

**A REVIEW OF THE COST EFFECTIVENESS ANALYSIS OF INHALED
INSULIN (EXUBERA) VS. STANDARD SUB-CUTANEOUS THERAPY FOR
DIABETES MELLITUS PATIENTS**



Summary

- In April 2006, Pfizer submitted a cost effectiveness and budget impact analysis comparing inhaled insulin (€188 to €1984 per patient per year) to standard sub-cutaneous insulin therapy (€425 to €667 per patient per year) for use in patients with diabetes mellitus, to support its application for reimbursement of inhaled insulin under the Community Drugs Schemes.
- Although Pfizer submitted cost-effectiveness data for six potential scenarios for use of inhaled insulin, only one scenario looking at the use of inhaled insulin in Type 2 diabetics uncontrolled on oral hypoglycaemic agents was considered in this review due to the lack of substantial evidence underpinning the other analyses. The accuracy of the estimates for the single scenario considered here is compromised by the hypothetical nature of the utility and preference data incorporated in the model.
- In the base case economic model with most credible assumptions, our assessment indicates an incremental cost effectiveness ratio of €44,526/QALY for Exubera plus metformin versus long acting sub-cutaneous insulin plus metformin and €45,339/QALY for Exubera plus metformin versus pre-mixed sub-cutaneous insulin plus metformin under the GMS Scheme. This could be considered borderline cost-effective (threshold approximately €45,000/QALY). However, had a probabilistic analysis been provided, the confidence intervals would almost certainly have exceeded the cost-effectiveness threshold.
- Sensitivity analysis indicates that reimbursement at or below 90% of the proposed price on the GMS Scheme would result in ICERs of €39,831/QALY and €40,496/QALY thereby increasing the probability of cost-effectiveness.
- The 50% mark-up on the Long Term Illness Scheme (LTI) (37.1% of potential Exubera patients) renders Exubera not cost-effective for patients on this scheme with ICERs of €65,720/QALY and €68,167/QALY respectively providing an argument for restructuring of pharmacist reimbursement under the Community Drugs Schemes.
- The results of the cost effectiveness analysis were also sensitive to the utility associated with inhaled insulin. Increasing the utility associated with inhaled insulin improves cost-effectiveness e.g. at a utility increment of 0.02 the ICERs

were €39,807/QALY and €40,393/QALY for inhaled versus long acting and pre-mix subcutaneous insulin respectively (utility value of 0.015 in the base case).

- The total budget impact of Exubera could be significant i.e. almost €1 million/year by 2010 taking account of additional monitoring costs, dispensing fees and the 50% mark-up for patients on the LTI scheme. Expenditure on Exubera alone is projected to increase from approximately €420,000 in 2006 to €7.4 million in 2010 due to increased numbers of patients accessing the product.
- **Exubera is an innovative product associated with a substantial budget impact which may be considered borderline cost-effective under the GMS Scheme in the Irish setting. Prescribing under the LTI Scheme renders the product not cost-effective. The cost-effectiveness profile may improve as the evidence base underpinning its use develops.**

**A COMPARISON OF THE BUDGET IMPACT OF INHALED INSULIN
(EXUBERA) ON THE HIGH TECH DRUG SCHEME
VS THE GMS & LTI SCHEMES**



Summary

- In June 2006, the National Centre for Pharmacoeconomics conducted a review of the cost-effectiveness and budget impact data submitted by Pfizer to support its application for reimbursement of inhaled insulin under the GMS and LTI Schemes.
- In the base case economic model with most credible assumptions, our assessment indicated an incremental cost effectiveness ratio of €44,526/QALY for Exubera plus metformin versus long acting sub-cutaneous insulin plus metformin and €45,339/QALY for Exubera plus metformin versus pre-mixed sub-cutaneous insulin plus metformin under the GMS Scheme in Type 2 diabetics uncontrolled on oral hypoglycaemic agents. This could be considered borderline cost-effective (threshold approximately €45,000/QALY).
- Subsequent to our initial review, Pfizer have decreased the cost of the drug by 15%. The device cost remains unchanged. The total cost has decreased from €1188 to €984 per patient per year to €1028 to €705 per patient per year.
- The total budget impact of Exubera at the new price if available on the LTI and GMS schemes could be significant i.e. approximately €9.5 million/year by 2010 taking account of additional monitoring costs, dispensing fees, the 50% mark-up for patients on the LTI scheme and the 3% rebate by the pharmaceutical companies for items prescribed on the GMS Scheme. Expenditure on Exubera alone is projected to increase from approximately €360,000 in 2006 to €6.4 million in 2010 due to increased numbers of patients accessing the product.
- If Exubera is made available on the High Tech Drugs Scheme instead of on the GMS and LTI schemes, the estimated total budget impact is higher at approximately €10.7 million due to increased expenditure on the High Tech Drugs Scheme's patient care fee for pharmacists and loss of the rebate by the pharmaceutical company for Exubera prescribed on the GMS Scheme.
- **The budget impact analysis indicates that reimbursement of Exubera on the High Tech Drugs Scheme in preference to reimbursement on the GMS and LTI Schemes could be associated with increased costs of approximately €1.2 million per year by 2010.**

