Australian Government

Medical Services Advisory Committee

Public Summary Document

Application 1156: The diagnostic use of thyrogen for patients with well-differentiated thyroid cancer

Applicant: **Genzyme Australasia**

Date of MSAC consideration: **29 March 2012.**

1. Purpose of application

In December 2010, the Department of Health and Ageing received an application from Genzyme Australasia, the Australian distributor of the Thyrogen® brand of thyrotropin alfa-rch, requesting an extension of the current Medicare Benefits Schedule (MBS) listing for thyrotropin alfa-rch (recombinant human thyroid stimulating hormone).

Recombinant human thyroid-stimulating hormone (thyrotropin alfa-rch) is used as a component of a diagnostic test for recurrence of thyroid cancer. Patients who have had well-differentiated thyroid cancer and who have been successfully treated by surgical removal of the thyroid gland (thyroidectomy), followed by treatment with radioactive iodine, require monitoring for the recurrence of thyroid cancer. Patients who have had a thyroidectomy are typically treated with synthetic thyroid hormone therapy (THT) to replace the thyroid hormone that would otherwise have been produced by the patient's own thyroid gland.

The recurrence of thyroid cancer is assessed by the measurement of serum thyroglobulin, a protein that is only produced by thyroid gland tissue. Thyroglobulin testing can be performed in conjunction with a radioactive iodine diagnostic whole body scan (dxWBS). To increase the sensitivity of these tests for the recurrence of thyroid cancer, the release of thyroglobulin and the uptake of radioactive iodine by the thyroid tissues can be promoted by increasing the patient's thyroid stimulating hormone (TSH) levels. This can be achieved by having the patient discontinue their THT to stimulate the production of their own TSH, or by the administration of another form of TSH, such as recombinant human thyroid-stimulating hormone.

Thyrotropin alfa-rch is currently available on the MBS; however it is only available to patients in whom an increase in endogenous TSH by the method of withdrawal of THT is either contraindicated on not tolerated. The applicant proposes that Thyrogen® be made available to all patients with well-differentiated thyroid cancer as part of a diagnostic test for recurrence of thyroid cancer.

Thyroid cancer, although relatively rare, is the most common endocrine malignancy. Thyroid cancer affects women more commonly than men and the majority of cases occur between ages 25 and 65. Well differentiated thyroid cancer accounts for approximately 80-90% of all thyroid cancers and is generally regarded as slow-growing with the potential for prolonged remission,

with relatively good long-term survival rates for most patients who have definitive primary (initial) treatment and comply with ongoing monitoring.

2. Background

In 2002, MSAC first considered evidence in relation to the use of thyrotropin alfa-rch as a component of a diagnostic procedure to detect recurrence of well-differentiated thyroid cancer. At that time MSAC concluded that the increase in TSH by administration of thyrotropin alfa-rch was associated with a lower diagnostic accuracy of detection of recurrent thyroid cancer compared with increase in TSH by withdrawal from THT. Accordingly, the MBS item was restricted to patients in whom THT-withdrawal is medically contraindicated or not tolerated.

3. Prerequisites to implementation of any funding advice

Thyrogen® (thyrotropin alfa-rch) 0.9 mg powder for injection has Therapeutic Goods Administration (TGA) approval for use as a preparatory agent "with serum Tg testing, with or without radioiodine imaging and undertaken for the detection of thyroid remnants and well-differentiated thyroid cancer in post-thyroidectomy patients maintained on hormone suppression therapy".

Thyrogen® (thyrotropin alfa-rch) is also approved for "therapeutic use in post-thyroidectomy patients maintained on hormone suppression therapy in the ablation of thyroid remnant tissue in combination with radioiodine". Thyrogen® (thyrotropin alfa-rch) has an Authority Required PBS listing for "Ablation of thyroid remnant tissue, in combination with radioiodine, in a post thyroidectomy patient without known metastatic disease". No further prerequisites (e.g., specific qualifications or training or accreditation of specialists) are specified.

