Executive Summary

☐ Budget impact analysis of changing osteoporosis reimbursement criteria

In this study, a budget impact analysis of changing reimbursement criteria for osteoporosis drug therapy was conducted to help rational improvements on the current reimbursement criteria which has been criticized for years by the professional society. This study considered the impact of the reimbursement expansion in both increased medical expenditure and reduced osteoporotic fracture related expenditure from preventing osteoporosis progression into a serious stage.

A series of systematic literature reviews were used to extract osteoporotic fracture prevention effect of osteoporosis drug therapies. The NHS report from England, the CADTH report from Canada and the Cochrane Collaboration report on osteoporosis drug therapies were found to include most of clinical trial results required in the budget impact analysis of this study. Therefore, these reports were evaluated by a quality tool AMSTAR and the effect values were extracted based on the quality evaluation results. In addition, each systematic review for ibandronate and elcatonin was conducted since no systematic literature review for these medications was available. The results of meta analysis by integrating all types of ibandronate showed that the occurrence of vertebral fracture was significantly lowered compared to the control group (RR=0.64, 95%CI=[0.47,0.87], p=0.004), but the difference between the two groups was not found to be statistically significant in other fractures (RR=0.98, 95%CI=[0.78,1.25], p=0.88). No problem was detected from heterogeneity test. Since only one study was available for elcatonin, no meta analysis was performed for the medication.

The values for baseline probability, fracture event probability,

transition probability for drug treatment / no treatment were extracted from an analysis of the Health Insurance Review and Assessment Services (HIRA) claims data between 2006 and 2008. Excess mortality and normal mortality information for the budget impact analysis was gathered from a separate Korean literature reviews and vital statistics published by the Statistics Korea.

Three scenarios of reimbursement criteria change were considered in the budget impact analysis: 1) reimburse for the patients with the lowest T-score (the minimum value among L1-L4 average, femoral neck, and other parts) less than -3.0 upto one year (i.e. just extending coverage period to one year), 2) reimburse for the patients with the lowest T-score less than -2.5 and extending the reimbursement period to one year (extending the covered T-score range to -2.5 and coverage period to one year), 3) even reimburse for the patients with osteopenia (-2.5 < the lowest T-score $\leq$ -1.0) but high risk for fracture (major osteoporotic fracture risk $\geq$ 20% or hip fracture risk $\geq$ 3%). The above scenarios reflected the issue of discrepancy between diagnostic criteria and reimbursement criteria for osteoporosis in Korea along with the recommended treatment guideline of the Korean Society of Bone Metabolism and the fact that all the large trials evaluated the treatment effects of osteoporosis medications at least continuously administered for more than one year.

The budget impacts calculated from this study considered both osteoporotic medication cost increase and osteoporotic fracture related medical cost decrease by extension of reimbursement coverage in the next five years. The results showed all 3 scenarios increase the budget compared to the current criteria, but the increase tends to declining over time. Since the patients with osteoporosis receiving treatment will be increased by the expansion of criteria and osteoporotic fracture related costs will be reduced as a result, the budget impact will be gradually decreased as fracture prevention benefits grows. To examine the validity of budget impact model,

various sensitivity analyses were performed for the input parameters and the assumptions used in the model. Throughout the sensitivity analyses, the trend of budget impact did not change. Two most significant parameters were treatment rate for those who became newly eligible and treatment rate change of those who were already covered but not treated. This result indicates that a rise in those two parameters increases the treatment probability for osteoporosis (i.e. increases the number of patients treated), which is the most important component of our budget impact analysis results. During the present research project, the Korean Ministry of Health and Welfare (MOHW) suggested the National Health Insurance (NHI) Coverage Enforcement Plan including osteoporosis drug therapy coverage extension at the Health Insurance Policy Review Committee (HIPRC) held on June, 2009. As a follow up on the plan, MOHW announced on December 2010, if the NHI financing is sound enough, the coverage will be extended on October 2011 to the lowest T-score less than -2.5 and one year coverage (our scenario 2). The budget impact of osteoporosis coverage extension plan was suggested as 147 billion Korean won in the 2009 plan and 133.3 billion Korean won in the 2010 announcement. In comparison to these numbers, the present study results (scenario 2), considering fracture prevention benefits of osteoporosis treatment extension, showed 87 billion Korean won in the first year and gradually reduced to approximately 50 billion Korean won in the 5th year. More specifically, osteoporosis treatment cost increase was estimated about 100 billion Korean won in the first year and 450 Korean won for the 5 year period total whereas fracture cost savings was estimated 17 billion Korean won in the first year and 120 billion Korean won during the 5 year total. Considering offset savings on osteoporotic fracture preventions, osteoporosis drug therapy coverage extension is less costly than MOHW estimated.

