CLINICAL INVESTIGATION

A Comparative Pharmacoeconomic Assessment of Two Surfactants for the Prevention of Respiratory Distress Syndrome

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OBJECTIVE The use of exogenous surfactants among preterm infants for the prevention and treatment of respiratory distress syndrome (RDS) has led to economic and cost-effectiveness evaluations of these products. Lucinactant (Surfaxin), a novel, peptide-based, synthetic surfactant, has been shown to significantly reduce RDS-related mortality, compared with the most commonly prescribed animal-derived surfactant, beractant (Survanta). Infants who survive expend significant healthcare resources; therefore, the impact of improved survival through 1-year corrected age was evaluated in a prospectively defined pharmacoeconomic analysis. The objectives of this study were to estimate the healthcare resource utilization, economic impact, and cost-effectiveness of lucinactant versus beractant for the prevention of RDS among surviving very low birth weight (VLBW) preterm infants weighing 600 to 1250 grams.

METHODS A decision-analytic model was developed to compare the healthcare resource utilization, economic impact, and cost-effectiveness of lucinactant versus beractant.

RESULTS Infants who received lucinactant had fewer neonatal intensive care unit (NICU) days and fewer NICU days on mechanical ventilation compared with infants who received beractant. Total healthcare costs for the initial stay in the NICU were lower by $8,803 among infants who received lucinactant compared with infants who received beractant. The incremental cost per life saved was $40,309 for lucinactant compared with beractant.

CONCLUSIONS Administration of lucinactant to surviving VLBW preterm infants resulted in fewer NICU days and fewer NICU days on mechanical ventilation compared with beractant. Fewer NICU days translates into lower total costs among infants who received lucinactant. This comprehensive pharmacoeconomic analysis indicates that lucinactant is a cost-effective therapy for the prevention of RDS among preterm infants.

KEYWORDS beractant, lucinactant, economics, respiratory distress syndrome, surfactant

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INTRODUCTION

Respiratory distress syndrome (RDS) is the most common respiratory disorder among preterm infants. In 2002, RDS ranked as the sixth leading cause of infant mortality.[1] In the United States (U.S.), approximately 60,000 infants receive surfactant therapy for RDS each

ABBREVIATIONS AWP, average wholesale price; BPD, bronchopulmonary dysplasia; HPM, Health Process Management; MV, mechanical ventilation; NCHS, National Centers for Health Statistics; PCA, post-conception age; RDS, respiratory distress syndrome; VLBW, very low birth weight; VON, Vermont Oxford Network

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year.[2] The incidence of RDS declines with the degree of maturity at birth, occurring in 60% of babies born at less than 28 weeks gestation, in 30% of infants born at 28 to 34 weeks, and in less than 5% of infants born after 34 weeks.[1] Early administration of exogenous surfactant therapy has significantly reduced mortality and morbidity among preterm infants.[3] By decreasing the sequelae of RDS, exogenous surfactant therapy has also reduced healthcare costs.[2,4]

The three currently approved exogenous surfactants in the U.S.—including beractant (Survanta, Abbott Laboratories, Inc.), calfactant (Infasurf, Forest Laboratories, Inc.), and poractant alfa (Curosurf, Dey L.P.–Chiesi Farmaceutici, S.p.A.)—are all of animal origin. Beractant is the most widely prescribed of these products. Lucinactant (Surfaxin, Discovery Laboratories, Inc.), a novel, peptide-containing, synthetic surfactant that mimics the function of the essential human surfactant protein SP-B, is currently under review by the Food and Drug Administration for approval in the U.S. for the prevention of RDS, following successful completion of two phase 3 clinical trials.[5,6]

Randomized controlled trials of exogenous surfactant therapy have been extensively published, making it one of the most widely studied therapies in neonatal medicine.[2] Studies have also evaluated the cost of preventing RDS and the economic impact and cost-effectiveness of surfactant replacement.[7-18] Compared to mechanical ventilation alone, both prophylactic and treatment strategies with surfactants provide economic benefits for preterm infants during their hospital stay.[9,10,13,15-17,19] Reductions in daily hospital charges among surfactant-treated infants have been reported to be substantial, ranging from 25% to 39%.[16,17] However, other published data have shown a more modest reduction in overall cost of care among treated preterm infants in the range of 1% to 10%.[10] Healthcare costs associated with surviving preterm infants are significantly greater than those for infants who do not survive– two- to four-fold higher.[16,19] Nevertheless, the cost to produce a survivor among infants treated with surfactant is less than among non-surfactant-treated infants, with a reduction in healthcare costs of $11,880 to $18,500 per treated infant.[16]

Whereas studies have examined the direct costs of surfactants compared with placebo or mechanical ventilation alone, none have extensively evaluated differences in resource utilization and economic outcomes among different surfactant therapies. Moya and colleagues recently reported that among very low birth weight (VLBW) preterm infants weighing 600 to 1250 grams, lucinactant significantly reduced RDS-related mortality compared with beractant.[5] In addition, overall survival through 36 weeks post-conception age (PCA) trended in favor of lucinactant (P = .051),[5] with similar observations out to 1-year corrected age.[20] In light of these observations, and the fact that preterm infants at risk for RDS who survive expend substantially more resources over the course of their hospitalization, this comprehensive pharmacoeconomic comparison of lucinactant versus beractant focused on surviving infants.

