15 national tariff. The spell tariff is £4,568, or c. £4,945 with a includes a market forces factor (MFF) uplift of 10%, and an efficiency factor of -3.5% and inflation rate of 1.9% for 2015/16 prices.

[xliv] This is expected to include the cost of the device. (Source: based on discussions with the policy working group)

[xlv] Based on discussions with the policy working group

[xlvi] Based on discussions with the policy working group

[xlvii] Based on discussions with the policy working group

[xlviii] Based on discussions with the policy working group

[xlix] The lower bound assumes each patient receives two CT scans at a cost of £77 each. The upper bound assumes four MRI scans at a cost of £330 each.

[l] Please note that figures are rounded to the nearest £1,000

[li] Based on the cost per 3 week cycle of dacarbazine of £53 (Source: Scottish Medicines Consortium (2015), "ipilimumab 5mg/mL concentrate for solution for infusion (Yervoy®)" [available online] https://www.scottishmedicines.org.uk/files/advice/ipilimumab_Yervoy_FINAL_Oct_2014_Amended_24.10.14_for_website.pdf) and 6 months of 3 weekly delivery of chemotherapy (Source: 2014/15 National tariff, HRG code SB14Z and SB15Z. Prices include a 10% MFF uplift, an efficiency factor of -3.5% and an inflation uplift of 1.9%).

[lii] Based on the estimated costs for systemic chemotherapy and immunotherapy costs per 6 months for either ipilimumab or pembrolizumab (based on discussions with the policy working group) from Scottish Medicines Consortium (2015), "pembrolizumab 50mg powder for concentrate for solution for infusion (Keytruda®)", [available online] https://www.scottishmedicines.org.uk/files/advice/pembrolizumab__Keytruda___FINAL_October_2015_SMC1086_for_website.pdf.

[liii] Based on discussions with the policy working group.

[liv] This is based on the 'mid' cost estimate in M2.1.

[lv] This assumes that 8-10 patients would instead receive TACE, and the remainder would receive systemic therapy (50% with immunotherapy and 50% without). 'Mid' cost estimates from M2.1 are used.

[lvi] Please note that figures may not sum due to rounding.

[lvii] Based on discussions with the policy working group.