

The London Cancer New Drugs Group – Recommendations November 2007

The London Cancer New Drugs Group is a sub-committee of the London Cancer Networks Steering Group. Members are nominated by and represent the six cancer networks in London and Herts. The group has delegated responsibility to develop recommendations for the managed entry of new treatments in cancer across London. *The terms of reference of the group are available on: www.london.nhs.uk and www.nelm.nhs.uk.*

In July 2005 the group reformatted this presentation of recommendations. This allows a more complete presentation of the issues discussed which may merit further consideration locally.

Ongoing work and potential topics identified for future work programme

Ongoing Work			
Drug	Indication	Date last reviewed	Review documents
Lenalidomide	Multiple myeloma	Sept 2006	LCNDG briefing (link – NHS password required) – awaiting full publication of the clinical trial data (expected Nov 07) before issuing guidance.
Docetaxel	Head and neck cancer	Sept 2006	LCNDG briefing (link – NHS password required) –clinical trial data now published and will be reviewed in Jan 08.
Gemcitabine-based combination regimens	Pancreatic cancer	Sept 2007	LCNDG briefing to be published during Nov 07 – guidance expected by Mar 08.
Rituximab: NB: The group will be reviewing the evidence base but not producing recommendations for these indications	Mantle Cell Lymphoma Hodgkin's Lymphoma Marginal Zone Lymphoma Waldenstroms Post-transplant proliferative disease ITP Haemolytic anaemia	July 2007 Nov 2007 Sep 2007	LCNDG briefing: link Review anticipated Dec 2007 LCNDG briefing: link
Sunitinib	First-line use in renal cell carcinoma	Jul 2007	The evidence base was reviewed again and it was felt that the data, although promising, are not mature enough to allow the group to produce guidance supporting first-line use at this time. This decision will be reviewed when more mature data become available but until then the existing recommendation supporting second-line use remains valid (see later)
Sorafenib	Hepatocellular carcinoma		First draft review anticipated Jan 08
Posaconazole	Treatment and prophylaxis of fungal infections		First draft review anticipated Nov 07
Topotecan and cisplatin	Cervical cancer		First draft review anticipated Jan 08

Potential Topics For Future Work Programme

Drug	Indication	Date last reviewed	Review documents
Bevacizumab	Breast cancer	Jan 2007	Now on NICE agenda (expected Jul 2008) but will use review by Regional Drug & Therapeutics Centre in Newcastle to inform interim guidance if necessary (link).
Bevacizumab	NSCLC.		Was on NICE agenda – but announced that they have suspended the appraisal. Keep monitoring developments
Capecitabine (ECX)	oesophago-gastric cancer		Keep monitoring developments
Carboplatin/gemcitabine	2 nd line ovarian cancer		Keep monitoring developments
Carboplatin/gemcitabine	2nd-line treatment in metastatic breast		Keep monitoring developments
Docetaxel	Gastric cancer		Keep monitoring developments
Exjade	Various oncological conditions		Keep monitoring developments
Ibandronic acid	Bone metastases	Sep 2007	Keep monitoring in light of developments on impact on service.
Lapatinib	Breast cancer		Keep monitoring developments – now on NICE programme (date of publication unknown).
Nilotinib	CML		Keep monitoring developments
Palifermin	prevention of mucositis in autologous transplants.		Keep monitoring developments
Temsirolimus	Advanced renal cell carcinoma		Keep monitoring developments – applied for licence Oct 06. Now on NICE work programme, due Jan 09.
Thalidomide	First line treatment in multiple myeloma		Keep monitoring developments

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Drug	Indication	Date last revised	Status	NICE guidance
Fludarabine and cyclophosphamide	Chronic Lymphocytic Leukaemia (CLL)	Nov 07	Final	None anticipated
<p><u>LCNDG Recommendation</u></p> <p>Combination therapy is not recommended as a first-line therapy although there may be exceptional circumstances when use may be justified (for example when an autograft is being considered).</p>				
<p><u>Specific Issues for further local consideration</u></p> <p>NICE recommends against the use of fludarabine as monotherapy for the first-line treatment of CLL. Although the company additionally supplied supporting data for the use of fludarabine in combination with cyclophosphamide, this was not considered by the Committee as it falls outside of the UK license.</p> <p>The BCSH guideline on the diagnosis and management of CLL, published in 2004, recommends fludarabine or chlorambucil as first-line therapy; FC is recommended if there was an initial response to fludarabine but progression within one year. These guidelines however predated the publication of initial results from CLL4 and are in the process of being updated.</p> <p>The results of a cost utility analysis submitted by the manufacturer to the SMC indicated an incremental cost of FC compared to chlorambucil of £2600-£3200 per QALY, depending on the assumptions made in the calculations of life years.</p> <p>The cost per treatment cycle with FC is lower than that associated with FDR due to a reduced dose of fludarabine (cost of cyclophosphamide is minimal in comparison).</p>		<p><u>Evidence considered by the group</u></p> <p>The main study of interest is the UK Chronic Lymphocytic Leukaemia Trial 4 (CLL4); a three-arm study directly comparing fludarabine plus cyclophosphamide (FC; n=196) to fludarabine monotherapy (FDR; n=194) and chlorambucil (n=387) in the first-line treatment of CLL – i.e. comparing the combination to the current first-line treatments recommended by BCSH. The main findings so far are as follows, after a median follow-up of three years and five months:</p> <ul style="list-style-type: none"> • FC has not demonstrated any superiority in terms of overall survival (OS), which is the study's primary endpoint. The 5-year OS is 54% for the combination, compared to 52% for FDR and 59% for chlorambucil • FC was statistically significantly superior in terms of 5-year PFS – 36% versus 10% for FDR (HR 0.45; 95% CI 0.35-0.59, p<0.00005) and 10% for chlorambucil (HR 0.45; 95% CI 0.37-0.54, p<0.00005) • FC was associated with statistically significantly higher rates of CR (p<0.0001), CR or nodular partial remission (p<0.0004) and overall response (p<0.0001) than FDR monotherapy. <p>FC was associated with a higher incidence of grade 3 or 4 adverse events, including neutropenia, haemolytic anaemia, and nausea and vomiting.</p> <p>Further randomised data are needed to confirm whether the use of oral fludarabine is associated with a comparable efficacy to the IV formulation in the treatment of CLL.</p>		
<p>Links LNDG review of fludarabine plus cyclophosphamide in the treatment of Chronic Lymphocytic Leukaemia (CLL) (link).</p>				

Drug	Indication	Date last revised	Status	NICE guidance
Rituximab	Maintenance treatment for relapsed/refractory follicular lymphoma responding to induction therapy with chemotherapy with or without rituximab.	May 2007	Final	Rituximab for recurrent/refractory stage III/IV follicular NHL expected Dec 2007.

