NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

Single technology appraisal (STA)

Denosumab for the Prevention of Osteoporotic Fractures in Postmenopausal Women

Manufacturer Response to Clarification Questions Received 11 February 2010

Amgen UK Ltd.

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Section A Clarification on effectiveness data

A.1 Based on the alendronate arms of the clinical trials, please provide information on whether there are any differences in baseline characteristics (and hence fracture risk) of patients who could and could not tolerate oral bisphosphonates.

There are too few patients in the 20050141 (DECIDE) and 20050234 (STAND) studies to allow for any meaningful post hoc statistical analysis for whether there are any differences in baseline characteristics (and hence fracture risk) of patients who could and could not tolerate oral BPs.

Subjects who could not tolerate oral bisphosphonates (BPs) were excluded from the 20050141 (DECIDE) and 20050234 (STAND) trials by the exclusion criteria, and with the minimum requirements for prior alendronate exposure and alendronate run-in in trial 20050234 (STAND).

Subjects were not eligible for trial 20050141 (DECIDE) or trial 20050234 (STAND) if alendronate therapy was contraindicated or poorly tolerated. Contraindications for alendronate therapy included the following:

- Abnormalities of the oesophagus, which delay oesophageal emptying such as stricture or achalasia
- Inability to stand or sit upright for at least 30 minutes
- Hypersensitivity to alendronate or other constituents of alendronate tablets

Additional exclusion criteria were included consistent with alendronate labelling to exclude subjects with impaired renal function; significantly impaired renal function as determined by serum creatinine ≥ 2.0 mg/dL (20050141 [DECIDE]) or significantly impaired renal function as determined by a derived creatinine clearance (using the Cockroft-Gault formula) of ≤ 35 mL/min calculated by the central laboratory (20050234 [STAND]) (Amgen data on file [20050141 (DECIDE) clinical study report (CSR), section 7.5.2]; Amgen data on file [20050234 (STAND) CSR, section 7.5.2]).

Subjects enrolled in the 20050234 (STAND) trial were required to have received alendronate treatment at a dose of 70 mg once weekly (QW) or equivalent

(i.e., 10 mg/day) for at least the past 6 months before screening. After screening and before randomisation, all eligible subjects received open-label alendronate 70 mg QW orally for 1 month (4 doses) (Amgen data on file [20050234 (STAND) CSR, sections 7.5.1 and 7.7.2]).

In trial 20050141 (DECIDE), a similarly small proportion of subjects in each treatment group could not tolerate (discontinued) investigational product due to adverse events ([redacted] subjects [redacted%] in the denosumab group and [redacted] subjects [redacted%] in the alendronate group) (20050141 [DECIDE] CSR, section 11.6 [Table 11-3]).

In trial 20050234 (STAND), the number of subjects who could not tolerate (discontinued) investigational product due to adverse events was also small and balanced between treatment groups (20050234 [STAND] CSR, section 11.6 [Table 11-4]). [redacted] ([redacted%) subjects in the denosumab group and [redacted] ([redacted%) subjects in the alendronate group discontinued investigational product as a result of an adverse event. The relatively small proportion of patients who could not tolerate (discontinued) alendronate in trials 20050234 (STAND) and 20050141 (DECIDE) is to be expected given that patients with known contraindications were excluded from the trials, in addition to the entry criteria for prior alendronate exposure and 1 month open-label alendronate run-in in the 20050234 (STAND) trial.

The discontinuations of alendronate in the [redacted] patients in the DECIDE study and the [redacted] patients in the STAND study are too small to allow for any meaningful post hoc statistical analysis for whether there are any differences in baseline characteristics (and hence fracture risk) of patients who could and could not tolerate oral BPs. The reasons for unsuitability for oral BPs relate to inability to comply with treatment, a contraindication or intolerance, rather than to demographic or disease characteristics; there is no evidence to suggest that baseline fracture risk will be different in patients who are are suitable for oral BPs compared to those that are not.

A.2 The manufacturer's submission states that there are no trials of IV ibandronate versus placebo with fractures as the outcome (page 24). Please provide the rationale for not including the trials of oral ibandronate versus placebo (BONE), and IV ibandronate versus oral ibandronate (DIVA), in an indirect comparison of IV ibandronate with denosumab via oral ibandronate and placebo.

