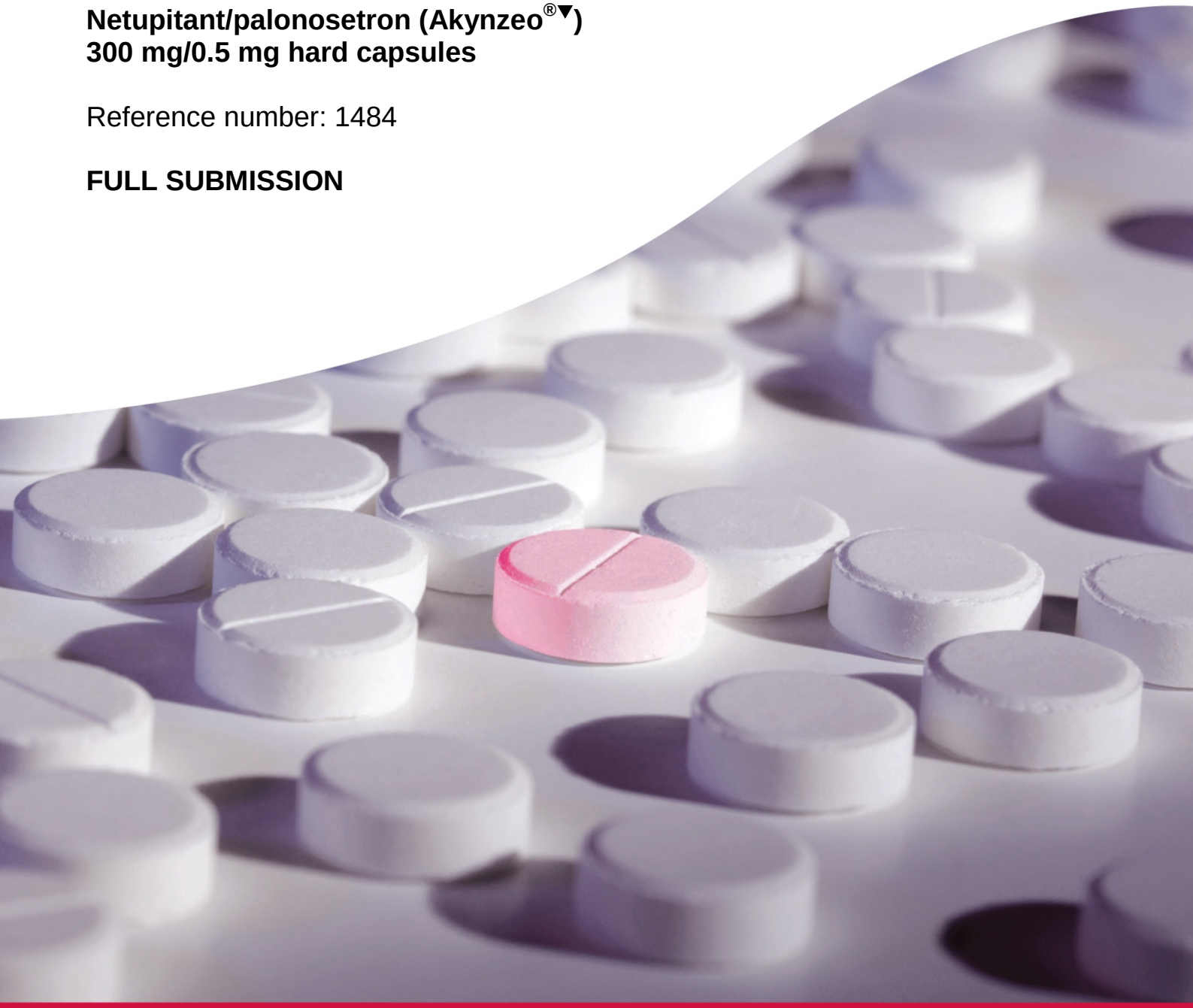
All Wales Therapeutics and Toxicology Centre
Canolfan Therapiwteg a Thocsicoleg Cymru Gyfan

AWMSG SECRETARIAT ASSESSMENT REPORT

Netupitant/palonosetron (Akynzeo®▼)
300 mg/0.5 mg hard capsules

Reference number: 1484

FULL SUBMISSION



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AWMSG Secretariat Assessment Report
Netupitant/palonosetron (Akynzeo®▼) 300 mg/0.5 mg hard capsules

This assessment report is based on evidence submitted by Chugai Pharma UK Ltd[1].