Economic assessments of surfactant therapy are warranted to measure the value of the different products in this class. As healthcare costs continue to rise to over 15% of the U.S. gross national product ($1,678.9 billion),[21] the economic evaluation of pharmaceutical therapies has become an important part in the clinical decision-making process. The value of economic data has become as important as that of efficacy or safety data when determining therapeutic choices.[22] The Academy of Managed Care Pharmacy produced guidelines for formulary submissions, which emphasize the need for economic evaluation.[23] Health economic studies assess the relationship between clinical, economic, and humanistic outcomes in order to facilitate the more efficient use of scarce medical resources. The results of these studies are useful in developing practice guidelines, making formulary decisions, and for budgeting and planning. Developing these types of data for use in evaluating different surfactant therapies is necessary. The objectives of this study were to estimate the healthcare resource utilization, economic impact, and cost-effectiveness of lucinactant versus beractant for the prevention of RDS among surviving VLBW preterm infants weighing 600 to 1250 grams.

METHODS

Decision Model

A decision-analytic model was developed to compare the healthcare resource utilization, economic impact, and cost-effectiveness of lucinactant versus beractant. A decision model is a mathematical prediction of health-related events with the goal to aid in decision-making. Health-related events are linked to costs and health outcomes. Modeling involves data synthesis and the use of values determined in clinical trial-based studies to essentially "predict" economic outcomes over a much longer period of time than for which data are currently available.[22,24] This study considered direct costs to a hospital. The analyses were performed using Crystal Ball 2000.2 (Decisioneering, Inc., Denver, Colorado) and Excel 2003 (Microsoft, Inc., Redmond, Washington). The decision-analytic model calculated outcomes based on the application of mathematical formulas and calculations (defined in the 'Analysis' section below) and the synthesis of available data[1,25-28] in order to simulate and predict real-world scenarios.

Data Sources and Model Inputs

Prospectively defined clinical outcomes and healthcare resource utilization data were derived from the SELECT (Safety and Effectiveness of Lucinactant vs Exosurf in a Clinical Trial) phase 3 lucinactant trial and the 1-year follow-up results.[5,20,25] SELECT is a randomized, masked clinical trial of very preterm infants, weighing 600 grams to 1250 grams and of less than 32 weeks gestational age. Included were 527 patients in the lucinactant group and 258 infants in the beractant group. Model inputs included the mean number of days per infant in the neonatal intensive care unit (NICU) and the mean number of days per infant in the NICU off mechanical ventilation (MV) by two birth weight cohorts: 600 to 1000 grams and 1001 to 1250 grams. Within each birth weight cohort, the inputs were further stratified by infants with bronchopulmonary dysplasia (BPD, defined as the need for supplemental oxygen to maintain saturations of 88%-96% at 28 days or 36 weeks PCA[5]) and infants without BPD (Figure 1). Therefore, the analysis adjusts for weight (600 to 1000 grams and 1001 to 1250 grams) and BPD status.

Economic inputs included the average cost of a day in the NICU on MV ($2,386) and the average cost of a day in the NICU off MV ($1,565).[26] Surfactant drug acquisition costs for beractant were based on the average wholesale price (AWP) in April, 2005, which was $459.60 for the 4 mL, 25 mg/mL vial and $813.46 for the 8 mL, 25 mg/mL vial.[27] Drug acquisition costs for lucinactant were not available at the time of the analysis and were assumed to be at parity per vial with the price of the 8 mL vial of beractant. Expenditure was calculated according to the number of vials used per infant within each birth weight cohort. The cost of the entire vial was used, even if the dose was less than the full vial, to account for wastage. Based on the recommended dosing for beractant of 4 mL/kg[29] and the average number of doses used in the SELECT trial of 1.7 (SD 1.2),[5] among infants 600 to 1000 grams it was estimated that two 4-mL (25 mg/mL, 100 mg/kg) vials would be required with a total per-infant cost of $919.20. Among infants 1001 to 1250 grams it was estimated that two 8-mL (25 mg/mL, 100 mg/kg) vials would be required with a total per-infant cost of $1,626.92. Based on the recommended dosing for lucinactant of 5.8 mL/kg[30] and the average number of doses used in the SELECT trial of 1.9 (SD 1.2),[5] within both birth weight cohorts it was estimated that two 8-mL (30 mg/mL, 175 mg/kg) vials of lucinactant would be required with a total per-infant cost of $1,626.92.

