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Opdatering af notat om medicin med begrænset effekt

Erfaringer fra NICE om prioritering af sygehus-medicin

Det Nationale Institut
for Kommuners og Regioners
Analyse og Forskning

Opdatering af notat om medicin med begrænset effekt – Erfaringer fra NICE om prioritering af sygehusmedicin kan hentes fra hjemmesiden www.kora.dk

Udgiver: KORA
ISBN: 978-87-7509-909-2
Projekt: 10986

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Forord

Regionernes udgifter til sygehusmedicin har været stigende gennem de senere år, og meget tyder på, at denne udvikling vil fortsætte de kommende år. Dette har fået diskussion vedrørende prioritering af brugen af lægemidler til at blusse op på ny, og herunder diskussion af, om økonomiske overvejelser af forholdet mellem lægemidlets pris og effekt bør inkluderes som vurderingsgrundlag ved godkendelse af sygehusmedicin.

I nærværende notat foretages en opdatering af Dansk Sundhedsinstituts (DSI) tidligere udgivne notat *"Medicin med begrænset effekt. Erfaringer fra NICE om prioritering af sygehusmedicin"*.

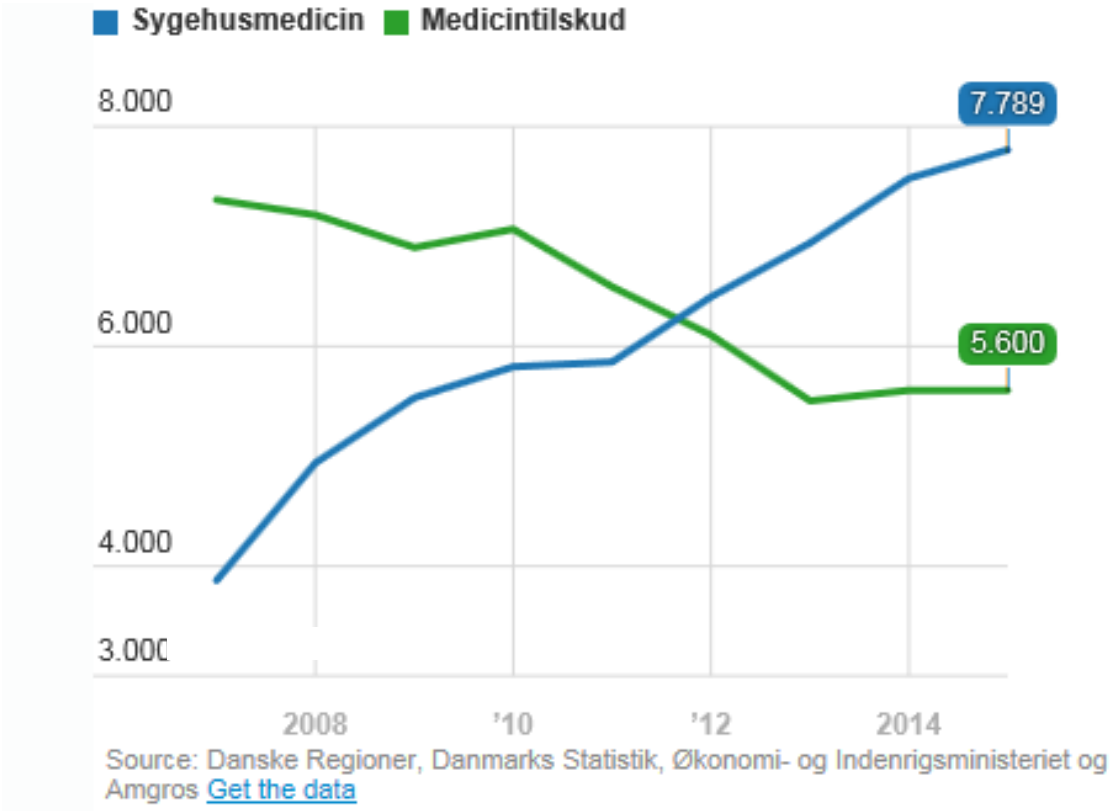
Forfatterne
September 2015

Indhold

1 Indledning

Sygehusmedicin er lægemidler, der er indkøbt af sygehuse og anvendes til behandling af patienter, som fysisk befinder sig på hospitalet (1).[1] Det er Regionerne, som afholder og prioriterer udgifterne til sygehusmedicin. Regionernes udgifter til sygehusmedicin har været stigende gennem de senere år, jf. figur 1.1. Således steg regionernes udgifter til sygehusmedicin med 1,1 milliard kroner mellem 2011 og 2013 (2). I 2014 brugte Regionerne over 7,5 milliarder kroner på sygehusmedicin (3). Til sammenligning skal det nævnes, at det danske sundhedsvæsen årligt koster lidt over 100 milliarder kr. Meget tyder på, at udgifterne til sygehusmedicin også i de kommende år vil stige grundet teknologiske fremskridt og øget overlevelse og sygelighed. Amgros forventer en udgiftsvækst på cirka 10 procent i 2015 og 2016 svarende til en udgift på 8,7 mia. kroner i 2016, eller en merudgift på 7-800 mio. kroner hvert år.

Figur 1.1 Regionernes udgifter til medicin i millioner kroner fra perioden 2007 til 2015



Kilde: Reference (3).

Regionerne har ved flere forskellige tiltag forsøgt at holde udgifterne til sygehusmedicin nede. I 2007 oprettede regionerne således Amgros. Amgros varetager indkøb af medicin til alle offentlige sygehuse i Danmark. En central indkøbsfunktion som Amgros kan give fordele i relation til rabatforhandlinger (1). Amgros er ejet af de fem regioner. Danske Regioner etablerede endvidere i 2009 *Rådet for Anvendelse af Dyr Sygehusmedicin* (RADS) og i 2011 *Koordineringsrådet for ibrugtagning af sygehusmedicin* – KRIS. RADS formål er at ensrette

[1] Patienter med kroniske eller længerevarende sygdomme kan imidlertid i nogle tilfælde få medicin udleveret fra et hospital, selvom de ikke fysisk befinder sig på sygehuset. I disse tilfælde vil medicinen være del af en behandling, der varetages af hospitalslæger fra et hospitalsambulatorium.

brugen af dyr sygehusmedicin på tværs af regionerne. Dette sker, ved at RADS udfærdiger rekommandationslister for, hvilken medicin der skal være lægernes førstevalg, samt behandlingsanvisninger for medicinen. Endvidere understøtter RADS Amgros i deres udbudsprocesser. Det fælles beslutningsgrundlag skaber potentiale for bedre indkøbspriser. KRIS koordinerer ibrugtagning af ny sygehusmedicin, herunder især kræftmedicin. KRIS' vurdering af, hvorvidt ny godkendt medicin og nye gokendte indikationsudvidelser skal ibrugtages som standardbehandling, baseres udelukkende på en faglig vurdering af effekten. Sundheds- og samfundsøkonomiske aspekter indgår således ikke i KRIS' vurderinger.

Modsat Danmark inddrager England aktivt sundhedsøkonomiske vurderinger ved vurdering af ny dyr sygehusmedicin og nye indikationer til eksisterende sygehusmedicin. National Institute for Health and Clinical Excellence (NICE) varetager den eksplicitte prioritering på sygehusmedicinområdet i England. Dette sker ved, at NICE foretager vurdering af omkostningseffektiviteten ved introduktion af ny dyr sygehusmedicin og ved nye indikationer til eksisterende dyr sygehusmedicin.

I 2011 udgav Dansk Sundhedsinstitut (DSI) notater *"Medicin med begrænset effekt. Erfaringer fra NICE om prioritering af sygehusmedicin"* (2). Notatet gennemgik erfaringer fra NICE omkring ibrugtagen af sygehusmedicin, og sammenlignet med danske beslutningsprocesser og omkostningsniveauer, for at se, om der er væsentlige forskelle mellem de to lande.

1.1 Formål

Formålet med dette notat er at opdatere notatet *"Medicin med begrænset effekt. Erfaringer fra NICE om prioritering af sygehusmedicin"*. Det vil sige, at der på baggrund af engelske erfaringer fra NICE identificeres sygehusmedicin med begrænset effekt og/eller stor økonomisk betydning, der er anvendt i Danmark i perioden november 2011 og frem. Samtidig gives der et overblik over udvalgte kommende vurderinger fra NICE.

2 Metode

Indledningsvis gives en kort beskrivelse af, hvilke kriterier der ligger til grund for NICE's anbefalinger, hvilke typer anbefalinger, de giver, samt hvad der sker, hvis NICE ikke anbefaler rutinemæssig brug af et lægemiddel. Herefter er relevante NICE-retningslinjer blevet gennemgået i forhold til, hvilke anbefalinger vurderingen har afstedkommet.

Til identifikation af relevante NICE-retningslinjer blev samtlige teknologivurderinger fra NICE fra oktober 2011 og frem til juli 2015 gennemgået. I udvælgelsesprocessen blev følgende teknologivurderinger sorteret fra:

- Teknologivurderinger, der omhandler ikke-farmakologiske interventioner (fx kirurgi eller medicinsk udstyr)
- Teknologivurderinger, der omhandler lægemidler, der i Danmark hovedsagligt udleveres på apotek (udleveringsgruppe A eller B og håndkøbsmedicin)
- Teknologivurderinger, der siden er blevet erstattet af en ny, revurderet teknologivurdering.

De inkluderede vurderinger af syghuslægemidler (defineret som lægemidler, der i Danmark kun må udleveres på sygehusapotek (BERG) eller udskrives af speciallæge (NBS) til givne indikationer), blev herefter gennemgået i forhold til oplysninger om omkostninger og effekt (målt ved kvalitetsjusterede leveår, QALY's), omkostningseffektivitet (meromkostninger per vunden QALY) ved de enkelte nye lægemidler og/eller indikation, samt hvilken anbefaling vurderingen har afstedkommet. Endeligt blev der udarbejdet en oversigt over omsætningsdata i Danmark i 2014 fra AMGROS for de enkelte lægemidler (i form af hospitalsapotekernes indkøbspriser).

På baggrund heraf er der udarbejdet en oversigt over NICE-beslutninger. Dernæst fremhæves eksempler på de mest udgiftstunge lægemidler (i Danmark), der er:

A. Afvist af NICE
B. Godkendt til begrænset indikation af NICE, eller
C. Godkendt efter indgåelse af aftale om prisnedslag i forhold til listeprisen.

Endvidere blev teknologivurderinger under udarbejdelse af NICE gennemgået for identifikation af nært forestående vurderinger af relevans.

3 NICE's vurderinger

Til grund for sin vurdering af ny dyr sygehusmedicin inkluderer NICE omkostningseffektiviteten i deres teknologivurderinger. Omkostningseffektiviteten af det enkelte lægemiddel opgøres i form af meromkostningen per vundet kvalitetsjusteret leveår (QALY). Siden 2004 har NICE anvendt en tærskelværdi på mellem 20.000 og 30.000 GBP per QALY[2]. Lægemidler med en lavere omkostning end 20.000 GBP per vundet QALY vil typisk blive anbefalet til rutinemæssig brug, mens anbefalingen af lægemidler i tærskelintervallet 20.000 – 30.000 GBP vil afhænge af, om der findes alternative behandlingstilbud til den pågældende patientgruppe, og om teknologien vurderes lovende og dermed giver løfte om udvikling af bedre behandlinger i fremtiden.

Når NICE afgiver sine anbefalinger, falder de overodnet set i tre kategorier:

1. Anbefalet til brug med den af Det Europæiske Lægemiddelagenturs (European Medicines Agency, EMA) godkendte indikation
2. Anbefalet med indikationsbegrænsning i forhold til EMA's godkendelse. Det vil sige for eksempel kun til patienter med svær sygdom, selv om lægemidlet er godkendt til både moderat og svær sygdom
3. Ikke anbefalet.

NICE's anbefaling af et lægemiddel er i nogle tilfælde endvidere betinget af indgåelse af en såkaldt risikodelingsaftale eller aftale om prisnedslag i forhold til listeprisen med producenten af lægemidlet. Ved risikodelingsaftalerne skal producenten af lægemidlet tilbagebetale dele af behandlingsomkostningerne, hvis lægemidlet bruges ud over et vist omfang eller ikke har den ønsket effekt.

3.1 Hvad sker der, hvis NICE siger nej?

Hvis NICE ikke anbefaler rutinemæssig brug af et lægemiddel, er de enkelte NHS trusts ikke forpligtede til at ibrugtage det lægemiddel. NHS trusts kan i princippet vælge at ibrugtage produktet alligevel, men der stilles blot ikke økonomiske midler til rådighed for den enkelte trust til at gøre det. I praksis betyder et NICE afslag derfor, at patienter som er omfattet at NICE afslaget i udgangspunktet ikke vil have mulighed for at modtage offentlig betalt behandling med det givne lægemiddel.

For kræftpatienter er situationen dog anderledes. I april 2011 blev der etableret en særlig Cancer Drug Fund, som har til formål at give adgang til kræftlægemidler, som NICE ikke har anbefalet til rutinemæssig brug. En Cancer Drug Fund-bevilling kræver en individuel ansøgning fra patientens behandlingsansvarlige læge. Herefter gennemføres en sagsbehandling baseret på informationer om tidligere behandling, stadie af sygdommen etc.

Når KRIS godkender et lægemiddel til national ibrugtagning i Danmark, så er det den behandlede læges ansvar at anvende lægemidler på en hensigtsmæssig måde. Principielt adskiller dette sig ikke fra fx den praktiserende læges ansvar for brugen af lægemidler, der er omfattet af generelt tilskud i Danmark. Dette kan i princippet sidestilles med situationen, hvori NICE har anbefalet brugen af et givet lægemiddel. Men hvis NICE har afvist rutinemæssig brug af et kræftlægemiddel, som Cancer Drug Fond efterfølgende vælger at finansiere, så udarbejdes der centrale behandlingsretningslinjer, hvor samtlige kriterier skal

[2] I 2009 blev en mindre gruppe af patienter, hvor restlevetiden forventedes at være kort, og hvor produktet kunne forlænge levetiden med mindst tre måneder, undtaget fra denne grænse.

overholdes, hvis produktet skal opnå offentlig finansiering. Sagsbehandlingen i Cancer Drug Fond, kan således bedst sammenlignes med den sagsbehandling der sker i Danmark ved tildeling af enkelttilskud til medicin i primærsektoren i Danmark, når lægemidler ikke har opnået klausuleret tilskud eller generelt tilskud.

Abiraterone til behandling af prostatakræft er et eksempel på et produkt, som NICE ikke har anbefalet til rutinemæssig brug med begrundelsen, at behandlingen med lægemidlet ikke var tilstrækkelig omkostningseffektivt, men som er omfattet af Cancer Drug Fund. I boks 3.1 er de 10 kriterier oplistet, som patienter skal opfylde, for at offentligt betalt behandling med Abiraterone kan igangsættes i England. I Danmark skal kræftafdelinger i vid udstrækning have udarbejdet lignende behandlingsvejledninger for brugen af Abiraterone. De danske retningslinjer vil ikke nødvendigvis adskille sig markant fra dem, som NICE anvender i England. Men muligheden for at fortolke retningslinjerne i England er markant mindre end i Danmark. Dette følger samme analogi, som når et lægemiddel i primærsektoren i Danmark ikke har opnået generelt tidskud, som følge af, at den behandlingsmæssige effekt ikke er vurderet til at stå i et rimeligt forhold til lægemidlers pris. I det tilfælde vil behandlingsvejledninger sjældent afvige fra den, der ville være gældende, hvis lægemidlet havde været omfattet af generelt tilskud. Erfaringsmæssigt er forbruget imidlertid noget mindre for lægemidler med enkeltskud end for lægemidler med generelt tilskud.

Boks 3.1 Behandlingskriterier for Abiraterone, National Cancer Drug Fund List, 19. januar 2015

DRUG	*NCDF APPROVED CRITERIA*
Abiraterone **Form ref: ABI1_v2.1**	*The treatment of metastatic castration resistant prostate cancer where all the following criteria are met:*
	1. Application made by and first cycle of systemic anti-cancer therapy to be prescribed by a consultant specialist specifically trained and accredited in the use of systemic anti-cancer therapy
	2. *a. Histologically/ cytologically confirmed adenocarcimoma of the prostate* *OR* *b. Clinical suspicion of prostate cancer is high due to high PSA value (>100ng/ml) and evidence of bone metastases (identified by a positive isotope bone scan or sclerotic metastases on plain radiographs)*
	3. Documented metastatic disease
	4. Either PSA progression according to Prostate Cancer Clinical Trials Working Party Group 2 criteria or radiographic progression
	5. Continuing androgen deprivation
	6. Performance status 0 or 1
	7. Asymptomatic (0 or 1) or mildly symptomatic (2-3) as scored on the Brief Pain Inventory Short Form question 3
	8. No visceral disease
	9. No previous chemotherapy
	10. No previous treatment with enzalutamide unless enzalutamide has had to be stopped within 3 months of its start solely as a consequence of dose-limiting toxicity and in the clear absence of disease progression

Lægemidler, der er på Cancer Drug Fund-listen, bliver efter prisreduktioner ofte efterfølgende anbefalet af NICE til rutinemæssig brug. At lægemiddelfirmaet er villigt til at reduce-

re prisen for lægemidlet mod at blive flyttet væk fra Cancer Drug Fund-listen, kan ses som en indikation på, at det for lægemiddelfirmaet er forbundet med betydelige omsætningsmæssige udfordringer at være på Cancer Drug Fund-listen frem for at være generelt anbefalet af NICE.

Cancer Drug Fund administreres af den private velgørende organisation Cancer Research UK, som også indsamler penge til forskning mv. i kræftsygdomme. Fonden blev oprettet som en midlertidig foranstaltning dækkende 2011-2016 med udgangspunkt i et valgløfte fra David Cameron. Fonden var oprindelig på 200 millioner pund om året, men siden er der dog flere gange blevet tilført ekstra midler. For perioden april 2015 til marts 2016 er fondens budgetramme i alt 340 millioner GBP. Dette er dog ikke tilstrækkeligt til at dække alle omkostningerne relateret til de lægemidler, som NICE ikke har anbefalet til rutinemæssig brug. Per marts 2015 blev der således fjernet 16 af de 84 cancerlægemidler/-indikationer, som tidligere var omfattet af Cancer Drug Fund. Det er således ikke længere muligt at søge om "enkelttilskud" til disse behandlinger i det offentlige system i England. Fjernelsen af disse lægemidler fra Cancer Drug Fund forventes at reducere udgifterne med 80 millioner GBP årligt, hvoraf en del forventes skaffet ved, at man giver den farmaceutiske industri et yderligere incitament til prisforhandlinger, nu med udgangspunkt i truslen om helt at fjerne lægemidler fra listen, hvis der ikke kan opnås enighed om prisniveauet.

Lægemidler, som det ikke længere er muligt at få via Cancer Drug Fund, er fx Avastin til indikationen avanceret blære cancer og Halaven, Tyverb and Afinitor, som er rettet mod brystkræft og Jevtana til prostatacancer. Fjernelse af lægemidlerne fra Cancer Drug Fund-listen er sket med henvisning til, at effekten ikke stod mål med omkostningerne, altså, samme argumentation, som da NICE oprindeligt afviste dem.

Cancer Drug Fund udløber til marts 2016, og der pågår p.t. en evaluering af, om den skal fortsætte, og i så fald under hvilke vilkår. Fonden har i dens levetid været stærkt kritiseret for at være urimelig og ulighedsskabede, da den giver kræft en særstilling frem for andre sygdomme, ligesom den har været kritiseret for at underminere NICE i dets arbejde med kontrollere sundhedsvæsenets omkostninger.

4 Vurdering af erfaringer fra NICE

NICE har i alt foretaget 80 vurderinger af syghuslægemidler i perioden oktober 2011 til juli 2015. Den komplette liste over de 80 vurderinger er vedlagt som bilag 1. Tabel 4.1 viser NICE's beslutning i forhold til de 80 lægemidler. I næsten en tredjedel af afgørelserne afviser NICE ibrugtagning af lægemidlet til en given indikation (31,6 %). Den hyppigste afgørelse (35,4 %) er, at NICE anbefaler præparatet med indikationsbegrænsning i forhold til EMA's godkendelse. Det vil sige for eksempel kun til patienter med svær sygdom, selv om lægemidlet er godkendt til både moderat og svær sygdom. I 32,9 % af tilfældene anbefaler NICE lægemidlet uden indikationsbegrænsning.

Tabel 4.1 Overblik over de 80 beslutninger om sygehusmedicin truffet af NICE fra oktober 2011 til juli 2015

Vurdering fra NICE	Andel
Ikke anbefalet	**31,6 %**
Anbefalet med indikationsbegrænsning	**35,4 %**
• Med prisnedslag	(25,3 %)
• Uden prisnedslag	(10,1 %)
Anbefalet	**32,9 %**
• Med prisnedslag	(16,5 %)
• Med Risikodeling	(1,3 %)
• Uden prisnedslag	(15,2 %)
Total	**100 %**

Kilde: Reference (4) og Bilag 1.