4. Proposal for public funding

The proposed MBS item is summarised below:

Category 2 – MISCELLANEOUS DIAGNOSTIC PROCEDURES AND INVESTIGATIONS
12201 Administration arranged by a specialist or consultant physician in the practice of his or her specialty, of thyrotropin alfa-rch (recombinant human thyroid-stimulating hormone) for use with serum thyroglobulin (Tg), with or without radioactive iodine imaging, undertaken for the detection of thyroid remnants and well differentiated thyroid cancer in post-thyroidectomy patients maintained on hormone suppression therapy.
Fee: $2,348.30 Benefit: 75% = $1,761.25 85% = $2,274.60

The proposed MBS item descriptor seeks to expand the eligible population beyond that defined by the current item descriptor, mainly by removing restrictions to particular subgroups.

5. Consumer Impact Statement

Nil.

6. Proposed intervention's place in clinical management

Thyrotropin alfa-rch is assumed to be a direct substitute for stimulation of endogenous TSH by THT-withdrawal, which in turn promotes the release of Tg and the uptake of radioactive iodine. Both approaches are used prior to the assessment of serum Tg, with or without dxWBS, for the purposes of the detection of recurrence of well-differentiated thyroid cancer in patients maintained on hormone suppression therapy post-thyroidectomy with I-131 remnant ablation. Thyrogen® would be used instead of THT-withdrawal.

The submission of evidence from the applicant advises that there will be no change to the clinical management algorithm for follow-up of patients with well-differentiated thyroid cancer as a result of the proposed changes to the MBS listing for thyrotropin alfa-rch. The only proposed change is the method used to elevate TSH prior to serum Tg assessment with or without radioactive iodine whole body scan.

Although the submission of evidence suggests that the only use of thyrotropin alfa-rch (followed by serum Tg assessment) is as a substitute for THT-withdrawal (followed by serum Tg assessment), the economic evaluation presented in the submission of evidence also suggests that thyrotropin alfa-rch might also be used as a substitute for unstimulated Tg assessment in patients who are not compliant with recommendations to discontinue THT (due to the unpleasantness of the hypothyroid state that occurs as a consequence of withdrawal of THT).

7. Other options for MSAC consideration

The Protocol Advisory Sub-Committee (PASC) is a standing sub-committee of MSAC. Its focus is in determining the Decision Analytic Protocols (DAPs). This involves defining the decision option/s and seeking the answers to questions raised by the Committee prior to lodgement with MSAC for the consideration of public funding.

Proposal for public funding

In determining the DAP, PASC raised an issue relating to the clinical need for TSH elevation given the current availability of ultrasensitive Tg assays. PASC suggested that the utility of unstimulated ultrasensitive Tg measurement needed to be considered along with the use of thyroglobulin alfa-rch stimulated assessments for this patient group. PASC also indicated that it may be important from an efficiency point of view that MSAC is informed about the relative cost-effectiveness of each of these alternatives for THT-withdrawal stimulated Tg assessment.

The MBS item considered in the submission of evidence from the Applicant differs from that suggested in the Final DAP in the following ways:

1 The proposed item descriptor does not restrict the patient population to those who have had a total thyroidectomy and at least one ablative dose of radioactive iodine. As noted by the Final DAP, the term “post-thyroidectomy patients” may be interpreted more broadly than intended, i.e., to include patients who have had partial thyroidectomy and to include patients who have not received an ablative dose of radioactive iodine post-thyroidectomy.

2 The proposed item descriptor is also broader than suggested by PASC in the Final DAP in that it permits use for detection of thyroid remnants in post-thyroidectomy patients maintained on hormone suppression therapy as well as use for the detection of recurrent well-differentiated thyroid cancer.

3 Unlike the item descriptor proposed in the Final DAP, the item descriptor considered in the Applicant’s submission-based assessment does not limit use of the item up to the time at which the patient achieves two consecutive assessments of stimulated serum Tg reporting undetectable levels of Tg. This may lead to inappropriate overuse of the item.