The indirect comparison and mixed treatment comparison analysis did include the oral ibandronate trial versus placebo (Chesnut et al., 2004; BONE) for evaluation of morphometric vertebral, clinical vertebral and non-vertebral fracture outcomes. See tables B3 in the restructured submission. A second trial of ibandronate versus alendronate (Miller et al., 2008; MOTION) was also included evaluating clinical vertebral and non-vertebral fracture outcomes. See table B3 in the restructured submission. The reasons for the exclusion of the other ibandronate studies, specifically the DIVA study (Eisman et al., 2008) and the MOBILE study (Reginster et al., 2006), was that these studies only recorded clinical osteoporotic fractures, which was not one of the five fracture categories analysed. Clinical osteoporotic fractures were not evaluated in our indirect and mixed treatment comparisons because firstly this fracture type was not included in the economic model, and secondly the definition of clinical osteoporotic fractures varied across studies. Only a few studies specifically evaluated clinical osteoporotic fractures, while the remaining studies summarised overall clinical fractures, thereby limiting the reliability when combining studies for comparison. Finally, the DIVA and MOBILE studies only recorded fractures as adverse events, which would have limited their inclusion to only sensitivity analyses, as our primary analysis included only studies that reported fractures as primary or secondary endpoints.

Section B Clarification on cost-effectiveness data

Probabilities and model calculations

B.1 Please clarify whether the baseline risk of fracture increases over time in the modelling. If so, is such an increase in baseline fracture risk linked to decreasing BMD or linked to increasing fracture prevalence? Please clarify how this was calculated.

The Z-score is calculated as follows:

$$Z_{score} = \frac{BMD_{pat} - BMD_{age-matched\ mean}}{BMD_{age-matched\ sd}}$$

The link between bone mineral density (BMD) and fracture risk is typically measured as the risk compared to the normal population (Z-score). Thus, it is a relative risk measure and is generally calculated as the increased risk per age-matched standard deviation of BMD compared to the age adjusted mean. The relative risk (RR) per age-matched standard deviation below the age-matched mean BMD is generally denoted: $RR_{fx/sd}$

The baseline risk is the normal population risk adjusted for BMD, prior fracture and age. Age is accounted for in the normal population data; however, it also modulates the effect of BMD and prior fracture in the RR. For example, a T-score of –2.5 SD may be considered good for an 80-year-old patient but very poor for a 60-year-old. Also, a prior fracture may indicate a greater RR for a younger patient, as prior fracture is less common in the normal population at younger ages.

The model itself does not run on BMD but the RR of fracture is updated each year to account for the fact that the $RR_{fx/sd}$ declines, and that a prior fracture will contribute less to the RR compared to the normal population (because more patients in the normal population will have a prior fracture at older ages).

B.2 When running the model for a population with no prior fractures, please clarify whether fracture risk increases if the modelled women experience a fracture, and whether this is dependent upon the site of fracture.

The modeled fracture risk does not increase if the women experience a fracture, although this is accounted for by the input incidence of fractures by site. fx risk is thus only adjusted at baseline and the risk of the total cohort contains the risk of 1st, 2nd, 3rd fracture (and so on) for all analyzed patients.

The model estimates fracture risk by reference to the modelled and age-matched populations' Z-scores at baseline with adjustments for the prevalence of prior fracture at baseline. These adjustments reflect the fact that RRs comparing patients with and without prior vertebral morphometric fracture require adjustment in applying

these to the normal population, as the population will contain a proportion of individuals who themselves have suffered morphometric fractures. The model architecture constrains the number of fractures a patient can suffer, so that increasing risk in a specific individual with a modelled fracture would be of little relevance.

B.3 Please clarify how the “below threshold” risks of fracture were estimated.

A patient with a given mean T-score will not have the mean risk of fracture as risk is non-linear with respect to T-score. The ‘below threshold’ approach therefore estimates risk for points along the distribution of T-score below the specified threshold. These risks are then weighted according to the distribution of T-scores in order to derive a mean risk.

B.4 Please clarify how the sub-group analysis for different T-score thresholds were conducted (i.e. were all the subgroup analyses conducted using “below threshold” risks, or were any done using at threshold risks?). Please also clarify whether analysis was carried out by band (2.5 to 2.9, 3.0 to 3.4, etc).

The model estimates the risk of fracture for a given population having a T-score below a defined value. The subgroup analyses examine different values for this threshold T-score, with risk estimation based on the below-threshold approach. Thus, the subgroups examine T-scores of –2.5 and below, –3.00 and below, and so on.