Sammenligning af NICE's nyeste beslutninger om sygehusmedicin (Tabel 4.1.) med tidligere beslutninger om sygehusmedicin (Tabel 4.2) viser, at der er sket en stor stigning i andelen af afgørelser, som resulterer i en afvisning af ibrugtagningen af lægemidlet til en given indikation. Endvidere er der sket en udvikling, hvor risikodeling ikke længere spillere en rolle, men hvor krav om prisnedslag i forhold til listeprisen i stedet er afgørende. Det er således i 61 % af anbefalingerne for anvendelse af lægemidlet (med og uden indikationsbegrænsning) en forudsætning for NICE's anbefaling, at der er indgået aftale med producenten om prisnedslag i forhold til listeprisen.

Tabel 4.2 Overblik over 183 beslutninger om sygehusmedicin truffet af NICE i årene 2001 til oktober 2011

Vurdering fra NICE	Andel
Ikke anbefalet	**25,1 %**
Anbefalet med indikationsbegrænsning	**17,5 %**
Anbefalet	**57,4 %**
• Med Risikodeling	(8.7 %)
• Uden risikodeling	(48,6 %)
Total	**100 %**

Kilde: Reference (5).

I de efterfølgende afsnit fremhæves eksempler på konkrete lægemidler og indikationer, der enten er afvist af NICE eller ibrugtaget med restriktion eller med krav om prisnedslag i forhold til listeprisen, men som er anvendt i Danmark i 2014.

Tabellerne er sorteret efter lægemidlets omsætning i Danmark i 2014. Opgørelsen er baseret på lægemiddelstatistiske udtræk fra AMGROS, og omsætningen er opgjort ved brug af hospitalsapotekernes indkøbspriser. Det skal bemærkes, at AMGROS lige som NICE også får prisnedslag i forhold til listeprisen, men at AMGROS prisnedslagene er mindre systematiske i forhold til effekten. AMGROS aftalepriser er ikke offentligt tilgængelige, men i 2013 oplyste Sundhedsministeriet, at ca. 20 % af omsætningen af sygehusmedicin sker til listepriser (6).

Det skal endvidere bemærkes, at statistikken for lægemidlets omsætning i Danmark desværre ikke tillader identificering af lægemiddelbrug på enkelte indikationer. Herved kan de efterfølgende nævnte omsætningstal i Danmark for fx lægemidler, der er afvist af NICE, ikke direkte benyttes til at beregne det direkte besparelsespotentiale, hvis lægemidlerne også i Danmark blev afvist til behandling af de pågældende indikationer. For at kunne beregne besparelsespotentialet af ændret lægemiddelsanvendelse kræves mere detaljeret data, end det har været muligt at skaffe til dette projekt.

4.1 Eksempler på lægemidler, der er afvist af NICE

Af nedenstående tabel fremgår de lægemidler, der 1) er blandt de mest omsatte i Danmark og 2) har fået én eller flere indikationer afvist af NICE.

Tabel 4.3 Udvalgte lægemidler afvist af NICE til givne indikation, sorteret efter totalomsætning på alle indikationer i Danmark 2014

Lægemiddel	Handelsnavn	Indikation	Omsætning
Trastuzumab (i kombination med aromatasehæmmer)	Herceptin®	Metastatisk brystkræft hormon-receptorpositive, der overudtrykker HER-2, førstevalgsbehandling	188 mio. kr.*
Bevacizumab	Avastin®	- Metastatik brystkræft, førstevalgsbehandling. - Fremskreden kræft i æggestokkene, førstevalgsbehandling. - Første gentagelse af platinsensitiv fremskreden kræft i æggestokkene	187 mio. kr.**
Imatinib (Høj dosis)	Glivec®	Kronisk accelereret eller philadelphiakromosompositiv kronisk myeloid leukæmi blastkrise, som er resistent til standarddosis Imatinib	96 mio. kr.***
Pemetrexed (Vedligeholdelsesbehandling)	Alimta®	Ikke-småcellet lungekræft	74 mio. kr.*
Tocilizumab	RoActemra	Systemisk juvenil idiopatisk artritis, som responder på methotrexat, eller som ikke er blevet behandlet med methotrexat	62 mio. kr.*

*Godkendt til andre, større indikationer, **NICE har tidligere afvist brug af Avastin til behandling af kolorektalkræft, nyrecellekræft og ikke-småcellet lungekræft (5).*** NICE har tidligere afvist brug af Glivec® til behandling af adjuvant gastro-intestinale bindevævstumor (GIST) og dosisøgning ved GIST (5).

Kilde: (4), bilag 1 og omsætningsdata fra AMGROS 2014.

De fire øverste lægemidler i tabellen er biologiske kræftlægemidler, mens det sidste lægemiddel er et biologisk antireumatikum.

Herceptin® er primært et brystkræftlægemiddel. Af tabel 4.3 fremgår det, at NICE afviser Herceptin® i kombination med aromatasehæmmer som førstevalgsbehandling til metasta-

tisk HER-2 brystkræft. NICE har tidligere anbefalet anvendelsen af Herceptin® til behandling af en række brystkræftindikationer (7,8). Endvidere har NICE godkendt Herceptin® til en afgrænset gruppe af patienter med mavekræft (9). Herceptin indgår ikke i CDF's liste.

Kræftlægemidlet Avastin® er afvist af NICE (eller vurderingen er afbrudt) på alle sine fem indikationer – metastatisk brystkræft, kræft i æggestokkene, kolorektalkræft, nyrecellekræft og ikke-småcellet lungekræft (Tabel 4.2 samt (10-18)). CDF giver, hvis specifikke kriterier yderligere er opfyldt, adgang til behandling med Avastin® til indikationerne fremskreden kræft i æggestokkene (1. linjebehandling), metastatisk brystkræft, kolorektalkræft (2. og 3. linjebehandling), 3. linjebehandling af lav kvalitet gliom hos børn og epitelial ovariecancer, æggeleder eller primær bughindekræft. Fra marts 2015 er Avastin® fjernet fra CDF's liste ved indikationen kolorektalkræft (1. linjebehandling) og 2. linjebehandling af epitelial ovariecancer, tuba eller primær peritonealcancer. I Danmark anbefaler KRIS Avastin (bevacizumab) i kombination med paclitaxel, topotecan eller pegyleret liposomal doxorubicin – som standardbehandling af patienter med platinresistent recidiverende epitelial ovariecancer, tubacancer eller primær peritonealcancer, der ikke har gennemgået mere end to kemoterapier, og som ikke tidligere har fået behandling med bevacizumab, andre VEGF-hæmmere eller med VEGF-receptormålrettede lægemidler (19).

Glivec® anvendes primært til leukæmi men er også godkendt til behandling af gastrointestinale bindevævstumorer (GIST). NICE anbefaler ikke høj dosis Glivec®-behandling til kronisk accelereret eller philadelphiakromosompositiv kronisk myeloid leukæmi blastkrise, som er resistent over for standarddosis Glivec® (20). Det skal i den forbindelse nævnes, at NICE anbefaler standarddosis Glivec® som en mulighed som første linjebehandling af voksne med kronisk fase philadelphiakromosompositiv kronisk myeloid leukæmi (21). RADS har i forhold til Glivec® kun foretaget lægemiddelrekommandation for nye patienter med kronisk myeloid leukæmi, Glivec® er her det eneste anbefalede lægemiddel (22).

Alimta® anvendes til behandling af visse former for lungekræft og lungehindekræft. NICE afviser brug af Alimta® til vedligeholdelsesbehandling af patienter med lokalt fremskreden eller metastatisk ikke-planocellulær, ikke-småcellet lungekræft (23). Det kan i den forbindelse nævnes, at RADS i deres *Behandlingsvejledning for medicinsk behandling af ikke-småcellet lungecancer (NSCLC) i stadium IV* fra december 2014 skriver, at de vurderer, at "*ca. 95 % af populationen kan behandles med de regimer, der alene indeholder pemetrexed* [Alimta®] *i vedligeholdelsesfasen"* (24). NICE har tidligere behandlet Alimta® i forhold til andre indikationer. NICE har her afvist brug af Alimta® til behandling af lokalt fremskreden eller metastatisk ikke-småcellet lungekræft (25), mens NICE har anbefalet Alimta® som en mulig behandling for lokalt fremskreden eller metastatisk ikke-småcellet lungecancer (NSCLC) (26), som en mulig vedligeholdelsesbehandling for nogle mennesker med ikke-småcellet lungekræft (27), samt en mulig behandling i forhold til lungehindekræft (28).

NICE anbefaler ikke brug af RoActemra til behandling af Juvenil Idiopatisk artritis, også kaldet børnegigt, hos patienter, som responder på methotrexat, eller som ikke er blevet behandlet med methotrexat (29). Jf. tabel 4.5. anbefaler NICE under forudsætning af aftale om prisreduktion RoActemra til behandling af børnegigt, hvor behandling med non-steroide anti-inflammatoriske lægemidler (NSAID), systemiske glukokortikoider og methotrexat er utilstrækkelig (29). RADS har ikke udformet en lægemiddelrekommandation for behandling af børnegigt i Danmark, da patientgruppen er for heterogen og patientantallet samlet er lille. Således er der ca. 1.000 børn under 16 år med børnegigt i Danmark, heraf er ca. 120 nye tilfælde om året. Af disse vil ca. 30-40 børn årligt sættes i biologisk terapi (30). RoActemra anvendes også til behandling af reumatoid artritis (leddegigt) i Danmark (31). NICE anbefaler RoActemra i kombination med methotrexat, som en mulig behandling for leddegigt hos voksne (32).

4.2 Eksempler på lægemidler, der er godkendt af NICE med indikationsbegrænsning

Af nedenstående tabel fremgår de lægemidler, der 1) er blandt de mest omsatte i Danmark og 2) har fået én eller flere indikationer begrænset af NICE.

Tabel 4.4 Udvalgte lægemidler godkendt af NICE til en indskrænket indikation, sorteret efter totalomsætning på alle indikationer i Danmark i 2014

Lægemiddel	Handelsnavn	Indikation	Omsætning	Betinget af prisnedslag
Rituximab	MabThera®	- Follikulært lymfom stadium III-IV, tidligere ubehandlede personer - Alvorligt aktiv granulomatose	205 mio. kr.*	Nej
Abiraterone	Zytiga	Metastaserende kastrationsresistent prostatacancer	151 mio. kr.	Ja
Aflibercept	Eylea	Aldersbetinget nedbrydning af nethinden (våd AMD)	151 mio. kr.	Ja
Ranibizumab	Lucentis®	- Synsnedsættelse grundet maculaødem som følge af retinal veneokklusion - Synsnedsættelse grundet diabetisk macularødem	141 mio. kr.**	Ja
Fingolimod	Gilenya®	meget aktiv attack-vis (recidiverende-remitterende) multipel sklerose, efter beta-interferon svigt	136 mio. kr.	Ja
Sofosbuvir	Sovaldi®	Specifikke grupper af patienter med kronisk hepatitis C	107 mio. kr.	Ja
Imatinib	Glivec®	Adjuvant gastro-intestinale bindevævstumor, ved høj risiko for tilbagefald	96 mio. kr.*	Nej
Dimethyl fumarate	Tecfidera	Aktiv (recidiverende-remitterende) multipel sklerose	62 mio. kr.	Ja
Ustekinumab	Stelara®	Aktiv psoriasis artritis	57. mio. kr.*	Ja

Godkendt til andre, større indikationer. Lucentis® anvendes ved synssvækkelse som følge af skader på nethinden, også skader, som er forårsaget af andre årsager end de her nævnte indikationer, fx aldersbetinget nedbrydning af nethinden og unormal vækst af lækkende blodårer i øjet.

Kilde: (4), bilag 1 og omsætningsdata fra AMGROS 2014.

Af tabel 4.4 fremgår det, at for syv ud af ni af de lægemidler med størst omsætning i Damarker, der er godkendt af NICE med indikationsbegrænsning, gælder det yderligere, at deres godkendelse er betinget af producenten giver prisnedslag i forhold til listeprisen.

MabThera® i kombination med binyrebarkhormon er godkendt af NICE med begrænsning til behandling af patienter med Wegeners Granulomatose, hvor Sendoxan® af forskellige grunde ikke kan anvendes, eller patienter, der har kræft i urinblæren (33). NICE har endvidere godkendt MabThera® i kombination med visse kemoterapeutika, som en mulig behandling for patienter med follikulært lymfom stadium III-IV (første linje behandling) (34). RADS har ikke foretaget behandlingsvejledninger for MabThera® i forhold til ovenstående diagnoser, men det skal nævnes, at MabThera® er anbefalet af RADS som 2. prioritet til biologisk behandling af reumatoid artritis (35).

Zytiga anbefales af NICE i kombination med prednison eller prednisolon som en mulighed for behandling af metastaserende kastrationsresistent prostatacancer hos voksne, hvis deres sygdom har udviklet sig under eller efter behandling med docetaxel (36). RADS anbefaler omvendt, at Abiraterone (Zytiga) er førstevalg, mens docetaxel anbefales som anden linjebehandling af metastatisk kasterationsresistent prostatacancer (37). Zytiga til behandling af metastaserende kastrationsresistent prostatacancer er på CDF's liste.

Øjenlægemidlerne Eylea og Lucentis® er af NICE godkendt med begrænsning. Injektion med Eylea til behandling af aldersbetinget nedbrydning af nethinden (våd AMD) er således kun godkendt af NICE til anvendelse i overensstemmelse med indikationsbegrænsningerne i tidligere retningslinje (38) for Lucentis® (39). I RADS behandlingsvejledning for våd aldersrelateret maculadegeneration anbefales Eylea som første linje behandling. Der er imidlertid nogle kriterier for igangsætning af behandlingen (40). Lucentis® er kun anbefalet af NICE til behandling af synsnedsættelse grundet maculaødem som følge af central eller grenretinal veneokklusion (RVO), hvis behandling med laserfotokoagulation ikke har været gavnlig, eller når laserfotokoagulation ikke er egnet på grund af omfanget af makulær blødning og nedsættelse (41). Af RADS behandlingsvejledning af retinal veneokklusion fremgår det, at Lucentis® er det eneste anbefalede lægemiddel til behandling ved grenveneokklusion (BRVO), mens Lucentis® er anden linjebehandling ved centralveneokklusion (CRVO) (42). NICE anbefaler kun brug af Lucentis® til behandling af synsnedsættelse grundet diabetisk maculaødem, hvis øjet har en central retinal tykkelse på 400 mikrometer eller mere ved begyndelsen af behandlingen (43). I RADS behandlingsvejledning for diabetisk maculaødem genfindes ikke samme krav til retinal tykkelse for påbegyndelse af behandling med Lucentis® (44).

Gilenya® anvendes til behandling af meget aktiv og tilbagevendende multipel sklerose. NICE anbefaler kun brug af Gilenya® til behandling af meget aktiv attakvis (recidiverende-remitterende) multipel sklerose (hvor beta-interferon ikke tidligere har haft den ønskede effekt), hvis patienten har en uændret eller øget tilbagefaldsrate eller vedvarende alvorlige tilbagefald sammenlignet med det foregående år på trods af behandling med beta-interferon (45). Af RADS behandlingsvejledning for behandling af attakvis (recidiverende-remitterende) multipel sklerose (RRMS) fremgår det, at Gileneya® er anden linje behandling, men at Gileneya er første linje behandling af patienter med særlig høj sygdomsaktivitet (46). Tecfidera® anbefales af NICE som en mulig behandling af aktiv (recidiverende-remitterende) multipel sklerose, hvis patienten ikke har meget aktiv eller hurtigt udviklende svær recidiverende-remitterende multipel sklerose. RADS anbefaler Tecfidera® som første linje behandling. I 2014 omsatte Gilenya® i Danmark for 136. mio. kr., mens Tecfidera® omsatte for 62 mio. kr. Prisen per patient per år er lige under 140.000 kr. ved Gilenya®, mens Tecfidera® koster lige over 120.000 kr. Til sammenligning kan det nævnes, at Betaferon® koster omkring 100.000 kr. per patient per år.

Sovaldi® i kombination med henholdsvis peginterferon alfa og ribavirin eller ribavarin alene er nyligt blevet anbefalet af NICE til behandling af visse undergrupper af patienter med kronisk hepatitis C genotype 1-6 (47). I Danmark synes målgruppen for brug af Sovaldi® at være større, jf. RADS behandlingsvejledning for kronisk hepatitis C infektion (48).

NICE anbefaler Glivec® som en mulighed til opfølgende behandling (i op til 3 år) for patienter, der har høj risiko for tilbagefald efter operation for KIT (CD117) positiv gastrointestinal bindevævstumor (baseret på tumorstørrelse, beliggenhed og mitotisk sats) (49). Jf. afsnit 4.1 har RADS i forhold til Glivec® kun foretaget lægemiddelrekommandation for nye patienter med kronisk myeloid leukæmi. Glivec® er på CDF's liste i forhold til adjuvant behandling af gastrointestinal bindevævstumor.

Stelara® er et biologisk lægemiddel til behandling af psoriasis og psoriasisgigt. NICE anbefaler Stelara® (givet alene eller sammen med methotrexat) til behandling af aktiv psoriasis, når tumornekrosefaktor (TNF)-alpha-hæmmere er kontraindiceret, eller hvis personen er blevet behandlet med én eller flere TNF-alpha-hæmmere (50). RADS anbefaler ikke Stelara® som 1. linjebehandling af psoriasisgigt, men Stelara® indgår som efterfølgende linjebehandling i RADS lægemiddelrekommandation (51). NICE har tidligere anbefalet Stelara®, som en behandlingsmulighed for voksne med plaque psoriasis, som opfylder visse kriterier i

forhold til sværhedsgrad og behandlingshistorik, samt under forudsætning af, at producenten tilbagebetaler merudgiften til patienter, som får brug for en højere dosis end standarddosis (52).

4.3 Eksempler på lægemidler, der er godkendt af NICE efter indgåelse af aftale om prisreduktion

Af nedenstående tabel 4.5 fremgår de lægemidler, der 1) er blandt de mest omsatte i Danmark og 2) har fået én eller flere indikationer godkendt efter indgåelse af aftale om prisreduktion i forhold til listeprisen mellem producenten og NICE.

På de to første pladser i tabellen er de to øjenlægemidler Lucentis® og Eylea®, der tilsammen havde en omsætning på tæt ved 300 mio. kr. i 2014. En aftale om prisnedsættelse er et krav fra NICE i alle de tre gældende retningslinjer omhandlende brugen af Lucentis® (41,43,53), men, som det fremgår af afsnit 4.2, er der yderligere indikationsbegrænsninger for anvendelsen af Lucentis® i de to andre retningslinjer (41,43). NICE har udarbejdet to retningslinjer for brugen af Eylea®, den i tabel 4.5 nævnte retningslinje (54) og den i tabel 4.4 nævnte retningsline (39). Af RADS' behandlingsvejledning, gældende fra januar 2015, fremgår det, at Eylea® er første linje behandling af CRVO (55).

Simponi er af NICE godkendt til behandling af tarmsygdommen colitis culcerosa under betingelse af, at producenten tilbyder 100 mg dosis til samme pris som 50 mg dosis.

Kræftlægemidlet Yervoy®, der i Danmark årligt omsætter for 96 mio. kr., er godkendt af NICE til to indikationer (39,54) under betingelse af en prisreduktion. Yervoy® anbefales af KRIS som 1. linjebehandling af patienter med metastaserende malignt melanom i performance status 0-2 uden symptomgivende cerebrale metastaser (19).

Det biologiske gigtmiddel RoActemra er, under forudsætning af aftale om prisreduktion, godkendt af NICE til behandling af børnegigt, hvor behandling med non-steroide antiinflammatoriske lægemidler (NSAID), systemiske glukokortikoider og methotrexat er utilstrækkelig (29). Jf. tabel 4.3 anbefaler NICE ikke brug af RoActemra til behandling af juvenil idiopatisk artritis, også kaldet børnegigt, hos patienter, som responderer på methotrexat, eller som ikke er blevet behandlet med methotrexat (29).