1.0 PRODUCT DETAILS

Licensed indication under consideration	Netupitant/palonosetron (Akynzeo®▼) in adults for the prevention of acute and delayed nausea and vomiting associated with highly emetogenic cisplatin-based cancer chemotherapy and for the prevention of acute and delayed nausea and vomiting associated with moderately emetogenic cancer chemotherapy[2].
Dosing	The recommended dose is one netupitant/palonosetron 300 mg/0.5 mg oral capsule administered approximately one hour before the start of each chemotherapy cycle. Refer to the Summary of Product Characteristics (SPC) for further information regarding dosing[2].
Marketing authorisation date	27 May 2015[3]

2.0 DECISION CONTEXT

2.1 Background

Nausea and vomiting are common side effects of chemotherapy which have a major adverse impact on quality of life for people undergoing cancer treatment[4,5]. Susceptibility to drug-induced nausea and vomiting varies; those affected more often include women, people under 50 years of age, people with anxiety and people who have motion sickness[6].

Chemotherapy regimens vary in the extent to which they cause nausea and vomiting and are usually classed as having minimal, low, moderate or high degree of emetogenicity[6]. The Multinational Association of Supportive Care in Cancer (MASCC) and European Society for Medical Oncology (ESMO) antiemetic guideline 2016 defines cisplatin chemotherapy as highly emetogenic, with an incidence of nausea and vomiting in over 90% of people receiving the treatment[7]. Nausea and vomiting can be either acute (< 24 hours after chemotherapy) or delayed (> 24 hours after chemotherapy)[3]. Delayed vomiting is more common in people who have experienced acute vomiting after cisplatin chemotherapy[5].

The company has focused its submission on the use of netupitant/palonosetron with cisplatin-based highly emetogenic chemotherapy (HEC). The company has not supplied an economic analysis for its use with moderately emetogenic chemotherapy (MEC) and has requested consideration of a restricted recommendation for the HEC sub-population[1].

The MASCC/ESMO guideline recommends that people receiving HEC are given a three-drug regimen of a $5HT_3$ antagonist, dexamethasone and a neurokinin-1 (NK_1) antagonist (aprepitant, fosaprepitant, netupitant [given in a fixed-dose oral combination with palonosetron] or rolapitant [not licensed in the UK]) to prevent nausea and vomiting[7].

Akynzeo®▼ is a fixed-dose combination of netupitant 300 mg and palonosetron 0.5 mg. Netupitant is a selective antagonist of NK_1 receptors and inhibits substance P-mediated responses which are associated with delayed emesis. Palonosetron is a second generation $5HT_3$ antagonist that acts by blocking the action of serotonin on the vomiting reflex[2].

2.2 Comparators

The comparator included in the company's submission was the combination of aprepitant (Emend®) and ondansetron[1].

2.3 Guidance and related advice

- MASCC/ESMO (2016) Antiemetic guideline[7]
- Velindre NHS Trust (2011) Guidelines for the management of chemotherapy-induced and radiotherapy-induced nausea and vomiting[8]

3.0 SUMMARY OF THE EVIDENCE ON CLINICAL EFFECTIVENESS

The company's submission includes details of a phase II study (NETU-07-07) and two phase III studies (NETU-10-29 and NETU-08-18)[1]. NETU-07-07 was a dose-ranging study for netupitant in cisplatin-based HEC; the results reported in section 3.1 are for the licensed dose only. NETU-10-29 was a safety study; results from the HEC group will be briefly described as supportive efficacy and safety data. The company's submission focuses on the HEC sub-population alone and therefore study NETU-08-18 of netupitant/palonosetron in preventing nausea and vomiting in moderately emetogenic chemotherapy (MEC) will not be discussed here. The submission also includes a network meta-analysis discussed in section 3.3[1].