4 Additionally, the submission-based assessment does not include an evaluation of a second listing as suggested by the PASC for patients who have had two consecutive assessments of stimulated serum Tg reporting undetectable levels of Tg but in whom recurrence of thyroid cancer is clinically suspected.

5 The listing evaluated in the submission of evidence from the applicant does not restrict the item to be payable once only in any twelve month period as suggested by the PASC and as

per the current MBS listing for thyrotropin alfa-rch. There is the potential for overuse of the item without this restriction.

6 The proposed MBS item descriptor, in relation to administration of thyrotropin alfa-rch, requires that administration be "*arranged* by a specialist or consultant physician" whereas the item descriptor proposed in the Final DAP, like the current MBS listing of thyrotropin alfa-rch, requires that thyrotropin alfa-rch be *administered* by a specialist or consultant physician.

8. Comparator to the proposed intervention

The submission of evidence from the Applicant nominates TSH stimulation by THT-withdrawal as the appropriate comparator on the grounds that it is the procedure most likely to be replaced in practice by thyrotropin alfa-rch for patients who are excluded by the current item descriptor.

This is consistent with PASC's determination.

9. Comparative safety

Three studies (Haugen 1999, Ladenson 1997 and Pacini 2001) involving within-patient comparisons of thyrotropin alfa-rch stimulated assessments for recurrence of thyroid cancer with THT-withdrawal stimulated assessments for recurrence of thyroid cancer constitute the primary source of evidence. The submission of evidence from the Applicant does not provide a summary of the comparative safety outcomes from the studies presented in the submission of evidence. The submission of evidence states that an "independent government evaluation concluded that Thyrogen® was safe and efficacious for therapeutic use".

The submission of evidence states that: "Thyrogen® is typically well-tolerated with short-lived (<48 hours) and generally mild adverse effects. The most common of these adverse effects include: nausea (approximately 10% incidence), headache (approximately 7% incidence) and asthaenia (approximately 3% incidence). No serious adverse events (life-threatening or requiring hospitalisation) were related to Thyrogen® administration.

Very rare manifestations of hypersensitivity to Thyrogen® have been reported in both clinical, post-marketing settings and in special treatment groups with advanced disease, such as urticaria, rash, pruritus, flushing and respiratory signs and symptoms. Enlargement of residual thyroid tissue or metastases has been reported to occur following treatment with Thyrogen®. This may lead to acute symptoms which depend on the anatomical location of the tissue. It is recommended that pre-treatment with corticosteroids be considered for patients in whom local tumour expansion may compromise vital anatomic structures".

Additionally, the submission of evidence states that the adverse events associated with thyrotropin alfa-rch administration should be considered in the context of adverse events associated with profound hypothyroidism secondary to THT-withdrawal. However, the submission does not provide direct evidence comparing the safety profile of thyrotropin alfa-rch with adverse events associated with hypothyroidism secondary to THT-withdrawal.

In the study reported by Haugen 1999, headache was the most commonly reported adverse event (9.2%) followed by nausea (6.1%) and asthenia (3.5%) in the thyrotropin alfa-rch phase of the study. These adverse effects were usually mild and transient. No serious adverse events (life-threatening or requiring hospitalization) were related to administration of thyrotropin alfa-rch. Two patients had chest pain and palpitations during the withdrawal phase of the study and one patient had syncope on the eighth day of thyroid hormone withdrawal.

Of the 152 patients enrolled in the study reported by Ladenson 1997, 48 (32%) had adverse events, which were interpreted by their treating physicians as definitely caused by thyrotropin

alfa-rch in 6 patients, probably caused by it in 20, and possibly caused by it in 22. The only common adverse event was nausea, which occurred in 25 patients (16%), but was usually mild and short-lived. One patient with recurrent invasive thyroid carcinoma died of an apparent pulmonary embolus six days after administration of thyrotropin alfa-rch. Pacini 2001 did not report any results of safety assessments.

10. Comparative effectiveness

The same three studies (Haugen 1999, Ladenson 1997 and Pacini 2001) constitute the primary source of evidence.