Tabel 4.5 Udvalgte lægemidler godkendt af NICE efter indgåelse af aftale om prisnedsættelse, sorteret efter totalomsætning på alle indikationer i Danmark 2014

Lægemiddel	Handelsnavn	Indikation	Omsætning
Aflibercept	Eylea®	Nedsat syn på grund af maculaødem sekundært til retinal centralveneokklusion (CRVO)	150 mio. kr.*
Ranibizumab	Lucentis®	Synsnedsættelse grundet choroidal neovaskularisering (CNV) som følge af patologisk myopi (PM)	140 mio. kr.**
Golimumab	Simponi	Moderat til svær, aktiv colitis ulcerosa, hvor konventionel behandling har haft utilstrækkelig effekt eller ikke er egnet	100 mio. kr.***
Ipilimumab	Yervoy®	• For tidligere ubehandlet fremskreden (inoperabel eller metastatisk) melanom • For tidligere behandlet fremskreden (inoperabel eller metastatisk) melanom	96 mio. kr.
Tocilizumab	RoActemra	Systemisk juvenil idiopatisk artritis hos børn og unge i alderen 2 år og ældre, hvor behandling med non-steroide anti-inflammatoriske lægemidler (NSAID), systemiske glukokortikoider og methotrexat er utilstrækkelig	61 mio. kr.****

*Også godkendt til behandling af neovaskulær (våd), aldersrelateret maculadegeneration. ** Også godkendt til behandling af: 1)neovaskulær (våd) aldersrelateret maculadegeneration (AMD) og 2) Synsnedsættelse grundet diabetisk maculaødem (DME) eller på grund af maculaødem som følge af retinal veneokklusion (RVO).*** Også godkend til behandling af moderat til svær aktiv reumatoid artritis, spondylartritis og psoriasisartritis. ****Også godkendt til behandling af moderat til svær reumatoid artritis som monoterapi eller i kombination med methotrexat til patienter, der ikke tidligere har været i behandling med methotrexat, eller hvor behandling med methotrexat, DMARDs eller TNF-antagonister er utilstrækkelig eller ikke tåles.

Kilde: (56), bilag 1 og omsætningsdata fra AMGROS 2014.

4.4 Eksempler på lægemidler der behandles af NICE i øjeblikket

Af nedenstående tabel 4.6 fremgår 8 lægemidler/indikationer, der 1) er under aktuel behandling af NICE (56), og 2) må forventes at have et vist udgiftsmæssigt potentiale. Listen er således suppleret med oplysninger om lægemiddelomkostninger per måned eller år, baseret på EMAS godkendte produktresumeer (57) og danske lægemiddelpriser (58) til Apotekets Indkøbspris (AIP).

Tabel 4.6 Udvalgte lægemidler på vej gennem vurdering hos NICE

Lægemiddel	Handelsnavn	Indikation	NICE-vurdering forventet	Omkostninger
Olaparib	Lynparza®	Kræft i æggestokkene, æggeleder og bughinde	Sept. 2015	Ca. 50.000 kr. per måned
Adalimumab, etanercept, infliximab og golimumab	Humira®, Enbrel®, Remicade® og Simponi®	Rygsøjlegigt	Sept. 2015	Ca.138.000 -152.000 kr. per år
Ombitasvir/paritaprevie/ritonavir	Viekirax®	Kronisk hepatitis C	Sept. 2015	Ca. 140.000 kr. per måned
Enzalutamide	Xtandi®	Metastatisk hormonrecidiverende prostatacancer	Sept. 2015	Ca. 34.000 kr. per måned
Idelalisib	Zydelig®	Kronisk lymfatisk leukæmi	Sept. 2015	Ca. 42.000 kr. per måned
Degarelix	Firmagon®	Fremskreden hormonafhængig prostatakræft	Okt. 2015	Ca. 22.000 kr. per år
Adalimumab, etanercept, infliximab, certolizumab pegol, golimumab, tocilizymab og abatacept	Humira®, Enbrel®, Remicade®,Cimzia, Simponi®, RoActemra® og Ovencia®	Leddegigt ikke tidligere behandlet med sygdomsmodificerende antireumatiske lægemidler (disease-modifiying anti-rheumatic drugs – DMARDs), eller efter konventionelle DMARDs har svigtet	Okt. 2015	Ca.125.000 -157.000 kr. per år
Certinib	Zykadia®	Tidligere behandlet anaplastisk lymfom kinase-positiv (ALK-positiv) ikke-småcellet lungecancer	Jan. 2016	Ca. 58.000 kr. per måned

Kilde: (56-58).

I høringsversionen af retningslinje for Lynparza® anbefalede NICE ikke lægemidlet anvendt til behandling af kræft i æggestokkene, æggeleder og bughinde, da effekten vurderes at være for lille i forhold til prisen. Den endelige retningslinje forventes offentliggjort i september 2015. KRIS har i juni i år derimod besluttet at anbefale Lynparza®, som standardbehandling af patienter med platinsensitiv recidiverende BRCA-muteret (germline og/eller somatisk) high-grade serøs epitelial ovarie-, tuba- eller primær peritonealcancer, som responderer (komplet eller maksimalt partielt) på platinbaseret kombinationskemoterapi (57).

De biologiske lægemidler til behandling af henholdsvis rygsøjlegigt og leddegigt (Humira® ,Enbrel®, Remicade®, Cimzia, Simponi®, RoActemra® og Ovencia®) er alle inkluderet i RADS' behandlingsvejledning for behandling af henholdsvis rygsøjlegigt (59) og leddegigt (60). Visse kriterier skal imidlertid være opfyldt for behandling med biologisk lægemiddel, ligesom beslutningen om behandling med biologiske lægemidler altid skal træffes ved en ekspertvurdering af patientens diagnose, sygdomsstatus og behandlingserfaring.

Det orale lægemiddel Viekirax® til behandling af kronisk hepatitis C er i 2015 blevet tilføjet RADS' behandlingsvejledning (48).

KRIS besluttede i februar 2015 at anbefale lægemidlet Xtandi® til behandling af prostata kræft før kemoterapi, som standardbehandling på alle behandlende afdelinger i Danmark (61). Ligeledes besluttede KRIS i december 2014, at anbefale Zydelig® til behandling af patienter med kronisk lymfatisk leukæmi, CLL (62).

Lægemidlet Firmagon® indgår i RADS' behandlingsvejledning for endokrin behandling af prostatakræft (63).

EMA godkendte i maj 2015 Zykaida® til behandling af patienter med fremskreden anaplastisk lymfomkinase-positiv (ALK positiv) ikke-småcellet lungekræft, der tidligere er behandlet med crizotinib. På nuværende tidspunkt anvendes Zykaida® ikke rutinemæssigt i Danmark.

5 Konklusion

I dette notat er NICE's beslutninger vedrørende ibrugtagen af sygehusmedicin fra november 2011 og frem gennemgået og sammenlignet med danske beslutningsprocesser og omkostningsniveauer.

Af analyserne fremgår det, at der er eksempler på, at NICE og de danske myndigheder når til samme beslutning om restriktiv brug af lægemiddel til en given indikation. Der er imidlertid også en række eksempler på lægemidler, der i Danmark anvendes til specifikke indikationer, mens disse er afvist af NICE (fx kræftlægemidlerne Avastin® og Alimta®). Ligeledes er der en række eksempler på, at NICE kun har godkendt lægemidler til en afgrænset del af den oprindelige indikation, mens de samme lægemidler i Danmark anvendes til den brede indikation (fx Eylea® og Lucentis®). Yderligere ses en tendens til, at mange af NICE's anbefalinger for anvendelse af et givent lægemiddel er betinget af et krav om prisnedslag i forhold til listeprisen.

Overordnet er det fundne mønster i dette notat det samme, som i notatet fra 2011. NICE afviser således stadig en del lægemidler, og for en del lægemidler giver de kun godkendelse til en afgrænset del af den oprindelige indikation, hvor vi i Danmark anvender lægemidlet til en bredere indikation. I forhold til 2011 ses der imidlertid en udvikling, hvor risikodeling ikke længere spillere en rolle, men hvor krav om prisnedslag i forhold til listeprisen i stedet er afgørende. Det er således i 61 % af anbefalingerne for anvendelse af lægemidlet (med og uden indikationsbegrænsning) en forudsætning for NICE's anbefaling, at der er indgået aftale med producenten om prisnedslag i forhold til listeprisen. Foruden den store andel af anbefalinger, der er betinget af en prisreduktion, ses det hyppigt i England, at et produkt flytter fra Cancer Drug Fund-listen til NICE's liste over mere generelt godkendte lægemidler, efter der er aftalt en prisreduktion.

Litteratur

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(3) Toft ONM. Ubehagelig medicindiskussion presser sig på. Altinget: Sundhed 2015;11. marts.

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NICE technology appraisal guidance [TA242]. 2012.

(13) National Institute for Health and Care Excellence (NICE). Bevacizumab in combination with a taxane for the first-line treatment of metastatic breast cancer. NICE technology appraisal guidance [TA 214]. 2011.

(14) National Institute for Health and Care Excellence (NICE). Bevacizumab in combination with oxaliplatin and either fluorouracil plus folinic acid or capecitabine for the treatment of metastatic colorectal cancer. NICE technology appraisal guidance [TA212]. 2010.

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NICE technology appraisal guidance [TA 178]. 2009.

(17) National Institute for Health and Care Excellence (NICE). Bevacizumab for the treatment of non-small-cell lung cancer (terminated appraisal).

NICE technology appraisal guidance [TA148]. 2008.

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(21) National Institute for Health and Care Excellence (NICE). Dasatinib, nilotinib and standard-dose imatinib for the first-line treatment of chronic myeloid leukaemia (part review of technology appraisal guidance 70). NICE technology appraisal guidance [TA251]. 2012.

(22) Rådet for Anvendelse af Dyr Sygehusmedicin. Lægemiddelrekommandation for nye patienter med kronisk myeloid leukæmi (CML). 31. januar 2013.

(23) National Institute for Health and Care Excellence (NICE). Pemetrexed maintenance treatment following induction therapy with pemetrexed and cisplatin for non-squamous non-small-cell lung cancer. NICE technology appraisal guidance [TA309]. 2014.

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(26) National Institute for Health and Care Excellence (NICE). Pemetrexed for the first-line treatment of non-small-cell lung cancer. NICE technology appraisal guidance [TA181]. 2009.

(27) National Institute for Health and Care Excellence (NICE). Pemetrexed for the maintenance treatment of non-small-cell lung cancer. NICE technology appraisal guidance [TA190] 2010.

(28) National Institute for Health and Care Excellence (NICE). Pemetrexed for the treatment of malignant pleural mesothelioma. NICE technology appraisal guidance [TA135]. 2008.

(29) National Institute for Health and Care Excellence (NICE). Tocilizumab for the treatment of systemic juvenile idiopathic arthritis. NICE technology appraisal guidance [TA238]. 2011.

(30) Rådet for Anvendelse af Dyr Sygehusmedicin. Baggrundsnotat for biologisk behandling af juvenil idiopatisk artritis (JIA). Version 1.1. 2014.

(31) Rådet for Anvendelse af Dyr Sygehusmedicin. Lægemiddelrekommandation for biologisk behandling af reumatoid artritis. Version 2.4. 2014.

(32) National Institute for Health and Care Excellence (NICE). Tocilizumab for the treatment of rheumatoid arthritis (rapid review of technology appraisal guidance 198). NICE technology appraisal guidance [TA247]. 2012.

(33) National Institute for Health and Care Excellence (NICE). Rituximab in combination with glucocorticoids for treating anti-neutrophil cytoplasmic antibody-associated vasculitis. NICE technology appraisal guidance [TA308]. 2014.

(34) National Institute for Health and Care Excellence (NICE). Rituximab for the first-line treatment of stage III-IV follicular lymphoma: (review of NICE technology appraisal guidance 110). NICE technology appraisal guidance [TA243]. 2012.

(35) Rådet for Anvendelse af Dyr Sygehusmedicin. Lægemiddelrekommandation for biologisk behandling af reumatologiske lidelser. 2013.

(36) National Institute for Health and Care Excellence (NICE). Abiraterone for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen. NICE technology appraisal guidance [TA259]. 2012.

(37) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning for medicinsk behandling af metastatisk kastrationsresistent prostatacancer, mCPRC. Version 1.1. 2014.

(38) National Institute for Health and Care Excellence (NICE). Ranibizumab and pegaptanib for the treatment of age-related macular degeneration. NICE technology appraisal guidance [TA155]. 2008.

(39) National Institute for Health and Care Excellence (NICE). Aflibercept solution for injection for treating wet age related macular degeneration. NICE technology appraisal guidance [TA294]. 2013.

(40) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning inklusiv lægemiddelrekommandation for behandling af våd aldersrelateret maculadegeneration (Våd AMD). Version 1. 2014.

(41) National Institute for Health and Care Excellence (NICE). Ranibizumab for treating visual impairment caused by macular oedema secondary to retinal vein occlusion. NICE technology appraisal guidance [TA283]. 2013.

(42) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning inklusiv lægemiddelrekommandation for behandling af retinal veneokklusion. Version 1.0. 2014.

(43) National Institute for Health and Care Excellence (NICE). Ranibizumab for treating diabetic macular oedema (rapid review of technology appraisal guidance 237). NICE technology appraisal guidance [TA274]. 2013.

(44) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning inklusiv lægemiddelrekommandation for behandling af diabetisk maculaødem. Version 1.0. 2014 .

(45) National Institute for Health and Care Excellence (NICE). Fingolimod for the treatment of highly active relapsing–remitting multiple sclerosis. NICE technology appraisal guidance [TA254]. 2012.

(46) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning inklusiv lægemiddelrekommandation for sygdomsmodificerende behandling af multipel sklerose. Version 3.6. 2015.

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(48) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning for behandling af kronisk hepatitis C infektion. Version: 2.2. 2015.

(49) National Institute for Health and Care Excellence (NICE). Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (review of NICE technology appraisal guidance 196). NICE technology appraisal guidance [TA326]. 2014.

(50) National Institute for Health and Care Excellence (NICE). Ustekinumab for treating active psoriactic arthritis (rapid reviews of technology appraisal guidance 313). NICE technology appraisal guidance [TA340]. 2015.

(51) Rådet for Anvendelse af Dyr Sygehusmedicin. Lægemiddelrekommandation for biologisk behandling af Psoriasis Artritis (PsA). Version 2.2. 2014.

(52) National Institute for Health and Care Excellence (NICE). Ustekinumab for the treatment of adults with moderate to severe psoriasis. NICE technology appraisal guidance [TA180]. 209.

(53) National Institute for Health and Care Excellence (NICE). Ranibizumab for treating choroidal neovascularisation associated with pathological myopia. NICE technology appraisal guidance [TA298]. 2013.

(54) National Institute for Health and Care Excellence (NICE). Aflibercept for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion. NICE technology appraisal guidance [TA305]. 2014.

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(60) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning for biologisk behandling af Reumatoid Artitis (RA). Version: 2.2. 2014.

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(63) Rådet for Anvendelse af Dyr Sygehusmedicin. Behandlingsvejledning for Endokrin behandling af Cancer Prostatae. Version 2.0. 2013.

Bilag 1 Oversigt over de inkluderede NICE-retningslinjer

Appraisal Number	Year of Publication	Process	Technology	Condition	Categorisation	Comment	Cost in £	QALYs gained	Cost pr. QALY	Reference	Omsætn. DK 2013 1000 kr.	Handelsnavn
TA238	2011		Tocilizumab	Treatment of systemic juvenile idiopathic arthritis in children and young people aged 2 years and older whose disease has responded inadequately to non-steroidal anti-inflammatory drugs (NSAIDs), systemic corticosteroids and methotrexate	Recommended	The recomendation is based on that the manufacturer makes tocilizumab available with the discount aggreed as part of the patient access scheme	The average cost of treatment is £7987.20 per year for a 30 kg patient and £9984 per year for a 25 kg patient, assuming no wastage. The manufacturer of tocilizumab (Roche Products) has agreed a patient access scheme with the Department of Health wich makes tocilzumab available with a discount applied to all invoices.		Committee concluded that the resulting cost-effectiveness estimate would be at the lower end of this range.	http://www.nice.org.uk/guidance/ta238/resources/guidance-tocilizumab-for-the-treatment-of-systemic-juvenile-idiopathic-arthritis-pdf	61.701	RoActemra
TA238	2011		Tocilizumab	Treatment of systemic juvenile idiopathic arthritis in children and young people aged 2 years and older whose disease continues to respond to methotrexate or who have not been treated with methotrexate	Not Recommended		The average cost of treatment is £7987.20 per year for a 30 kg patient and £9984 per year for a 25 kg patient, assuming no wastage. The manufacturer of tocilizumab (Roche Products) has agreed a patient access scheme with the Department of Health wich makes tocilzumab available with a discount applied to all invoices.			http://www.nice.org.uk/guidance/ta238/resources/guidance-tocilizumab-for-the-treatment-of-systemic-juvenile-idiopathic-arthritis-pdf	61.701	RoActemra
TA239	2011		Fulvestrant	Treatment of locally advanced or metastatic breast cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The first month of treatment with fulvestant 500 mg includes an additonal loading dose adminstered 2 weekes after the initial dose, resulting in a cost of £1044.82 for the first month, and £522.41 per month in subsequent months.		ICER £35,000 per QALY gained	http://www.nice.org.uk/guidance/ta239/resources/guidance-fulvestrant-for-the-treatment-of-locally-advanced-or-metastatic-breast-cancer-pdf	23.429	Faslodex*
TA240	2011		Panitumumab in combination with chemotherapy	Treatment of metastatic colorectal cancer (terminated appraisal)	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta240/resources/guidance-panitumumab-in-combination-with-chemotherapy-for-the-treatment-of-metastatic-colorectal-cancer-terminated-appraisal-pdf	19.929	Vectibix
TA241	2012		Nilotinib	Treatment of chronic or accelerated phase Philadelphia-chromosome-posiive chronic myeloid leukaemia (CML) in adults: Whose CML is resitant to treatment with standard-dose imatinib or who have imatinib intolerance	Recommended	Partially updates of guidance TA70. Recommendation in line with marketing authorisation. The recomendation is based on that the manufacturer makes tocilizumab available with the discount aggreed as part of the patient access scheme	Costs £2643 for a 200 mg tablet pack (excluding VAT). The cost of nilotinib treatment is £31,711 per year, asuming a treatemnt regimen of 400 mg twice daily		The Novartis' adjusted ICER of £22,800 er QALY gained was too optimistic, however, with the patient access scheme in place, the use of nilotinib for the treatment of imatibib-rsistant CML could be regarded as a cost-effecite use of NHS resources	http://www.nice.org.uk/guidance/ta241/resources/guidance-dasatinib-highdose-imatinib-and-nilotinib-for-the-treatment-of-imatinibresistant-chronic-myeloid-leukaemia-cml-part-review-of-nice-technology-appraisal-guidance-70-and-dasatinib-and-nilotinib-for-peo-pdf	24.748	Tasigna
TA241	2012		Dasatinib	Treatment of chronic, accelerated or blast-crisis phase CML in adults with imatinib intolerance or whoose CML is resistant to treatment with standard-dose imatinib	Not Recommended	Partially updates of guidance TA70. At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Dasatinib is available at a cost of £2504.96 for a 100 mg 30-tablet pac (excluding VAT). The cost of dasatinib is £30,477 per year, assuming a treatmeent regimen of 100 mg once daily.		The Committee noted that treatment for the blast-crisis phase is different from that used in the other phases. To the extent that dasatinib could be considered a stand-alone treatment, the Committee concluded that the evidence was particularly limited	http://www.nice.org.uk/guidance/ta241/resources/guidance-dasatinib-highdose-imatinib-and-nilotinib-for-the-treatment-of-imatinibresistant-chronic-myeloid-leukaemia-cml-part-review-of-nice-technology-appraisal-guidance-70-and-dasatinib-and-nilotinib-for-peo-pdf	36.050	Sprycel
TA241	2012		High-dose imatinib	Treatment of chronic, accelerated or blast-crisis phase Philadelphia-crhomosome-positive CML that is resistant to standard-dose imatinib	Not Recommended	Partially updates of guidance TA70. At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Imatinib costs £1724 for a 400 mg (december 2010, excluding VAT). The cost is £41,960 per year assuming a treatment regimen of 400 mg twice daily.		dominated (more expensive and less effective) in all models	http://www.nice.org.uk/guidance/ta241/resources/guidance-dasatinib-highdose-imatinib-and-nilotinib-for-the-treatment-of-imatinibresistant-chronic-myeloid-leukaemia-cml-part-review-of-nice-technology-appraisal-guidance-70-and-dasatinib-and-nilotinib-for-peo-pdf	95.933	Glivec*
TA242	2012		Cetuximab (montherapy or combination chemotherapy)	Treatment of people with metastatic colorectal cancer that has progressed after first-line chemotherapy	Not Recommended	Updates of guidance TA150 and TA 118. At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Cetuximab plus best supportive care: Estimated mean time 4,8 months, drug costs £14,400, drug administration costs £5500. Cetuximab plus irniotecan versus best supportive care: Estimated mean time 8.8 months, drug costs £32,000 and drug administration £12,700		The most plausible ICER for cetuximab plus best supportive care was £90.000 per QALY gained and for Cetuximab plus irinotecan plus best supportive care the ICER was £ 88,000 per QALY gained, both compared with best supportive care	http://www.nice.org.uk/guidance/ta242/resources/guidance-cetuximab-bevacizumab-and-panitumumab-for-the-treatment-of-metastatic-colorectal-cancer-after-firstline-chemotherapy-pdf	32.485	Erbitux*