Cost inputs per day for nine hospital reporting departments included: 1) room, 2) laboratory, 3) pharmacy, 4) respiratory therapy, 5) other therapy, 6) imaging, 7) general supply, 8) operating room, and 9) other costs (Table 1).[26] The total NICU days on and off MV were calculated by day and not per infant in the source data; therefore, several assumptions were made when calculating the budget impact by hospital department. All costs by hospital department were assumed to occur on each day in the NICU on or off MV, except operating room costs. Operating room costs were found to occur on approximately 1% of the days in the NICU. Therefore, operating room costs were only calculated for 1% of the days in each cohort. Additionally, costs by pharmacy department were assumed not to include surfactant costs

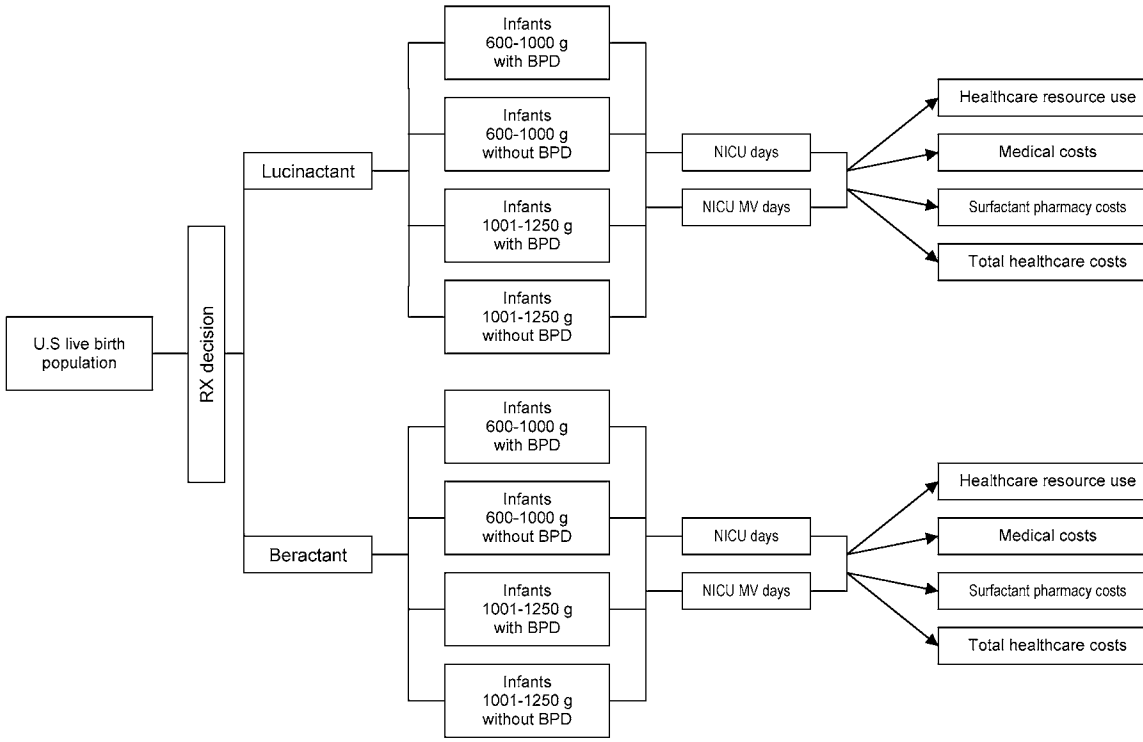

Figure 1. Surfactant economic decision tree.

based on the low mean total pharmacy cost and the inability to determine if surfactant therapy was administered to all infants. Finally, costs are only included for the nine hospital departments identified and may not be inclusive of all services received during the initial NICU stay. Based on these assumptions, the total budget impact and the sum of the budget impact by hospital departments are not equal.

Study Population

The study population included the total U.S. live birth population from the most current National Centers for Health Statistics (NCHS) annual birth file (2002) of 4,021,726 births (Table 2).[1] Epidemiologic data were estimated from the Vermont Oxford Network (VON) 2003 annual VLBW database summary.[28] Inputs included: the percent of live births stratified by the two weight cohorts of 600 to 1000 grams and 1001 to 1250 grams; the percent of infants receiving surfactant therapy in each of these weight cohorts; and the percent of infants who survived in each weight cohort. The VON maintains a database for infants 401 to 1500 grams who are born at participating hospitals or are admitted to them within 28 days of birth.