LCNDG Recommendation

The use of rituximab as maintenance therapy for patients with relapsed follicular lymphoma who have responded to induction treatment but have not been exposed to rituximab during prior treatment is supported by the group. Maintenance therapy should be administered as per license at a dose of 375mg/m² every 3 months for a maximum of two years.

Specific Issues for further local consideration

There are few data on long term safety of maintenance treatment therefore risk of any long term complications unknown.

The optimal maintenance dosing regimen and duration of treatment is unknown and there is a lack of data to show R maintenance improves quality of life.

It is not know if choice of induction chemotherapy influences outcome of R maintenance treatment.

The cost of a 2 year maintenance course of R in a patient with average body surface area of 1.73m² is approximately £9800.

The Scottish Medicines Consortium (SMC) has accepted for restricted use within NHS Scotland, R maintenance therapy for patients with relapsed/refractory follicular lymphoma responding to induction therapy with chemotherapy with or without R. Maintenance therapy was considered to be cost effective (£7721 per QALY) by the SMC.

Evidence considered by the group

Short term follow-up from two phase III studies suggest a survival advantage for rituximab R maintenance therapy over observation; one in previously untreated patients and the other in relapsed follicular.

The EORTC 20981 Intergroup study compared R maintenance treatment with observation (OBS) in relapsed or resistant FL (n= 465) after induction with R-CHOP or CHOP. It reported that median PFS was 51.5 months in the R-maintenance group vs 14.9 months in the observation group (HR 0.4, p < 0.001). R maintenance treatment also increased 3 year overall survival rates after second randomisation from 77.1% in the OBS group to 85.1% in the R maintenance group (HR 0.52, p = 0.011).

The unpublished ECOG 1496 study evaluated the efficacy of 2 years of R maintenance therapy in prolonging PFS after CVP induction therapy in 304 previously untreated patients with follicular or small lymphocytic lymphoma. Survival for all patients favoured R for PFS (HR 0.38; 95% CI, 0.28-0.54, p = 3 x 10⁻⁸) and there was a trend towards better OS (0.66; 0.36 to 1.22, p = 0.09). Data for the 237 patients with FL showed that PFS after randomisation was longer in the R group (0.39; 0.27 to 0.57, p = 3 x 10⁻⁷). The estimated PFS at 4 years was 56% for R group vs 33% for OBS group. Estimated OS at 4 years was 88% for R vs 72% (p = 0.03) for OBS.

The studies to date have not reported any unexpected toxicities, but longer follow up is needed to confirm this. The only significant adverse event of note in the EORTC 20981 Intergroup study, was neutropenia which occurred in 10.8% on R maintenance and 5.4 % in the observation arm (p = 0.07), which probably contributed to the higher rate of grade III-IV infection in the R maintenance group (9% vs 2.4%, p = 0.009).

Links

LCNDG review of rituximab for maintenance therapy for follicular non-Hodgkin's lymphoma ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
Sunitinib	Gastrointestinal stromal tumour (GIST) that is resistant to standard doses of imatinib	May 2007	Final	For standard dose imatinib only (2004)

LCNDG Recommendation

Patients who become unresponsive to, or are intolerant of, standard-dose imatinib (400mg daily) should be discussed with a specialist centre (Marsden or UCLH) for consideration and, if appropriate, mutational analyses. In cases of imatinib-resistance the results of mutational analyses should inform treatment choice including eligibility for ongoing clinical trials. (see related guidance on high-dose imatinib in GIST)

Specific Issues for further local consideration

Use of mutational analysis should help target therapy more appropriately but a validated QC process for this is not yet available and may only ever be available in a few centres.

There are clinical trials of treatment strategies for imatinib-resistant GIST underway in a few centres in London – to maximise patient recruitment to these trials it may be appropriate to limit treatment to those centres

How should treatment response be monitored? Should it be restricted to those patients who are genuinely benefiting based on GIST-specific CT response criteria, or exceptionally, the use of FDG-PET?

There is little direct evidence that increasing the dose of imatinib in patients that develop resistance leads to an improvement in outcomes like progression free survival – conversely as stated there is published evidence that sunitinib is associated with a 17 week increase in time to disease progression.

A one year course of imatinib 800mg daily costs approximately £36,000 (excl VAT) compared with about £26,400 for sunitinib

Experts suggest that the incidence of primary resistance to imatinib is approximately 15%, and 50% for secondary resistance at 2 years.

The Scottish Medicines Commission rejected the use of sunitinib in the treatment of imatinib-resistant GIST on the basis that the economic case was not proven. In their analysis they state that when used in this way sunitinib cost around £65,000 per QALY gained over best supportive care.

Evidence considered by the group

There is one fully published Phase III randomised trial which compared sunitinib with placebo in patients that were either resistant to, or intolerant of, imatinib therapy – this trial shows that sunitinib is associated with a 21 week increase in time to disease progression compared to no treatment.

Sunitinib Phase III study

312 patients with imatinib intolerance or resistant GIST randomised to sunitinib 50mg/day or placebo. Results: Longer median TTP with sunitinib vs placebo (27.3 vs 6.4 weeks, HR, 0.28, 95% CI, 0.23- 0.47, p < 0.0001) but a median overall survival could not be calculated. Unpublished data suggest overall survival at 6 months was 79.4% in the sunitinib and 56.9% in the placebo group (HR 0.49; 0.29 to 0.83, p = 0.007, equating to an NNT of 5 to produce one additional survivor at 6 months). At this stage the study was unblinded and all placebo patients crossed over to open label sunitinib. Current analysis from combined and blinded open label phases showed similar median TTP whilst the survival rate in placebo group began to improve at approx 13 weeks, by which time, 83 of 118 (70%) on placebo were on sunitinib. OS at that stage was similar between groups (HR 0.76; 0.54- 1.06, p = 0.107). Adverse events: diarrhoea, hypertension, bleeding, mucositis, skin abnormalities, and altered taste, grade III/IV laboratory abnormalities, elevated LFTs, pancreatic enzymes and creatinine, decreased LVEF, myelosuppression, and electrolyte disturbances more common in sunitinib group.