3.1 NETU-07-07

NETU-07-07 was a phase II, multicentre, randomised, double-blind, double-dummy, parallel group, dose-ranging study that investigated three doses of netupitant co-administered with palonosetron 0.5 mg in 694 adults diagnosed with solid tumors[9]. Patients entering the study were chemotherapy-naive and had a Karnofsky Performance Scale score of ≥ 70% (equivalent to ECOG 0–1). All were scheduled to receive a first course of cisplatin-based chemotherapy at a dose of ≥ 50 mg/m^2, either alone or in combination with other chemotherapy agents.

Patients were randomised 1:1, stratified by gender, to one of the following treatment groups:

- palonosetron 0.5 mg once daily plus dexamethasone 20 mg once daily plus placebo on day 1 followed by dexamethasone 8 mg twice daily on days 2–4
- netupitant either 100 mg, 200 mg or 300 mg once daily plus palonosetron 0.5 mg once daily plus dexamethasone 12 mg once daily on day 1 followed by dexamethasone 4 mg twice daily on days 2–4
- aprepitant 125 mg once daily plus intravenous ondansetron 32 mg once daily plus dexamethasone 12 mg once daily on day 1; followed by aprepitant 80 mg once daily plus dexamethasone 4 mg twice daily on days 2-3, followed by dexamethasone 4 mg twice daily on day 4.

Each patient completed a diary from the start of cisplatin infusion on day 1 until the morning of day 6 (0–120 h)[9]. Episodes of vomiting were recorded and severity of nausea was evaluated daily by the patient[9].

The primary efficacy endpoint was complete response defined as no vomiting and no use of rescue medication during the post-chemotherapy phase (0-120 h)[9]. For the netupitant/palonosetron 300 mg/0.5 mg dose, statistically significantly more people

achieved complete response overall compared with those treated with palonosetron 0.5 mg. Netupitant/palonosetron 300 mg/0.5 mg was more effective than palonosetron 0.5 mg for the secondary efficacy endpoints: complete protection (defined as complete response and no significant nausea); no emesis and no significant nausea. Although the study was not designed to compare netupitant/palonosetron with aprepitant plus ondansetron, the netupitant/palonosetron 300 mg/0.5 mg dose group had numerically higher response rates for all efficacy endpoints (see Table 1)[9].

Table 1: Results from the exploratory analysis of study NETU-07-07[1,9]

	NEPA* n = 135	APR + OND* n = 134	Difference between NEPA and APR + OND
Primary endpoint			
Complete response overall (0-120 h) as a percentage (95% CI)	89.6 (84.5 to 94.8)	86.6 (80.8 to 92.3)	3.0 (-4.7 to 10.8)
Secondary endpoints			
Complete response acute (0-24 h) as a percentage (95% CI)	98.5 (96.5 to 100)	94.8 (91.0 to 98.5)	3.7 (-0.5 to 8)
Complete response delayed (25-120 h) as a percentage (95% CI)	90.4 (85.4 to 95.3)	88.8 (83.5 to 94.1)	1.6 (-5.7 to 8.9)
Complete protection, as a percentage (95%CI)			
Acute (0-24 h)	97.0 (94.2 to 99.9)	89.6 (84.4 to 94.7)	7.5 (1.6 to 13.4)
Delayed (25-120 h)	84.4 (78.3 to 90.6)	82.1 (75.6 to 88.6)	2.4 (-6.6 to 11.3)
Overall (0-120 h)	83.0 (76.6 to 89.3)	78.4 (71.4 to 85.3)	4.6 (-4.8 to 14)

* in combination with dexamethasone
APR: aprepitant; CI: confidence interval; Complete protection: complete response plus no significant nausea; Complete response: no emesis, no rescue medication; NEPA: netupitant/palonosetron 300 mg/0.5 mg; OND: ondansetron