Table 1. Cost inputs by hospital departments per day[26]

Hospital Reporting Department	NICU off MV	NICU on MV
Room	$693	$814
Laboratory	$167	$254
Pharmacy	$146	$228
Respiratory Therapy	$105	$329
Other Therapy	$98	$75
Imaging	$74	$107
General Supply	$120	$98
Operating Room*	$1146	$853
Other	$145	$188

**Operating room costs were only calculated for 1% of the days in each study cohort*
MV, mechanical ventilation; NICU, neonatal intensive care unit

There are over 485 member hospitals and data on over 35,000 VLBW infants each year. This includes over 50% of all VLBW infants born each year in the U.S.

The average, unadjusted initial NICU stay for surviving infants was 56.99 days, and the average cost of a day in the NICU was $1938, resulting in a total mean cost of $110,443 per surviving VLBW preterm infant.[26,28] The average, unadjusted initial NICU stay for non-surviving infants was 15.00 days,[28] with

Table 2. Study population

Populations	Infants (%)	Source
U.S. live births	4,021,726 (100)	NCHS
VLBW births	56,304 (1.4)	NCHS,VON
VLBW births, 600-1000 g	35,303 (62.7)	VON
Infants 600-1000 g receiving surfactant therapy	29,301 (83)	VON
Infants 600-1000 g receiving surfactant who survived	22,855 (78)	VON
VLBW births, 1001-1250 g	21,001 (37.3)	VON
Infants 1001-1250 g receiving surfactant therapy	13,021 (62)	VON
Infants 1000-1250 g receiving surfactant who survived	12,240 (94)	VON
Total number of surviving infants receiving surfactant therapy in the U.S.	35,095	

NCHS, National Centers for Health Statistics; VON, Vermont Oxford Network

a mean total cost per non-surviving VLBW preterm infant of $29,070.[22] Mean NICU costs for surviving infants were $81,373 greater than the mean costs for non-surviving infants. Therefore, in the total U.S. population, among VLBW preterm infants, surviving infants accounted for approximately 80% of aggregate NICU costs; thus, this study was conducted on the surviving infant population.

Analysis and Impact on Medical Resource Utilization Analysis

Three primary outcomes were analyzed to compare lucinactant versus beractant: 1) impact on medical resource utilization, 2) total budget impact, and 3) incremental cost-effectiveness. Medical resource utilization was defined as the number of days an infant was hospitalized in the NICU and the number of days an infant was in the NICU on MV. Impact on medical resource utilization outcomes consisted of the following: 1) Mean NICU days per infant, per product, 2) Mean NICU days on MV per infant, per product, 3) Impact on medical resource use by NICU days per infant, 4) Impact on medical resource use by NICU days on MV per infant, and 5) Total impact on medical resource use across the entire U.S. population.

Budget Impact Analysis

Budget impact was defined as the difference between the mean costs for lucinactant and beractant for each outcome. The budget impact (pharmacy costs + medical costs = healthcare costs) was calculated from the hospital perspective. It addresses the question: what is the budget impact on a hospital among infants who receive lucinactant versus beractant? The budget impact outcomes included: 1) Average surfactant pharmacy costs per infant, per product, 2) Average medical costs per infant, per product, 3) Average medical costs by hospital department per infant, per product, 4) Average healthcare costs per infant, per product, 5) Budget impact by hospital department per infant, 6) Overall surfactant pharmacy budget impact per infant, 7) Overall medical budget impact per infant, 8) Overall healthcare budget impact per infant, and 9) Total budget impact across the U.S. population.

Incremental Cost-effectiveness Analysis

A cost-effectiveness analysis was conducted to examine the incremental cost per life saved among all VLBW preterm infants who received lucinactant versus beractant. Examining the cost-effectiveness of lucinactant provides additional information for healthcare decision-makers regarding the risks and benefits of surfactants.

Sensitivity Analysis

A sensitivity analysis was performed using a Monte Carlo simulation to measure the robustness of model results to changes in base case inputs and to determine which inputs most impact the results. Inputs were varied independently while holding all other variables constant for a range of 20% around the mean base case input. This was repeated for 1,000 trials to determine a budget impact range. The sensitivity analysis provides confidence that, when adjusting the input values ± 20%, the results of the model will be similar to those reported. The tornado diagram in the Results section (Figure 2, Table 6) provides the results of the sensitivity analysis based on the adjusted inputs.

RESULTS

Survival

In the pivotal clinical prevention trial SELECT, 14-day RDS-related mortality was reported at 4.7% for lucinactant versus 10.5% for beractant [OR 0.35 (95% CI, 0.18-0.66); P=.001], and all-cause mortality rates at 36 weeks PCA were 21.1% (78.9% survival rate) for lucinactant and 26.4% (73.6% survival rate) for beractant [OR 0.67 (95% CI, 0.45-1.00); P=.051].[5] In the long-term follow-up study, 1-year corrected age results demonstrated a survival rate of 71.9% for lucinactant and 69% for beractant.[20]

When the long-term 1-year corrected age results, adjusted by weight strata and BPD, were applied to the U.S. population, the decision-analytic model estimated the survival rates among all VLBW preterm infants to be 69.1% and 64.6% for those given lucinactant and beractant, respectively. These results translated into an estimated 4.5% survival benefit in the lucinactant-treated infants. The survival benefit demonstrated in the model established that the number of lucinactant patients needed-to-treat to save one life is 22 infants.