The survival data are hard to interpret as 70% of patients on placebo had crossed over to sunitinib at week 13 and the trial is now basically a comparison of immediate vs delayed treatment with sunitinib.

There is a view that the trial design used may not reflect clinical practice in that patients with imatinib-resistance might be expected to continue treatment to control the growth of cells that remain sensitive to the drug – in this trial that treatment was stopped.

Links: LCNDG review of high-dose imatinib and sunitinib for imatinib-resistant GIST ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
High dose imatinib (ie 600-800mg daily)	Gastrointestinal stromal tumour (GIST) that is resistant to standard doses of imatinib.	May 2007	Draft	For standard dose imatinib only (2004)
<u>LCNDG Recommendation</u>				
Patients who become unresponsive to, or are intolerant of, standard-dose imatinib (400mg daily) should be discussed with a specialist centre (Marsden or UCLH) for consideration and, if appropriate, mutational analyses. In cases of imatinib-resistance the results of mutational analyses should inform treatment choice including eligibility for ongoing clinical trials. (see related guidance on sunitinib in GIST).				
<u>Specific Issues for further local consideration</u>		<u>Evidence considered by the group</u>		
<p>Use of mutational analysis should help target therapy more appropriately but a validated QC process for this is not yet available and may only ever be available in a few centres.</p> <p>There are clinical trials of treatment strategies for imatinib-resistant GIST underway in a few centres in London – to maximise patient recruitment to these trials it may be appropriate to limit treatment to those centres</p> <p>There is little direct evidence that increasing the dose of imatinib in patients that develop resistance leads to an improvement in outcomes like progression free survival – conversely there is published evidence that sunitinib is associated with a 17 week increase in time to disease progression.</p> <p>How should treatment response be monitored? Should it be restricted to those patients who are genuinely benefiting based on GIST-specific CT response criteria, or exceptionally, the use of FDG-PET?</p> <p>A one year course of imatinib 800mg daily costs approximately £36,000 (excl VAT) compared with about £26,400 for sunitinib.</p> <p>No relevant health economic analyses were identified to help assess the cost-effectiveness of using high-dose imatinib for this indication.</p>		<p>No Phase III studies were identified which directly address this question.</p> <p>Two Phase III studies have compared imatinib 400mg od with 400mg bd, but only in patients who had not previously been treated with imatinib. However, in these studies crossover to higher dose was allowed in cases of disease progression. These data may provide some insight into the efficacy of high-dose treatment in patients that do not respond to conventional therapy. Neither study was designed to quantify the incremental effect of high-dose imatinib on clinically relevant outcomes like overall survival and neither study assessed the impact of high-dose imatinib on quality of life. There is also a phase II study (imatinib 400mg vs 600mg)</p> <p><u>EORTC-STBSG/ISG/AGITG study</u></p> <p>Both regimens associated with similar response rates but statistically significantly better PFS for BD regimen (disease progressed in 263 (56%) on OD vs 235 (50%) on BD; estimated HR; 0.82; 95% CI, 0.69- 0.98; p = 0.026). Interim analysis of 133 patients who had crossed over from OD to BD dose after disease progression (median 112 days on treatment after crossover) noted 3 partial responses and further disease stabilisation in 36 patients – ie a response rate of 29%. The median duration of documented stabilisation in these 39 patients was 153 days. Most common adverse events haematological: anaemia and granulocytopenia. Non haematological: oedema, fatigue, nausea, pleuritic pain, diarrhoea and rash. Most of these events occurred more frequently in the higher dose group.</p> <p><u>S0033 Intergroup study</u></p> <p>This unpublished study of similar design found no survival difference between two doses imatinib. Of 164 patients on OD dose whose disease had progressed, 88 were crossed over to higher dose. Median follow up on crossover 307 days and 5 of 68 evaluable patients (7%) had PR, and additional 20 (29%) developed stable disease. Median PFS 4 months and OS 19 months following crossover. Experts suggest that the incidence of primary resistance to imatinib in patients with GIST is approximately 15%, and 50% for secondary resistance at 2 years.</p>		
Links: LCNDG review of high-dose imatinib and sunitinib for imatinib-resistant GIST (link)				

Drug	Indication	Date last revised	Status	NICE guidance
Docetaxel (as part of the FEC→T regimen)	The adjuvant treatment of node positive breast cancer.	May 2007	Final	Issued Sept 2006

LCNDG Recommendation

The use of the FEC→T regimen as an alternative to the TAC regimen endorsed by NICE for the adjuvant treatment of node positive breast cancer is supported by the group on the basis that although it is unlicensed it appears to be similarly effective but is better tolerated and less expensive.

Specific Issues for further local consideration

FEC→T (fluorouracil, epirubicin, cyclophosphamide, followed by docetaxel) is not currently licensed for use in this indication. Thus NICE was unable to address or endorse its use but did acknowledge that the vast majority of clinical oncologists would prefer to use FEC→T rather than TAC which is licensed.

Based on an average surface area of 1.75m² NICE estimate that six cycles of FEC costs £1608 (or £1728 including wastage), six cycles of TAC costs £6366 (or £7578 including wastage). Using the same baseline costs it can be calculated that 6 cycles of the FEC-T regimen would cost £4308 (or £4869 including wastage)

According to the costing template produced by NICE to support implantation of this guidance it would cost an additional £17,000 per 100,000 population if 18% of eligible patients were switched from FEC to TAC. On the basis of the figures outlined above this cost impact could be reduced by around 30% if FEC→T was used instead of TAC. However if this switch leads to a 30% increase in the percentage of women considered eligible for a docetaxel-containing regimen the overall costs may be increased above the original NICE estimate of cost impact.

Evidence considered by the group

The licence, and subsequent NICE approval, for the use of docetaxel as part of the TAC regimen was based on data reported from a trial (BCIRG001) which compared TAC with FAC (the previously accepted standard therapy) on disease-free survival, overall survival, quality-of-life measures and adverse effects. This study showed that at a median follow-up of 55 months, the estimated rates of disease-free survival (DFS) at five years were 75% among the patients randomised to receive TAC and 68% among those assigned to receive FAC (fluorouracil, doxorubicin, cyclophosphamide). The estimated rates of overall survival (OS) at 5 years were 87% and 81%, respectively. However the incidence of grade 3 or 4 neutropenia was 65.5% in the TAC group and 49.3% in the FAC group and rates of febrile neutropenia were 24.7% and 2.5%, respectively.