BACKGROUND

In June 2006, Pfizer submitted a report on the clinical and cost effectiveness of inhaled insulin (Exubera®) versus sub-cutaneous insulin in patients with diabetes mellitus in support of their application for reimbursement on the GMS and LTI Schemes. A budget impact analysis was also provided.

Exubera provides a therapeutic alternative to sub-cutaneously injected insulin, which appears as effective and is associated with greater patient preference. This patient preference could lead to improved blood glucose control in some Type 1 patients through improved compliance and in some Type 2 patients through an earlier switch to insulin therapy. Improved blood glucose control leads to the avoidance of diabetic complications, related costs and negative impact on patients.

As outlined in our earlier report, the base case cost-effectiveness analysis suggests that Exubera is borderline cost-effective under the GMS Scheme with an incremental cost effectiveness ratio of €44,526/QALY for Exubera plus metformin versus long acting sub-cutaneous insulin plus metformin and €45,339/QALY for Exubera plus metformin versus pre-mixed sub-cutaneous insulin plus metformin¹. However, had a probabilistic analysis been provided, the confidence intervals around the incremental cost effectiveness ratio would almost certainly have exceeded the threshold of €45,000/QALY. Sensitivity analysis indicates that the result of the cost-effectiveness analysis are sensitive to the utility increment associated with inhaled versus injected insulin and to the cost of the product e.g. taking account of the 50% mark-up on the Long Term Illness Scheme renders Exubera not cost-effective for patients on this scheme.

In June 2006, Pfizer applied to have Exubera considered for reimbursement under the High Tech Drugs Scheme instead of reimbursement under the GMS and LTI Schemes. In addition, Pfizer have dropped the price of Exubera by 15% since our earlier review. The device cost remains unchanged. The total cost has decreased from €1188 to €984 per patient per year to €1028 to €705 per patient per year. The following is an assessment of the budget impact of Exubera under either the GMS & LTI schemes or under the High Tech Drugs Scheme taking account of the new price.

BUDGET IMPACT ON THE GMS AND LTI SCHEMES

The accuracy of the budget projections was enhanced by incorporating data extracted by NCPE from the Community Drugs Schemes data files as described in the earlier report¹. The total budget impact of Exubera was recalculated adjusting for the 15% price cut as mentioned above. The estimated total budget impact of Exubera if reimbursed under the GMS and LTI schemes could be significant i.e. almost €9.5 million/year by 2010 taking account of additional monitoring costs, dispensing fees the 50% mark-up for patients on the LTI scheme and the 3% rebate by the pharmaceutical companies for items prescribed on the GMS Scheme (Table 1). Expenditure on Exubera alone is projected to increase from approximately €360,000 in 2006 to €6.4 million in 2010.