3.2 NETU-10-29

NETU-10-29 was a phase III, international, multicentre, randomised, double-blind, double-dummy, parallel group study that assessed the safety and efficacy of netupitant/palonosetron in 412 chemotherapy-naive patients with cancer undergoing HEC or MEC[10]. Patients (≥ 18 years) diagnosed with a malignant tumour and scheduled to received repeated consecutive courses of chemotherapy were randomised 3:1 to receive a single oral dose of the fixed-dose combination of netupitant/palonosetron 300 mg/0.5 mg, or aprepitant 125 mg once daily plus palonosetron 0.5 mg once daily on day 1 and aprepitant 80 mg once daily on days 2–3; both groups also received dexamethasone (12 mg once daily [day 1]; 8 mg once daily [days 2–4]).

Results for the 100 patients who received one cycle of HEC (95 of whom received cisplatin) showed that during the overall post-chemotherapy phase (0–120 h) 83.8% of patients receiving netupitant/palonosetron achieved a complete response (no vomiting; no use of rescue medication) compared with 57.7% of patients receiving aprepitant plus palonosetron[1]. The proportions of patients in the netupitant/palonosetron and aprepitant plus palonosetron groups achieving complete response in the delayed phase were 87.8% and 57.7%, respectively; in the acute phase these were 91.9% and 96.2%, respectively[1]. In cycles 2,3,5 and 6 the proportion of patients with complete response was consistently numerically higher for the netupitant/palonosetron group than for the aprepitant plus palonosetron group; in cycle 4 the results were similar[1].

3.3 Network meta-analysis

The company submitted results from a network meta-analysis (NMA) comparing the fixed-dose combination of netupitant/palonosetron 300 mg/0.5 mg and a range of comparator treatments for preventing chemotherapy-induced nausea and vomiting in patients undergoing HEC and MEC[1]. Although the analysis included a wide range of comparators, the data focus on aprepitant 125 mg plus ondansetron with concomitant dexamethasone because this represents the comparator most widely used in clinical practice in Wales[11]. Results for the HEC sub-population were analysed and the NMA showed no difference in outcomes for complete response overall and for the acute and delayed phases[11]. For complete protection in the acute phase however, there was a difference in favour of the fixed-dose combination of netupitant/palonosetron[11].

3.4 Comparative safety

In the NETU-07-07 study the overall incidence, type, frequency and intensity of treatment-related adverse events were comparable across treatment groups[9]. In total, across all treatment groups, 106/679 patients had at least one treatment-related adverse event; hiccups and headache were the most common events[9]. In the NETU-10-29 safety study, the overall incidence, type and frequency of adverse events was comparable for both treatment groups[10]. The most frequent treatment-related adverse events for the netupitant/palonosetron combination included constipation (3.6%) and headache (1.0%); no cardiac safety concerns based on adverse events and electrocardiograms were reported[10].

The Committee for Medicinal Products for Human Use (CHMP) considered that the fixed-dose combination of netupitant/palonosetron was well tolerated overall, with many adverse reactions likely to be associated with the underlying condition or cytotoxic therapies[3]. A total of 1,538 patients were exposed to the netupitant/palonosetron 300 mg/0.5 mg dose during the clinical programme (one phase II study and three phase III studies)[3]. The Summary of Product Characteristics describes common adverse reactions of headache (3.6%), constipation (3.0%) and fatigue (1.2%); none were considered serious[2]. Similar frequencies of headache, constipation and fatigue were seen in patients receiving palonosetron alone therefore no common adverse reactions are attributable to netupitant[3].

3.5 AWTTC critique

- A post-hoc analysis of study NETU-07-07 reported the combination of netupitant/palonosetron is comparable for efficacy and safety to aprepitant plus ondansetron and numerically superior for all efficacy endpoints in people receiving HEC[1]. The study was not designed to compare netupitant/palonosetron with aprepitant plus ondansetron.
- Akynzeo®▼ (netupitant/palonosetron) is the first fixed-dose combination product for chemotherapy-induced nausea and vomiting[1]. CHMP states that the combination product may provide a more simple and convenient therapy and therefore may improve patient compliance[3].
- Clinical opinion sought by AWTTC suggests that aprepitant plus ondansetron is the most appropriate comparator for preventing nausea and vomiting in patients receiving HEC.
- There were no quality-of-life data in the studies submitted.
- Study NETU-07-07 used a dose of 32 mg ondansetron in the comparator arm[9], which is higher than the dose used in clinical practice in Wales[1,8]. Clinical experts reported that doses of intravenous ondansetron of 8 mg were most commonly used, with a maximum dose of 16 mg[1].