The concordance between results generated during the thyrotropin alfa-rch stimulated dxWBS phase and THT-withdrawal stimulated dxWBS phase of the study were reported by Haugen 1999 and Ladenson 1997. Where there were discordant results following thyrotropin alfa-rch stimulated assessment and following THT-withdrawal stimulated assessment, a higher classification rating was given to the assessment that revealed the presence of thyroid remnant or thyroid cancer not seen on the other scan.

In the study reported by Haugen 1999, scans were concordant between the two testing methods in 101/113 (89.4%) patients and discordant in 12/113 (10.6%) of patients. Overall, there was a trend toward a higher rate of detection of thyroid tissue or cancer in the THT-withdrawal phase of the study than in the thyrotropin alfa-rch phase (57/113 [50.4%] vs. 51/113 [45.1%]) however the difference did not reach statistical significance. For nine of the twelve cases where the scans in the two phases of the study resulted in discordant results (75% of discordant cases), a superior rate of detection of thyroid tissue or cancer was found in THT-withdrawal phase of the study and for three of the twelve cases where discordant results were observed (25% of discordant cases) a superior rate of detection was found in the thyrotropin alfa-rch phase of the study.

In the study reported by Ladenson 1997, scans were concordant between the two testing methods in 106/127 (83.5%) patients and discordant in 21/113 (18.6%) of patients. Overall, there was a trend toward a higher rate of detection of thyroid tissue or cancer in the THT-withdrawal phase of the study than in the thyrotropin alfa-rch phase (59/127 [46.5%] vs 44/127 [34.6%]) however the difference did not reach statistical significance.

For 18 of the 21 cases where the scans in the two phases of the study resulted in discordant results (86% of discordant cases), a superior rate of detection of thyroid tissue or cancer was found in THT-withdrawal phase of the study and for 3 of the 21 cases where discordant results were observed (14% of discordant cases) a superior rate of detection was found in the thyrotropin alfa-rch phase of the study. These results suggest superiority of TSH stimulation by THT-withdrawal over TSH stimulation by administration of thyrotropin alfa-rch prior to dxWBS.

Ladenson 1997 conclude “[we] found that recombinant thyrotropin was efficacious and safe for stimulating the uptake of radioactive iodine in patients with thyroid carcinoma who continued thyroid hormone therapy, but not as effective as withdrawal of thyroid hormone.”

In the study reported by Pacini 2001, the overall concordance between thyrotropin alfa-rch stimulated and THT-withdrawal stimulated serum Tg was 67/72 (93.1%). Overall, there was a trend toward a higher rate of positive serum Tg assay in the THT-withdrawal phase of the study than in the thyrotropin alfa-rch phase (36/72 [50.0%] vs 31/72 [43.0%]) however the difference did not reach statistical significance. For all five cases where the results across the two phases of the study were discordant (100% of discordant cases) the results were positive during the THT-withdrawal phase of the study and negative in the thyrotropin alfa-rch phase of the study.

The submission of evidence from the applicant describes thyrotropin alfa-rch as equivalent in

terms of comparative effectiveness; however there appears to be a consistent trend toward higher rates of detection of thyroid tissue or cancer by dxWBS or by serum Tg assessment when endogenous TSH is stimulated by THT-withdrawal compared with the administration of exogenous thyrotropin alfa-rch in the studies.

11. Economic evaluation

The submission of evidence estimated the incremental cost-effectiveness ratio (ICER) for thyrotropin alfa-rch over THT withdrawal as $41,145 per extra quality-adjusted life-year (QALY) gained (base case from Step 3). This estimate incorporated a correction from the initial estimate of $39,130 when a modelled "48-week" year in the original calculations is corrected to a full "52-week" year. The primary assumption of the economic evaluation was that diagnostic performance under thyrotropin alfa-rch stimulation is non-inferior to THT withdrawal.