The FEC→T regimen was investigated in the PACS01 study. In this study, researchers investigated the impact on disease-free-survival (DFS) at 5 years of the sequential administration of docetaxel following FEC (FEC→T) vs. FEC alone amongst 1944 patients with node positive operable breast cancer and showed that the 5-year DFS rates were 73.2% for FEC and 78.4% for FEC→T. The 5-year OS rates were 86.7% with FEC and 90.7% with FEC→T.

A significantly higher proportion of patients in the FEC group compared to the FEC→T group experienced neutropenia (33.6% vs. 28.1% respectively, p=0.008). However, more patients in the FEC→T group experienced febrile neutropenia (p=0.03) although it was also noted that a significantly higher proportion of patients in the FEC group compared to the FEC→T group required filgrastim (27.0% vs. 22.2%, p=0.01).

Links

LCNDG review of evidence of the FEC→T regimen in the adjuvant treatment of node positive breast cancer ([link](#)).

Drug	Indication	Date last revised	Status	NICE guidance
Dasatinib	The treatment of CML in patients that have failed treatment with imatinib.	May 2007	Final	None anticipated

LCNDG Recommendation

The use of dasatinib (at a maximum dose of 70mg BD) is supported in patients with CML (all phases) who meet European LeukaemiaNet criteria for imatinib failure or have experienced Grade 3 or 4 adverse events when treated with imatinib.

Specific Issues for further local consideration

It costs £37,180 (including VAT) to treat a patient with dasatinib (70mg BD) for one year. This compares with between £22,100 and £44,200 for imatinib used at a dose of between 400mg and 800mg daily.

The Scottish Medicines Consortium (SMC) accepted dasatinib for restricted use within NHS Scotland for the treatment of adults with chronic phase CML and resistance or intolerance to prior therapy including imatinib. However they rejected it for use in patients with accelerated or blast phase disease on the basis that they could not accept the manufacturer's justification of treatment cost in relation to its health benefits.

If dasatinib is accepted for use in the NHS for patients with CML who have failed treatment with imatinib we might expect an average of 1 case per 100,000 population to be eligible for treatment at this moment and for this to increase incrementally over the next few years to perhaps reach a steady state level of 2 cases per 100,000 population. At this level of use, the drug budget would increase by between £37,000 and £74,000 per 100,000 population. If treatment is restricted to patients with chronic phase disease as per the SMC recommendation this would reduce uptake – the SMC state that 26% of patients that are resistant to imatinib have chronic phase disease and therefore the cost impact would decrease by about 60%.

Evidence considered by the group

There are no published Phase III studies of dasatinib available.

There is one fully published Phase II study which compared outcomes in patients randomised to receive dasatinib or high-dose imatinib with chronic-phase disease who are either unresponsive to standard-dose imatinib. With a median follow up of 15 months (range 1 to 21 months) a major cytogenetic response (MCyR) was seen in 52% of dasatinib- treated patients and 33% of imatinib- treated patients. It was also reported that complete cytogenetic responses (CCyR) were seen in 40% and 16% of dasatinib and imatinib treated patients respectively after a minimum of 15 months follow up. 28% and 82% of dasatinib and imatinib treated patients were categorised as treatment failures during a 15 month follow up. The median time to treatment failure was 3.5 months for imatinib and despite 15 months follow up had not yet been reached for dasatinib.

There are single non-comparative Phase II studies of dasatinib in patients with chronic phase, accelerated phase and blast phase disease who are either intolerant of, or unresponsive to imatinib. These describe treatment response rates in terms of haematological and cytogenetic response rates but it is difficult to set the data they provide into any meaningful clinical context. The results available suggest that complete haematological responses can be achieved with dasatinib in 90%, 39% and 26% of patients with chronic, accelerated and blast phase disease respectively. The corresponding results for complete cytogenetic response are 39%, 33% and 24% respectively.

In the comparative trial of dasatinib and high-dose imatinib it is reported that dasatinib is associated with an excess of pleural effusion (17% vs 0), Grade3 to 4 neutropenia (61% vs 39%), Grade 3 to 4 thrombocytopenia (56% vs 14%), an increased need for red-cell transfusions (23% vs 12%) and an increased need for platelet transfusions (14% vs 0). Dasatinib was associated with lower incidences of superficial oedema and fluid retention (15% and 30% respectively compared with 42% and 45% in the imatinib group).