TA242	2012		Bevacizumab in combination with non-oxaliplatin (fluoropyrimidine-based) chemotherapy	Treatment of people with metastatic colorectal cancer that has progressed after first-line chemotherapy	Not Recommended	Updates of guidance TA150 and TA 118. At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available. It was not possible to confirm by how much bevacizumab in combination with non-oxaliplatin (flueropyrimidine-based) chemotherapy would extend life when used as second-line therapy, and evidence from previous assesments of bevacizumab with other combination regimens or for first-line treatmen does not allow a justification for a postive recommendation	The recommended dosage is 5 or 10 mg/kg of body weight once every 2 weeks or 7.5 or 15 mg/kg of body weight once every 3 weeks. The price o af 100-mg vial is £242.66, and a 400-mg vial is £924.40 (excluding VAT).			http://www.nice.org.uk/guidance/ta242/resources/guidance-cetuximab-bevacizumab-and-panitumumab-for-the-treatment-of-metastatic-colorectal-cancer-after-firstline-chemotherapy-pdf	187.032	Avastin*
TA242	2012		Panitumumab monotherapy	Treatment of people with metastatic colorectal cancer that has progressed after first-line chemotherapy	Not Recommended	Updates of guidance TA150 and TA 118. At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The recommende dosage is 6 mg/kg of body weight once every 14 days. The price of a 100-mg vial is £379.29, and a 400-mg vial is £1517.16 (excluding VAT).		The Committee noted the most plausible ICER lies between £110.000 and £150,000 per QALY gained	http://www.nice.org.uk/guidance/ta242/resources/guidance-cetuximab-bevacizumab-and-panitumumab-for-the-treatment-of-metastatic-colorectal-cancer-after-firstline-chemotherapy-pdf	19.929	Vectibix
TA243	2012		Rituximab	Treatment of stage III-IV follicular lymphoma	Option	Update of guidance TA110. Recommended as a option for use in previously untreated people.	The recommended dose of rituximab in combination with chemotherapy for induction treatment of previusly untreated pateins with follicular lymphoma is 375 mg/m body survace area, per cycle, for up to eight cycles, adminstered on day 1 of the chemotherapy cycle. The cost of one 10-ml (100-mg) vial is £174.63 and one 50-ml(500-mg) vial is £873.15 (excluding VAT). For a person with a body survace area of 1.85 m and assuming vial wastage, the cost per infusion of rituximab induction treatment is £1222.41 (excluding VAT).		The assessment Group calculated an ICER of £7720 per QALY gained for rituximab plus CVP, £10,800 per QALY gained for rituximab plus CHOP and £9320 per QALY gained for rituximab plus MCP. The committee did not acept hat the analyses fully reflectd how rituximab was used in clinical practice and the ICERs increased when it was assumed that rituximab first-line maintenance treatment was provided and if there was a loss of efficay when rituximab was used as a re-treatment. However, the Committee was persuaded that this uncertainty was not such that t increaed the ICERs to above the treshold range (£20,000-30,000).	http://www.nice.org.uk/guidance/ta243/resources/guidance-rituximab-for-the-firstline-treatment-of-stage-iiiiv-follicular-lymphoma-pdf	205.206	Mabthera*
TA247	2012		Tocilizumab in combination with methotrexate		Option	Update of guidance TA198. Recommended as an option for use in adults if the disease has resonded inadequately to disease-modifying anti-rheumatic drugs (DMARDs) and it is used as described for tumour necrosis factor (TNF) inhibtor treatmens in Adalimumab, etanercept and infliximab for the treatment of rheumatoid arthritis. Or if the disease has resonded inadequately to DMARDs and a TNF inhibitor and the person cannot receive rituximab. Or the disease has responded inadequately to one or more TNF inhibitor treatments and to rituximab. The recommendation is based on that the manufacturer makes tocilizumab available with the discount aggreed as part of the patient access scheme	The recommended dosage is 8 mg/kg, given once every 4 weeks. For people whose body weight is more tahn 100 kg, doses exceeding 800 mg per infusion are not reccomended. Tocilizumab is available in three vial sizes, which are prices at £102.40 for an 80-mg vial, £256 for a 200-mg vial and £512 for a 400-mg vial. The cost for tocilizumab as reported by the manuacturer is £9295 per year for a patient weighing approximately 70 kg.		DMARD-IR population: three sequences were extendendly dominated (less effective than and at least as costly as a combination of other drug sequences. When tocilizumab is the third biological in the sequence the most plausible estimate of the ICER is £28,400 per QALY gained. The committee accepted that some uncertainty around the point estimates of the ICERs was likely. DMARD-IR rituximab intolerant population: ICER ranged form £10,700 per QALY gained for the sequence in which entanercept followed tocilizumab to £30,100 per QALU gained in the sequence where tocilizumab followed etanercept. TNF-IR population: ICER of £18,500 per QALY gained for tocilizumab following rituximab.	http://www.nice.org.uk/guidance/ta247/resources/guidance-tocilizumab-for-the-treatment-of-rheumatoid-arthritis-rapid-review-of-technology-appraisal-guidance-198-pdf	61.701	RoActemra
TA250	2012		Eribulin	Treatment of locally advanced or metastatic breast cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The cost of eribulin mesilate is £313 per 2 ml vial (0.44 mg/ml eribulin;excluding VAT). The manufacturer has agreed a patient access scheme with the Department of Health, wich makes eribulin avilable at a discounted price.		Eribulin compared with TPC £68,600 per QALY gained. However, the Committee considerds that this figure was likely to underestimate the true cost per QALY gained of eribulin relative to TPC because it did not incorporate the full toxicity profile of eribulin, including the disutility associated with alopecia. iSgnificant uncertainties remained about heath-related quality of life associated with eribulin.	http://www.nice.org.uk/guidance/ta250/resources/guidance-eribulin-for-the-treatment-of-locally-advanced-or-metastatic-breast-cancer-pdf	12.111	Halaven
TA251	2012		Imatineb	Treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML)	Recommended	Update of guidance TA70. Standard-dose imatinib[1] is recommended as an option for the first-line treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML).	Imatinib is avialable at a cost of £1724.39 for a 400 mg 30-tablet pack (excluding VAT) resulting in an annual cost of imatinib treatment of £20,980 per year, asuming a treatment regimen of 400 mg per day.		The ICER for first-line nilotinib followed by imatinib compared with first-line imatinib followed by nilotinib was £11,000 per QALY gained for both scenarios.	http://www.nice.org.uk/guidance/ta251/resources/guidance-dasatinib-nilotinib-and-standarddose-imatinib-for-the-firstline-treatment-of-chronic-myeloid-leukaemia-part-review-of-technology-appraisal-guidance-70-pdf	95.933	Glivec*
TA251	2012		Nilotinib	Treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML)	Recommended	Nilotinib is recommended as an option for the first-line treatment of adults with chronic phase Philadelphia-chromosome-positive CML if the manufacturer makes nilotinib available with the discount agreed as part of the patient access scheme.	Nilotinib is availbale at a cost of £2432.85 for a 150 mg 112-tablet pack (excluding VAT). The cost of nilotinib treatment is £31,715 per year, assuming a treatment regimen of 300 mg twice a day. The manufacturer of nilotinib (Novartis) has agreed a patient access scheme with the Department of Health which makes nilotinib available with a discount applied to all invoices.		The ICER for first-line nilotinib followed by imatinib compared with first-line imatinib followed by nilotinib was £11,000 per QALY gained for both scenarios.	http://www.nice.org.uk/guidance/ta251/resources/guidance-dasatinib-nilotinib-and-standarddose-imatinib-for-the-firstline-treatment-of-chronic-myeloid-leukaemia-part-review-of-technology-appraisal-guidance-70-pdf	24.748	Tasigna
TA251	2012		Dasatinib	Treatment of adults with chronic phase Philadelphia-chromosome-positive chronic myeloid leukaemia (CML)	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Dasatinib is available at a cost of £2504.96 for a pack of 30 100 mg tablets (excluding VAT). The cost of dasatinib treatment is £30,477 per year, assuming a treatment regimen of 100 mg once daily.		Dasatibib was associated with fewer QALYs gained and was more costly than nilotinib in all scenarios. The ICERs for dasatinib compared with standard-dose imatinib exceeded £200,000 per QALY gained	http://www.nice.org.uk/guidance/ta251/resources/guidance-dasatinib-nilotinib-and-standarddose-imatinib-for-the-firstline-treatment-of-chronic-myeloid-leukaemia-part-review-of-technology-appraisal-guidance-70-pdf	36.050	Sprycel
TA252	2012		Telaprevir	Treatment of genotype 1 chronic hepatitis C	Option	Telaprevir in combination with peginterferon alfa and ribavirin is recommended as an option for the treatmen of genotype 1 chronic hepatitis C in adults with compensated liver diseas: Who are previously untreated or in whom previous treatment with interferon alfa (pegylated or non-pegylated) alone or in combination with ribavirin has failed, including people whose condition has relapsed, has partially responded or did not respond.	Telaprevir has a list price of £1866.50 for a 1-week, 42-tablet pack (excluding VAT; Monthly index of medical specilaities [MIMS] January 2012). This ezuates to £22,398 for a 12-week course of therapy.		The mos plausible ICERs were £18,000 and £10,000 per QALY gained for the previously untreated and previously treated patients respectively.	http://www.nice.org.uk/guidance/ta252/resources/guidance-telaprevir-for-the-treatment-of-genotype-1-chronic-hepatitis-c-pdf	646	Incivo

TA253	2012		Boceprevir	Treatment of genotype 1 chronic hepatitis C	Option	Boceprevir in combination with peginterferon alfa and ribavirin is recommended as an option for the treatmen of genotype 1 chronic hepatitis C in adults with compensated liver diseas: Who are previously untreated or in whom previous treatment has failed.	Boceprevir is priced at £2800 for a 28-day, 336-tablet pack (excluding VAT: Monthly Index of Medical Specialities [MIMS] january 2012) and costs 30,800 for a 44 week course		ICERs for boceprevir plus peginterferon alfa and ribavirin compared with peginterferon alfa and ribavirin alone for the treatment-naive population, £11,601 per QALY gained, and the previously treated population £2909 per QALY gained.	http://www.nice.org.uk/guidance/ta253/resources/guidance-boceprevir-for-the-treatment-of-genotype1-chronic-hepatitisc-pdf	285	Victrelis
TA254	2012		Fingolimod	Treatment of highly acive relapsing-remitting multiple sclerosis	Option	Fingolimos is recommended as an option for the treatment of highly active relapsing-remitting multiple sclerosis in adutls, only if: they have an unchanged or increased relapse rate or ongoing severe relapses compared with the previous year despite treatment with beta interferon, and the manufacturer provides fingolimod with the discount agreed as part of the patient access scheme.	The list price of fingolimod is £1470 for 28 capsules (excluding VAT; MIMS july 2011) which is equivaltent to an annual cost of approximately £19,169 per person. The manufacturer of fingolimod has agreed a patient access scheme with the Department of _Health, in which a discount on the list price of fingolimod is offered.		The most plausible ICER for fingolimod compared with the weighted average of the comparators form the manufacturer's model was likely to be in the range of £25,000 to £35,000 per QALY gained. The Committee recognised that including all of the benefits of fingolimod which may not be adequately captured in the QALY calculation (as suggested by the manufacturer and the patient experts) could decrease the ICER level.	http://www.nice.org.uk/guidance/ta254/resources/guidance-fingolimod-for-the-treatment-of-highly-active-relapsingremitting-multiple-sclerosis-pdf	136.284	Gilenya
TA255	2012		Cabazitaxel	Treatment for hormone-refractory metastatic prostate cancer previously treated with a docetaxel-containing regimen	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The cost of a 1.5 ml vial containing 60 mg cabazitaxel (40 mg/ml) is £3696 (excluding VAT). The average cost of one cycle of treatment is £3696 excluding VAT. The median number of cycles was six in the key clinical trial.	base-case population, treatment with cabazitaxel was associated with a gain of 0.298 QALYs	The Committee considered that the most plausible ICER would be above £87,500 per QALY gained. The Committtee further noted that there remains considereabl euncertainty in the robustness of this ICER becuase the utility values that were used in the model were based on unpublished data from an interim analysis of a small number of patients, and the costs assosicated with managing febrile neutropenia were underestimated.	http://www.nice.org.uk/guidance/ta255/resources/guidance-cabazitaxel-for-hormonerefractory-metastatic-prostate-cancer-previously-treated-with-a-docetaxelcontaining-regimen-pdf	27.559	Jevtana*
TA257	2012		Lapatinib in combination with an aromatase inhibitor	first-line treatment of metastatic hormone-receptorpositive breast cancer that overexpresses HER2	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Lapatinib is administered orally at a dosage of 1500 mg (six tablets) per day. The net price per pack of 84 tablets is £965.16 (excluding VAT). The acquisition cost for a lifetime of treatment with lapatinib plus the aromatase inhibitor letrozole is £28,212 (£27,024 for lapatinib and £1188 for letrozole), assuming a mean treatment duration of 55.2 weeks and excluding administration costs.	Lapatinib plus letrozole compared with letorzle alone: incremenal QALY gained was 0.467.	The Committee concluded that the most plausible ICER for lapatinib plus an aromatase inhibitor would be near to £74,000 per QALY gained.	http://www.nice.org.uk/guidance/ta257/resources/guidance-lapatinib-or-trastuzumab-in-combination-with-an-aromatase-inhibitor-for-the-firstline-treatment-of-metastatic-hormonereceptorpositive-breast-cancer-that-overexpresses-her2-pdf	3.799	Tyverb
TA257	2012		Trastuzumab in combination with an aromatase inhibitor	first-line treatment of metastatic hormone-receptorpositive breast cancer that overexpresses HER2	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The net price per 150 mg vial is £407.40 (excluding VAT; BNF 62). Assuming an average patient weight of 67 kg, a mean treatment period of 15 months and excluding administration, monitoring and wastage costs, the acquisition cost for a lifetime of treatment with trastuzumab plus anastrozole is £26,018 (£24,852 for trastuzumab and £1166 for anastrozole) for a weekly schedule and £26,832 (£25,666 for trastuzumab and £1166 for anastrozole) for a 3-weekly schedule.	Trastuzumab plus anastorzole compared with anastrozole alone gave an incremental QALY gain of 0.58.	The Committee concluded that the most plausible ICER for trastuzumab plus an aromatase inhibitor would be at least £51,000 per QALY gained.	http://www.nice.org.uk/guidance/ta257/resources/guidance-lapatinib-or-trastuzumab-in-combination-with-an-aromatase-inhibitor-for-the-firstline-treatment-of-metastatic-hormonereceptorpositive-breast-cancer-that-overexpresses-her2-pdf	188.399	Herceptin*
TA258	2012		Erlotinib	First-line treatment of locally advanced or metastatic EGFR-TK mutation-positive nonsmall-cell lung cancer	Option	Erlotinib is recommended as an option for the first-line treatment of people with locally advanced or metastatic non-small-cell lung cancer (NSCLC) if: they test positive for the epidermal growth factor receptor tyrosine kinase (EGFRTK) mutation and the manufacturer provides erlotinib at the discounted price agreed under the patient access scheme (as revised in 2012).	Erlotinib is given orally at a recommended dosage of 150 mg/day. The cost of a pack of 30 (150-mg) tablets is £1631.53 (excluding VAT). Dosage reductions (typically to 100 or 50 mg/day) are possible if the clinician considers it appropriate, and erlotinib is also available in tablet strengths of 100 mg and 25 mg. The manufacturer of erlotinib has agreed a patient access scheme (revised in 2012) with the Department of Health in which a confidential discount from the list price is applied to original invoices.		The Committee discussed the results from the updated analyses and on balance agreed that the sums of money either saved or spent are small given the uncertainties associated with the analysis.	http://www.nice.org.uk/guidance/ta258/resources/guidance-erlotinib-for-the-firstline-treatment-of-locally-advanced-or-metastatic-egfrtk-mutationpositive-nonsmallcell-lung-cancer-pdf	25.874	Tarceva*
TA259	2012		Abiraterone	Treatment for castration-resistant metastatic prostate cancer previously treated with a docetaxel-containing regimen	Option	Abiraterone in combination with prednisone or prednisolone is recommended as an option for the treatment of castration-resistant metastatic prostate cancer in adults, only if: their disease has progressed on or after one docetaxel-containing chemotherapy regimen, and the manufacturer provides abiraterone with the discount agreed in the patient access scheme. The maunfacturer of abiraterone has agreed a single conficential discount applied to the list price of abiraterone.	The cost of abiraterone is £2930 for 120 tablets (excluding VAT). Abiraterone is administered as a single dose of 1 g per day, taken as four 250-mg tablets. The manufacturer of abiraterone (Janssen) has agreed a patient access scheme with the Department of Health. This involves a single confidential discount applied to the list price of abiraterone. The Department of Health considered that this patient access scheme does not constitute an excessive administrative burden on the NHS. The manufacturer has agreed that the patient access scheme will remain in place until any review of this NICE technology appraisal guidance is published.		The Committee agreed that, for nearly all analyses presented, mitoxantrone was extendedly dominated by abiraterone. In the Committee's view, a reasonable starting point was the manufacturer's base-case ICER for abiraterone plus prednisolone compared with prednisolone alone of £46,800 per QALY gained for the one prior chemotherapy subgroup.	http://www.nice.org.uk/guidance/ta259/resources/guidance-abiraterone-for-castrationresistant-metastatic-prostate-cancer-previously-treated-with-a-docetaxelcontaining-regimen-pdf	151.104	Zytiga