Per-Infant Impact

Impact on medical resource utilization estimated that infants who received lucinactant had 5.65 fewer NICU days per infant and 0.51 fewer NICU days on MV per infant compared to infants who received beractant (Table 3). The budget impact analysis demonstrated that the total surfactant pharmacy costs among surviving VLBW preterm infants were $461 higher for infants who received lucinactant compared with infants who received beractant (Table 3). Total medical costs, however, were $9,264 lower among infants who received lucinactant. Thus, total healthcare costs for the initial stay in the NICU were $8,803 lower among infants who received lucinactant compared to infants who received beractant. Infants who received lucinactant had lower costs in all nine hospital departments assessed compared to infants who received beractant (Table 4).

U.S. Impact

The total impact on medical resource use and

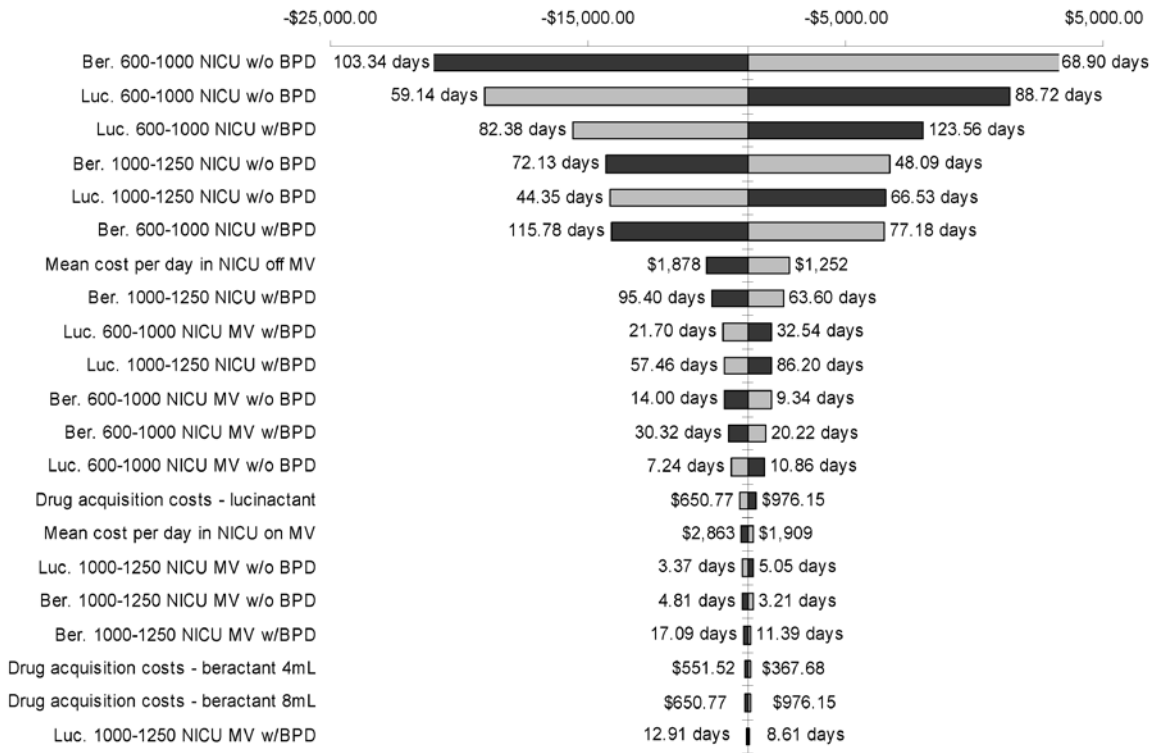

Figure 2. Sensitivity analysis tornado diagram—impact of varying base case values on the total healthcare budget impact per infant. Ber, Beractant; BPD, bronchopulmonary dysplasia; Luc, Lucinactant.

Table 3. Per-infant impact among surviving VLBW preterm infants

	Lucinactant	Beractant	Difference
Mean NICU days per infant	74.30	79.95	-5.65
Mean NICU days on MV per infant	11.45	11.96	-0.51
Surfactant pharmacy cost	$1,627	$1,166	$461
Medical costs	$125,667	$134,931	-$9,264
Total costs	$127,294	$136,097	-$8,803

MV, mechanical ventilation; NICU, neonatal intensive care unit; VLBW, very low birth weight

total budget impact for all U.S. live births of preterm VLBW infants who received surfactant therapy and survived (n=35,095) projected that lucinactant infants had 198,308.41 fewer NICU days, 17,905.81 fewer NICU days on MV, and $308,937,956 lower costs for the initial NICU stay compared with beractant infants (Table 5). The U.S. impact is the total impact on the U.S. healthcare system if all U.S. live births of preterm VLBW infants who received surfactant therapy and survived (n=35,095) received lucinactant versus beractant. By modeling the difference, there would be considerably fewer total NICU days and NICU days on MV if all VLBW infants received lucinactant, with a savings of over $300 million to the U.S. healthcare system.