Links: LCNDG review of dasatinib which includes European LeukaemiaNet criteria for imatinib treatment failure ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
Sorafenib	Renal cell carcinoma	July 2007	Final	Anticipated Jan 2009
<p><u>LCNDG Recommendation</u></p> <p>Sunitinib may be used in patients who become unresponsive to, or are intolerant of interferon alfa and in patients for whom interferon alfa is contraindicated. Sorafenib may be used instead of sunitinib in patients for whom it is contraindicated. There is currently no evidence to support the sequential use of sunitinib and sorafenib.</p> <p>The data available to support first-line use of sunitinib, although promising, are not felt to be mature enough to support the use of this agent for this indication at this time.</p>				
<p><u>Specific Issues for further local consideration</u></p> <p>Sorafenib is currently licensed in the EU for the second-line treatment of patients who have failed prior IFNa and/or IL-2 therapy; it is additionally licensed to be used first-line as treatment for those patients for which IFNa or IL-2 therapy is considered to be unsuitable. Patients who may be considered unsuitable for interferon therapy may include the elderly, patients with poor renal function, patients with poor performance status and those with an autoimmune or inflammatory disease.</p> <p>There are no data for the efficacy of sorafenib in first-line treatment versus IFNa or IL-2.</p> <p>There are no set durations of treatment – sorafenib is given continuously until disease progression, unacceptable toxicity or patient refusal. The cost of 24 weeks of treatment (median PFS in the phase III sorafenib trial) would be £15,027 for sorafenib and £13,216 for sunitinib. Given an estimated advanced RCC annual incidence of 6.6 patients per 100,000 population, additional drug costs could reach £99,182 for sorafenib and £87,226 for sunitinib.</p> <p>Quality of life was assessed as a secondary outcome in the phase III TARGETs study, using the Functional Assessment of Cancer Therapy General (FACTG) and the FACT: Kidney Cancer Symptom Index (FKSI). Sorafenib was not associated with an improvement in the mean overall score using either index (significant treatment-related improvements were only observed for three single items in the FKSI, but the study was not adequately powered to detect such differences).</p>		<p><u>Evidence considered by the group</u></p> <p>TARGET is an ongoing phase III trial, which randomised 903 patients with advanced and/or metastatic clear-cell RCC to second-line treatment with sorafenib 400mg BD or placebo. The main results so far are:</p> <ul style="list-style-type: none"> • Median PFS in the sorafenib group of 24 weeks, versus 12 weeks in the placebo group (HR 0.44, 95% CI 0.35-0.55, p<0.000001). • Median OS of 19.3 months for patients in the sorafenib group and 15.9 months for patients in the placebo group (HR 0.77; 95% CI 0.63-0.95, p=0.02). <p>The positive PFS data were from a preliminary analysis, and following this, patients receiving placebo were permitted to cross over to active treatment. The first OS analysis was therefore performed immediately prior to the medication crossover (median follow up of 6.6 months). At this time, the median OS was 14.7 months in the placebo group, and had not been reached in the sorafenib group (HR 0.72; 95% CI 0.54-0.94; p=0.02). The results of a second analysis, performed after 216 out of 452 patients originally randomised to placebo had crossed over to sorafenib, are summarised above.</p> <p>As the predefined levels of significance for the interim survival analyses were however not met (p=0.0005 and 0.009 respectively), a statistically significant difference between the groups has yet to be demonstrated and more mature survival data are awaited.</p> <p>The NCRI Renal Clinical Studies Group prepared the following position statement: “Existing standard therapies for metastatic renal cell cancer are inadequate. Both sorafenib and sunitinib significantly prolong progression free survival in metastatic renal cell cancer and should now be made routinely available in the management of this disease in the UK.”</p> <p>The SMC rejected sorafenib on the basis that cost effectiveness has not been demonstrated (overall cost-effectiveness estimate of £35,523/QALY).</p>		
<p>Links:</p> <p>LNDG review of sunitinib and sorafenib in renal cell carcinoma (link)</p> <p>SMC review of sunitinib in renal cell carcinoma (link)</p> <p>SMC review of sorafenib in renal cell carcinoma (link)</p>				

Drug	Indication	Date last revised	Status	NICE guidance
Sunitinib	Renal cell carcinoma	July 2007	Final	Anticipated Jan 2009

LCNDG Recommendation

Sunitinib may be used in patients who become unresponsive to, or are intolerant of interferon alfa and in patients for whom interferon alfa is contraindicated. Sorafenib may be used instead of sunitinib in patients for whom it is contraindicated. There is currently no evidence to support the sequential use of sunitinib and sorafenib.

The data available to support first-line use of sunitinib, although promising, are not felt to be mature enough to support the use of this agent for this indication at this time.

Specific Issues for further local consideration

Sunitinib is currently licensed in the EU for the second-line treatment of patients who have failed prior IFNa and/or IL-2 therapy. This approval was based on pooled phase II data and mature follow-up data are awaited. It has recently received additional approval from the EMEA for use as first-line therapy, based upon promising preliminary Phase III data versus IFNa.

Sunitinib is given continuously (four weeks 'on treatment' and two weeks 'off treatment') until disease progression, unacceptable toxicity or patient refusal. The cost of 24 weeks of treatment (drug costs only) is £13,216 for sunitinib compared to £15,027 for sorafenib. Given an estimated advanced RCC annual incidence of 6.6 patients per 100,000 population, additional drug costs could reach £87,226 for sunitinib, compared to £99,182 for sorafenib.

Decreases in LVEF of $\geq 20\%$ and below the lower limit of normal occurred in approximately 4% of sunitinib-treated patients and 2% of placebo-treated patients. It is unknown if patients with pre-existing cardiac disease are at a higher risk of developing treatment-related left ventricular dysfunction, as patients who presented with cardiac events within 12 months prior to the trial initiation were excluded from the study. The manufacturer recommends that sunitinib be discontinued in the presence of clinical manifestations of CHF, and the dose should be interrupted and/or reduced in patients without clinical evidence of CHF but with an ejection fraction $< 50\%$ and $> 20\%$ below baseline.

Evidence considered by the group

Data from two phase II studies (n=168) of sunitinib (50mg daily for four weeks, then two weeks 'off therapy', i.e. six week cycles) in patients with metastatic RCC who had failed on or could not tolerate cytokine therapy (IFN alfa or IL-2) have been published. Pooled results showed an ORR of 42% and a median PFS of 8.2 months. The median OS at the time of reporting was 16.4 months for one study, and had not been met in the other.

Recently published interim results from a Phase III study suggest that the use of sunitinib in the first-line treatment of metastatic RCC is associated with an improved PFS (11 months; 95% CI 10-12) over IFNa (5 months; 95% CI 4-6). The median overall survival (secondary endpoint) had not been reached at this time and a final survival analysis will be reported when the data become mature.

The NCRI Renal Clinical Studies Group prepared the following position statement: "Existing standard therapies for metastatic renal cell cancer are inadequate. Both sorafenib and sunitinib significantly prolong progression free survival in metastatic renal cell cancer and should now be made routinely available in the management of this disease in the UK."

The SMC has rejected the second-line use of sunitinib (following failure of IL-2 or IFa) on the basis that cost-effectiveness has not been demonstrated (overall cost effectiveness estimate of £39,000 per QALY gained).

Links

LNDG review of sunitinib and sorafenib in renal cell carcinoma ([link](#))

SMC review of sunitinib in renal cell carcinoma ([link](#))

SMC review of sorafenib in renal cell carcinoma ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
Trastuzumab	Adjuvant treatment of early-stage HER2-positive breast cancer.	Sept 06	Final	Aug 06
<p><u>LCNDG Recommendation</u></p> <p>LCNDG supports the indications approved by NICE but recommends that clinicians refer to the more detailed patient selection and monitoring criteria outlined in the relevant NCRI Clinical Guideline.</p>				
<p>Links</p> <p>NICE – TA 107: Trastuzumab for the adjuvant treatment of early-stage HER2-positive breast cancer (link)</p> <p>NCRI - UK Clinical Guidelines for the Use of Adjuvant Trastuzumab (Herceptin®) With or Following Chemotherapy in HER2-positive Early Breast Cancer (link)</p>				

Drug	Indication	Date last revised	Status	NICE guidance
Gemcitabine	Advanced bladder cancer	July 2006	Final	None anticipated

LCNDG Recommendation

The use of gemcitabine/ cisplatin is supported as it is similarly effective to, and better tolerated than, MVAC.