TA260	2012		Botulinum toxin type A	For preventin of headaches in adults with chronic migraine	Option	Botulinum toxin type A is recommended as an option for the prophylaxis of headaches in adults with chronic migraine (defined as headaches on at least 15 days per month of which at least 8 days are with migraine): that has not responded to at least three prior pharmacological prophylaxis therapies and whose condition is appropriately managed for medication overuse. Treatment with botulinum toxin type A that is recommended according to above should be stopped in people whose condition: is not adequately responding to treatment (defined as less than a 30% reduction in headache days per month after two treatment cycles) or has changed to episodic migraine (defined as fewer than 15 headache days per month) for three consecutive months.	The net price of a 200 unit vial is £276.40 (excluding VAT). The manufacturer estimates that the administration cost is £73 per treatment, based on a total treatment time of less than 30 minutes. The total cost for treatment and administration of treatment per 12 week cycle, assuming no vial sharing, is therefore expected by the manufacturer to be £349.40.		The Committee concluded that the most plausible ICER was £18,900 per QALY gained, because it incorporated the Committee's preferred inputs and assumptions including a 30% negative stopping rule, applied different utilities to treatment arms, and equalised the non-MSQ parameter values in the utility mapping functions.	http://www.nice.org.uk/guidance/ta260/resources/guidance-botulinum-toxin-typea-for-the-prevention-of-headaches-in-adults-with-chronic-migraine-pdf	10.550	Botox	
TA262	2012		Adalimumab	Treatment of moderate to severe ulcerative colitis (terminated appraisal)	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta262/resources/guidance-adalimumab-for-the-treatment-of-moderate-to-severe-ulcerative-colitis-terminated-appraisal-pdf	419.141	Humira	eksklusiv til pæ
TA263	2012		Bevacizumab in combination with capecitabine	First-line treatment of metastatic breast cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Bevacizumab is available in 100 mg and 400 mg vials at net prices of £242.66 and £924.40, respectively (excluding VAT). The recommended dose is 10 mg/kg body weight given once every 2 weeks or 15 mg/kg body weight given once every 3 weeks. The manufacturer estimated the price of bevacizumab (excluding VAT and assuming wastage) to be £2577 for a patient weighing 72.1 kg at a dosage of 15 mg/kg every 3 weeks, amounting to an average monthly cost of £3689.	The base-case results indicated incremental QALYs of 0.5034 for bevacizumab plus capecitaine alone.	The Committee concluded that given all of the uncertainties, it was not possible to determine the most plausible ICER for bevacizumab plus capecitabine compared with capecitabine alone for the subgroup of patients who were previously treated with a taxane. However, it was convinced that the ICER would be higher than the ICER of £82,000 per QALY gained resulting from the ERG explorations. The Committee considered that the ICER for bevacizumab plus capecitabine compared with capecitabine alone in the ITT population would be even higher.	http://www.nice.org.uk/guidance/ta263/resources/guidance-bevacizumab-in-combination-with-capecitabine-for-the-firstline-treatment-of-metastatic-breast-cancer-pdf	187.032	Avastin*	
TA264	2012		Alteplase	For treating acute ischaemic stroke	Recommended	Update of guidance TA122. Alteplase is recommended within its marketing authorisations for treating acute ischemic stroke in adults if: tretatment is started as early as possible within 4.5 hours of onset of stroke symptoms, and intracranial haemorrhrage has been excluded by appropriate minaging techniques	The cost of alteplase is £135 per 10-mg pack, £180 per 20-mg pack and £300 per 50-mg pack (excluding VAT). The cost per course of treatment depends on the body weight of the patient, and can range from £300 to £600 based on a recommended dose of 0.9 mg per kilogram of body weight.	Alteplase compared with standard care: Incremental QALYs 0.333	The Committee agreed that alteplase either dominated standard care or had an ICER below £10,000 per QALY gained depending on the time-to-treatment window considered.	http://www.nice.org.uk/guidance/ta264/resources/guidance-alteplase-for-treating-acute-ischaemic-stroke-review-of-technology-appraisal-guidance-122-pdf	14.104	Actilyse*	
TA265	2012		Denosumab	Prevention of skeletal-related events in adults with bone metastases from solid tumours	Option	Denosumab is recommended as an option for preventing skeletal-related events (pathological fracture, radiation to bone, spinal cord compression or surgery to bone) in adults with bone metastases from breast cancer and from solid tumours other than prostate if: bisphosphonates would otherwise be prescribed and the manufacturer provides denosumab with the discount agreed in the patient access scheme.	The cost of a 120 mg vial is £309.86 (excluding VAT; British National Formulary [BNF] 63). A year of treatment (13 doses) would cost £4028.18 (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts. The manufacturer of denosumab has agreed a patient access scheme with the Department of Health, in which a discount on the list price of denosumab is offered.	Breast cancer denosumab when wcompared with zoledronic acid was associated with an incremental QALY gain of 0.07. When compared with ibandronic acid and disodium pamidronate denosumab was associated with incremental QALYs of 0.005. For other solid tumorus including non-small cell lung cancer, in the subgroup of patients with painful bone metastases and who have experinced a prior skeletal-related event, denosumab when compared with zoledronic acid was associated with an incremental QALY gain of 0.004	Without the patient access scheme, denosumab could not be recommended as a cost-effective use of NHS resources. For breast cancer, the patient access scheme reduced the cost of denosumab so that it became less costly and more effective than zoledronic acid. For people with bone metastases from solid tumours other than breast and prostate, the patient access scheme reduced the ICER for denosumab compared with zoledronic acid to less than £16,000 per QALY gained and to less than £6000 per QALY gained in the non-small cell lung cancer subgroup. For all 3 patient groups, compared with best supportive care, denosumab was associated with high ICERs even with the patient access scheme in the Assessment Group's analyses. The lowest of these remained above £70,000 per QALY gained.	http://www.nice.org.uk/guidance/ta265/resources/guidance-denosumab-for-the-prevention-of-skeletalrelated-events-in-adults-with-bone-metastases-from-solid-tumours-pdf	27.583	Prolia og Xgeva	27.583.533,61

TA265	2012		Denosumab	Prevention of skeletal-related events in adults with bone metastases from solid tumours	Not Recommended	Denosumab is not recommended for preventing skeletal-related events in adults with bone metastases from prostate cancer.	The cost of a 120 mg vial is £309.86 (excluding VAT; British National Formulary [BNF] 63). A year of treatment (13 doses) would cost £4028.18 (excluding VAT). Costs may vary in different settings because of negotiated procurement discounts. The manufacturer of denosumab has agreed a patient access scheme with the Department of Health, in which a discount on the list price of denosumab is offered.	Prostate cancer: In the subgroup of patientw with painful bone metastases and who have experienced a prior skeleal-related event, denosumab when compared with zoledronic acid was associated with an incremental QALY gain of 0.006	Without the patient access scheme, denosumab could not be recommended as a cost-effective use of NHS resources. For breast cancer, the patient access scheme reduced the cost of denosumab so that it became less costly and more effective than zoledronic acid. For people with bone metastases from solid tumours other than breast and prostate, the patient access scheme reduced the ICER for denosumab compared with zoledronic acid to less than £16,000 per QALY gained and to less than £6000 per QALY gained in the non-small cell lung cancer subgroup. For all 3 patient groups, compared with best supportive care, denosumab was associated with high ICERs even with the patient access scheme in the Assessment Group's analyses. The lowest of these remained above £70,000 per QALY gained.	http://www.nice.org.uk/guidance/ta265/resources/guidance-denosumab-for-the-prevention-of-skeletalrelated-events-in-adults-with-bone-metastases-from-solid-tumours-pdf	27.583	Prolia og Xgeva
TA266	2012		Mannitol dry powder for inhalation	Treating Cystic firbosis	Option	Mannitol dry powder for inhalation is recommended as an option for treating cystic fibrosis in adults: who cannot use rhDNase because of ineligibility, intolerance or inadequate response to rhDNase and whose lung function is rapidly declining (forced expiratory volume in 1 second [FEV1] decline greater than 2% annually) and for whom other osmotic agents are not considered appropriate.	Mannitol is available as a 40 mg powder capsule for inhalation. The list price for a 14-day pack of 280 capsules and 2 inhalers is £231.66 (excluding VAT; 'Monthly Index of Medical Specialities' [MIMS] September 2012). This equates to £0.83 per 40 mg capsule, or an average cost of £16.55 per day, including the cost of the inhaler. These prices do not include VAT.		The Committee noted that if mannitol treatment was offered only to patients with a rapid decline in lung function, the ICER would most likely be lower than in the whole population because of this group's lower quality of life and lung function, and a greater potential to improve. The Committee concluded that the ICER for mannitol in patients for whom hypertonic saline is not considered appropriate, who cannot use rhDNase because of ineligibility, intolerance or inadequate response to rhDNase, and whose lung function is rapidly declining would be under £30,000 per QALY gained. It also took into account the severity of the disease and the importance of treatment options for people with cystic fibrosis who have few alternative options.	http://www.nice.org.uk/guidance/ta266/resources/guidance-mannitol-dry-powder-for-inhalation-for-treating-cystic-fibrosis-pdf	-	Bronchitol
TA268	2012		Ipilimumab	Treatment for previously treated advanced (unresectable or metastatic) melanoma	Recommended	Ipilimumab is recommended as an option for treating advanced (unresectable or metastatic) melanoma in people who have received prior therapy, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme.	The summary of product characteristics states that all 4 doses should be administered 'as tolerated, regardless of the appearance of new lesions or growth of existing lesions'. Ipilimumab costs £3750 for 50 mg and £15,000 for 200 mg (excluding VAT, British national formulary, September 2012). Assuming an average body weight of 70 kg, each dose of ipilimumab would need a 200 mg vial and a 50 mg vial costing £18,750. A 4-dose course would therefore cost £75,000, not including administration costs. Costs may vary in different settings because of negotiated procurement discounts. The manufacturer of ipilimumab has agreed a patient access scheme with the Department of Health, in which a discount on the list price of ipilimumab is offered.		The Committee concluded that the manufacturer's ICER of £42,200 per QALY gained was a plausible estimate, but recognised that the ICER could be higher using other approaches to overall survival modelling.	http://www.nice.org.uk/guidance/ta268/resources/guidance-ipilimumab-for-previously-treated-advanced-unresectable-or-metastatic-melanoma-pdf	92.969	Yervoy*
TA269	2012		Vemurafenib	Treating locally advanced or metastatic BRAF V600 mutation-positive malignant melanoma	Recommended	Vemurafenib is recommended as an option for treating BRAF V600 mutation-positive unresectable or metastatic melanoma only if the manufacturer provides vemurafenib with the discount agreed in the patient access scheme.	The recommended dose of vemurafenib is 960 mg (4 × 240 mg tablets) twice daily (equivalent to a total daily dose of 1920 mg). The summary of product characteristics states that the doses should be given approximately 12 hours apart, and that treatment with vemurafenib should continue until 'disease progression or the development of unacceptable toxicity'. Vemurafenib costs £1750 for 1 pack of 56 × 240 mg tablets (1 week's supply) (excluding VAT; 'British national formulary' [BNF] September 2012). The manufacturer of vemurafenib has agreed a patient access scheme with the Department of Health, in which a discount on the list price of vemurafenib is offered.		The most plausbile ICER was in the range of £44,000 to £51,800 per QALY gained.	http://www.nice.org.uk/guidance/ta269/resources/guidance-vemurafenib-for-treating-locally-advanced-or-metastatic-brafv600-mutationpositive-malignant-melanoma-pdf	8.124,00	Zelboraf
TA270	2012		Decitabine	Treatment of acute myeloid leukaemia	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta270/resources/guidance-decitabine-for-the-treatment-of-acute-myeloid-leukaemia-terminated-appraisal-pdf	254	Dacogen
TA272	2013		Vinflunine	Treatment of advanced or metastatic transitional cell carcinoma of the urothelial tract	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Vinflunine is available in 50 mg and 250 mg vials, costing £212.50 and £1062.50 respectively (excluding VAT; 'British National Formulary' edition 64). The acquisition cost of vinflunine for an entire course of treatment is £9817.50, assuming an average of 4.2 cycles, a dose of 287 mg/m2 and a body surface area of 1.85 m2.	The manufacturer's base case: incremental QALYs of 0.131	The most plausible estimate of the ICER for vinflunine plus best supportive care compared with best supportive care alone was above £120,000 per QALY gained.	http://www.nice.org.uk/guidance/ta272/resources/guidance-vinflunine-for-the-treatment-of-advanced-or-metastatic-transitional-cell-carcinoma-of-the-urothelial-tract-pdf	5.305	Javlor*

TA274	2013		Ranibizumab	Treating diabetic macular oedema	Option	Update of guidance TA237. Ranibizumab is recommended as an option for treating visual impairment due to diabetic macular oedema only if: the eye has a central retinal thickness of 400 micrometres or more at the start of treatment and the manufacturer provides ranibizumab with the discount agreed in the patient access scheme revised in the context of this appraisal.	Ranibizumab is administered as a single intravitreal injection of 0.5 mg. Each vial of ranibizumab contains 2.3 mg in 0.23 ml; overfilling is considered necessary to achieve an injectable dose of 0.5 mg. The list price of ranibizumab is £742.17 per vial (excluding VAT; 'British national formulary' [BNF] edition 64). The manufacturer of ranibizumab (Novartis) has agreed a patient access scheme with the Department of Health which makes ranibizumab available with a discount applied to all invoices.		The most plausible ICER for the treatment of all people with diabetic macular oedema was likely to be above £30,000 per QALY gained, and that it therefore could not recommend ranibizumab as an effective use of NHS resources. The most plausible ICER for the subgroup of people with thicker retinas was likely to be higher than the manufacturer's estimate, but would be under £25,000 per QALY gained.	http://www.nice.org.uk/guidance/ta274/resources/guidance-ranibizumab-for-treating-diabetic-macular-oedema-rapid-review-of-technology-appraisal-guidance-237-pdf	140.599	Lucentis*
TA276	2013		Tobramycin dry powders for inhalation	Treating pseudomonas lung infection in cystic fibrosis	Option	Tobramycin dry powder for inhalation (DPI) is recommended as an option for treating chronic pulmonary infection caused by Pseudomonas aeruginosa in people with cystic fibrosis only if: nebulised tobramycin is considered an appropriate treatment, that is, when colistimethate sodium is contraindicated, is not tolerated or has not produced an adequate clinical response and the manufacturer provides tobramycin DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.	The recommended dosage for tobramycin DPI is 112 mg tobramycin (4×28-mg capsules), administered twice daily for 28 days using the Podhaler device in alternating cycles of 28 days on treatment followed by 28 days off treatment. The price for a pack of 56×28-mg capsules and 1 Podhaler device is £447.50 (excluding VAT; 'British national formulary' [BNF] edition 64). The list price cost for 56 days of treatment is therefore £1790 excluding VAT. The manufacturer of tobramycin DPI (Novartis) has agreed a patient access scheme with the Department of Health which makes tobramycin DPI available with a discount applied to all invoices.		Tobramycin DPI consistently dominated nebulised tobramycin with inclusion of the patient access scheme, that is, there was a cost saving and QALY gain for tobramycin DPI compared to nebulised tobramycin.	http://www.nice.org.uk/guidance/ta276/resources/guidance-colistimethate-sodium-and-tobramycin-dry-powders-for-inhalation-for-treating-pseudomonas-lung-infection-in-cystic-fibrosis-pdf	701	Tobi
TA276	2013		Colistimethate sodium and tobramycin dry powders for inhalation	Treating pseudomonas lung infection in cystic fibrosis	Option	Colistimethate sodium DPI is recommended as an option for treating chronic pulmonary infection caused by P. aeruginosa in people with cystic fibrosis only if: they would clinically benefit from continued colistimethate sodium but do not tolerate it in its nebulised form and thus tobramycin therapy would otherwise be considered and the manufacturer provides colistimethate sodium DPI with the discount agreed as part of the patient access scheme to primary, secondary and tertiary care in the NHS.	The recommended dosage for colistimethate sodium DPI is 1 capsule (approximately equal to 125 mg of colistimethate sodium) to be inhaled twice daily using the 'Turbospin' inhaler device (PH&T Pharma) which is a breathactivated, reusable dry powder inhaler. The price for a 28-day pack including 1 Turbospin inhaler is £968 (excluding VAT; price provided by the manufacturer). The list price cost for 56 days of treatment is therefore £1936 excluding VAT. The manufacturer of colistimethate sodium DPI (Forest) has agreed a patient access scheme with the Department of Health which makes colistimethate sodium DPI available with a discount applied to all invoices.		The Committee noted the small QALY loss for colistimethate sodium DPI compared with nebulised tobramycin but also the substantial cost saving (£38,000 with the list price for nebulised tobramycin).	http://www.nice.org.uk/guidance/ta276/resources/guidance-colistimethate-sodium-and-tobramycin-dry-powders-for-inhalation-for-treating-pseudomonas-lung-infection-in-cystic-fibrosis-pdf	-	Colobreathe
TA278	2013		Omalizumab	Treating severe persistent allergic asthma	Option	Updates of guidance TA133 and TA201. Omalizumab is recommended as an option for treating severe persistent confirmed allergic IgE-mediated asthma as an add-on to optimised standard therapy in people aged 6 years and older: who need continuous or frequent treatment with oral corticosteroids (defined as 4 or more courses in the previous year), and only if the manufacturer makes omalizumab available with the discount agreed in the patient access scheme. Optimised standard therapy is defined as a full trial of and, if tolerated, documented compliance with inhaled high-dose corticosteroids, long-acting.	The cost of omalizumab ranges from approximately £1665 per patient per year (excluding VAT) for a 75 mg dose administered every 4 weeks to approximately £26,640 per patient per year (excluding VAT) for a 600 mg dose (the maximum recommended dose in the summary of product characteristics) administered every 2 weeks. The manufacturer of omalizumab has agreed a patient access scheme with the Department of Health, which makes omalizumab available with a discount applied to all invoices.		The most plausible ICER was £23,200 per QALY gained for the combined population of adults, adolescents and children on continuous or frequent courses of oral corticosteroids, defined as 4 or more courses in the year before receiving omalizumab incorporating the patient access scheme for omalizumab.	http://www.nice.org.uk/guidance/ta278/resources/guidance-omalizumab-for-treating-severe-persistent-allergic-asthma-review-of-technology-appraisal-guidance-133-and-201-pdf	35.900	Xolair*
TA280	2013		Abatacept in cobination with methotrexate	Treating rheumatoid arthritis after the failure of conventional disease-modifying anti-rheumatic drugs	Option	Updates of guidance TA234. Abatacept in combination with methotrexate is recommended as an option for treating rheumatoid arthritis in adults whose disease has responded inadequately to 2 conventional disease-modifying anti-rheumatic drugs (DMARDs), including methotrexate, only if: it is used in accordance with the recommendations for other biological DMARDs in Adalimumab, etanercept and infliximab for the treatment of umatoid arthritis (NICE technology appraisal guidance 130) and the manufacturer provides abatacept with the discount agreed in the patient access scheme.	Abatacept is available in 250-mg vials at a cost of £302.40 per vial (excluding VAT; 'British national formulary' [BNF] edition 64). The annual drug costs associated with abatacept vary according to body weight and the number of infusions needed. For a person weighing 60–100 kg, the cost is £12,700.80 in the first year, and £11,793.60 in subsequent years.		The cost effectiveness of abatacept plus methotrexate (with the patient access scheme) is comparable with that of other biological DMARDs recommended by NICE, with an ICER of less than £30,000 per QALY gained compared with conventional DMARDs.	http://www.nice.org.uk/guidance/ta280/resources/guidance-abatacept-for-treating-rheumatoid-arthritis-after-the-failure-of-conventional-diseasemodifying-antirheumatic-drugs-rapid-review-of-technology-appraisal-guidance234-pdf	28.250	Orencia*
TA281	2013		Canakinumab	Treating gouty arthritis attacks and reducing the frequency of subsequent attacks	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta281/resources/guidance-canakinumab-for-treating-gouty-arthritis-attacks-and-reducing-the-frequency-of-subsequent-attacks-terminated-appraisal-pdf	7.106	Ilaris*
TA282	2013		Pirfenidone	Treating idiopathic pulmonary fibrosis	Option	Pirfenidone is recommended as an option for treating idiopathic pulmonary fibrosis only if: the person has a forced vital capacity (FVC) between 50% and 80% predicted and the manufacturer provides pirfenidone with the discount agreed in the patient access scheme. Treatment with pirfenidone that is recommended above should be discontinued if there is evidence of disease progression (a decline in per cent predicted FVC of 10% or more within any 12 month period).	Pirfenidone is priced at £501.92 for a 14-day, 63-capsule starter pack, £2007.70 for a 28-day, 252-capsule blister pack and £2151.10 for a 30-day, 270-capsule bottle (costs from manufacturer's submission; all excluding VAT). The annual cost of ongoing treatment is £26,171.72, assuming no wastage. The manufacturer of pirfenidone has agreed a patient access scheme with the Department of Health that makes pirfenidone available with a discount.		Subgroup results form patients with FVC 80% predicted or less: The manufacturer's probabilistic ICER was £24,000 per QALY gained.	http://www.nice.org.uk/guidance/ta282/resources/guidance-pirfenidone-for-treating-idiopathic-pulmonary-fibrosis-pdf	19.692	Esbriet