Cost-effectiveness

Based on the increased survival benefit and decreased total costs, the incremental cost per life saved was $40,309 for lucinactant compared to beractant, producing a cost-benefit of administering lucinactant. The results of the cost-effectiveness analysis demonstrate that lucinactant is a cost-effective medication in the prevention of RDS in VLBW preterm infants.

Sensitivity Analysis

A univariate sensitivity analysis was conducted around each resource utilization and economic input to determine its relative impact on the study results. Each input was independently increased and decreased by 20% from the base input. The results of the sensitivity analysis indicate that the model was influenced the greatest by the mean number of days in the NICU (length of stay). The model was relatively insensitive to changes in the drug acquisition costs; therefore, these costs could increase or decrease widely with little effect on the magnitude of the results. The tornado diagram demonstrates the impact that specific increases and decreases to the base inputs would have on the study results (Figure 2, Table 6). For example, the top bar of the diagram indicates that if the initial NICU length of stay among infants 600 to 1000 grams without BPD who received beractant increased or decreased by 17.22 days, the budget impact per infant would yield a range of -$21,631 to $4,026 among infants who received lucinactant compared with beractant (assuming all other inputs remain the same).

DISCUSSION

We performed an extensive comparative pharmacoeconomic analysis of the novel peptide-containing synthetic surfactant, lucinactant, versus the most widely used animal-derived surfactant therapy in the U.S., beractant. This study evaluated differences in healthcare resource utilization, budget impact, and incremental cost-effectiveness between these two classes of surfactants. Fewer NICU days and fewer NICU days on MV were observed with lucinactant compared with beractant in surviving VLBW preterm infants. These differences in hospital stay translate into lower total hospitalization costs, and the survival benefit demonstrated with lucinactant indicates that lucinactant is a cost-effective therapy for the prevention of RDS among VLBW preterm infants.

Reducing days in the NICU and days on MV are important factors in decreasing the costs associated with initial NICU stays. In this study, where all infants received surfactant therapy, the mean lengths of initial stay in the NICU for surviving infants ranged between 74.3 days (lucinactant) and 79.9 days (beractant). These lengths of stay are consistent with those reported in contemporary databases. For example, the Vermont Oxford Network average length of stay is 105 (SD 31), 60 (SD 28), and

Table 4. Budget impact by hospital department among surviving VLBW preterm infants

Hospital Reporting Department	Lucinactant	Beractant	Difference
Room costs	$52,873	$56,850	-$3,978
Laboratory costs	$13,404	$14,392	-$988
Pharmacy costs	$11,786	$12,653	-$867
Respiratory therapy costs	$10,366	$11,074	-$708
Other therapy costs	$7,018	$7,560	-$542
Imaging costs	$5,876	$6,311	-$435
General supply costs	$8,664	$9,330	-$667
Operating room costs	$818	$881	-$63
Other costs	$11,265	$12,107	-$841

VLBW, very low birth weight

57 (SD 23) days for infants discharged home in the birth weight categories of 501 to 750 grams, 751 to 1000 grams, and 1001 to 1250 grams, respectively, compared with 13 (SD 29), 18 (SD 34), and 16 (SD 33) days, respectively, in patients who died.[28] The historical mean length of stay for infants on MV has been reported to be approximately 15 days.[15] The findings in this study of a slightly lower average length of stay in the NICU on MV of 11.4 days for infants receiving lucinactant and 11.9 days for infants receiving beractant may be related to continued advances in respiratory care and changes in ventilatory strategies among these infants.

The majority of previous studies reporting on the healthcare resource utilization and economic outcomes associated with surfactant therapy have focused on the benefits compared with MV alone.[7-18] When compared to no surfactant therapy or placebo, surfactant therapy has demonstrated great clinical success as well as economic benefits to hospitals and society. There is, however, no comprehensive, published literature which assesses the differences in total healthcare costs (medical and drug costs) between the different classes of surfactants. The current study demonstrated lower costs among patients who received lucinactant compared with beractant. Total U.S. healthcare costs for the initial NICU stay were $127,294 (lucinactant) and $136,097 (beractant) per infant. These costs are higher than previous studies which report mean hospitalization costs ranging from $60,134 to $103,042 (after adjusted to 2003 dollars[31]) among **s**urviving VLBW preterm infants who received surfactant therapy.[13,16] Higher costs in the current study may be accounted for by the presently accelerated inflation rate of overall healthcare costs. In the setting of increasing hospitalization costs, surfactant drug acquisition costs become even more nominal compared with the costs associated with healthcare resource utilization in this population, as addressed in the sensitivity analysis.