Specific Issues for further local consideration

Despite no clear consensus that gemcitabine-cisplatin had established itself as the gold standard regimen for the treatment of bladder cancer it was selected by the EORTC/MRC as the control arm of a follow up study several years ago. This makes it ethically difficult to promote MVAC over gemcitabine-cisplatin when it has already been endorsed as a gold standard treatment.

The cost of the MVAC regimen based on an average body surface area of 1.6m² is approximately £202 per cycle whereas the cost of the gemcitabine-cisplatin combination is approximately £843 per cycle (excluding VAT), If 10 people per 100,000 population received four cycles of gemcitabine-cisplatin instead of MVAC per year it would increase treatment costs by almost £26,000 (excluding VAT). Some of this increased cost may be offset from savings resulting from reduced hospitalisation due to adverse effects. Conversely the cost differential could increase if patients are able to tolerate more cycles of GC treatment.

As gemcitabine-cisplatin has been used in both the clinical trial setting and in clinical practice for several years there is a view that the additional costs described may already be reflected in contracts with provider units.

A cost-effectiveness analysis estimates that by using GC instead of MVAC patients would gain an average 0.13 QALYs at an incremental cost of just under £23,000 per QALY (based on 2001 costs).

Evidence considered by the group

Cisplatin-based regimens are the standard choice of treatment for or advanced cancers of the bladder; traditionally the methotrexate, vinblastine, doxorubicin and cisplatin (MVAC) combination was accepted as the regimen of choice

There are a number of Phase II studies assessing the efficacy and tolerability of gemcitabine plus cisplatin in advanced bladder cancer.

One fully published phase III study has evaluated the efficacy and toxicity of GC vs. the standard MVAC regimen. In this study it was shown that the regimens appear to be similarly efficacious, in that median survival with gemcitabine-cisplatin was 13.8 months and 14.8 months with the MVAC regimen. Long-term follow up analysis showed that the 3, 4 and 5 year survival rates for GC were 19%, 16.4% and 13% respectively and those for MVAC were 20.4%, 17.3% and 15.3% (no statistically significant differences)

GC would appear to be better tolerated than MVAC in the treatment of this cancer – with fewer patients developing neutropenia, fever, infection, mucositis and alopecia but more developing anaemia and thrombocytopenia.

In the comparative study patients that had GC received a median 6 cycles of chemotherapy (mean of 4.6 cycles) whereas patients that had MVAC received a median of 4 cycles (mean 3.9 cycles).

Links

LNDG Review of gemcitabine for advanced bladder cancer ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
Cetuximab (Erbix®)	Squamous cell cancer of the head and neck (SCCHN).	May 2006	Final	Expected June 2007 but remains unpublished

LCNDG Recommendation

There is no evidence that cetuximab provides any advantage over the current standard treatment which is chemo-radiotherapy. However the addition of cetuximab to radiotherapy might be considered in patients who cannot tolerate platinum-based chemotherapy and would therefore be treated with radiotherapy alone.

Specific Issues for further local consideration

The use of concurrent chemotherapy and radiotherapy is fast becoming the treatment of choice for locally-advanced SCCHN, and the Phase III trial did not use this as the comparator arm. Therefore the data as it stands currently supports a role of cetuximab plus radiotherapy over radiotherapy alone in the treatment of patients who cannot tolerate platinum-based chemotherapy, which represents a small minority of patients.

The annual incidence of locally-advanced SCCHN (stage III or IV) in England is approximately 12 per 100,000. It is estimated that 30% of these patients will receive radiotherapy alone; if it is assumed that this patient group represent those unable to tolerate chemotherapy (i.e. suitable for treatment with cetuximab), then the additional use of cetuximab in 80% of cases would lead to an estimated additional drug cost of £17,607 per 100,000 population.

When considering costs, it will be important to clarify at present the number of patients who are receiving radiotherapy alone as they are unsuitable for platinum-based chemotherapy. This is likely to be the limited role of cetuximab in SCCHN as there has been no comparison of its efficacy versus chemoradiotherapy, which remains the treatment of choice of this patients group in the majority of centres. Further well designed RCTs are awaited to see whether the role of cetuximab in SCCHN could be expanded.

Evidence considered by the group

In the Phase III trial on which the licensing application was based, patients with locoregionally-advanced SCCHN were randomised to receive high-dose radiotherapy (n=213) or radiotherapy plus weekly cetuximab (n=211) as first-line treatment. After a median follow-up of 54 months, the use of cetuximab plus radiotherapy was associated with benefits over radiotherapy alone in:

- Median duration of locoregional control (24.4 months vs. 14.9 months, p=0.005) – primary outcome
- Median duration of progression-free survival (17.1 months vs. 12.4 months, p=0.006)
- Median duration of overall survival (49.0 months vs. 29.3 months, p=0.03)

The most common adverse events associated with cetuximab are acneiform rash (87% vs. 10% radiotherapy alone) and mild-moderate infusion reactions (11% vs. 5% respectively).

There are Phase II data available (abstract only) for cetuximab monotherapy in the second-line treatment of platinum-refractory recurrent/metastatic SCCHN, demonstrating an overall response rate of around 12%.

One small Phase III trial (n=117) assessed cetuximab in combination with cisplatin in patients with recurrent or metastatic SCCHN – there was no statistically significant difference between the groups in the primary endpoint of progression-free survival (2.7 months cisplatin vs. 4.2 months cisplatin plus cetuximab, p=NS).

Links

LNDG review of cetuximab in head and neck cancer ([link](#))

Drug	Indication	Date last revised	Status	NICE guidance
Lenalidomide	Myelodysplastic syndromes (IPSS Low to Intermediate-1, deletion of chromosome 5q31.1).	May 2006	Final	None anticipated

LCNDG Recommendation

The use of lenalidomide in myelodysplastic syndrome is not recommended as there is a lack of controlled trial evidence available to assess its efficacy and safety.

Specific Issues for further local consideration

Current national treatment recommendations for the IPSS Low grouping state that neither intensive chemotherapy nor stem cell transplantation can currently be recommended for this group and in the IPSS Intermediate-1 (IPSS Int-1) it is recommended that all patients under 65 years should be assessed for fitness/eligibility for allogeneic stem cell transplantation (SCT) as soon as possible after diagnosis. Patients >65 years or <65 years and not suitable for SCT should be offered supportive care and/or considered for growth factor therapy (e.g. erythropoietin).