B.5 When running the model over the lifetime of younger cohorts, relative fracture risks cease to update with age after 30 years. For example, when running the model for a 50 year old cohort, the relative risk of a hip fracture at age 90 is equal to the relative risk at age 80, despite the fact that age dependent relative risks are held up to age 100 (Worksheet titled “RR below”). Please provide the rationale for this approach.

Columns C-F in the model data sheet referred to a lookup array defined as:

RR below'!$A$2:A**3**2

This represented a model bug in that the array should have been referenced as

RR below'!$A$2:A**5**2

For younger ages this bug gives rise to a situation where in later cycles the relevant age is not available to the lookup function, causing Excel to match to the nearest alternative, and hence resulting in constant risks after a certain age. This does not affect the base-case results or associated sensitivity analysis. For analyses of cohorts of younger patients, the bug has no impact until approximately 30 years into the model time horizon. Mortality, discounting and the withdrawal of treatment after 5 years mean that younger cohorts results are not significantly affected.

An updated model version is available with this bug corrected, and with the at-threshold risk option for fracture risk prediction enabled (see C1). Updated sub-group analyses are presented in Tables B1a and B1b for primary comparisons (to replace Tables B86 and B87 in our restructured submission). Those cost-effectiveness results impacted by the bug correction are highlighted in bold with grey shading.

The correction of the bug has no effect on the cost-effectiveness results in the cohort with no prior fracture for all the sub-groups presented in our restructured submission. The correction of the bug has a negligible and insignificant numerical impact on cost-effectiveness results in the 55 and 60 year old cohorts with a prior fracture and no effect in the 65 year and older cohorts with a prior fracture. In the cohort of no prior fracture, RRs for non-hip fracture compared to the general population are constant, whereas the RRs are age dependent for all fractures in the prior fracture cohort, reflecting the changing prevalence of prior fracture in the aging general population.

No further impact of the bug would be seen in the probabilistic analysis, as the data that retrieved by the bug-affected lookup function are deterministic only.

Table B1a Subgroup analysis: primary comparison: denosumab, strontium, raloxifene and no treatment (no prior fracture)

		QALYs				Costs				ICERs for comparison with Denosumab				
T	age	Denosumab	Strontium	Raloxifene	No Treatment	Denosumab	Strontium	Raloxifene	No Treatment	Strontium	Raloxifene	No Treatment	Highest NMHB	Position for Denosumab
–2.5	55	13.00	12.97	12.97	12.97	11,392	11,182	10,714	9,368	8,421	29,572	68,330	No Treat	2
–2.5	60	11.37	11.34	11.34	11.34	11,316	11,126	10,667	9,328	7,966	28,175	71,319	No Treat	2
–2.5	65	9.77	9.74	9.74	9.73	11,318	11,187	10,755	9,425	4,348	19,390	49,140	No Treat	2
–2.5	70	8.05	8.01	8.01	7.99	11,135	11,138	10,764	9,455	Domt	9,289	29,223	Dmab	1
–2.5	75	6.54	6.50	6.50	6.49	10,578	10,759	10,455	9,201	Domt	3,346	30,359	No Treat	2
–3	55	12.86	12.83	12.83	12.82	14,628	14,474	14,030	12,678	4,787	19,306	47,436	No Treat	2
–3	60	11.24	11.21	11.21	11.20	14,493	14,362	13,929	12,583	4,269	18,317	49,597	No Treat	2
–3	65	9.66	9.62	9.62	9.60	14,462	14,413	14,018	12,678	1,250	11,396	34,194	No Treat	2
–3	70	7.95	7.90	7.90	7.88	14,182	14,326	14,015	12,690	Domt	3,069	19,313	Dmab	1
–3	75	6.47	6.42	6.42	6.41	13,402	13,785	13,563	12,301	Domt	Domt	18,007	Dmab	1
–3.5	55	12.67	12.63	12.63	12.61	19,144	19,081	18,679	17,316	1,453	10,711	31,786	No Treat	2
–3.5	60	11.07	11.03	11.03	11.02	18,895	18,858	18,466	17,110	932	10,140	33,504	No Treat	2
–3.5	65	9.50	9.45	9.45	9.43	18,789	18,867	18,530	17,174	Domt	4,893	22,977	Dmab	1
–3.5	70	7.83	7.75	7.75	7.72	18,344	18,700	18,486	17,136	Domt	Domt	11,728	Dmab	1
–3.5	75	6.37	6.32	6.31	6.29	17,223	17,897	17,794	16,519	Domt	Domt	8,600	Dmab	1
–4	55	12.43	12.37	12.36	12.35	25,434	25,523	25,187	23,809	Domt	3,962	20,198	Dmab	1
–4	60	10.85	10.79	10.79	10.77	24,971	25,081	24,755	23,384	Domt	3,670	21,665	Dmab	1
–4	65	9.30	9.24	9.23	9.21	24,713	24,986	24,737	23,359	Domt	Domt	14,512	Dmab	1
–4	70	7.66	7.57	7.56	7.52	23,985	24,660	24,591	23,206	Domt	Domt	5,772	Dmab	1
–4	75	6.25	6.18	6.17	6.15	22,334	23,426	23,496	22,200	Domt	Domt	1,238	Dmab	1