An assessment of the impact of treatments on healthcare costs and cost-effectiveness is standard across categories of efficacious products and is expected in other areas of medical specialties. Economic research is necessary in neonatal medicine, specifically as it relates to surfactant therapy. Seeking ways to reduce healthcare costs is essential, and options are provided through published research. Cost-effectiveness analyses compare the value of different clinical strategies, specifically focusing on new strategies versus current practice. The analysis in this study assessed the cost-effectiveness of lucinactant (new strategy) to beractant (current strategy) to determine incremental cost per life saved. The results of the analysis can be interpreted as the 'cost' of the additional survival benefit by switching from the current practice to the new strategy. If the cost falls below an acceptable threshold, the new strategy is considered cost-effective. Widely accepted standards for cost-effectiveness state that a treatment is appropriate if it costs less than $50,000 for a quality-adjusted life-year gained.[32,33] The number of quality-adjusted life-years among preterm infants is not available for analysis when comparing surfactants; therefore, this study measured the cost per life saved. When comparing this value to the $50,000 standard per life-year gained, the cost per life saved can be amortized over an infant's total number of

Table 5. U.S. Impact among surviving VLBW preterm infants

	Lucinactant	Beractant	Difference
U.S. total impact NICU days	2,607,395.50	2,805,703.91	-198,308.41
U.S. total impact NICU days on MV	401,843.52	419,749.32	-17,905.81
U.S. total budget impact	$4,467,334,800	$4,776,272,756	-$308,937,956

MV, mechanical ventilation; NICU, neonatal intensive care unit; VLBW, very low birth weight

life-years. For example, based on an incremental cost of $40,309 per life saved for infants who live to age 70 years, the incremental cost would be $575 per life-year gained. Therefore, at an incremental cost of $40,309 per life saved, lucinactant is a particularly cost-effective therapy for the prevention of RDS among VLBW preterm infants.

These findings are consistent with those of previous studies reporting on the use of surfactant replacement therapy compared to no surfactant therapy. The cost to produce a 28-day survivor was shown to be $41,020 for infants who received beractant compared to $44,339 for infants with air shams.[13] Additionally, the administration of colfosceril palmitate resulted in an average cost per life saved of $71,500.[26] The findings of the research conducted in this study demonstrate that lucinactant is favorable compared to beractant (and colfosceril palmitate) in terms of cost-effectiveness.

The actual cost of a formulary decision to a healthcare provider relies heavily on resource utilization, cost of care, and drug pricing. Therefore, a sensitivity analysis was conducted to identify the most critical factors that impacted the model results. Among the economic inputs, the sensitivity analysis indicated that the budget impact was most dependent on the cost of a day in the NICU off MV and least dependent on the drug acquisition costs of surfactant therapy; however, changes to either of these inputs only had minor effects on the results of the analysis. This is of 'real-world' relevance as we recognize that true acquisition costs differ from AWP, as discounts are typical in this therapeutic category. Hospitals should consider that if the cost of a NICU day off MV in their hospital is lower than $1,565, the potential cost savings to the hospital are lower than demonstrated in this analysis. However, if the costs are higher, then greater cost savings may be realized than seen in this study (Table 7). The sensitivity analysis also demonstrated that surfactant drug acquisition costs are nominal compared to the costs associated with healthcare resource utilization. Differences in total surfactant costs were $461, while differences in medical costs were $8,803. Drug costs for lucinactant can increase significantly over the cost of beractant, and this study demonstrated that lucinactant will still generate cost savings and be cost-effective.

The methods and inputs used in estimating the healthcare resource use, economic impact, and cost-effectiveness are subject to certain limitations. The cost per day in the NICU on and off MV among VLBW preterm infants was based on primary sourced data from Health Process Management (HPM), a national database that typically would not be reported in peer-reviewed literature.[26] The 244 patients enrolled in the HPM study represent data captured across NICUs in the U.S. associated with 11,967 days in the NICU off MV and 5,318 days in the NICU on MV. The representations of NICUs in the database and the data on hospital charges reflect current average healthcare costs across units in the U.S. Moreover, the sensitivity analysis indicated that changes in these variables continue to generate lower costs among infants who received lucinactant.