4.0 SUMMARY OF THE EVIDENCE ON COST-EFFECTIVENESS

4.1 Cost-effectiveness evidence

4.1.1 Context

The company's submission focuses the economic evaluation on netupitant/palonosetron (Akynzeo®▼), co-administered with dexamethasone in patients receiving cisplatin-based HEC[1]. The company did not include cost-effectiveness information for the MEC population based on a survey of clinical experts which reported that a combination of a NK_1 antagonist and a 5-HT_3 antagonist would not be considered in clinical practice for the prevention of nausea and vomiting for patients with MEC[1].

The company provided a cost-minimisation analysis (CMA) and a cost-utility analysis (CUA) comparing netupitant/palonosetron with the combination of aprepitant and ondansetron, both co-administered with dexamethasone for the prevention of nausea and vomiting associated with cisplatin-based HEC in adults in Wales.

The company first developed a de novo CMA to estimate the incremental costs over the time horizon of the model: a single cycle of chemotherapy (maximum of five days of antiemetic treatment). The analysis assumes that netupitant/palonosetron 300 mg/0.5 mg (as a fixed-dose combination) is administered before the start of chemotherapy on day 1 with dexamethasone. The comparator is aprepitant and ondansetron and dexamethasone, which represents the standard of care in Wales for chemotherapy-induced nausea and vomiting in cisplatin-based HEC. The analysis assumes that aprepitant is administered orally on days 1, 2 and 3 of the chemotherapy cycle: 125 mg on day 1 before starting chemotherapy and 80 mg on days 2 and 3. The analysis assumes on day 1, ondansetron was administered intravenously in 70% of patients, and orally in 30%. On day 2, the model assumes all patients received oral ondansetron. The dosing regimens used in the model were based on clinical practice reported in a survey of clinical experts in Wales[1].

The company justified the use of a CMA on direct clinical evidence from the NETU-07-07 study showing at least comparable efficacy and safety between netupitant/palonosetron and the combination of aprepitant plus ondansetron[9]. The company stated that netupitant/palonosetron was associated with numerically better efficacy compared with aprepitant plus ondansetron across all key primary and secondary endpoints. The combination of aprepitant plus intravenous ondansetron was included as an exploratory arm in the study. Although only descriptive statistics were pre-specified in the statistical analysis plan, post-hoc analyses showed that the 95% confidence intervals for the differences for all key endpoints crossed zero with the exception of no nausea and complete protection in the acute phase[12].

The costs included in the CMA are medicine acquisition and administration costs. The medicine acquisition cost of netupitant/palonosetron is based on a Wales patient access scheme (WPAS). The analysis assumes that 15 minutes of nurse time would be associated with the use of intravenous ondansetron, based on feedback from the clinical experts in Wales[1]. Costs attributable to dexamethasone and patient monitoring were excluded from the analysis because they were assumed to be the same for both netupitant/palonosetron and aprepitant plus ondansetron. The costs of consumables associated with the administration of intravenous ondansetron were considered minor and not included. Adverse events, and their associated costs, were not considered in the analysis.

The company subsequently developed a CUA to estimate the incremental costs and effects over a time horizon of five days (a single cycle of chemotherapy). This was developed to demonstrate how numerical differences in clinical outcomes translate into potential quality-adjusted life year (QALY) differences. The model uses a simple

three health state decision analytical design; the three health states are: 'complete protection', 'complete response at best' and 'incomplete response'. This is in line with previous models in the prevention of chemotherapy-induced nausea and vomiting.