The ICER also relied on a 13-week period of disutility due to *symptomatic* hypothyroidism following THT withdrawal. By contrast, the profile and duration of QoL differences in the QoL studies reported a 4-6 week period in which symptoms differed between patients receiving THT withdrawal or thyrotropin alfa-rch. Applying a six-week period in the Step 1 version of the model increased its base case ICER from $70,077 per extra QALY gained to $98,698.

The ICER was also affected by the estimation of any "additional costs" relating to specialist visits and co-ordination of assessment for recurrence of thyroid cancer ($400.83 based on the current MBS fee for the thyrotropin alfa-rch-associated professional service minus the dispensed price of thyrotropin alfa-rch). A sensitivity analysis reduced this estimate from $400.83 to $100, which increased the Step 1 ICER to $81,652.

When both these changes were made to the model, the Step 1 ICER increased to $114,993.

The main effect of changing the Step 1 version of the model to the Step 3 version of the model was to examine the flow on effect of experiencing hypothyroidism symptoms on reducing subsequent compliance to repeat testing with THT withdrawal. The Step 3 estimate of noncompliance was 14.4% with THT withdrawal compared with 0% with thyrotropin alfa-rch. This difference in compliance contributed to differences in the extent and severity of late stage thyroid cancer recurrence, further contributing to both utility differences (a disutility of -0.33 was assumed for late-stage cancer) and mortality differences.

For MSAC's view of the economic evaluation, see 15 "Summary of consideration and rationale for MSAC's advice".

12. Financial/budgetary impacts

The cost of rendering each thyrotropin alfa-rch service was assumed to only reflect the PBS-dispensed price of thyrotropin alfa-rch, and no other costs for the associated medical service as reflected in the current MBS fee were included.

The estimates of utilisation were assumed to range from 727 extra services in year 1 increasing to 942 services in year 5.

The estimated incremental costs to the MBS overall ranged from $1,073,705 in year 1 increasing to $1,482,915 in year 5. When revised to use the current MBS fee rather than the PBS-dispensed price, these estimates increased to $1,273,719 in year 1 and $1,758,408 in year 5

13. MSAC key issues

MSAC proposed to consider only expanding the MBS-eligible population to patients who have had a total thyroidectomy and at least one ablative dose of radioactive iodine. This is consistent

with the advice of PASC, and narrower than the request of the applicant.

14. Other significant factors

MSAC considered that the patient perspective was important given that the immediate claim in support of the proposal was that it improved the quality of life by avoiding hypothyroidism during the THT withdrawal period. The committee further commented that a patient impact statement outlining the implications of how this period of hypothyroidism may impact on a patient's financial, physical and emotional wellbeing may be beneficial to complement the quality of life studies presented in any future application.

MSAC further noted the applicant had proposed to broaden the additional population groups being sought for public funding beyond that agreed by PASC.

15. Summary of consideration and rationale for MSAC's advice

Clinical context considerations

MSAC noted that there have been changes in the diagnosis and treatment of well-differentiated thyroid cancer over the last decade. With the advancement of diagnostic technologies and subsequent earlier detection of thyroid cancer, morbidity and mortality rates have reduced, though the rate of diagnosis has increased approximately four fold. This is because more patients are newly diagnosed with early-stage, low-risk thyroid cancer. The Committee noted that, for the majority of such low-risk cases, aggressive therapy which included radioactive iodine (I-131) ablation of remnant thyroid tissue is no longer indicated. Monitoring under conditions of high thyroid stimulating hormone (thyrotropin, TSH) levels – whether produced endogenously following withdrawal of thyroid hormone therapy (THT) or administered exogenously as recombinant human thyrotropin alfa-rch – is only warranted after thyroid remnant ablation. Thus, MSAC proposed to consider only expanding the MBS-eligible population to patients who have had a total thyroidectomy and at least one ablative dose of radioactive iodine. This is consistent with the advice of PASC, and narrower than the request of the applicant. Similarly, MSAC supported maintaining the current requirement for administration by a specialist or consultant physician (as specifically defined for the existing item) as opposed to allowing the specialist or consultant physician to arrange for this administration (as proposed by the applicant).