NMHB, Net Monetary Health Benefit

ICERs for treatments that are recommended by NICE according to age, T-score and prior fracture are provided in bold text to enable readers to compare with recommendations in TA160/161

Table B1b Subgroup analysis: primary comparison: denosumab, strontium, raloxifene and no treatment (prior fracture)

		QALYs				Costs				ICERs for comparison with Denosumab				
T	age	Denosumab	Strontium	Raloxifene	No Treatment	Denosumab	Strontium	Raloxifene	No Treatment	Strontium	Raloxifene	No Treatment	Highest NMHB	Position for Denosumab
–2.5	55	12.67	12.61	12.61	12.58	15,101	15,093	14,713	13,349	**136**	**6,999**	**18,735**	Dmab	1
–2.5	60	11.11	11.06	11.06	11.03	14,447	14,419	14,033	12,675	**539**	**8,636**	**22,953**	Dmab	1
–2.5	65	9.57	9.51	9.52	9.48	14,075	14,079	13,717	12,359	Domt	6,995	19,113	Dmab	1
–2.5	70	7.92	7.84	7.85	7.80	13,543	13,698	13,410	12,060	Domt	2,046	12,381	Dmab	1
–2.5	75	6.47	6.42	6.42	6.39	12,533	12,877	12,644	11,380	Domt	Domt	14,436	Dmab	1
–3	55	12.44	12.36	12.36	12.32	19,785	19,953	19,653	18,270	Domt	**1,697**	**12,277**	Dmab	1
–3	60	10.91	10.84	10.85	10.81	18,729	18,849	18,531	17,154	Domt	**3,043**	**15,587**	Dmab	1
–3	65	9.41	9.33	9.34	9.29	18,101	18,255	17,967	16,582	Domt	1,979	13,308	Dmab	1
–3	70	7.79	7.69	7.70	7.63	17,299	17,660	17,481	16,087	Domt	Domt	7,986	Dmab	1
–3	75	6.38	6.31	6.31	6.28	15,886	16,493	16,376	15,087	Domt	Domt	7,741	Dmab	1
–3.5	55	12.14	12.04	12.03	11.98	26,455	26,914	26,742	25,333	Domt	Domt	**6,959**	Dmab	1
–3.5	60	10.67	10.58	10.58	10.54	24,723	25,077	24,865	23,463	Domt	Domt	**9,629**	Dmab	1
–3.5	65	9.20	9.10	9.11	9.05	23,659	24,046	23,869	22,450	Domt	Domt	8,479	Dmab	1
–3.5	70	7.62	7.50	7.50	7.43	22,412	23,089	23,069	21,621	Domt	Domt	4,197	Dmab	1
–3.5	75	6.27	6.18	6.18	6.13	20,387	21,371	21,422	20,098	Domt	Domt	2,195	Dmab	1
–4	55	11.78	11.64	11.63	11.58	35,998	36,932	36,961	35,521	Domt	Domt	**2,320**	Dmab	1
–4	60	10.37	10.25	10.25	10.20	33,129	33,856	33,805	32,372	Domt	Domt	**4,558**	Dmab	1
–4	65	8.94	8.83	8.83	8.77	31,323	32,072	32,061	30,603	Domt	Domt	4,149	Dmab	1
–4	70	7.41	7.26	7.26	7.18	29,337	30,501	30,713	29,205	Domt	Domt	579	Dmab	1
–4	75	6.12	6.01	6.01	5.96	26,369	27,896	28,186	26,819	Domt	Domt	Domt	Dmab	1

NMHB, Net Monetary Health Benefit

ICERs for treatments that are recommended by NICE according to age, T-score and prior fracture are provided in bold text to enable readers to compare with recommendations in TA160/161.