Table 1: Total projected cost of Exubera per patient group under GMS & LTI

Patient group	2006	2007	2008	2009	2010
Cost of treating Type 1					
Exubera	€9,606	€197,991	€105,089	€849,532	€1,223,981
SC insulin savings	-€19,446	-€55,313	-€13,171	-€237,336	-€341,946
Additional monitoring	€14,211	€10,421	€2,702	€173,438	€249,885
Dispensing fees	€788	€2,243	€1,589	€9,624	€13,865
50% mark-up LTI	€16,855	€17,942	€8,090	€205,709	€296,379
Rebate (Exubera)	-€30	-€2,646	-€5,413	-€11,352	-€16,356
Rebate (other)	€70	€199	€107	€54	€1,230
Total cost of Type 1	€81,154	€230,837	€172,293	€990,469	€1,427,038
Cost of treating Type 2 uncontrolled on oral hypoglycaemics					
Exubera	€74,640	€781,197	€1,598,329	€3,351,935	€4,829,370
SC insulin savings	-€0	-€0	-€0	-€0	-€0
Additional monitoring	€108,855	€9,634	€33,511	€1,328,567	€1,914,161
Dispensing fees	€5,846	€6,629	€4,024	€1,353	€102,803
50% mark-up LTI	€5,333	€157,391	€22,021	€75,327	€72,992
Rebate (Exubera)	-€5,807	-€16,519	-€3,798	-€70,879	-€102,121
Rebate (other)	-€2,302	-€6,548	-€13,396	-€28,094	-€10,477
Total cost of Type 2 uncontrolled on oral hypoglycaemics	€136,565	€1,241,784	€2,540,691	€5,328,209	€7,676,728
Cost of treating Type 2 uncontrolled on sc insulin + orals hypoglycaemics					
Exubera	€18,996	€4,033	€10,552	€231,844	€334,034
SC insulin savings	-€1,169	-€1,858	-€2,263	-€50,883	-€73,310
Additional monitoring	€5,796	€16,487	€3,732	€70,741	€101,922
Dispensing fees	€26	€28	€1,899	€982	€5,737
50% mark-up LTI	€597	€10,232	€20,935	€43,904	€63,256
Rebate (Exubera)	-€61	-€1,027	-€2,102	-€4,408	-€6,351
Rebate (other)	-€31	-€88	-€180	-€78	-€44
Total cost of Type 2 uncontrolled on sc insulin + oral hypoglycaemics	€24,154	€68,707	€140,573	€294,803	€424,745
Exubera cost for all diabetics	€63,242	€1,033,221	€2,113,970	€4,433,311	€6,387,385
Total cost for all diabetics	€41,873	€1,541,328	€3,153,557	€6,613,481	€9,528,511

BUDGET IMPACT ON THE HIGH TECH DRUGS SCHEME

A limited list of high tech high cost items are reimbursed under the High Tech Drugs Scheme (HTDS). A form giving details of the patient, indication for treatment and a nominated pharmacy must be completed by the prescriber (usually a hospital consultant) and sent to the HSE prior to the drug being made available to the patient. The wholesaler is paid by the HSE to supply the drug to the patient's pharmacy and the pharmacist is paid a standard patient care fee of €49.64 per month to cover dispensing, patient counselling and administration.

Estimating the budget impact on the High Tech Drugs Scheme as opposed to on the GMS and LTI Schemes involved the following changes to the original analysis:

- Under the terms of the agreement between the Irish Pharmaceutical Healthcare Association and the Dept of Health & Children, the pharmaceutical companies must pay a 3% rebate on all items prescribed on the GMS Scheme. Switching to the High Tech Drugs Scheme would involve loss of this rebate.
- Under the terms of the High Tech Drugs Scheme, wholesalers are paid a 10% mark-up on the ex-manufacturer cost of the drug as opposed to the standard 15% mark-up. The ex-wholesaler cost of Exubera was adjusted to take consideration of this.
- On the High Tech Drugs Scheme, pharmacists are paid a standard patient care fee of €49.64 per month². This is offset to some extent by savings on the dispensing fees on the GMS Scheme and savings on dispensing fees and 50% mark-up on the LTI Scheme.
- The cost associated with monitoring tests and sub-cutaneous insulin is calculated for the GMS and LTI Schemes as before.
- We retained the same assumptions with regard to patient population and disease profile as in the previous budget impact assessments.
- Initiation of new therapy in diabetics may be shared by general practitioners and hospital consultants. Most Type 1 diabetics attend hospital based clinics but some Type 2 diabetics are managed primarily by general practitioners. Consideration needs to be given to whether prescribing would be restricted to hospital initiation of therapy as commonly occurs with the High Tech Drug Scheme or whether general practitioners would be allowed to initiate

treatment. There is a possibility that restricting Exubera to the HTDS and the associated administrative burden may act as a disincentive to prescribers and result in a delay in uptake of the product. However, prescribing on the HTDS avoids the impact of increased drug expenditure for GMS patients and the negative impact for GPs who are trying to meet their indicative drugs budget targets.

