Cost effectiveness of nab-paclitaxel (Abraxane®) + gemcitabine as a combination therapy for metastatic pancreatic cancer in Ireland, eligible for reimbursement as a hospital only product.

The National Centre for Pharmacoeconomics (NCPE) has issued a recommendation regarding the use of nab-paclitaxel (Abraxane®) + gemcitabine as a combination therapy for metastatic pancreatic cancer. The NCPE does not recommend reimbursement of nab-paclitaxel (Abraxane®) in combination with gemcitabine for this indication.

The HSE has asked the NCPE to evaluate the manufacturer's (Celgene Ltd.) economic dossier on the cost effectiveness of nab-paclitaxel (Abraxane®) in combination with gemcitabine. The NCPE uses a decision framework to systematically assess whether a technology is cost effective. This includes clinical effectiveness and health related quality of life benefits that the new treatment may provide and whether the cost requested by the pharmaceutical company is justified.

Following the recommendation from the NCPE, the HSE examine all the evidence that may be relevant for the decision; the final decision on reimbursement is made by the HSE. As this is an oncology drug, the NCPE recommendation is also considered by the National Cancer Control Programme Technology Review Group.

About the National Centre for Pharmacoeconomics

The NCPE are a team of clinicians, pharmacists, pharmacologists and statisticians who evaluate the benefit and costs of medical technologies and provide advice to the HSE. We also obtain valuable support from clinicians with expertise in the specific clinical area under consideration. Our aim is to provide impartial advice to help decision makers provide the most effective, safe and value for money treatments for patients. Our advice is for consideration by anyone who has a responsibility for commissioning or providing healthcare, public health or social care services.

National Centre for Pharmacoeconomics **September 2014**

Cost effectiveness of nab-paclitaxel (Abraxane®) + gemcitabine as a combination therapy for metastatic pancreatic cancer in Ireland, eligible for reimbursement as a hospital only product.

Nab-paclitaxel (Abraxane®) is a solvent-free paclitaxel formulation. It was approved by the European Medicines Agency on 20th December 2013 for first-line treatment of patients with metastatic adenocarcinoma of the pancreas in combination with gemcitabine.

In May 2014, Celgene Ltd. submitted an economic evaluation to the National Centre for Pharmacoeconomics on the cost effectiveness of nab-paclitaxel (Abraxane®) + gemcitabine for this indication, eligible for reimbursement as a hospital only product. The basecase analyses consider the comparators gemcitabine monotherapy and gemcitabine + oxaliplatin. In a scenario analyses FOLFIRINOX was also considered.

1. Comparative Effectiveness

Clinical evidence for nab-paclitaxel comes from the CA046 Study of 861 adults, (≥18yrs; Karnofsky Performance Score (KPS) ≥ 70 (on a scale from 0 to 100, with higher scores indicating better performance status)) with histologically or cytologically confirmed metastatic adenocarcinoma of the pancreas. Patients were randomised to nab-paclitaxel + gemcitabine (n=431) or to gemcitabine monotherapy (n=430). The median overall survival was 8.5 months in the nab-paclitaxel + gemcitabine group vs. 6.7 months in the gemcitabine group. The median progression free survival was 5.5 months (nab-paclitaxel + gemcitabine) and 3.7 months (gemcitabine). For patient subgroup KPS = 70-80, the median overall gain was 3.3 months and the median progression free survival gain was 1.3 months [1].

In the Treated Population the most common ≥ Grade 3 adverse events were neutropenia (38% (nab-paclitaxel + gemcitabine) vs. 27% (gemcitabine)), fatigue (17% vs. 7%), and neuropathy (17% vs. 1%), febrile neutropenia (3% vs. 1%) [1].

In the absence of head-to-head data, data was combined in a Mixed Treatment Comparison and results were used to estimate the relative clinical efficacy of nab-paclitaxel + gemcitabine compared to gemcitabine + oxaliplatin and to FOLFIRINOX.