TA283	2013		Ranibizumab	Treating visual impairment caused by macular oedema secondary to retinal vein occlusion	Option	Ranibizumab is recommended as an option for treating visual impairment caused by macular oedema: following central retinal vein occlusion or following branch retinal vein occlusion only if treatment with laser photocoagulation has not been beneficial, or when laser photocoagulation is not suitable because of the extent of macular haemorrhage and only if the manufacturer provides ranibizumab with the discount agreed in the patient access scheme revised in the context of NICE technology appraisal guidance 274.	Ranibizumab is administered as a single 0.5 mg intravitreal injection. Each vial of ranibizumab contains 2.3 mg in 0.23 ml; overfilling is considered necessary to achieve an injectable dose of 0.5 mg. The list price of ranibizumab is £742.17 per vial (excluding VAT; 'British national formulary' [BNF] edition 64). The manufacturer of ranibizumab (Novartis) has agreed a patient access scheme with the Department of Health, revised in the context of technology appraisal guidance 274, which makes ranibizumab available with a discount applied to all invoices.		Ranibizumab was associated with an ICER of £26,200 per QALY gained compared with best supportive care in CRVO. The Committee concluded that the most plausible ICER for ranibizumab compared with standard care in treating BRVO was in excess of £44,800 per QALY gained.	http://www.nice.org.uk/guidance/ta283/resources/guidance-ranibizumab-for-treating-visual-impairment-caused-by-macular-oedema-secondary-to-retinal-vein-occlusion-pdf	140.599	Lucentis*	
TA284	2013		Bevacizumab in combination with paclitaxel and carboplatin	First-line treatment of advanced ovarian cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Bevacizumab is available in 100 mg and 400 mg vials at prices of £242.66 and £924.40 respectively (excluding VAT; 'British national formulary' [BNF] edition 64). The manufacturer estimated the cost of bevacizumab (excluding VAT and assuming wastage) to be £36,078 for a patient weighing 65 kg at a dosage of 15 mg/kg every 3 weeks, amounting to an average monthly cost of £2577.		With a treatment duratin of 15 months or a time horizon of 25 years or both, the range of ICERs from £128,000 to £161,000 per QALY gained.	http://www.nice.org.uk/guidance/ta284/resources/guidance-bevacizumab-in-combination-with-paclitaxel-and-carboplatin-for-firstline-treatment-of-advanced-ovarian-cancer-pdf	187.032	Avastin*	
TA285	2013		Bevacizumab in combination with gemcitabine and carboplatin	Treating the first recurrence of platinum-sensitive advanced ovarian cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Bevacizumab is available in 100 mg and 400 mg vials at net prices of £242.66 and £924.40 respectively (excluding VAT; 'British national formulary' edition 65). The manufacturer estimated the cost of a course of treatment with bevacizumab (excluding VAT and assuming vials are not shared between patients) to be £25,208 for a patient weighing 60.5 kg at a dosage of 15 mg/kg every 3 weeks for a mean treatment duration of 10.8 cycles (7.5 months).		The Committee agreed that the manufacturer's base-case ICER, using the September 2010 overall survival data of £149,000 per QALY gained, was likely to be an optimistic cost-effectiveness estimate and that the most plausible ICER could be much higher than this.	http://www.nice.org.uk/guidance/ta285/resources/guidance-bevacizumab-in-combination-with-gemcitabine-and-carboplatin-for-treating-the-first-recurrence-of-platinumsensitive-advanced-ovarian-cancer-pdf	187.032	Avastin*	
TA286	2013		Loxapine inhalation	Treating acute agitation and disturbed behaviours associated with schizophrenia and bipolar disorder	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta286/resources/guidance-loxapine-inhalation-for-treating-acute-agitation-and-disturbed-behaviours-associated-with-schizophrenia-and-bipolar-disorder-terminated-appraisal-pdf	5	Adasuve	
TA289	2013		Ruxolitinib	For disease-related splenomegaly or symptoms in adults with myelofibrosis	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The cost of ruxolitinib is £3600 for a 60-tablet pack of 15 mg or 20 mg tablets, or £1800 for a 60-tablet pack of 5 mg tablets (excluding VAT; British National Formulary [BNF] online, November 2012). This corresponds to an annual cost of approximately £43,200 per patient (assuming a 15 mg or 20 mg dose, taken twice daily, 30 days per month).	Manufacturer provided revised base case - a 15-year time horizon, Australian utiity values, survival hazard ratios estimated form patients who recievd ruxolitinib and had a least a 35% reduction in spleen volum on COMFORT II: Incremenatl QALYs 1.36. ERG conducted an analysis of the revised base case, without the dose intensity adjustment: incremenal QALYs 1.36.	The Committee considered the ICER could be approaching £149,000 per QALY gained as presented by the ERG's alternative scenario, but acknowledged that this may have overestimated the ICER because of the uncertainty in the utility and survival estimates. It considered that the base-case ICERs presented by the manufacturer (£74,000 and £57,000 per QALY gained) were likely to have underestimated the ICER because of the structural limitations of the model.	http://www.nice.org.uk/guidance/ta289/resources/guidance-ruxolitinib-for-diseaserelated-splenomegaly-or-symptoms-in-adults-with-myelofibrosis-pdf	23.343	Jakavi	
TA291	2013		Pegloticase	Treating severe debilitating chronic tophaceous gout	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The acquisition cost of a single vial containing 8 mg of pegloticase concentrate for 1 infusion is £1770 (cost from manufacturer's submission; excludes VAT). The average cost of a course of 6 months' treatment is £23,010.	Manufacturer's: Revised base-case - Pegloticase compared with best supportive care: QALY gain of 0.267. The ERG: 0.23 gain in QALY	ICER is in excess of £54,000 per QALY gained	http://www.nice.org.uk/guidance/ta291/resources/guidance-pegloticase-for-treating-severe-debilitating-chronic-tophaceous-gout-pdf	-	Krystexxa	
TA293	2013		Eltrombopag	Treating chronic immune (idiopathic) thrombocytopenic purpura	Option	Update og guidance TA205. Eltrombopag is recommended as an option for treating adults with chronic immune (idiopathic) thrombocytopenic purpura, within its marketing authorisation (that is, in adults who have had a splenectomy and whose condition is refractory to other treatments, or as a second-line treatment in adults who have not had a splenectomy because surgery is contraindicated), only if: their condition is refractory to standard active treatments and rescue therapies, or they have severe disease and a high risk of bleeding that needs frequent courses of rescue therapies and the manufacturer provides eltrombopag with the discount agreed in the patient access scheme.	The 'British national formulary' (BNF; edition 64) states that the net price of a 28-tablet pack of 25 mg eltrombopag is £770 (a single 25 mg dose costs £27.50). The net price of a 28-tablet pack of 50 mg eltrombopag is £1540 (a single 50 mg dose costs £55). The cost per patient will vary with dose adjustment and treatment duration. The manufacturer indicated that the average daily cost of eltrombopag (based on the mean dose of eltrombopag in the EXTEND study of 51.3 mg per day) is £56.43. The manufacturer of eltrombopag (GlaxoSmithKline) has agreed a patient access scheme with the Department of Health that makes eltrombopag available with a discount.		The Committee considered the analysis that mirrored its preferred assumptions and parameters. It noted that the resulting ICERs for eltrombopag compared with romiplostim were £389,000 saved per QALY lost for patients who had had a splenectomy and £271,000 saved per QALY lost for patients who had not had a splenectomy.	http://www.nice.org.uk/guidance/ta293/resources/guidance-eltrombopag-for-treating-chronic-immune-idiopathic-thrombocytopenic-purpura-review-of-technology-appraisal-205-pdf	5.611	Revolade	

TA294	2013		Aflibercept solution for injection	Treating wet age-related macular degeneration	Option	Aflibercept solution for injection is recommended as an option for treating wet age-related macular degeneration only if: it is used in accordance with the recommendations for ranibizumab in NICE technology appraisal guidance 155 (re-issued in May 2012) and the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme.	The list price of aflibercept 40 mg/ml solution for injection is £816 per 100-microlitre vial (excluding VAT; 'British national formulary' [BNF] edition 52). The manufacturer of aflibercept solution for injection has agreed a patient access scheme with the Department of Health. This involves a confidential discount applied to the list price of aflibercept solution for injection.		The Committee noted that its preferred analyses incorporated the confidential discount to the list price of aflibercept and a range of discounts (from 0 to 50%) to the list price of ranibizumab. It also noted that, when discounts to the list price of ranibizumab ranged from 0 to 45%, aflibercept had lower costs and quality-adjusted life years (QALYs) than ranibizumab, which resulted in ICERs for aflibercept compared with ranibizumab ranging from £1,690,000 to £16,700 saved per QALY lost and that, when a 50% discount was applied to the list price of ranibizumab, aflibercept was dominated by ranibizumab in both the worse-seeing eye and better-seeing eye models. However, the Committee was aware that, in both the manufacturer's and the ERG's analyses, the differences in total costs and QALYs were very small.	http://www.nice.org.uk/guidance/ta294/resources/guidance-aflibercept-solution-for-injection-for-treating-wet-agerelated-macular-degeneration-pdf	150.820	Eylea	
TA295	2013		Everolimus in combination with exemstane	Treating advanced HER2-negative homrone-receptor-prositive breast cancer after endocrine therapy	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	Everolimus is administered orally. The recommended dosage is 10 mg once daily and treatment should continue as long as patients benefit clinically, or until they experience unacceptable adverse reactions. Adverse reactions that are severe and/or intolerable may be managed by reducing the dosage to 5 mg daily or temporarily stopping treatment followed by reintroducing it at 5 mg daily. The price for a pack (30 tablets per pack) of 10 mg tablets and 5 mg tablets is £2970 and £2250 respectively (excluding VAT; 'British National Formulary' [BNF] edition 65).	Using the 'non-parallel exponential' model of overall survival, the ERG estimated an 0.269 incremental QALYs gained	The Committee concluded that the ERG's estimate of the ICER (including the patient access scheme for everolimus) of £68,000 per QALY gained for everolimus plus exemestane compared with exemestane alone was more plausible than the manufacturer's base-case estimate.	http://www.nice.org.uk/guidance/ta295/resources/guidance-everolimus-in-combination-with-exemestane-for-treating-advanced-her2negative-hormonereceptorpositive-breast-cancer-after-endocrine-therapy-pdf	12.634	Afinitor	
TA296	2013		Crizotinib	For previoulsy treated non-small-cell lung cancer associated with an anaplastic lymphoma kinase fusion gene	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The acquisition cost of crizotinib is £4689 for 1 pack of 60×200 mg (or 250 mg) capsules (30-day supply) (excluding VAT; 'British national formulary' [BNF] edition 64). The summary of product characteristics states that the recommended dose of crizotinib is 250 mg twice daily (500 mg daily) taken continuously. It further states that 'Treatment should be continued until disease progression or unacceptable toxicity. Prolongation of treatment after objective disease progression in selected patients may be considered on an individual basis but no additional benefit has been demonstrated'. Assuming treatment until disease progression, the cost of a course of treatment would be £37,512 using the median progression-free survival in the study PROFILE 1007 as the number of cycles of treatment (that is, 7.7 months or 8 packs of capsules), or £46,890 using the number of treatment cycles calculated from the duration of progression-free survival in the manufacturer's economic model (that is, 9.6 months or 10 packs of capsules). Using the median number of crizotinib treatment cycles started in PROFILE 1007 (that is, 10.5 months or 11 packs of capsules) the cost of a course of treatment would be £51,579.		The Committee concluded that the ICER on which to base a decision for crizotinib compared with docetaxel would be more than £100,000 per QALY gained. The Committee concluded that the ICER on which to base a decision for crizotinib compared with best supportive care would be more than £50,200 per QALY gained. However, the Committee further concluded that this ICER was associated with a substantial amount of uncertainty, which it was not possible to quantify because of the lack of a robust mixed treatment comparison between crizotinib and best supportive care.	http://www.nice.org.uk/guidance/ta296/resources/guidance-crizotinib-for-previously-treated-nonsmallcell-lung-cancer-associated-with-an-anaplastic-lymphoma-kinase-fusion-gene-pdf	11.485	Xalkori	
TA297	2013		Ocriplasmin	Treating vitreomacular traction	Option	Ocriplasmin is recommended as an option for treating vitreomacular traction in adults, only if: an epiretinal membrane is not present and they have a stage II full-thickness macular hole with a diameter of 400 micrometres or less and/or they have severe symptoms.	The cost of an ocriplasmin injection is £2500 (excluding VAT) (0.5 mg in 0.2 ml solution; MIMS, July 2013). Because repeat injections are not recommended, this is the cost for a full course of treatment.	ERG estimates: VMT without ERM incremental QALY 0.100, VMT with ERM incremental QALY 0.038, VMT with MH indremental QALY 0.038	ICER for ocriplasmin to treat vitreomacular traction without an epiretinal membrane or a stage II macular hole was likely to be no greater than £20,900 per QALY gained (as presented by the ERG). The ICER for ocriplasmin to treat vitreomacular traction with an epiretinal membrane but without a stage II macular hole and recognised that ocriplasmin was not clinically effective or cost effective for these people. ICER was likely to be lower than 30,500 per QALY gained and therefore ocriplasmin was a cost-effective use of NHS resources for treating people with vitreomacular traction and a stage II macular hole without an epiretinal membrane.	http://www.nice.org.uk/guidance/ta297/resources/guidance-ocriplasmin-for-treating-vitreomacular-traction-pdf	342	Jetrea	
TA298	2013		Ranibizumab	Treating choroidal neovascularisation associated with pathological myopia	Recommended	Ranibizumab is recommended as an option for treating visual impairment due to choroidal neovascularisation secondary to pathological myopia when the manufacturer provides ranibizumab with the discount agreed in the patient access scheme.	The list price of ranibizumab 10 mg/ml is £742.17 per 0.23-ml vial (excluding VAT; 'British national formulary' [BNF] edition 66). The manufacturer of ranibizumab (Novartis) has agreed a patient access scheme with the Department of Health, revised in the context of Ranibizumab for treating diabetic macular oedema (NICE technology appraisal guidance 274), which makes ranibizumab available with a discount applied to all invoices.	The manufacturer's bese-case deterministic cost-effectivenss analysis reults showed taht ranibizumb compared to vPDT resulting in more QALYs (13.18 compared with 12.75). ERG's exploratory analysis: incremental QALYs ere 0.344 or 0.266, respectively.	The Committee noted that manufacturer's base-case analysis showed that ranibizumab dominated vPDT (that is, it was more effective and less costly), resulting in more QALYs (13.18 compared with 12.75) and lower costs (£9694 compared with £12,455). The Committee considered the uncertainties in the manufacturer's model and noted that they were unlikely to have an effect on the overall results of the base-case analysis, which showed that ranibizumab dominated vPDT.	http://www.nice.org.uk/guidance/ta298/resources/guidance-ranibizumab-for-treating-choroidal-neovascularisation-associated-with-pathological-myopia-pdf	140.599	Lucentis*	
TA299	2013		Bosutinib	For previously treated chronic myeloid leukaemia	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The manufacturer has stated that bosutinib is available in 2 pack sizes: 500 mg×28 tablets (£3436.67) and 100 mg×28 tablets (£859.17), with an average cost of £122.74 for 500 mg/day (all costs exclude VAT). The annual cost of bosutinib at this dose is £44,799 per patient.	For Chronic phase incremental QALYs of 1.7066.	For chronic phase CML the most plausible available ICER was £43,000 per QALY gained, but taking into account the limited potential for post-bosutinib benefit and a proportion of people taking bosutinib after loss of complete cytogenetic response an estimated range of £40,000 to £50,000 was appropriate for the purposes of its decision making. For accelerated phase CML and blast phase CML the most plausible ICERs were £58,000 per QALY gained and £60,000 per QALY gained respectively.	http://www.nice.org.uk/guidance/ta299/resources/guidance-bosutinib-for-previously-treated-chronic-myeloid-leukaemia-pdf	3.319	Bosulif	

TA300	2013		Peginterferon alfa and ribavirin	Treating chronic hepatitis C in children and young people	Recommended	Updates and replacement of section 1.7, bullet 2 only of TA75 an par of section 1.6 of TA106. Peginterferon alfa in combination with ribavirin is recommended, within its marketing authorisation, as an option for treating chronic hepatitis C in children and young people.	The price of peginterferon alfa-2a is £107.76 for a 135-microgram prefilled syringe or pen and £124.40 for a 180-microgram prefilled syringe or pen (excluding VAT; 'British national formulary' [BNF] edition 65). The price of peginterferon alfa-2b is £1.33 per microgram and it is available in 50-, 80-, 100-, 120- and 150-microgram pens costing £66.46, £106.34, £132.92, £159.51 and £199.38 respectively (BNF edition 65). The Assessment Group calculated that, based on an average age of 11 years, a body weight of 35.5 kg and a body surface area of 1.19 m2, a 24-week course of peginterferon alfa-2a plus ribavirin costs approximately £3700 and a 48-week course of treatment costs approximately £7400; a 24-week course of peginterferon alfa-2b plus ribavirin oral solution costs approximately £4000 and a 48-week course of treatment costs approximately £8100.	The Assessment Group's base-case results for peginterferon alfa-2a compared with peginterferon alfa-2b showed that peginterferon alfa-2a was more effective than peginterferon alfa-2b (22.25 QALYs compared with 22.19 QALYs). For people with genotype 1 or 4, peginterferon alfa-2a was also more effective than peginterferon alfa-2b (£21,278 compared with £22,316; 22.00 QALYs compared with 21.97 QALYs). However, for people with genotype 2 or 3, peginterferon alfa-2a was less effective than peginterferon alfa-2b (£11,831 compared with £11,202; 23.05 QALYs compared with 23.21 QALYs).	The manufacturer's and Assessment Group's base-case results showed that peginterferon alfa-2a and peginterferon alfa-2b (both plus ribavirin) dominated best supportive care in all genotypes, except Roche's cost-effectiveness results for children and young people with HCV genotype 1, 4 or 5, which resulted in an ICER of £3900 per QALY gained.	http://www.nice.org.uk/guidance/ta300/resources/guidance-peginterferon-alfa-and-ribavirin-for-treating-chronic-hepatitisc-in-children-and-young-people-pdf	25674	Pegasys og PegIntron	25674152,14
TA302	2013		Canakinumab	Treating systemic juvenile idiopathic arthritis	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta302/resources/guidance-canakinumab-for-treating-systemic-juvenile-idiopathic-arthritis-terminated-appraisal-pdf	7.106	Ilaris*	
TA303	2014		Teriflunomide	Treating relapsing-remitting multiple sclerosis	Option	Teriflunomide is recommended as an option for treating adults with active relapsing–remitting multiple sclerosis (normally defined as 2 clinically significant relapses in the previous 2 years), only if they do not have highly active or rapidly evolving severe relapsing–remitting multiple sclerosis and the manufacturer provides teriflunomide with the discount agreed in the patient access scheme.	The manufacturer has stated that the list price of teriflunomide is £1037.84 per 28-tablet pack (excluding VAT). The length of teriflunomide treatment may vary because it is anticipated to be used continuously until a joint decision is made between the patient and clinician to stop treatment. Based on the list price, the manufacturer has estimated the annual cost of teriflunomide to be £13,529 per patient per year. The manufacturer of teriflunomide has agreed a patient access scheme with the Department of Health. This is a simple discount scheme, with the discount applied at the point of purchase or invoice.	Teriflunomide dominated the blanded comparator in the base case: incremental QALYS 0.201. Teriflunomide compared with glatiramer acetate: incremental QALYs 0.041. Rebif-22 compared with teriflunomide: incremental QALYs 0.130. Base-case MTC with secondary progressive multiple sclerosis treatment: ingremental QALYs 0.111.	The Committee concluded that teriflunomide dominated the beta interferons. For the comparison with glatiramer acetate, the Committee noted the varying ICERs from the different analyses but accounting for the benefits not captured in the QALY, such as the oral administration of teriflunomide, the Committee concluded that, on balance, the most plausible ICER for teriflunomide compared with glatiramer acetate would be below £20,000 per QALY gained.	http://www.nice.org.uk/guidance/ta303/resources/guidance-teriflunomide-for-treating-relapsingremitting-multiple-sclerosis-pdf	45.662	Aubagio	
TA305	2014		Aflibercept	Treating visual impairment caused by macular oedema secondary to retinal vein occlusion	Recommended	Aflibercept solution for injection is recommended as an option for treating visual impairment caused by macular oedema secondary to central retinal vein occlusion only if the manufacturer provides aflibercept solution for injection with the discount agreed in the patient access scheme.	The list price of aflibercept 40 mg/ml solution for injection is £816.00 per 0.1-ml vial (excluding VAT; 'British national formulary' [BNF] edition 66). The manufacturer of aflibercept solution for injection has agreed a patient access scheme with the Department of Health which makes aflibercept solution for injection available with a discount applied to the list price.	The manufacturer's base-case results showed result showede taht ranibizumab dominate: Incremental QALYS 0.054	The Committee noted that the manufacturer's base-case analysis showed that aflibercept dominated ranibizumab (that is, it was more effective and less costly), resulting in more QALYs and lower costs. The Committee considered the uncertainties in the manufacturer's model and noted the ERG's exploratory analysis, which resulted in slightly more cost savings with aflibercept. It also noted that aflibercept continued to dominate ranibizumab despite the changes made by the ERG.The Committee noted that the ERG's exploratory analysis, which included the confidential discount applied to the list price for aflibercept, resulted in an incremental cost-effectiveness ratio (ICER) of £12,300 per QALY gained for aflibercept compared with dexamethasone. The Committee also noted that even using the Brown utilities for the 'better-seeing eye', that is to say, the 'worst case scenario', the ICER was below the top end of the range that would normally be considered a cost-effective use of NHS resources (£20,000–£30,000 per QALY gained).	http://www.nice.org.uk/guidance/ta305/resources/guidance-aflibercept-for-treating-visual-impairment-caused-by-macular-oedema-secondary-to-central-retinal-vein-occlusion-pdf	150.820	Eylea	
TA306	2014		Pixantrone monotherapy	Treating multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma	Option	Pixantrone monotherapy is recommended as an option for treating adults with multiply relapsed or refractory aggressive non-Hodgkin's B-cell lymphoma only if: the person has previously been treated with rituximab and the person is receiving third- or fourth-line treatment and the manufacturer provides pixantrone with the discount agreed in the patient access scheme.	Pixantrone is priced at £553.50 per 20-ml vial containing 29 mg free base pixantrone, which is equivalent to 50 mg pixantrone dimaleate (excluding VAT; 'British national formulary' [BNF] edition 66). The estimated cost of a course of treatment is £19,926 (costs calculated over 4 cycles using an average of 3 vials per dose based on the median length of treatment in the PIX301 trial, described in section 3.2). The manufacturer of pixantrone has agreed a patient access scheme with the Department of Health that makes pixantrone available with a discount.	Pixanrone compared with treatment of physician's choice for several subgroups, including patients with aggressive B-cell lymphoma: incremental QALYs 0.20	The manufacturer's deterministic ICER incorporating the patient access scheme was £18,500 per QALY gained and the manufacturer's mean probabilistic ICER was £22,000 per QALY gained. The Committee noted that the exploratory analysis showed a high level of uncertainty around the ICER. However, the Committee was persuaded that this analysis could overestimate the uncertainty associated with the survival modelling and that the true value of the ICER might be lower. The Committee concluded that the probabilistic ICER was likely to be less than £22,000 per QALY gained pixantrone	http://www.nice.org.uk/guidance/ta306/resources/guidance-pixantrone-monotherapy-for-treating-multiply-relapsed-or-refractory-aggressive-nonhodgkins-bcell-lymphoma-pdf	-	Pixuvri	
TA307	2014		Aflibercept in combination with irinotecan and fluorouracil-based therapy	Treating metastatic colorectal cancer that has progressed following prior oxaliplatin-based chemotherapy	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The manufacturer states that the net price of a vial of 100 mg aflibercept is £295.65, and the net price of a vial of 200 mg aflibercept is £591.30. The cost per patient will vary with dose adjustment and treatment duration. The manufacturer of aflibercept (Sanofi) has agreed a patient access scheme with the Department of Health that makes aflibercept available with a discount.		ICER produced by the ERG using the Committee's preferred assumptions, but which used a utility value for progressed disease of 0.6: approximately £51,000 per QALY gained and would be higher if an extrapolation function with a less heavy tail had been used.	http://www.nice.org.uk/guidance/ta307/resources/guidance-aflibercept-in-combination-with-irinotecan-and-fluorouracilbased-therapy-for-treating-metastatic-colorectal-cancer-that-has-progressed-following-prior-oxaliplatinbased-chemotherapy-pdf	-	Zaltrap	