The estimated total budget impact of Exubera if reimbursed under the High Tech Drugs Scheme could be almost €10.7 million/year by 2010 taking account of additional monitoring costs, the patient care fee paid to pharmacists, the lower wholesaler mark-up and loss of the 3% rebate by the pharmaceutical companies for items prescribed on the GMS Scheme (Table 2). Expenditure on Exubera alone taking account of the lower wholesaler mark-up is projected to increase from approximately €50,000 in 2006 to €6.1 million in 2010.

Table 2: Total projected cost of Exubera per patient group under HTDS

Patient group	2006	2007	2008	2009	2010
Cost of treating Type 1					
Exubera	€66,580	€189,382	€387,476	€12,596	€1,170,764
SC insulin savings	-€19,446	-€55,313	-€113,171	-€37,336	-€41,946
Additional monitoring	€38,768	€110,273	€225,618	€73,154	€81,707
Dispensing fees*	€788	€2,243	€4,589	€9,624	€13,865
50% mark-up LTI(other)	-€2,446	-€6,959	-€14,237	-€9,858	-€3,018
Rebate (other)	€70	€199	€407	€54	€1,230
Total cost of Type 1	€97,736	€278,003	€568,795	€1,192,849	€1,718,622
Cost of treating Type 2 uncontrolled on oral hypoglycaemics					
Exubera	€62,699	€747,232	€1,528,836	€3,206,199	€4,619,398
SC insulin savings	-€0	-€0	-€0	-€0	-€0
Additional monitoring	€108,856	€309,634	€633,511	€1,328,567	€1,914,161
Dispensing fees*	€95,923	€72,847	€58,246	€1,170,726	€1,686,748
50% mark-up LTI (other)	€14,804	€42,110	€86,157	€180,684	€260,325
Rebate (other)	-€2,302	-€6,547	-€13,396	-€28,093	-€40,477
Total cost of Type 2 uncontrolled on oral hypoglycaemics	€479,980	€1,365,276	€2,793,354	€5,858,083	€8,440,155
Cost of treating Type 2 uncontrolled on sc insulin + orals hypoglycaemics					
Exubera	€18,170	€1,684	€105,746	€221,764	€319,511
SC insulin savings	-€4,169	-€1,859	-€22,263	-€50,883	-€73,310
Additional monitoring	€5,796	€16,487	€33,732	€70,741	€101,921
Dispensing fees*	€10,677	€30,371	€62,139	€130,315	€187,754
50% mark-up LTI (other)	€19	€38	€91	€1,449	€2,087
Rebate (other)	-€31	-€88	-€180	-€78	-€544
Total cost of Type 2 uncontrolled on sc insulin + oral hypoglycaemics	€30,562	€6,933	€177,865	€373,008	€537,419
Exubera cost for all diabetics	€347,449	€988,298	€2,022,058	€4,240,559	€6,109,673
Total cost for all diabetics	€608,278	€1,730,212	€3,540,014	€7,423,940	€10,696,196

* dispensing fees on GMS and LTI, patient care fees on HTDS as appropriate

CONCLUSION

Exubera is associated with a substantial budget impact due to the high cost of the product and the large number of patients who are likely to receive it. The estimated total budget impact of Exubera if reimbursed under the GMS and LTI schemes could be significant i.e. almost €9.5 million/year by 2010 taking account of additional monitoring costs, dispensing fees, the 50% mark-up for patients on the LTI scheme and 3% the rebate by the pharmaceutical companies for items prescribed on the GMS Scheme

The estimated total budget impact of Exubera if reimbursed under the High Tech Drug Scheme is even higher and could be almost €10.7 million/year by 2010 taking account of additional monitoring costs, the patient care fee paid to pharmacists, the lower wholesaler mark-up and loss of the 3% rebate by the pharmaceutical companies for items prescribed on the GMS Scheme.

The budget impact analysis indicates that reimbursement of Exubera on the High Tech Scheme in preference to reimbursement on the GMS and LTI Schemes could be associated with increased cost of approximately €1.2 million per year by 2010.

REFERENCES

1. National Centre for Pharmacoeconomics. A review of the cost-effectiveness of inhaled insulin (Exubera) Vs standard sub-cutaneous therapy for diabetes mellitus patients. Report submitted to the Dept of Health & Children June 2006.
2. General Medical Services (Payments) Board. Report for the year ended 31st December 2004.