Patients enter the model on day 1 (acute phase) and receive prophylactic antiemetics. Depending on the efficacy of the administered antiemetic, they will have different probabilities of avoiding emesis and not needing rescue medication (complete response in acute phase) or experiencing emesis and/or rescue medication (incomplete response in acute phase). From day 2–5 of chemotherapy (delayed phase), patients will be exposed to different probabilities of avoiding emesis and rescue medication (complete response in delayed phase), instead of failing to achieve response (incomplete response in delayed phase). 'Complete protection' is defined as no emetic episode, no use of rescue medication, and no more than mild nausea. 'Complete response at best' is defined as complete response (no emesis, no use of rescue medication) without complete protection. 'Incomplete response' is when patients do not achieve complete protection or complete response.

The model uses the same medicine acquisition and administration costs from the CMA but also includes costs for managing chemotherapy-induced nausea and vomiting. The costs attributable to emesis were obtained from a published UK study[13]. The model uses outcomes data from the NETU-07-07 study[9], supplemented by 95% confidence interval data from the clinical study report for the NETU-07-07 study[12]. Utility values for the different health states were obtained from the published literature[1].

The company commented that the small difference in QALYs generated in the model justifies the use of the CMA.

4.1.2 Results

Results of the base case analysis for the CMA are presented in Table 2. Netupitant/palonosetron results in cost savings of [commercial in confidence text removed] per patient per chemotherapy cycle when compared with aprepitant plus ondansetron.

Table 2. Company-reported results of the base case analysis (CMA)

Medicine	Costs per chemotherapy cycle (medicine acquisition cost and administration costs)	Total cost (including nurse time savings) per chemotherapy cycle up to 5 days
netupitant/palonosetron 300 mg/0.5 mg on day 1		¶¶*
aprepitant ondansetron orally† ondansetron intravenously†	£47.42 £2.24 £4.42	£54.08

*Wales patient access scheme (WPAS) price.
†Costs of ondansetron were based on average dose use and pro rata intravenous/oral use as reported in clinical expert survey.
¶¶ commercial in confidence
NEPA: netupitant/palonosetron

The company conducted scenario analyses to test key areas of uncertainty within the model. These included varying the dosage, formulation, and frequency of administration of ondansetron; varying the nurse time for administration and excluding nurse time for administering ondansetron. [commercial in confidence text removed]. In addition, the results from threshold analysis indicate that the proportion of patients receiving intravenous ondansetron which would result in cost neutrality between netupitant/palonosetron and aprepitant plus ondansetron is estimated to be 15.2%.

Results of the base case analysis for the CUA, using the WPAS price for netupitant/palonosetron, are presented in Table 3. The results show netupitant/palonosetron dominates aprepitant plus ondansetron with cost savings estimated and small QALY gains.

Table 3. Company-reported results of the base case analysis (CUA)

	NEPA	aprepitant plus ondansetron
Medicine costs	¶¶ (WPAS)	£49.66*
Administration costs	-	£4.42
Costs of CINV management	£9.05	£11.66
Total costs	¶¶	**£65.74**
QALDs	0.0427	0.0414
QALYs	0.0001170	0.0001134
Incremental costs (NEPA vs. comparator)	¶¶	
Incremental QALYs (NEPA vs. comparator)	0.0000036	
ICER NEPA vs. comparator	**NEPA dominates**	
Net monetary benefit (WTP threshold of ¶¶/QALY)	¶¶	

*Costs of ondansetron were based on average dose use and pro rata intravenous/oral use as reported in clinical expert survey.
¶¶ commercial in confidence
CINV: chemotherapy-induced nausea and vomiting; ICER: incremental cost-effectiveness ratio; NEPA: netupitant/palonosetron; QALD: quality adjusted life day; QALY: quality adjusted life year; WPAS: Wales patient access scheme; WTP: willingness to pay

The company conducted the same scenario/sensitivity analyses as those investigated in the CMA as well as additional sensitivity analyses around utilities and resource use (+/- 10% for all health state utilities and +/- 10% for costs of managing chemotherapy-induced nausea and vomiting). In all cases, netupitant/palonosetron remained dominant over aprepitant plus ondansetron. Probabilistic sensitivity analysis was not conducted.