TA308	2014		Rituximab in combinatin with glucocorticoids	Treating anti-neutrophil cytoplasmic antibody-associated vasculitis	Option	Rituximab, in combination with glucocorticoids, is recommended as an option for inducing remission in adults with anti-neutrophil cytoplasmic antibody [ANCA]-associated vasculitis (severely active granulomatosis with polyangiitis [Wegener's] and microscopic polyangiitis), only if: further cyclophosphamide treatment would exceed the maximum cumulative cyclophosphamide dose or cyclophosphamide is contraindicated or not tolerated or the person has not completed their family and treatment with cyclophosphamide may materially affect their fertility or the disease has remained active or progressed despite a course of cyclophosphamide lasting 3–6 months or the person has had uroepithelial malignancy.	Rituximab is priced at £174.63 per 10 ml vial and £873.15 per 50 ml vial (excluding VAT; British national formulary [BNF] edition 66). The recommended dosage for treating granulomatosis with polyangiitis and microscopic polyangiitis (2 types of anti-neutrophil cytoplasmic antibody [ANCA]-associated vasculitis) is 375 mg/m2 body surface area, administered intravenously once weekly for 4 weeks (4 infusions in total). The manufacturer's estimate of the average cost of a course of treatment is £4889.64 (based on 1.79 m2 body surface area and no vial sharing).	Comparison of rituximab with cyclophosphamide: incremental QALYs 0.24. Comparison of rituximab with cyclophosphamide : Incremental QALYs 0.24. Comparison of rituximab with cyclophosphamide: Incremental WALYs 0.14.	The Committee agreed that the most plausible ICER on which to base its decision for people who can have cyclophosphamide was £12,100 per QALY gained, provided by the comparison of 2 courses of cyclophosphamide followed by 1 course of rituximab with 2 courses of cyclophosphamide. The Committee concluded there was substantial uncertainty about the cost effectiveness of rituximab for people who cannot have cyclophosphamide, but on balance the ICER was likely to be lower than £30,000 per QALY gained.	http://www.nice.org.uk/guidance/ta308/resources/guidance-rituximab-in-combination-with-glucocorticoids-for-treating-antineutrophil-cytoplasmic-antibodyassociated-vasculitis-pdf	205.206	Mabthera®	
TA309	2014		Pemetrexed maintenance treatment following induction therapy with pemerexed and cisplatin	Non-squamous non-small-cell lung cancer	Not Recommended	At the time of appraisal, the technology was not considered to be an appropriate use of NHS resources based on the data available.	The list price for pemetrexed is £160 for a 100-mg vial and £800 for a 500-mg vial (excluding VAT; 'British national formulary' [BNF] January 2014). Using the manufacturer's estimated average body surface area of 1.79 m2 the drug cost for each treatment cycle is £1440. Because patients are treated until disease progression or toxicity, the number of cycles varies; in the clinical trial the mean number of cycles given for maintenance treatment was 7.86. Therefore, assuming 8 cycles of treatment, the average total treatment cost is approximately £11,520.	Nafees utility values: Incremental QALYs of 0.1583. Utility values from the unadjusted utility model: incremental QALYs of 0.1760.	Approximately £74,500 per QALY gained	http://www.nice.org.uk/guidance/ta309/resources/guidance-pemetrexed-maintenance-treatment-following-induction-therapy-with-pemetrexed-and-cisplatin-for-nonsquamous-nonsmallcell-lung-cancer-pdf	74.020	Alimta	
TA310	2014		Afatinib	Treating epidermal growth factor receptor mutation-positive locally advanced or metastatic non-small-cell lung cancer	Option	Afatinib is recommended as an option, within its marketing authorisation, for treating adults with locally advanced or metastatic non-small-cell lung cancer only if: the tumour tests positive for the epidermal growth factor receptor tyrosine kinase (EGFR-TK) mutation and the person has not previously had an EGFR-TK inhibitor and the manufacturer provides afatinib with the discount agreed in the patient access scheme.	The NHS list price, provided by the manufacturer, is £2023.28 per pack of 28 tablets (20 mg, 30 mg, 40 mg or 50 mg). The manufacturer stated that the NHS list price per course of treatment is expected to be around £22,000 per patient, based on a progression-free survival of 11 months. The manufacturer of afatinib has agreed a patient access scheme with the Department of Health in which a confidential discount is applied at the point of purchase or invoice.		Could not be estimated	http://www.nice.org.uk/guidance/ta310/resources/guidance-afatinib-for-treating-epidermal-growth-factor-receptor-mutationpositive-locally-advanced-or-metastatic-nonsmallcell-lung-cancer-pdf	1.448	Giotrif	
TA311	2014		Bortezomib for induction therapy	Multiple myeloma before hig-dose chemotherapy and autologous stem cell transplantation	Recommended	Bortezomib is recommended as an option within its marketing authorisation, that is, in combination with dexamethasone, or with dexamethasone and thalidomide, for the induction treatment of adults with previously untreated multiple myeloma, who are eligible for high-dose chemotherapy with haematopoietic stem cell transplantation.	The cost of bortezomib is £762 per 3.5-mg vial (excluding VAT; British National Formulary [BNF] edition 66). According to the marketing authorisation bortezomib should be given in combination with dexamethasone (4 cycles of 21 days each) or with dexamethasone and thalidomide (4 cycles of 28 days each; 2 additional cycles of 28 days each for patients with at least partial response after the fourth cycle). Four intravenous infusions or subcutaneous injections of bortezomib are administered per cycle, on days 1, 4, 8 and 11 of each cycle. The average cost of a course of treatment with bortezomib given with dexamethasone is estimated to be £12,261 and the average cost of a course of treatment with bortezomib given with dexamethasone and thalidomide is estimated to be £24,840.		Bortezomib, thalidomide and dexamethasone compared with thalidomide and dexamethasone: ICERs of £22,700 and £39,600 per QALY gained. For bortezomib and dexamethasone compared with cyclophosphamide, thalidomide and dexamethasone: the ICERs were £20,600, £24,300 and £33,400 per QALY gained	http://www.nice.org.uk/guidance/ta311/resources/guidance-bortezomib-for-induction-therapy-in-multiple-myeloma-before-highdose-chemotherapy-and-autologous-stem-cell-transplantation-pdf	58.408	Velcade	
TA312	2014		Alemtuzumab	Treating relapsing-remitting multiple sclerosis	Recommended	Alemtuzumab is recommended as an option, within its marketing authorisation, for treating adults with active relapsing–remitting multiple sclerosis.	The price of alemtuzumab is £7045 per 12 mg vial, which equates to £56,360 for the full course of treatment consisting of 5 daily consecutive 12 mg doses in year 1, followed by 3 daily consecutive 12 mg doses 12 months later in year 2.		The Committee concluded that the most plausible ICER for alemtuzumab compared with glatiramer acetate for people with active relapsing-remitting multiple sclerosis is likely to lie between £13,600 and £24,500 per QALY gained. The Committee noted that the most plausible ICER for patients with highly active relapsing-remitting multiple sclerosis despite beta interferon treatment was £8900 per QALY gained for alemtuzumab compared with fingolimod. The Committee noted that for patients with rapidly evolving severe relapsing-remitting multiple sclerosis, alemtuzumab dominated natalizumab.	http://www.nice.org.uk/guidance/ta312/resources/guidance-alemtuzumab-for-treating-relapsingremitting-multiple-sclerosis-pdf	9.245	Lemtrada	
TA316	2014		Enzalutamide	Metastatic homone-relapsed prostate cancer previously treated with a docetaxel-containing regimen	Recommended	Enzalutamide is recommended within its marketing authorisation as an option for treating metastatic hormone-relapsed prostate cancer in adults whose disease has progressed during or after docetaxel-containing chemotherapy, only if the manufacturer provides enzalutamide with the discount agreed in the patient access scheme.	Enzalutamide costs £2734.67 for 1 pack of 112 40-mg capsules, (excluding VAT; 'British national formulary' [BNF] website accessed March 2014). Assuming a daily dose of 160 mg and a mean length of treatment of 8.5 months, the manufacturer estimated that the average cost of treatment with enzalutamide, based on the list price, is £25,269. The manufacturer of enzalutamide has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the price listed above, with the discount applied at the point of purchase or invoice.		For patients who had received 1 previous cytotoxic chemotherapy regimen, the Committee noted that the analysis reflecting its preferred assumptions, but not the actual patient access scheme discount for abiraterone, gave an ICER of £22,600 per QALY gained for enzalutamide compared with abiraterone. The Committee agreed that enzalutamide would remain cost effective when the correct patient access scheme for abiraterone is taken into account. For patients who had received 2 or more previous courses of cytotoxic chemotherapy, the Committee noted that the ICER estimated by the manufacturer for enzalutamide compared with best supportive care was £45,500 per QALY gained and that the ERG's ICER was £48,000 per QALY gained.	http://www.nice.org.uk/guidance/ta316/resources/guidance-enzalutamide-for-metastatic-hormonerelapsed-prostate-cancer-previously-treated-with-a-docetaxelcontaining-regimen-pdf	29.747	Xtandi®	

TA319	2014		Ipilimumab	For previously untreated advanced (unresectable or metastatic) melanoma	Recommended	Ipilimumab is recommended, within its marketing authorisation, as an option for treating adults with previously untreated advanced (unresectable or metastatic) melanoma, only if the manufacturer provides ipilimumab with the discount agreed in the patient access scheme.	Ipilimumab is priced at £3750 per 10-ml vial (5 mg/ml) or £15,000 per 40-ml vial (5 mg/ml) (excluding VAT; 'British national formulary' [BNF] edition 67). The manufacturer of ipilimumab has agreed a patient access scheme with the Department of Health.		The most plausible ICER is £47,900 per QALY gained for ipilimumab compared with dacarbazine and £28,600 per QALY gained for ipilimumab compared with vemurafenib.	http://www.nice.org.uk/guidance/ta319/resources/guidance-ipilimumab-for-previously-untreated-advanced-unresectable-or-metastatic-melanoma-pdf	92.969,00	Yervoy*	
TA320	2014		Dimethyl fumarate	Treating relapsing-remitting multiple sclerosis	Option	Dimethyl fumarate is recommended as an option for treating adults with active relapsing-remitting multiple sclerosis (normally defined as 2 clinically significant relapses in the previous 2 years), only if: they do not have highly active or rapidly evolving severe relapsing-remitting multiple sclerosis and the manufacturer provides dimethyl fumarate with the discount agreed in the patient access scheme.	The recommended dosage is 120 mg twice daily in the first week of treatment and 240 mg twice daily thereafter. The frequency of flushing and gastrointestinal adverse reactions may be managed by temporarily (up to a month) reducing the dosage to 120 mg twice daily. The prices of a pack of 120-mg tablets (14 tablets per pack) and 240-mg tablets (56 tablets per pack) are £343 and £1373 respectively (excluding VAT; manufacturer's submission). The manufacturer of dimethyl fumarate has agreed a patient access scheme with the Department of Health, with a simple discount applied at the point of purchase or invoice.	Dimethyl fumarate compared with glatiramer acetate: incremental QALYs gained of 0.26	A comparison of dimethyl fumarate with glatiramer acetate: the most plausible ICER is below £27,700 per QALY gained, taking into consideration that waning of treatment effect may have been overestimated and also the benefits not captured in the economic modelling, such as the oral administration of dimethyl fumarate and its shorter washout period.	http://www.nice.org.uk/guidance/ta320/resources/guidance-dimethyl-fumarate-for-treating-relapsingremitting-multiple-sclerosis-pdf	62.338	Tecfidera	
TA321	2014		Dabrafenib	Treating unresectable or metastatic BRAF V600 mutation-positive melanoma	Recommended	Dabrafenib is recommended, within its marketing authorisation, as an option for treating unresectable or metastatic BRAF V600 mutation-positive melanoma only if the company provides dabrafenib with the discount agreed in the patient access scheme.	The list price of dabrafenib is £1400 for a pack of 75-mg capsules (28 capsules per pack) and £933.33 for a pack of 50-mg capsules (28 capsules per pack) (excluding VAT; 'British national formulary' [BNF] edition 67). It is taken orally at a recommended dose of 150 mg twice daily. GlaxoSmithKline has agreed a patient access scheme with the Department of Health that makes dabrafenib available with a discount applied at the point of purchase or invoice. The size of the discount is commercial in confidence.		The Committee noted that the company's base case ICER was £11,000 per QALY gained for dabrafenib compared with vemurafenib, but was much lower than this if a class effect was assumed for dabrafenib and vemurafenib. In the absence of any further numerical analysis by the ERG, the Committee could not give an estimate of the most plausible ICER for the comparison of dabrafenib with vemurafenib.	http://www.nice.org.uk/guidance/ta321/resources/guidance-dabrafenib-for-treating-unresectable-or-metastatic-brafv600-mutationpositive-melanoma-pdf	14.286	Tafinlar	
TA322	2014		Lenalidomide	Treating myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality	Recommended	Lenalidomide is recommended as an option, within its marketing authorisation, that is for treating transfusion-dependent anaemia caused by low or intermediate-1 risk myelodysplastic syndromes associated with an isolated deletion 5q cytogenetic abnormality when other therapeutic options are insufficient or inadequate, with the following condition: The drug cost of lenalidomide (excluding any related costs) for people who remain on treatment for more than 26 cycles (each of 28 days; normally a period of 2 years) will be met by the company.	Lenalidomide is available in 21-day packs of 10 mg and 5 mg capsules at net prices of £3780 and £3570 respectively (excluding VAT; 'British national formulary' [BNF] edition 67). The cost of a 28-day cycle of treatment with 10 mg of lenalidomide (excluding VAT) is £3780. The company (Celgene) has agreed a standard patient access scheme with the Department of Health, in which the NHS pays for lenalidomide treatment for up to 26 monthly cycles. The company subsequently provides free of charge lenalidomide for those people who receive more than 26 monthly cycles.		The revised company's base-case ICER, which included the patient access scheme and accounted for treatment interruptions (model 4), for lenalidomide compared with best supportive care was approximately £25,300 per QALY gained. The patient access scheme increased all of the uncertainties, and there was a risk that savings from the patient access scheme would not be realised in clinical practice, because of the uncertainty about survival estimates. The Committee acknowledged that the data collection committed to by the company will ensure that the uncertainties of the assumptions used to model the patient access scheme can be addressed when the guidance is reviewed. The Committee concluded that lenalidomide for treating MDS associated with an isolated deletion 5q cytogenetic abnormality was a cost-effective use of NHS resources, when taking these assurances into account.	http://www.nice.org.uk/guidance/ta322/resources/guidance-lenalidomide-for-treating-myelodysplastic-syndromes-associated-with-an-isolated-deletion-5q-cytogenetic-abnormality-pdf	65.708	Revlimid*	
TA323	2014		Erythropoiesis-stimulating agents (epoetin and darbepoetin)	Treating anaemia in people with cancer having chemotherapy	Recommended	Review of TA142. Erythropoiesis-stimulating agents (epoetin alfa, beta, theta and zeta, and darbepoetin alfa) are recommended, within their marketing authorisations, as options for treating anaemia in people with cancer who are having chemotherapy. If different erythropoiesis-stimulating agents are equally suitable, the product with the lowest acquisition cost for the course of treatment should be used.	Eprex and Binocrit are available in pre-filled syringes at net prices of £5.53 and £4.33 per 1000 units respectively (excluding VAT; British national formulary [BNF], March 2014). They are administered by subcutaneous injection at a recommended initial dose of 150 units/kg body weight 3 times weekly or 450 units/kg body weight once a week.		The Committee concluded that the scenario assuming equal survival and using contract prices was the most plausible. It noted that the probabilistic ICERs for this scenario were all below £30,000 per QALY gained and that the benefits of ESA treatment associated with avoiding blood transfusions and starting ESA treatment only at haemoglobin concentrations in line with the marketing authorisations would likely reduce the ICERs. The Committee agreed that the most plausible ICER was below £20,000 per QALY gained.	http://www.nice.org.uk/guidance/ta323/resources/guidance-erythropoiesisstimulating-agents-epoetin-and-darbepoetin-for-treating-anaemia-in-people-with-cancer-having-chemotherapy-including-review-of-ta142-pdf	113	Eprex	
TA326	2014		Imatinib	Adjuvant treatment of gatrointestinal stromal tumours	Option	Update of guideline TA196. Imatinib is recommended as an option as adjuvant treatment for up to 3 years for adults who are at high risk of relapse after surgery for KIT (CD117)-positive gastrointestinal stromal tumours, as defined by the Miettinen 2006 criteria[1] (based on tumour size, location and mitotic rate).	The summary of product characteristics recommends a dose of 400 mg per day of imatinib as an adjuvant treatment after surgery for GISTs. It states that optimal treatment duration is not yet established but that length of treatment in a supporting clinical trial was 36 months. Imatinib is available in doses of 100 mg (60-tab pack) and 400 mg (30-tab pack) at net prices per pack of £862.19 and £1724.39 respectively (excluding VAT; 'British national formulary' [BNF] edition 67). At a dose of 400 mg per day, drug costs for a course of treatment would be approximately £20,700 for 1 year and £62,100 for 3 years. The net price of imatinib has risen since the original appraisal of Imatinib for the adjuvant treatment of gastrointestinal stromal tumours (NICE technology appraisal guidance 196). At that time, drug costs for a 1-year course of treatment (400 mg per day) would have been approximately £19,500.	For the company's fully incremental analysis, the incremental QALYs for1 year's treatment with imatinib compared with no adjuvant treatment was 2.24 QALYs. For 3 years' treatment with imatinib compared with 1 year was the incremental QALYs 1.43.	The Committee concluded that the true value of the ICERs was between £3610 and £12,100 per QALY gained for 1-year adjuvant imatinib compared with no adjuvant treatment, and between £16,700 and £30,000 per QALY gained for 3-year adjuvant imatinib compared with 1-year adjuvant imatinib.	http://www.nice.org.uk/guidance/ta326/resources/guidance-imatinib-for-the-adjuvant-treatment-of-gastrointestinal-stromal-tumours-review-of-nice-technology-appraisal-guidance196-pdf	95.933,00	Glivec*	
TA328	2014		Idelalisib	Treating follicular lymphoma that is refractory to 2 prior treatments	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.				http://www.nice.org.uk/guidance/ta328/resources/guidance-idelalisib-for-treating-follicular-lymphoma-that-is-refractory-to-2-prior-treatments-terminated-appraisal-pdf	363,00	Zydelig	