The resource use and clinical inputs are derived from secondary measures in a single, phase 3 clinical trial of lucinactant (SELECT).[5] Data are from the lucinactant and beractant treatment groups and include results from the global neonatology community. The model applies the resource use and clinical inputs from this population where services and care may differ from a U.S.-only population. The resource use and clinical inputs were, in some circumstances, not statistically different or may not have been adequately powered to detect differences. Thus, the sensitivity analysis was conducted. Figure 2 represents the varying of each individual input by 20% from the base case (or

Table 6. Sensitivity analysis—impact of varying base case values on the total healthcare budget impact per infant

Variable	Decrease base input 20%	Increase base input 20%	Range
Beractant 600-1000 NICU days w/o BPD	$4,026.41	-$21,631.25	$25,657.66
Lucinactant 600-1000 NICU days w/o BPD	-$18,985.03	$1,380.19	$20,365.22
Lucinactant 600-1000 NICU days w/BPD	-$15,609.21	-$1,995.63	$13,613.57
Beractant 1000-1250 NICU days w/o BPD	-$3,290.55	-$14,314.29	$11,023.73
Lucinactant 1000-1250 NICU days w/o BPD	-$14,136.62	-$3,468.23	$10,668.39
Beractant 600-1000 NICU days w/BPD	-$3,508.26	-$14,096.58	$10,588.32
Mean cost per day in NICU off MV	-$7,190.44	-$10,414.41	$3,223.97
Beractant 1000-1250 NICU days w/BPD	-$7,413.88	-$10,190.97	$2,777.09
Lucinactant 600-1000 NICU MV days w/BPD	-$9,742.90	-$7,861.94	$1,880.96
Lucinactant 1000-1250 NICU days w/BPD	-$9,732.38	-$7,872.46	$1,859.92
Beractant 600-1000 NICU MV days w/o BPD	-$7,890.45	-$9,714.40	$1,823.95
Beractant 600-1000 NICU MV days w/BPD	-$8,074.99	-$9,529.85	$1,454.87
Lucinactant 600-1000 NICU MV days w/o BPD	-$9,456.33	-$8,148.51	$1,307.81
Drug acquisition costs - Lucinactant	-$9,127.80	-$8,477.04	$650.77
Mean cost per day in NICU on MV	-$8,561.74	-$9,043.10	$481.36
Lucinactant 1000-1250 NICU MV days w/o BPD	-$9,014.92	-$8,589.92	$425.00
Beractant 1000-1250 NICU MV days w/o BPD	-$8,609.52	-$8,995.32	$385.79
Beractant 1000-1250 NICU MV days w/BPD	-$8,671.94	-$8,932.90	$260.95
Drug acquisition costs – Beractant 4 mL	-$8,682.70	-$8,922.14	$239.45
Drug acquisition costs - Beractant 8 mL	-$8,688.94	-$8,915.90	$226.96
Lucinactant 1000-1250 NICU MV days w/BPD	-$8,875.50	-$8,729.34	$146.16

BPD, bronchopulmonary dysplasia; MV, mechanical ventilation; NICU, neonatal intensive care unit

actual input), while all other inputs remain the same. For example, if infants 600 to 1000 grams without BPD who received beractant had, on average, 74 days in the NICU versus 86 days (base case), lucinactant will have lower costs. Where length-of-stay estimates appear higher or lower than at a particular institution, base inputs can be varied throughout the model (i.e., if there are 10 fewer days for infants who received beractant, it can be assumed that there would be proportionally fewer days among the lucinactant infants as well, and, thus, the impact on resource utilization and costs would remain the same). This assumption applies to incidence of BPD; institutions where there are very low rates of BPD can assume that the low rates apply across weight cohorts and across surfactants received. Despite these limitations, this study provides currently unavailable data assessing the differences in resource utilization and costs among VLBW preterm infants who received two different surfactant therapies– important results for making healthcare treatment decisions. Future naturalistic studies should be conducted to validate the results found here.

CONCLUSIONS

Exogenous surfactants administered both prophylactically and for treatment of RDS are cost-effective therapies for high-risk preterm infants.[3] In the general NICU setting among this population, surfactant drug acquisition costs are nominal relative to the overall costs associated with healthcare resource utilization. Reducing days in the NICU and days on mechanical ventilation in surviving patients are the most important indicators for improving long-term healthcare resource utilization and reducing costs associated with the initial NICU stay among preterm infants. This study has shown that administration of the novel, peptide-based synthetic surfactant, lucinactant, to surviving VLBW preterm infants results in fewer NICU days and fewer days on mechanical ventilation compared with beractant, a commonly prescribed animal-derived surfactant. Fewer NICU days translates into $8,803 in total cost savings among infants who receive lucinactant. This comprehensive pharmacoeconomic analysis, including examination of the costs per life saved, indicates that lucinactant

Table 7. Overall per-infant cost difference of varying base case economic inputs by 20%

	Base case (current study)	Increase 20% from base case	Decrease 20% from base case
NICU day on MV	$2,386	$2,863	$1,909
NICU day off MV	$1,565	$1,878	$1,252
Overall per-infant cost difference	-$8,803	-$10,655	-$6,949

MV, mechanical ventilation; NICU, neonatal intensive care unit

is a cost-effective therapy for the prevention of RDS among VLBW preterm infants.

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