4.1.3 AWTTC critique

The reliability of the company's CMA depends on the extent to which netupitant/palonosetron is considered to be therapeutically equivalent to aprepitant plus ondansetron.

Strengths of the company's economic evidence include:

- The model structure is clear and in line with other models in chemotherapy-induced nausea and vomiting.
- The comparator and assumptions about treatment used in the model are based on clinical practice in Wales reported in a clinical expert survey.

Limitations of the economic evidence include:

- The economic analysis is limited to a restricted sub-population of the licensed indication.
- The assumption of equivalence used for the CMA was not based on a head-to-head equivalence study; it was based on the lack of statistical significance for numerical differences for most key endpoints in a post-hoc analysis of netupitant/palonosetron against aprepitant plus ondansetron, using exploratory data for aprepitant plus ondansetron.
- The dose of ondansetron used in NETU-07-07 is higher than that reported to be used in clinical practice. Similarly, ondansetron was only given on day 1 in the

study compared with day 1 and day 2 in the model. Consequently, the assumption of comparable efficacy is based on different dosing to that used in the model; however, the model reflects clinical practice in Wales and the assumption is conservative for netupitant/palonosetron.
- Lack of utility estimates from study NETU-07-07 meant that utility values were obtained from the literature, adding uncertainty to the model. In particular, the utility value for the complete protection health state is high. The utility values were not varied independently in the sensitivity analysis.

4.2 Review of published evidence on cost-effectiveness

Standard literature searches conducted by AWTTC did not identify any cost-effectiveness analyses of netupitant/palonosetron for the prevention of nausea and vomiting associated with cisplatin-based HEC in adults.

5.0 SUMMARY OF EVIDENCE ON BUDGET IMPACT

5.1 Budget impact evidence

5.1.1 Context and methods

The company reported there were 63,124 people with advanced stage cancer who were receiving HEC in the UK in 2011[14]. The population in Wales represents 4.8% of the UK population; therefore, it was estimated that 3,030 people received HEC in Wales in 2011[1]. Based on population projections in Wales for 2015[15], it was estimated that 3,088 people would receive HEC each year. It was estimated that 797 of these people would receive cisplatin-based HEC, based on the average cisplatin usage using sales data of reported use of four cycles of cisplatin-based chemotherapy per patient per year[1].

The company assumed that all eligible people receiving cisplatin-based chemotherapy will currently be receiving treatment to prevent chemotherapy-induced nausea and vomiting (with aprepitant plus ondansetron, and concomitant dexamethasone). The company estimates that uptake of netupitant/palonosetron will range from 20% in year 1 to 45% in year 5. Therefore the number of people treated with netupitant/palonosetron is estimated to range from 159 in year 1 to 359 in year 5.

The company has based its budget impact analyses on the same assumptions used in the CMA and CUA.

5.1.2 Results

The company estimates the acquisition costs of treatment with netupitant/palonosetron to be [commercial in confidence text removed] per patient per year (WPAS price). This compares to £198.64 for aprepitant plus ondansetron. This results in an estimated net saving in medicine costs of [commercial in confidence text removed] in year 1, increasing to [commercial in confidence text removed] in year 5. Including the nurse costs for administering intravenous ondansetron increases the net saving to [commercial in confidence text removed] in year 1, increasing to [commercial in confidence text removed] in year 5. The estimated number of patients and the associated costs as described by the company in its budget impact analysis are summarised in Table 4.