The cost of 1 year of treatment could be in the region of £40,000 per patient per year (excluding VAT). Given that there is an estimated MDS population of around 1750 patients who might currently be considered suitable for this drug the introduction of lenalidomide for the treatment of MDS may increase drug costs by £118,000 per 100,000 population (excluding VAT).

There is some evidence to support the use of thalidomide in this population although it is not actually recommended in the national treatment guidelines.

Evidence considered by the group

One fully published small study of lenalidomide in MDS (assessing 3 dose regimens: 10mg daily, 25mg daily and 25mg daily for 21 days out of every 28). In this study 24 out of 43 patients recruited (and 55 screened for eligibility) had a haematological response, 21 of which were classified as major (i.e. patients became transfusion independent).

In a larger unpublished Phase II study (n= 215) it is reported that 21.4% of patients treated with lenalidomide achieved transfusion independence.

Neutropenia (65%) and thrombocytopenia (74%) were the most common adverse events associated with treatment. Severe myelosuppression (grade 3 or higher) was dose dependent and necessitated treatment interruption or dose reduction in 25 (58%) patients. Other side-effects reported included pruritus, urticaria and diarrhoea.

Links

LNDG review of lenalidomide in myelodysplastic syndromes (MDS) ([Link](#) - NHS password needed)

Drug	Indication	Date last revised	Status	NICE guidance
Erlotinib (Tarceva)	Non-small cell lung cancer	Mar 2006	Final	Expected April 2007

LCNDG Recommendation

Erlotinib is not generally recommended as a second or third line treatment for locally advanced or metastatic non-small cell lung cancer.

However there is some evidence that certain groups of patients may benefit and might be considered for erlotinib – these include never-smokers and patients with bronchoalveolar disease that present with good performance status.

Specific Issues for further local consideration

It is uncertain at present whether EGFR testing is beneficial in selecting patients for erlotinib treatment and further studies are currently underway that should clarify this. Currently there are no requirements to test patients for eligibility.

Erlotinib is more expensive than currently available treatments, although there will be patient and service benefits associated with its oral formulation. The absence of haematological toxicity with erlotinib could be associated with cost savings to the NHS but it is uncertain whether these would offset the increased drug costs of erlotinib. If in future patient eligibility testing were introduced it would have both a service and cost impact.

The annual incidence of NSCLC in England and Wales is 52 per 100,000. It is estimated that 20% of patients would receive chemotherapy and approximately a third of these would go on to receive second line therapy (3 per 100,000). If this group of patients received 4 months of erlotinib instead of 4 cycles of docetaxel this would incur additional costs of £9300 per 100,000.

When considering costs it will be important to quantify the number of patients unsuitable for other second line therapy who are currently not receiving treatment and the proportion of patients failing other second line therapy who may benefit from a third line option where currently there is none. It is uncertain at present what the uptake will be in both these settings, but these costs will be additional to existing costs and as such will have the potential for significant impact.

Evidence considered by the group

The BR.21 trial (n=731) patients with advanced or metastatic NSCLC were randomised to receive erlotinib monotherapy or placebo, as second or third line treatment. Erlotinib demonstrated benefits over placebo in

- overall survival (6.7 vs 4.7 months, p<0.001)
- overall response rate (8.9 vs 0.9%, p<0.001)
- progression free survival (2.2 vs 1.8 months, p<0.001)
- quality of life.

The most frequent adverse effects associated with erlotinib are rash (76%) and diarrhoea (55%). These were generally mild to moderate in nature with grade 3 or 4 toxicities occurring in 9 and 6% respectively.

There are currently no trials comparing erlotinib with other second line agents. In the pivotal trial for pemetrexed the overall survival and response rates reported for pemetrexed and docetaxel were comparable at 8.3 and 7.9 months and 9.1 and 8.8% respectively.

It is important to note the BR.21 trial with erlotinib recruited more patients with a performance status of two than the pemetrexed/docetaxel trial, 25% compared with around 12% respectively. The BR.21 trial also included patients with a performance status of 3 (9%) and half the patients had received two prior therapies. These patient characteristics are associated with a poorer prognosis.

Links

LCNDG review (March 2006): [link](#)

Drug	Indication	Date last revised	Status	NICE guidance
Pemetrexed (Alimta)	Malignant pleural mesothelioma	July 2005	Final	Due September 2007
<p><u>LCNDG Recommendation</u></p> <p>The group supports the use of pemetrexed to treat mesothelioma in view of it being the only licensed product available for this indication.</p>				
<p><u>Specific Issues for further local consideration</u></p> <ul style="list-style-type: none"> This is the first and only licensed treatment for MPM in the UK. “Standard therapy” is hard to define for this disease and there is some question as to whether cisplatin alone represents this. So the question as to whether pemetrexed offers any real benefit over best supportive care in MPM is still debatable. Based on an incidence of MPM of 3.3 per 100, 000 population in England and cost of 6 courses of pemetrexed and cisplatin of £8737, the cost of using this regimen would be £28,832 per 100,000 population. <p>The increased neutropenia seen in the phase III study could in practice mean higher costs for treating neutropenia and its consequences.</p>		<p><u>Evidence considered by the group</u></p> <p>Main evidence from one phase III study (n=456) in patients with MPM who had not undergone prior chemotherapy and did not have a second primary malignancy or brain metastases. Patients were randomised to a combination of pemetrexed and cisplatin or cisplatin alone.</p> <ul style="list-style-type: none"> The combination regimen extended median survival by nearly 3 months (12.1 vs 9.3 months) from randomisation. <p>The incidence of grade 3 or 4 neutropenia and leukopenia was higher in the combination group, as was the incidence of nausea, vomiting, diarrhoea, dehydration and stomatitis.</p>		
<p>Links LCNDG review, April 2005 (link)</p>				

Recommendations made prior to new format

Treatment	Date last reviewed	Recommendation	Links to supporting documentation	Recommendation status
Neoadjuvant androgen deprivation therapy in prostate cancer	September 05 (confirmed March 2006)	This group recommended the use of neoadjuvant androgen deprivation therapy in specific prostate cancer patients prior to radiotherapy but not surgery.	Evaluation (link) Suggested criteria (link)	Final
Ibandronic acid for bone metastases	May 05 (confirmed March 2006) Currently under review (Nov 07)	There is no evidence to show superiority over existing bisphosphonate treatments in that there are no direct comparative studies available. However, the availability of an oral formulation means that there may be some situations where the use of this agent is preferable. (See also LCNDG recommendations on zoledronic acid).	Ibandronate evaluation (link)	Final
Alemtuzumab for relapsed CLL	May 05 (confirmed March 2006)	In accordance with guidelines from the British Committee for Standards in Haematology, alemtuzumab is recommended in patients without bulky lymphadenopathy, previously treated with alkylating agents refractory to fludarabine. This is a licensed indication.	Alemtuzumab for relapsed CLL Briefing Sheet (link) National Guidelines (link)	Final