2. Cost-Effectiveness Analysis

The evaluation uses an 'Area under the Curve' model with three health states, 'Pre-progression (subdivided into 'on' or 'off' first-line treatment)', 'Post-progression' and 'Death'. The Model has a 10 year time horizon; costs and consequences are discounted at 5%.

In the Economic Model, health state transitions are informed using survival models fitted to empirical data from CA046 for 'overall survival' data, 'progression free survival' data and 'time on treatment' data. Mixed Treatment Comparison derived hazard ratios for 'overall survival' and 'progression free survival' are used in the comparison to gemcitabine + oxaliplatin and FOLFIRINOX. The respective hazard ratios for 'progression free survival' were applied to the gemcitabine monotherapy 'time on treatment' in order to estimate hazard ratios for 'time on treatment' for gemcitabine + oxaliplatin and FOLRIRINOX. There are no clinical data available to support these assumptions; the incremental cost effectiveness ratios (ICERs) vs. gemcitabine + oxaliplatin and vs. FOLFIRINOX will therefore be uncertain.

Adverse event rates for input into the Model were not derived from the Mixed Treatment Comparison. The adverse event profile for gemcitabine + oxaliplatin was assumed to be equal to the profile of nab-paclitaxel + gemcitabine (from CA046). The adverse event rate for FOLFIRINOX was taken directly from a trial that compared FOLFIRINOX to gemcitabine [2]. Where this trial did not report data for particular adverse events, rates with nab-paclitaxel + gemcitabine (from CA046) were applied to FOLFIRINOX. There are no clinical data available to support these assumptions.

Results

According to the basecase analyses (Intention to Treat population), the incremental cost-effectiveness ratio (ICER) vs. gemcitabine is €68,605/QALY (incremental cost = €10,553; incremental QALY=0.154).

The ICER vs. gemcitabine + oxaliplatin is €116,788/QALY (incremental cost = €10,761; incremental QALY=0.092).

When compared to FOLFIRINOX in the Intention to Treat population, nab-paclitaxel + gemcitabine is less costly and less effective (incremental cost = -€3,406; incremental QALY= -0.18) and is not cost effective.

In the patient subgroup KPS= 70-80, the ICER vs. gemcitabine is €48,262/QALY (incremental cost = €10,226; incremental QALY=0.212).

Sensitivity Analysis

These basecase ICERs are based on the assumption that granulocyte colony-stimulating factor (G-CSF) is used to treat established febrile neutropenia. Locally, G-CSF is instead used to prevent febrile neutropenia in at risk patients (about 30% of patients) [3, 4]. Under this assumption, the deterministic ICERs increase to €71,591/QALY (vs. gemcitabine) and €119,892/QALY (vs. gemcitabine + oxaliplatin). These ICERs may be more realistic in our population.

The Review Group believes that the utility values (0.8 and 0.75 for the pre-progression and post-progression health states respectively) are high relative to the age/sex matched population norm value (0.78) [5]. Scenario analysis indicates that the basecase ICER (vs. gemcitabine) increases to €73,867/QALY when these utility values are decreased to 0.74 and 0.69 respectively.

The Model results are also sensitive to the choice of parameter models used to extrapolate the time to event data and the Model time horizon.

Probabilistic analysis indicates that there is a zero probability of nab-paclitaxel + gemcitabine being cost effective at €45,000/QALY for this indication.

3. **Budget Impact Analysis**

Based on the Company population estimates and an uptake rate of 50%, the Gross Budget Impact (drug acquisition cost for nab-paclitaxel + gemcitabine) will be about €0.5 million in Year 1, increasing to about €1 million per annum thereafter (5 year cumulative of about €4.5 million). The Net Budget Impact is estimated to be about €0.41 million in Year 1, increasing to about €0.83 million thereafter (5 year cumulative of about €3.7 million). In these Company Budget Impact figures, Year 1 is assumed to be of 6 months duration. It is possible that the uptake will be higher resulting in increased Budget Impact figures.

4. Conclusion

Following NCPE assessment of the Company submission, reimbursement of nab-paclitaxel in combination with gemcitabine is not recommended for metastatic pancreatic cancer.

References

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