TA329	2015		Infliximab	treating moderately to severely active ulcerative colitis after the failure of conventional therapy	Recommended	Including af review of TA140 and TA262	The price of infliximab is £419.62 for a 100 mg vial containing powder for reconstitution (excluding VAT; BNF edition 67). Assuming the patient weighs 77 kg and the recommended dose for infliximab is followed (see section 3.8), the cost of infliximab induction therapy is £5035; the cost of 4 weeks of infliximab maintenance therapy is £839.		In the company's model for adalimumab, the base-case ICER for adalimumab compared with conventional therapy was £34,400 per QALY gained. This was revised to £23,000 per QALY gained; a revision not critiqued by the Assessment Group. When the Assessment Group compared medical options only, infliximab was dominated by adalimumab, and golimumab was extendedly dominated by adalimumab and conventional therapy. The base-case ICER for adalimumab compared with conventional therapy was £50,600 per QALY gained.	http://www.nice.org.uk/guidance/ta329/resources/guidance-infliximab-adalimumab-and-golimumab-for-treating-moderately-to-severely-active-ulcerative-colitis-after-the-failure-of-conventional-therapy-including-a-review-of-ta140-and-ta262-pdf	335.348	Remicade
TA329			Infliximab	treating moderately to severely active ulcerative colitis after the failure of conventional therapy - in children and young people aged 6-17 years	Recommended	Including af review of TA140 and TA262	The price of infliximab is £419.62 for a 100 mg vial containing powder for reconstitution (excluding VAT; BNF edition 67). Assuming the patient weighs 77 kg and the recommended dose for infliximab is followed (see section 3.8), the cost of infliximab induction therapy is £5035; the cost of 4 weeks of infliximab maintenance therapy is £839.	j	For children and young people, the Assessment Group estimated an ICER of £68,400 per QALY gained for infliximab compared with conventional therapy.	http://www.nice.org.uk/guidance/ta329/resources/guidance-infliximab-adalimumab-and-golimumab-for-treating-moderately-to-severely-active-ulcerative-colitis-after-the-failure-of-conventional-therapy-including-a-review-of-ta140-and-ta262-pdf	335.348	Remicade
TA329	2015		Adalimumab	treating moderately to severely active ulcerative colitis after the failure of conventional therapy	Recommended	Including af review of TA140 and TA262	The price of adalimumab is £352.14 for a pre-filled 40 mg pen or syringe, or a 40 mg/0.8 ml vial (excluding VAT; 'British National Formulary' [BNF] edition 67). Assuming the recommended dosage for adalimumab is followed, the cost of adalimumab induction therapy is £2113; the cost of 4 weeks of adalimumab maintenance therapy is £704.		In the company's model for adalimumab, the base-case ICER for adalimumab compared with conventional therapy was £34,400 per QALY gained. This was revised to £23,000 per QALY gained; a revision not critiqued by the Assessment Group. When the Assessment Group compared medical options only, infliximab was dominated by adalimumab, and golimumab was extendedly dominated by adalimumab and conventional therapy. The base-case ICER for adalimumab compared with conventional therapy was £50,600 per QALY gained.	http://www.nice.org.uk/guidance/ta329/resources/guidance-infliximab-adalimumab-and-golimumab-for-treating-moderately-to-severely-active-ulcerative-colitis-after-the-failure-of-conventional-therapy-including-a-review-of-ta140-and-ta262-pdf	419.141	Humira
TA329	2015		Golimumab	treating moderately to severely active ulcerative colitis after the failure of conventional therapy	Recommended	Including af review of TA140 and TA262. Golimumab is recommended only if the company provides the 100 mg dose of golimumab at the same cost as the 50 mg dose, as agreed in the patient access scheme.	The price of golimumab is £762.97 for a pre-filled 50 mg pen or syringe and £1525.94 for a 100 mg pre-filled pen (excluding VAT; BNF edition 67). Merck Sharp & Dohme has agreed a patient access scheme with the Department of Health. This will make the 100 mg dose of golimumab available to the NHS at the same cost as the 50 mg dose. Including the patient access scheme and assuming that the recommended dosage for golimumab is followed (see section 3.5), the cost of golimumab induction therapy is £2289; the cost of 4 weeks of golimumab maintenance therapy is £763.		In the company's model for adalimumab, the base-case ICER for adalimumab compared with conventional therapy was £34,400 per QALY gained. This was revised to £23,000 per QALY gained; a revision not critiqued by the Assessment Group. When the Assessment Group compared medical options only, infliximab was dominated by adalimumab, and golimumab was extendedly dominated by adalimumab and conventional therapy. The base-case ICER for adalimumab compared with conventional therapy was £50,600 per QALY gained.	http://www.nice.org.uk/guidance/ta329/resources/guidance-infliximab-adalimumab-and-golimumab-for-treating-moderately-to-severely-active-ulcerative-colitis-after-the-failure-of-conventional-therapy-including-a-review-of-ta140-and-ta262-pdf	99.930	Simponi
TA330	2015		Sofosbuvir	Treating chronic hepatitis C	Recommended in addults as specified en the next collum	Sofosbuvir in combination with peinterferon alfa and ribavirin: Is recommended for adults with genotype 1 HCV, for adults with genotype 3 HCV treatment of treatment-naive patients is only reccomended for people with cirrhosis and recommended for all with treatmentexperienced, and for adults with genotype 4,5 or 6 HCV only reccomended for people with cirhosis. Sofosbuvir in combination with ribavirin: For Adults eith genotype 2 HCV it is only recommended for people who are intolerant to or ineligible for interferon, for adults with genotype 3 HCV it is only recommended for people with cirrhosis who are intolerant to or ineligible for interferon.	The cost of sofosbuvir is £11,660.98 per 28 tablet pack of 400 mg tablets (excluding VAT, 'British national formulary' [BNF] May 2014). The cost of a 12 week course of treatment is £34,982.94 and a 24 week course is £69,965.88 (both excluding VAT), not including the cost for ribavirin and peginterferon alfa. Costs may vary in different settings because of negotiated procurement discounts.		The Commitee considere sofosbuvir cost-effective en the recommended scenaries (under £30.000 per QALY gained)	http://www.nice.org.uk/guidance/ta330/resources/guidance-sofosbuvir-for-treating-chronic-hepatitisc-pdf	106.823	Sovaldi
TA331	2015		Simeprevir in combination with pegeinterferon	treating genotypes 1 and 4 chronic hepatitis C	Recommended	Recommended within its marketing authorisation as an option for treating genotype 1 and 4 chornic hepatitis C in adults	Simeprevir costs £1866.50 per pack of 7x150 mg tablets (excluding VAT, MIMS online, accessed July 2014). A course of simeprevir (for 12 weeks) plus peginterferon alfa and ribavirin (both for 24 weeks) costs £27,220. A course of simeprevir (for 12 weeks) plus peginterferon alfa and ribavirin (both for 48 weeks) costs £32,155. Costs may vary in different settings because of negotiated procurement discounts.		For treating genotype 1 HCV, the ICERs for simeprevir plus peginterferon alfa and ribavirin compared with peginterferon alfa and ribavirin alone was between £14,200 and £9800 per QALY. Simeprevir dominated both telaprevir and boceprevir (both with peginterferon alfa and ribavirin), that is simeprevir was less expensive and provided more QALYs. The Committee noted that, in all scenarios for genotype 4 HCV, the ICERs for simeprevir plus peginterferon alfa and ribavirin compared with peginterferon alfa and ribavirin remained below £20,000 per QALY gained.	http://www.nice.org.uk/guidance/ta331/chapter/9-Sources-of-evidence-considered-by-the-Committee	21.018	Olysio

TA333	2015		Axitinib	advanced renal cell carcinoma after failure of prior systemic treatment	Option	Axitinib is recommended as an option for treating adults with advanced renal cell carcinoma after failure of treatment with a first-line tyrosine kinase inhibitor or a cytokine, only if the company provides axitinib with the discount agreed in the patient access scheme.	Axitinib is available in 1-mg and 5-mg film-coated tablets at net prices of £703.40 and £3517 per 56-tablet pack respectively (excluding VAT, 'British national formulary' [BNF] November 2014). Axitinib is administered orally at a recommended starting dose of 5 mg twice daily. This dose may be increased to 7 mg and then up to 10 mg, or decreased to 3 mg and then down to 2 mg, depending on individual safety and tolerability. The company has agreed a patient access scheme with the Department of Health. The size of the discount is commercial in confidence.		The Committee considered that the more plausible ICER for the prior-sunitinib group was likely to lie between the base-case estimate with a progression-free to overall survival gain relationship of 1 to 1.6 (approximately £33,500 per QALY gained) and the estimate assuming no survival gain with a survival relationship of 1 to 1 (approximately £52,900 per QALY gained) and concluded that the ICER would be likely to be towards the middle of this range. For the prior-cytokine group, the Committee noted that the company's base-case ICER of approximately £55,300 per QALY gained (with the patient access scheme applied) compared with best supportive care was based on the overall survival for best supportive care of 24 months, but fell to £36,500 per QALY gained if 17.46 months for overall survival for best supportive care was used.	http://www.nice.org.uk/guidance/ta333/resources/guidance-axitinib-for-treating-advanced-renal-cell-carcinoma-after-failure-of-prior-systemic-treatment-pdf	7.578	Inlyta
TA334	2015		Regorafenib	metastatic colorectal cancer after treatment for metastatic disease	Terminated Appraisal - non submission	The single technology appraisal process is based on the manufacturer's submission. In the absence of a submission from the manufacturer the appraisal was terminated and a recommendation could not be made.					http://www.nice.org.uk/guidance/ta334/resources/guidance-regorafenib-for-metastatic-colorectal-cancer-after-treatment-for-metastatic-disease-terminated-appraisal-pdf	6.681	Stivarga
TA338	2015		Pomalidomide	For relapsed and refractory multiple myeloma previously treated with lenalidomide and bortezomib	Not Recommended	Pomalidomide, in combination with dexamethasone, is not recommended within its marketing authorisation for treating relapsed and refractory multiple myeloma in adults who have had at least 2 previous treatments, including lenalidomide and bortezomib, and whose disease has progressed on the last therapy.	Pomalidomide is administered orally. The recommended dosage is 4 mg once daily, taken on days 1 to 21 of repeated 28-day cycles. Treatment should continue until disease progression. Adverse reactions may be managed by interrupting or reducing the dose, as specified in section 4.2 of pomalidomide's summary of product characteristics. The price of a pack (21 tablets) of 1 mg, 2 mg, 3 mg or 4 mg tablets is £8884 (excluding VAT; British National Formulary [BNF] edition 67). Costs may vary in different settings because of negotiatedprocurement discounts.		ICERs presented for pomalidomide were over £50,000 per QALY gained compared with bortezomib, and over £70,000 per QALY gained compared with bendamustine plus thalidomide and dexamethasone. The Committee were of the view that the ICERs for pomalidomide would be more likely to increase than to decrease if the uncertainties were accounted for in the economic analysis.	http://www.nice.org.uk/guidance/ta338/resources/guidance-pomalidomide-for-relapsed-and-refractory-multiple-myeloma-previously-treated-with-lenalidomide-and-bortezomib-pdf	19.355	Imnovid
TA339	2015		Omalizumab	Previously treated chronic spontaneous urticaria	Option	Omalizumab is recommended as an option as add-on therapy for treating severe chronic spontaneous urticaria in adults and young people aged 12 years and over only if: the severity of the condition is assessed objectively, for example, using a weekly urticaria activity score of 28 or more the person's condition has not responded to standard treatment with H1-antihistamines and leukotriene receptor antagonists omalizumab is stopped at or before the fourth dose if the condition has not responded omalizumab is stopped at the end of a course of treatment (6 doses) if the condition has responded, to establish whether the condition has gone into spontaneous remission, and is restarted only if the condition relapses, omalizumab is administered under the management of a secondary care specialist in dermatology, immunology or allergy the company provides omalizumab with the discount agreed in the patient access scheme.	Omalizumab costs £256.15 for a 150 mg prefilled syringe (excluding VAT; 'British national formulary' [BNF] online October 2014). A single dose of 300 mg costs £512.30 and the cost for a 24-week course of treatment is £3073.80 (excluding VAT). The company has agreed a patient access scheme with the Department of Health. This scheme would provide a simple discount to the list price of omalizumab across all indications, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.		In the company's revised base-case analysis, the ICER was approximately £28,000 per QALY gained. However, because the model probably underestimated the response in patients on standard medications in the placebo arm of the trial, the Committee concluded that it was likely to be underestimated. For patients with severe disease at baseline, the revised base-case ICER was around £26,000 per QALY gained. The Committee noted that the model likely underestimated the severity of disease in the utility values used for the severe health state in the model and a more realistic value for severe disease would likely increase the incremental QALY gain and decrease the ICER. The Committee was also aware that the benefit of avoiding the side effects of immunosuppressant treatment was not accounted for in the model and, considering the lifelong nature of these effects, the actual ICER for severe disease may be lower.	http://www.nice.org.uk/guidance/ta339/resources/guidance-omalizumab-for-previously-treated-chronic-spontaneous-urticaria-pdf	35.900	Xolair
TA340	2015		Ustekinumab	active psoriatic arthritis	Option	This guidance replaces Ustekinumab for treating active psoriatic arthritis (NICE technology appraisal guidance 313 issued in May 2014). Ustekinumab is recommended as an option, alone or in combination with methotrexate, for treating active psoriatic arthritis in adults only when: treatment with tumour necrosis factor (TNF) alpha inhibitors is contraindicated but would otherwise be considered (as described in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis and golimumab for the treatment of psoriatic arthritis) or the person has had treatment with 1 or more TNF–alpha inhibitors. Ustekinumab is recommended only if the company provides the 90 mg dose of ustekinumab for people who weigh more than 100 kg at the same cost as the 45 mg dose, as agreed in the patient access scheme. Ustekinumab treatment should be stopped if the person's psoriatic arthritis has not shown an adequate response using the Psoriatic Arthritis Response Criteria (PsARC) at gained).lizumab became a dominant treatment option, that is, more effective and less costly than its comparators. packs of capsules) the cost of a course of treatment would be £51,579.riteria. As recommended in NICE technology appraisal guidance on etanercept, infliximab and adalimumab for the treatment of psoriatic arthritis, people whose disease has a Psoriasis Area and Severity Index (PASI) 75 response but whose PsARC	The list price for ustekinumab is £2147 per 45-mg vial (excluding VAT; British national formulary online [accessed February 2015]). The recommended dose of ustekinumab is an initial dose of 45 mg, followed by a dose 4 weeks later and further doses every 12 weeks thereafter. A dose of 90 mg may be used in people with a body weight over 100 kg. The summary of product characteristics notes that consideration should be given to stopping treatment in people whose psoriatic arthritis has shown no response after up to 28 weeks of treatment. The average annual acquisition cost for ustekinumab 45 mg is £10,735 in the first year and £9304 per year thereafter. The company has agreed a patient access scheme with the Department of Health, in which the company provides the 90-mg dose (2 vials) at the same cost as the 45-mg dose (1 vial), for people who weigh more than 100 kg and need the higher dose.		With the patient access scheme: In the TNF-alpha inhibitor-naive population, ustekinumab was extendedly dominated (that is, was more expensive and less effective than a combination of 2 comparators). In people who have not previously had TNF-alpha inhibitors and for whom TNF-alpha inhibitors are inappropriate because of contraindications, the Committee concluded that the most plausible ICER was £21,900 per QALY gained. In the TNF-alpha inhibitor-exposed population, the Committee noted that in the incremental analysis, the most plausible ICER was £25,400 per QALY gained (compared with conventional management). In the TNF-alpha inhibitor-exposed population, looking specifically at people for whom TNF-alpha inhibitors as a class had failed, the Committee considered that the most plausible ICER for ustekinumab compared with conventional management was £25,300 per QALY gained.	http://www.nice.org.uk/guidance/ta340/resources/guidance-ustekinumab-for-treating-active-psoriatic-arthritis-rapid-review-of-technology-appraisal-guidance-313-pdf	57.125	Stelara*

TA342	2015		Vedolizumab	Treating moderately to severely active ulcerative colitis	Option	Vedolizumab is recommended, within its marketing authorisation, as an option for treating moderately to severely active ulcerative colitis in adults only if the company provides vedolizumab with the discount agreed in the patient access scheme. Vedolizumab should be given until it stops working or surgery is needed. At 12 months after the start of treatment, people should be reassessed to see whether treatment should continue. Treatment should only continue if there is clear evidence of ongoing clinical benefit. For people in complete remission at 12 months, consider stopping vedolizumab, resuming treatment if there is a relapse. People who continue edolizumab should be reassessed at least every 12 months to see whether continued treatment is justified.	The NHS list price of vedolizumab is £2050 per 300 mg vial (excluding VAT; 'British national formulary' [BNF] edition 69). The company has agreed a patient access scheme with the Department of Health. This scheme provides a simple discount to the list price of vedolizumab, with the discount applied at the point of purchase or invoice. The level of the discount is commercial in confidence.		In the population in whom treatment with a TNF-alpha inhibitor had failed, the Committee expressed a preference for the use of published utility values from Woehl et al. or Swinburn et al. to those used in the company's base case and noted that the corresponding ICERs were £31,900 and £27,500 per quality-adjusted life year (QALY) gained, which were around the upper limit of the range normally considered to be a cost-effective use of NHS resources. In the population who had not had treatment with a TNF-alpha inhibitor before, the company's pairwise ICERs with adalimumab and conventional therapy were £7000 and £5000 per QALY gained, respectively. The Committee understood that in the ERG's exploratory incremental analysis, vedolizumab was dominated by adalimumab. However, if this analysis was adjusted by applying the Swinburn et al. rather than Woehl et al. utility values, and assuming a 1-year stopping rule, the ICER for vedolizumab was less than £20,000 per QALY gained relative to its comparators. This meant that vedolizumab became a dominant treatment option, that is, more effective and less costly than its comparators.	http://www.nice.org.uk/guidance/ta342/resources/guidance-vedolizumab-for-treating-moderately-to-severely-active-ulcerative-colitis-pdf	6.715	Entyvio
TA343	2015		Obinutuzumab	In combination with chlorambucil for untreated chronic lymphocytic leukaemia	Option	Obinutuzumab, in combination with chlorambucil, is recommended as an option for adults with untreated chronic lymphocytic leukaemia who have comorbidities that make full-dose fludarabine-based therapy unsuitable for them, only if: bendamustine-based therapy is not suitable and the company provides obinutuzumab with the discount agreed in the patient access scheme.	The price of obinutuzumab is £3312 per 1000-mg vial (excluding VAT; 'British national formulary' [BNF] February 2015). The company stated that a course of treatment costs £26,496 (£9936 for cycle 1 and £3312 for cycles 2–6, excluding VAT). The recommended dosage is 1000 mg administered over days 1 and 2, 1000 mg on day 8 and 1000 mg on day 15 of treatment cycle 1, followed by 1000 mg on day 1 of treatment cycles 2–6. The company has agreed a patient access scheme with the Department of Health that makes obinutuzumab available with a discount.		For people who cannot have bendamustine, the Committee noted that the most likely ICERs (including the patient access scheme) for obinutuzumab plus chlorambucil compared with chlorambucil alone and with rituximab and chlorambucil were within the range considered cost effective (£20,000–30,000 per QALY gained). For people who can have bendamustine, the Committee noted that the most likely ICERs (including the patient access scheme) for obinutuzumab plus chlorambucil compared with both bendamustine alone and with rituximab plus bendamustine were above the top end of the range that would normally be considered cost effective (£20,000–30,000 per QALY gained).	http://www.nice.org.uk/guidance/ta343/resources/guidance-obinutuzumab-in-combination-with-chlorambucil-for-untreated-chronic-lymphocytic-leukaemia-pdf	440	Gazyvaro
TA344	2015		Ofatumumab	in combination with chlorambucil or bendamustine for untreated chronic lymphocytic leukaemia	Option	Ofatumumab in combination with chlorambucil is recommended as an option for untreated chronic lymphocytic leukaemia only if: the person is ineligible for fludarabine-based therapy and bendamustine is not suitable and the company provides ofatumumab with the discount agreed in the patient access scheme.	The recommended dose and schedule in the summary of product characteristics is 300 mg on day 1 followed by 1000 mg on day 8 (cycle 1), followed by 1000 mg on day 1 of subsequent cycles, for a minimum of 3 cycles, until best response or a maximum of 12 cycles (every 28 days). Best response is defined as a clinical response that did not improve after 3 additional cycles of treatment. Ofatumumab is priced at £182 for a 100-mg vial and £1820 for a 1000-mg vial (British national formulary 66, 2014). Assuming 6 cycles and no drug wastage, the mean cost of a treatment course for ofatumumab is £11,466 for 6300 mg. The company has agreed a patient access scheme with the Department of Health that makes ofatumumab available with a discount.		The Committee concluded that the ERG's exploratory base-case ICER of £26,000 per QALY gained, which incorporated the ofatumumab PAS, was the most plausible for ofatumumab plus chlorambucil compared with chlorambucil alone. The Committee concluded that, when using the ofatumumab PAS price, the cost effectiveness of ofatumumab plus chlorambucil is likely to be similar to rituximab plus chlorambucil because of small differences in costs and QALYs.	http://www.nice.org.uk/guidance/ta344/resources/guidance-ofatumumab-in-combination-with-chlorambucil-or-bendamustine-for-untreated-chronic-lymphocytic-leukaemia-pdf	7.029	Arzerra