Table 4. Company-reported net costs associated with the use of netupitant/palonosetron for the prevention of nausea and vomiting in cisplatin-based HEC in adults

	Year 1	Year 2	Year 3	Year 4	Year 5
Number of eligible patients	797	797	797	797	797
Expected uptake of NEPA	20%	25%	30%	35%	45%
Number of patients expected to be treated with NEPA per year	159	199	239	279	359
NEPA cost per year	¶¶	¶¶	¶¶	¶¶	¶¶
Aprepitant + ondansetron cost per year*	£31,584	£39,529	£47,475	£55,421	£71,312
Net costs					
Net medicine costs	¶¶	¶¶	¶¶	¶¶	¶¶
Net administration/staff costs	-£2,809	-£3,516	-£4,223	-£4,929	-£6,343
Overall net cost	¶¶	¶¶	¶¶	¶¶	¶¶

*Costs of ondansetron were based on average dose use and pro rata intravenous/oral use as reported in clinical expert survey.
¶¶ commercial in confidence
NEPA: netupitant/palonosetron

The company conducted scenario analyses to assess the impact of varying input parameters on the overall budget impact. The scenarios considered were based on different dosing and changing the number of doses of ondansetron, lower and higher rates of uptake of netupitant/palonosetron and six cycles of cisplatin-based HEC per patient per year. All scenarios conducted used the discounted WPAS price for netupitant/palonosetron and all resulted in the net medicine cost and overall net cost being negative (that is, cost saving) each year over the five-year period, [commercial in confidence text removed].

5.1.3 AWTTC critique

- The cost estimates used in the budget impact are derived from the company's CMA (and CUA); therefore the limitations and uncertainties associated with the cost-effectiveness analysis also apply to the budget impact analysis.
- The company used data on the number of people with advanced cancer receiving HEC in the UK which appears to include children and adolescents. This would overestimate the number of patients.

5.2 Comparative unit costs

Table 5 includes example acquisition costs of other medicines for the prevention of nausea and vomiting associated with cisplatin-based HEC in adults in Wales. The example acquisition costs are based on a per patient per HEC cycle. The equivalent cost per patient for a person receiving netupitant/palonosetron would be £69.00 using the NHS list price and [commercial in confidence text removed] using the discounted WPAS price.

Table 5. Examples of acquisition costs per patient of medicines for the prevention of nausea and vomiting associated with cisplatin-based HEC in adults

Regimen	Example dose	Cost per patient per cycle
Netupitant/palonosetron (Akynzeo®▼)	300 mg/0.5 mg oral capsule administered approximately one hour before the start of each chemotherapy cycle.	£69.00 (list price)
Aprepitant (Emend®) capsules, 80 mg, 125 mg	Initially 125 mg, dose to be taken 1 hour before chemotherapy, then 80 mg once daily for 2 days.	£47.42
Fosaprepitant (Ivemend®) vial, 150 mg	150 mg, dose to be administered over 20–30 minutes and given 30 minutes before chemotherapy on day 1 of cycle only.	£47.42
Palonosetron (Aloxi®) capsule, 500 micrograms	500 micrograms, dose to be taken 1 hour before treatment.	£55.89
Granisetron tablet, 1 mg	1–2 mg, to be taken within 1 hour before start of treatment, then 2 mg daily in 1–2 divided doses for up to 1 week following treatment (based on total dose of 10 mg).	£41.64
Ondansetron tablet, 8 mg	24 mg, dose to be taken 1–2 hours before treatment, then 8 mg every 12 hours for up to 5 days (based on 5 days).	£4.58
This table does not imply therapeutic equivalence of medicines or doses. See relevant Summaries of Product Characteristics (SPCs) for full dosing details[16-18] Costs based on British National Formulary, March 2016[19]. Costs of administration and monitoring are not included.		

6.0 ADDITIONAL INFORMATION

6.1 Prescribing and supply

AWTTC is of the opinion that, if recommended, netupitant/palonosetron (Akynzeo®▼) is appropriate for specialist only prescribing within NHS Wales for the indication under consideration.

The company does not anticipate that netupitant/palonosetron (Akynzeo®▼) will be supplied by a home healthcare provider.

6.2 Ongoing studies

The company submission states that there are no ongoing studies from which additional evidence is likely to be available within the next 6–12 months.

6.3 AWMSG review

This assessment report will be considered for review three years from the date of the Final Appraisal Recommendation.

6.4 Evidence search

Date of evidence search: 4 March 2016
Date range of evidence search: No date limits were applied to database searches.

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