Treatment	Date last reviewed	Recommendation	Links to supporting documentation	Recommendation status
Zoledronic acid (Zometa)	March 05 (confirmed March 2006)	For breast and multiple myeloma the use should be guided by existing guidance from ASCO (for breast) and UK Myeloma Forum (outlined in related briefing document). However the evidence for prostate is still controversial and it was concluded there is simply not enough strong evidence to support this indication. Also concluded that choice of bisphosphonate for treatment of hypercalcaemia should be a local one. (See also LCNDG recommendations on ibandronic acid).	Briefing Sheet on zoledronic acid (link) UK Myeloma Forum guidance (link) ASCO guidance (link)	Final
Aprepitant for acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy	Sept 06	The use of aprepitant may be considered in highly emetogenic regimens	ASCO Clinical Guideline for anti-emetics in oncology – 2006 update (link) UKMI/NPC evaluation (link)	Final
¹³¹I tositumomab (Bexxar) and ⁹⁰Y ibritumomab tiuxetan (Zevalin) for non-Hodgkin's lymphoma	January 05 (confirmed March 2006)	Current data insufficient to make any formal recommendation. Awaiting further guidance from BCSH	Bexxar and Zevalin briefing document (link)	Provisional
Gliadel implants for recurrent glioma	March 04 (confirmed March 2006)	There is currently NICE guidance for temozolomide for brain cancer. The place in therapy for Gliadel is unclear in the context of this guidance.	Gliadel Overview briefing document (link)	Final

Treatment	Date last reviewed	Recommendation	Links to supporting documentation	Recommendation status
Interferon for malignant melanoma	March 04 (confirmed March 2006)	Insufficient evidence to support the use of high dose interferon in the adjuvant setting The London Cancer Networks asked to support meta-analysis of individual patient data.	Interferon in malignant melanoma briefing document (link) NICE Guidance on management of skin cancer (link)	Final
Paclitaxel for germ cell tumours in testis	March 04 (confirmed March 2006)	Use of paclitaxel for germ cell tumours in testis, as second line treatment is supported.	Paclitaxel for germ cell tumours of the testis briefing sheet (link)	Final
Thalidomide	February 04 (confirmed March 2006)	Group agreed to recommend that thalidomide should be used in the context of national guidelines on use from the British Myeloma Forum. Users should be aware of: a) differing risk management arrangements made by each supplier and b) should also carry out a local risk assessment. b)	Briefing Sheet on thalidomide (link) & Position paper prepared by the UKMF on behalf of the British Committee for Standards in Haematology (BCSH) (link)	Final
Erythropoietin	November 03 (confirmed March 2006)	LCNDG felt unable to endorse the replacement of blood transfusion by erythropoietin at this stage as the former remains the first line of treatment. However, where blood is not available, or difficult to obtain, and in a number of clinical settings, erythropoietin may be the treatment of choice. These exceptions are recognised and should be agreed locally.	Darbepoetin briefing document (link)	Final
Pegfilgrastim	November 03 (confirmed March 2006)	The currently licensed pegfilgrastim presentations represent a longer duration of treatment than is common in current UK clinical practice. There is no robust evidence to suggest that it offers an advantage in terms of clinical outcomes over filgrastim and, therefore, its routine replacement in place of filgrastim is not recommended. However, in certain clinical settings its use may be cost-effective. Such indications should be defined and agreed locally.	Briefing document to Pegfilgrastim (link)	Final

Treatment	Date last reviewed	Recommendation	Links to supporting documentation	Recommendation status
Rituximab for <ul style="list-style-type: none"> • post-transplant lymphoproliferative disorder • B-cell CLL • haemolytic anaemia • ITP <p>(see above for use as a first-line treatment in NHL)</p>	September 03 (confirmed March 2006) Evidence currently being updated	Use in individuals with: <ul style="list-style-type: none"> • post-transplant lymphoproliferative disorder • B-cell CLL • haemolytic anaemia • ITP may be appropriate and should be considered on a case by case basis”	NICE Guidance (link) Briefing sheet outlining potential indications available (link)	Final
Voriconazole	May 03 (confirmed March 2006)	Insufficient evidence at present to warrant changing to voriconazole from current first line agents; probable role as salvage therapy. More information is needed before roles can be defined by group.	Voriconazole Briefing Document (link)	Final
Bicalutamide in early prostate cancer	May 03 (confirmed March 2006)	In line with the recent MHRA advice use of bicalutamide 150mg tablets should be restricted to men with locally advanced prostate cancer who cannot tolerate treatment with LHRH analogues.	Bicalutamide in early prostate cancer Briefing Document (link) MHRA warning (link)	Final
Caspofungin	May 03 (confirmed March 2006)	Insufficient evidence at present to warrant changing to caspofungin from current first line agents. More information is needed before roles can be defined by group.	Caspofungin Briefing Document (link)	Final

Treatment	Date last reviewed	Recommendation	Links to supporting documentation	Recommendation status
Fulvestrant for advanced breast cancer	May 03 (confirmed March 2006 and again in July 2007)	Not recommended. Group considered that this product offered no clear benefits over existing treatments at this stage.	Briefing document to Fulvestrant (link) An updated review will be published during Nov 2007	Final
Bexarotene	September 02 (confirmed March 2006)	Recommendations made at meeting: <ul style="list-style-type: none"> ▪ Bexarotene may be used as a treatment option for advanced stage cutaneous T-cell lymphoma ▪ Treatment should be made through the one specialist centre in London ▪ Use and patient outcomes on treatment should be monitored and audited and fed back to the networks/PCTs ▪ Requests for funding should be accompanied by a business case – it is anticipated that most of the acquisition costs for bexarotene will be offset by other savings from its use. ▪ Use in the early stages of the disease should be within the context of appropriately controlled clinical trials ▪ GPs will not be asked to prescribe bexarotene 	Briefing Sheet on Bexarotene (link)	Final