B.6 The relative risk of fracture at a given age appears to depend on the start age of the cohort (i.e. the relative risk for hip fracture associated with osteoporosis in a 70 year old varies depending on the start age of the cohort). Please clarify the rationale for this approach, and whether it is assumed that T-scores become worse over time.

The osteoporotic population will lose BMD at the same rate as the normal population, and the Z-score can therefore be assumed to be constant. A patient who starts with a T-score of –2.5 at age 60 will implicitly have a lower T-score at age 70 (but the same Z-score). Consequently, taking two patients, one a 60-year-old with a T-score of –2.5 SD, and the other a 70-year-old with T-score –2.5 SD, the former will have greater fragility (lower T-score) upon reaching 75 years of age.

B.7 The reproduction of the FREEDOM trial validates the structure of the model but not the risk equations used to derive baseline risks in the osteoporotic population. Please clarify how well the risk equations predict the three year incidence of fractures observed in the placebo arm of the FREEDOM trial (when age, T-score, and fracture prevalence are set to match the average characteristics of participants in the Freedom trial).

The FREEDOM trial is used principally to source the treatment effect for denosumab. The model is run for specified population characteristics, including a maximum T-score (not the non-parametric distribution of T-scores represented in the trial), rather than for each individual profile represented within the FREEDOM trial. The mean results seen in the trial are based on actual outcomes in the limited (relative to the epidemiological studies employed in the risk modelling) set of patients enrolled in the trial. The cost-effectiveness model is designed to estimate outcomes for patients with a given risk profile, rather than the actual level of risk observed in the trial. Though based on population, rather than trial, baseline fracture risks, when set to the at-threshold risk option (rather than the below threshold), accordance between the modelled 3-year fracture risks and those observed in the placebo arm of the FREEDOM trial is good. This reproduction of the placebo arm of the FREEDOM trial validates the risk equations used to drive baseline risks in the osteoporotic population.

Table 1 Comparison of FREEDOM placebo arm and model 3-year fracture risk

Fracture type	FREEDOM	Model set to at-risk*
Hip	1.2%	1.52%
Vertebral	2.6%	2.76%
Non-vertebral (including hip)	8.0%	8.0%

* With patient characteristics set to age 72, prior fracture = 0.234, T-score = –2.16 (at threshold risk)

B.8 The mortality risk calculations following fracture are not clear. Please provide further details on how the relative risks of mortality were arrived at and how they are used in conjunction with the baseline mortality risks to estimate mortality following fractures (as in worksheet “Model data”: AQ - AU).

Relative risks are assigned for all-cause mortality following fracture events. These risks are based on sources in the literature; see discussion of these in section 6.3.4 of restructured submission document. A proportion of the excess mortality in fracture patients, relative to the general population, is assumed to be due to other co-morbidities. Consequently the model adjusts (downward) the additional risk implied by the initial RR estimate (removing the estimate of additional mortality due to co-morbidities). The resulting RRs are applied to population-based estimates of all-cause mortality. Where the basis for fracture risk prediction employed is FRAX, the application of the wider set of risk factors gives rise to further modification of mortality risk. FRAX calculates adjustments to mortality pre-fracture according to the patient risk factors. An additional term is employed in the mortality calculation when using FRAX to account for variation in mortality due to baseline risk factors. This adjustment is therefore in addition to the RRs post-fracture employed when using the ‘traditional’ risk prediction method.

Utilities

B.9 Health-related quality of life losses continue over the life time of all patients post hip fracture. Please clarify whether the utility multipliers are valid for the baseline population of the model (i.e. were these multipliers derived from populations of similar age with similar likelihood of admission to nursing homes following hip fracture).