Further, MSAC noted the changes in diagnostic technologies which may further reduce the clinical need for high TSH, especially in patients at lower risk of recurrence. In particular, there is increasing use of high-resolution neck ultrasound, which does not require high TSH levels, to detect local recurrences, and more sensitive assays which are capable of detecting lower circulating levels of the thyroid tissue marker, thyroglobulin (Tg), under conditions of normal or suppressed TSH.

MSAC agreed that, for patients with well-differentiated thyroid cancer who have had a total thyroidectomy and at least one ablative dose of radioactive iodine and who are monitored with serum Tg, with or without I-131 whole-body scanning, to detect recurrent disease, the appropriate comparator for thyrotropin alfa-rch is THT withdrawal to stimulate endogenous TSH.

Assessment of test performance

MSAC agreed that the claim for noninferiority had not been robustly established when comparing the results of whole body scanning and serum Tg between patients who had previously received thyrotropin alfa-rch or THT withdrawal. The Committee noted that the key prospective studies used to support this application were the same as identified in the previous application

(Application 1043). For the current assessment, data from these studies were presented as an analysis of concordance of results between THT withdrawal and thyrotropin alfa-rch administration.

MSAC noted that concordance was 89.4% (Haugen et al, 1999) and 83.5% (Ladenson et al, 1997) for whole body scanning and 93.1% (Pacini et al, 2001) for serum Tg. Although the proportions of test positive results overall were not statistically significantly different for any of the three studies (post-THT withdrawal and post-thyrotropin alfa-rch results being 50.4% and 45.1%, 46.5% and 34.6%, and 50.0% and 43.0%, respectively), MSAC also noted that the majority of discordant results were positive after THT withdrawal and negative after rhTSH administration (9/12, 18/21 and 5/5 of the discordant results, respectively), indicating a consistent trend towards lower rates of detection of thyroid tissue following rhTSH. Analysis of the same data in MSAC Application 1043 showed that the differences were statistically significant, at least for the largest of these studies, whilst acknowledging the difficulty of using an "imperfect" comparator (THT withdrawal) as the reference standard.

Assessment of quality of life consequences

In relation to the safety of thyrotropin alfa-rch, MSAC noted from the previous application that the most commonly reported adverse events associated with thyrotropin alfa-rch (Haugen et al, 1999 and Ladenson et al, 1997) were minor and short-lived: headache (3.5% to 11.1%) and nausea (7.7% to 17.4%). In comparison with THT withdrawal, statistically significant differences favouring thyrotropin alfa-rch were reported across all domains of the SF-36 quality of life instrument, with thyrotropin alfa-rch results being closer to the results from the general population norm (Schroeder et al, 2006). When summarised into a single SF-6D score, this statistically significant advantage was consistent across a subgroup who subsequently received diagnostic follow-up and a subgroup who subsequently received remnant ablation. The time course of the quality of life advantage became statistically significant 2 - 4 weeks after THT withdrawal and had returned to baseline by four weeks after restarting THT (Pacini et al, 2006). MSAC did acknowledge however that a patient impact statement would have been helpful as a supplement to the quality of life studies (QoLS) presented in the application.

Economic considerations

MSAC considered that the base case (Step 3) incremental cost-effectiveness ratio (ICER) presented for thyrotropin alfa-rch over THT withdrawal of $41,145 per extra quality-adjusted life-year (QALY) gained was an underestimate. This incorporates a correction from the initial estimate of $39,130 when a "48-week" year in the calculations is corrected to a "52-week" year.

The primary assumption of the economic evaluation is that diagnostic performance is not impaired by prior use of thyrotropin alfa-rch rather than THT withdrawal. As noted above, MSAC did not accept that this had been sufficiently established by the data presented.

MSAC identified that the ICER relied on a 13-week period of disutility due to *symptomatic* hypothyroidism following THT withdrawal. The committee noted the profile and duration of QoL differences in the QoL studies and commented that a 4-6 week symptomatic period was clinically more realistic and that this change would increase the ICER and so make it less favourable.