□ Measurement of Willingness to Pay (WTP) for the reduction in osteoporotic fracture risk

In the present study, a survey soliciting Willingness to Pay (WTP) of general population for the osteoporosis drug therapy was conducted. The purpose of this survey is to investigate Korean coverage cutoff based on the public willingness to pay. In the US, osteopenia (-2.5 < lowest T-score < -1.0) patients with more than 3% 10-year fracture risk in femoral parts or more than 20% 10-year major osteoporotic fracture risk are also covered for osteoporosis drug therapy based on the WHO FRAX US version and 60,000 US dollar cost effectiveness threshold.

In 2009, a pilot WTP survey on 100 individuals was conducted to prepare for the main WTP survey in 2010. The pilot survey questionnaire considered a treatment method reducing 10% mean vertebral fracture risk (about 6.818% risk of vertebral fracture in Korea) and a treatment method reducing 50% of the risk. The results showed that WTP for 10% risk reduction and 50% risk reduction were 660,000 Korean won and 1,350,000 Korean won for self and 820,000 Korean won and 1,600,000 Korean won for family member (about 20% more than self), respectively. In the case of hip fracture, WTP for a treatment method for 10% risk reduction (about 1.64% risk of hip fracture in Korea) and WTP for 50% risk reduction were 1,222,000 Korean won and 2,340,000 Korean won for self and thae amounts for a family member increased about 10% more than self. From a Generalized Linear Model (GLM) regression analysis on factors influencing WTP, age, education level, marital status, employment status, economic level of a family, and self/family member were found to be the significant variables on WTP level.

To confirm the maximum WTP amount for osteoporosis fracture risk reduction, the present study developed a face-to-face questionnaire based on the pilot study results. In the questionnaire, two treatment

efficacies 25% and 50% along with baseline risk 20% and 100% were used for vertebral fracture while same efficacies with 10% and 100% baseline risk were used for hip fracture. For vertebral fracture risk reductions, WTPs for 20% baseline risk with 25% efficacy and 50% efficacy were 560,000 Korean won and 610,000 Korean won respectively while 100% baseline risk with same efficacies were 750,000 Korean won and 820,000 Korean won respectively. For hip fracture risk reductions, WTPs for 10% baseline risk with 25% efficacy and 50% efficacy were 780,000 Korean won and 850,000 Korean won respectively while 100% baseline risk with same efficacies were 1,020,000 Korean won and 1,160,000 Korean won respectively.

The regression results showed that the variables of age, sex, region, marital status, number of family members, and monthly average income of family were found to be significant on WTP. After adjusting for these significant factors, the maximum annual WTPs increase 24,000 Korean won per 10% rise of the vertebral fracture risk and to increase 28,800 Korean won per 10% rise in hip fracture risk.

□ Korean osteoporotic fracture risk prediction model

To build a Korean osteoporotic fracture risk prediction model, two large hospital health examination center records were used. The records from Center A were between the periods of 2003 and 2008 (34,137 cases) and the records from Center B were between the periods of 2004 and 2008 (61,026 cases). To confirm the osteoporotic fractures, Health Insurance Review and Assessment Services (HIRA) claims data between 2005 and 2009 were matched to those subjects in the health examination records from two centers. Total number of subjects in the matched cohort was 61,786 and 34,300 subjects with more than 50 year of age were used in the analysis. These subjects are believed to be relatively healthy since

wealthier patients tends to use those two centers. Out of 34,300 subjects, the probability of osteoporosis related fractures (coded as vertebral fracture, hip fracture, wrist fracture, and humerus fracture in osteoporosis diagnosed patients and coded as osteoporotic fracture) in female was 3.53%, and the probability in male was 1.48%. The probabilities of major osteoporotic fractures (coded as vertebral fracture and hip fracture in osteoporosis diagnosed patients) were 1.53% in females and 0.86% in males. As mentioned earlier the subjects from these two centers are likely to be relatively healthier people than general population in same age, therefore, with a caution of bias, the osteoporotic fracture probability seems to increase as age increases and the lowest T-score decreases.

To build an osteoporotic fracture prediction model, logistic regression analyses were performed for each gender and two fracture groups (major osteoporotic fractures and all osteoporotic fractures). For females, the lowest T-score, age, and weight were significant factors predicting for both groups of fractures while the lowest T-score and age were only significant factors predicting for both groups of fractures in males.