The utility decrements applied in the model were age-dependent and hence considered appropriate to the baseline population of the model. The health-related quality of life (HRQL) losses for patients post–hip fracture were taken from a meta-analysis undertaken by Peasgood et al. (2009). Peasgood et al. (2009) included five studies in the meta-analysis on hip fracture used to derive utility multipliers in the first year post-fracture (Blomfeldt et al., 2005, Borgstrom et al., 2006, Murray et al., 2002, Söderqvist et al., 2006 and Tidermark et al., 2002) and three studies (Blomfeldt et al., 2005, Murray et al., 2002 and Tidemark et al., 2002) in the meta-analysis for the second and following years. The characteristics of patients in the studies incorporated into the meta-analysis are summarised in section 9.12 (appendix 12). The mean age of the patients included in these studies was 80 years (Blomfeldt et al., 2005), 81 years (Murray et al, 2002), 82.8 years (Söderqvist et al., 2006), 77.6 (Borgstrom et al., 2006) and 79.9 years (Tidermark et al., 2002). The age of these populations was therefore somewhat higher than those of baseline population of the model (70 years). HRQL was not reported by age subgroups in these studies to estimate HRQL multipliers by age. As described in Peasgood et al., one of the studies (Borgstrom et al., 2006) showed that utility loss after a hip fracture was function of baseline utility (the higher the baseline, the greater the absolute utility loss). This suggests that the utility loss is multiplicative in its effect, which is how the multiplier works in the model: the multipliers are applied to age-dependent UK population utilities. The absolute utility loss for patients with hip fracture is therefore modelled to be age-dependent.

The studies included in the meta-analysis appeared broadly to reflect the baseline population in terms of nursing home entry. Blomfeldt et al. (2005) reported that 89% of patients in the arthroplasty group and 70% of patients in the fixation group were living independently at 48 months post-fracture; Tidermark et al. (2002) reported that

after 17 months 88% of patients were living independently; whilst Borgstrom et al. (2006) reported that 5% of patients were living in special accommodation post–hip fracture at 12 months. The proportion of patients entering nursing home in the current model was considered age-dependent and estimated as 10% for the baseline population of women aged 70 years.

Costs

B.10 Please clarify whether applying costs for excess bed days was done using the trim points for specific healthcare resource groups (HRGs). Please also clarify the assumption relating to the 2 day trim point used to inflate the HRG costs.

It is important to be clear regarding how excess bed day HRG cost data are used in the analysis. There was an expectation that the average length of stay reflected in a given HRG cost (which would relate to all fracture patients) might be lower than for those patients with osteoporosis in particular due to the former being based on patients with a lower average age. For this reason, HES data were interrogated to establish the mean lengths of stay for the different fracture types for the patients aged 60-74 years and 75+ years, respectively. If the HES lengths of stay were more than 2 days greater than those relating to the HRG costs, then the latter costs were inflated to reflect that difference using Non-Elective Inpatient (Long Stay) excess bed day cost data. The latter were assumed to reflect the average cost per day for the relevant patient group (elderly and very elderly osteoporotic patients).

Regarding the choice of a margin of more than 2 days, this was considered more appropriate than inflating the HRG costs for any fractures where the mean length of stay was even slightly lower than that indicated in the HES data. Hence some margin was used to reflect the expected variability in the mean values. The use of a margin of this type can be considered conservative with in favour of less effective treatments, as it will reduce the mean costs of fractures compared to the approach of inflating all HRG costs with a mean length of stay lower than shown in the HES data. The choice of 2 days is ultimately arbitrary but was considered a reasonable compromise and was endorsed by clinical experts.

Section C Textual clarifications and additional points

Model functionality

C.1 Please clarify whether or not the “at threshold” risk estimation control should be functional in the model, as the internal calculations all seem to reference the “below threshold” risks.

A late edit of the model prior to our submission resulted in the ‘at threshold’ option requiring additional work. The analyses performed for the submission are based on the below threshold approach (which allows a clear T-score criterion to be employed for subgroup purposes). The additional edits required to update the at threshold option were not incorporated in the originally submitted model.

An updated version of the model that incorporates at-threshold risk is now available. Activation of the at-threshold risk option is required in order to output fracture risks for comparison with FREEDOM placebo arm results (see B7).

C.2 Please provide a version of the model in which the FRAX algorithm is enabled

We have discussed this with the owner of this information and it has been agreed that an executable version of the model with FRAX enabled can be provided to the Institute, Evidence Review Group and consultees on the proviso that every individual receiving the file enters into the same confidentiality agreement that was put in place during NICE’s previous appraisals in post-menopausal osteoporosis (TA 160/161).

References

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