Applying a six-week period in the Step 1 version of the model increased its base case ICER from $70,077 per extra QALY gained to $98,698. MSAC also noted that the estimation of any "additional costs" relating to specialist visits and co-ordination of assessment for recurrence of thyroid cancer ($400.83 based on the current MBS fee for the thyrotropin alfa-rch-associated

professional service minus the dispensed price of thyrotropin alfa-rch) was poorly substantiated, and when reduced to $100, increased the Step 1 ICER to $81,652. When both these changes were made to the model, the Step 1 ICER increased to $114,993, illustrating the extreme sensitivity of these results to assumptions made in regard to disutility associated with hypothyroidism and costs assumed for arranging and coordinating assessments for recurrence of thyroid cancer. MSAC also noted that no disutility was attributed in the ICER to the adverse effects of thyrotropin alfa-rch.

MSAC noted that there was little or poorly documented evidence of the flow on effect of hypothyroidism reducing subsequent compliance to repeat testing with THT withdrawal and that the estimate of noncompliance (14.4% with THT withdrawal compared with 0% with thyrotropin alfa-rch) was based on a survey with only a 24% (11/46) response rate. This is an important source of longer-term QALYs gained for thyrotropin alfa-rch over THT withdrawal in Steps 2 and 3 of the model, contributing to both utility differences (a disutility of -0.33 is assumed for late-stage cancer) and mortality differences due to late stage thyroid cancer. MSAC also considered that the assumption of zero noncompliance with thyrotropin alfa-rch was unrealistic and this also contributes to an underestimated base case ICER.

MSAC concluded that, even if noninferiority of diagnostic performance had been established, the base case ICER was highly likely to have been underestimated due to favourable assumptions for thyrotropin alfa-rch administration.

MSAC considered that a price reduction for thyrotropin alfa-rch would make the ICER more favourable. In the sensitivity analyses provided for the original base case ICER estimate in the submission, each 10% change in price is associated with a $4210 change in the ICER.

MSAC noted that the incremental costs to the MBS overall were assumed to reflect only the PBS-dispensed price of thyrotropin alfa-rch, and no other costs for the associated medical service as reflected in the current MBS fee were included. Corrected estimates should use 96% of the current fee to reflect current MBS practice with thyrotropin alfa-rch and the current rebate amount.

However the estimates of utilisation are also uncertain: the relevant incident population is likely to have been overestimated given the more restricted indication considered by MSAC, whereas the prevalent population is likely to be higher than the current utilisation of 160 per year.

16. MSAC's advice to the Minister

After considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of thyrotropin alfa-rch in the diagnosis of recurrence of patients with well differentiated thyroid cancer, MSAC advised the Minister that it did not support the application to broaden the current MBS item descriptor to include additional population groups.

17. Context for decision

This advice was made in accordance with MSAC Terms of Reference.

MSAC is to:

Advise the Minister for Health and Ageing on medical services that involve new or emerging technologies and procedures and, where relevant, amendment to existing MBS items, in relation to:

1 the strength of evidence in relation to the comparative safety, effectiveness, cost-effectiveness and total cost of the medical service;

2 whether public funding should be supported for the medical service and, if so, the circumstances under which public funding should be supported;

3 the proposed Medicare Benefits Schedule (MBS) item descriptor and fee for the service where funding through the MBS is supported;

4 the circumstances, where there is uncertainty in relation to the clinical or cost-effectiveness of a service, under which interim public funding of a service should be supported for a specified period, during which defined data collections under agreed clinical protocols would be collected to inform a re-assessment of the service by MSAC at the conclusion of that period;

5 other matters related to the public funding of health services referred by the Minister.

Advise the Australian Health Ministers' Advisory Council (AHMAC) on health technology assessments referred under AHMAC arrangements.

MSAC may also establish sub-committees to assist MSAC to effectively undertake its role. MSAC may delegate some of its functions to its Executive sub-committee.

18. Linkages to other documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.
The MSAC Assessment Report is available at
http://www.msac.gov.au/internet/msac/publishing.nsf/Content/app1156-1