



**57<sup>th</sup> MSAC Meeting  
29-30 November 2012**

**1334 Subcutaneous Immunoglobulins (SCIg)**

**Summary of consideration and rationale for MSAC's advice**

MSAC noted that applications to add subcutaneous immunoglobulin (SCIg) products to the National Products Price List (NPPL) under the National Blood Agreement had been made by Octapharma Australia Pty Ltd (for Gammanorm<sup>®</sup>) and by CSL Ltd (for Evogam<sup>®</sup>). MSAC further noted that the National Blood Authority (NBA) had prepared a Cycle 1 Assessment for the two applications which it proposed be provided to the Jurisdictional Blood Committee and had sought comment from the Evaluation Sub-Committee of MSAC and MSAC. MSAC first considered the applications and then the Cycle 1 Assessment.

Applications

MSAC accepted that immunoglobulin therapy had an established place in clinical management. A clinical need for SCIg products is established by their use in overseas markets and by the estimate of about one third of the intramuscular product being diverted to subcutaneous use.

MSAC accepted that intravenous immunoglobulin (IVIg) is the main comparator for the subcutaneous route of administration, but also noted that some SCIg use would replace immunoglobulins formulated for intramuscular use, but administered subcutaneously and some SCIg may be used for a small number of patients who, for some reason, cannot be treated with either intravenous or intramuscular immunoglobulins. MSAC noted that a potential advantage for SCIg was the possibility of arranging self-administration at home rather than receiving treatment in hospital.

MSAC noted that the applications were based primarily on pharmacological and pharmacokinetic data, which indicated that adequate trough levels were attained. There was no basis provided to assess these results in terms of comparative clinical effectiveness. Similarly, the trial data provided were underpowered to detect meaningful differences in bacterial infection rates as a basis to assess comparative clinical safety. The applications tended to rely on a long-established overseas market as the basis for providing reassurance on comparative safety. MSAC accepted that reduced infection was a plausible claim for those patients who no longer need a central line for the subcutaneous route of administration, but that this would apply only to a subgroup of patients (for example, patients with primary immunodeficiency), and not for other patients (for example, those with secondary immunodeficiency from cancer or its treatment who need a central line for other reasons).

MSAC noted that the applications did not formally justify the proposed equi-effective doses across the two routes of administration, but accepted that years of experience supported equivalence on a gram of immunoglobulin to a gram of immunoglobulin basis when treated for the same overall duration. MSAC also accepted that both applicants proposed to adopt a cost-minimisation approach from the NPPL perspective by aligning the price of their products with the price of IVIg on a gram of immunoglobulin to gram of immunoglobulin basis.

MSAC noted that both applications assumed that SCIG would result in home-based injection rather than hospital-based injection, and thus claimed a range of associated cost offsets from reduced use of hospital resources. As no home-based arrangements have yet been made, MSAC was unsure when these hospital-based resources would be freed following any addition of SCIG to the NPPL. Based on home-based arrangements for injection of medicines developed by hospitals in other therapeutic areas, MSAC also accepted advice from its ESC that it was likely that such arrangements would be accompanied by charges to patients, for example, to cover consumables. Depending on how these arrangements and charges were developed, such a cost shift would reduce likely uptake rates if patients had a choice, or disadvantage patients financially if they had no choice. There may also be flow-on consequences with any shifts from the public sector (tertiary hospitals) to the private sector (primary care). Thus an important omission in the analyses was a breakdown of how the costs would be re-distributed when moving from current hospital-based IVIg to proposed home-based SCIG in Australia. MSAC also agreed with advice from ESC about the importance of adequate training of all involved, that the analyses did not include any quality of life gains nor account for the increased likelihood of errors with immunoglobulin injection (including wastage) if it is delivered in the home setting, that cost offsets are greater if SCIG is administered via push injection than infusion pump, and that a small increase in SCIG per unit cost over IVIg would reverse the claimed overall cost saving in one of the evaluations presented.

MSAC noted that the applicants assumed no net cost to the NPPL a simple substitution of SCIG for IVIg on a patient for patient basis, with equal pricing for equal doses and overall cost savings to the health care system. MSAC noted that if SCIG resulted in an increase in the number of patients treated with immunoglobulin (especially for various neurological indications), then the cost neutral assumption would no longer apply. The larger the increase in the population treated with immunoglobulin overall, the bigger the cost to the NPPL. The assumption of net cost savings to the overall health care system would not be realised from a financial perspective if the freed hospital resources were simply redeployed for other uses.

#### Cycle 1 Assessment

MSAC noted that the NBA has issued criteria to identify clinical uses of IVIg which are appropriate for funding under the National Blood Agreement. MSAC noted that the demand for immunoglobulins exceeded supply, and so advised that these guidelines should also apply to SCIG if listed on the NPPL. MSAC further advised that more narrowly limiting SCIG to the circumstances identified in page 4 of the Cycle 1 Assessment would further reduce the risk of an expansion of use of immunoglobulins following any addition of SCIG products to the NPPL.

MSAC noted that the Cycle 1 Assessment report included studies not included in the applications, which suggested possible improvements in infection rates, quality of life and patient preference for SCIG over IVIg, but were largely confounded by SCIG being injected in the home via arrangements which were free of charge, whereas IVIg continued to be injected in the hospital. MSAC considered that it was difficult to isolate the effect of changing the route of administration from these studies and thought that the overall conclusions might not apply in Australia if different arrangements for injecting in the home were to apply here.

## **MSAC advice to the Minister, Commonwealth representative of the Jurisdictional Blood Committee, and the National Blood Authority (NBA)**

After considering the strength of the available evidence in relation to the safety, clinical effectiveness and cost-effectiveness of adding subcutaneous immunoglobulin (SCIg) products to the National Products Price List (NPPL) under the National Blood Agreement, MSAC's advice in respect to the following aspects of the NBA's Cycle 1 Assessment against the agreed Multi-Criteria Assessment (MCA) tool is as follows:

- MCA 2, comparative health gain: should be rated as “no impact”, because the direct comparative evidence weakly supports a non-inferiority conclusion rather than a superiority conclusion, and although there is a possibility of a theoretical incremental health gain, MSAC considered that this was better captured as part of MCA 10 (see below)
- MCA 3, comparative safety gain: should be rated as “no impact”, because the direct comparative evidence weakly supports a non-inferiority conclusion rather than a superiority conclusion, and although there is a possibility of a theoretical incremental safety benefit, MSAC considered that this was better captured as part of MCA 10 (see below)
- MCA 4, comparative cost-effectiveness: should be rated as “uncertain” in preference to “neutral”, because the direct comparative evidence weakly supports a non-inferiority conclusion rather than a superiority conclusion, the basis for accepting any QALY gain is largely theoretical (see also MCA 10, below), and the basis of accepting any cost offsets relies on separately accepting that adding SCIg to the NPPL would trigger the delivery of immunoglobulins in the home rather than the hospital setting (see MCA 5b, below)
- MCA 5a, financial implications for the national blood budget: should be rated as “uncertain” in preference to “no impact”, accepting that this cost-minimisation approach is supported by the clinical non-inferiority conclusion from MCA 2 and MCA 3, together with an acceptance that SCIg and intravenous immunoglobulin (IVIg) are equi-effective on a gram of immunoglobulin to gram of immunoglobulin basis, that SCIg products would have the same price as IVIg products on a gram of immunoglobulin to gram of immunoglobulin basis and also accepting NBA's assurance that its guidelines for use of immunoglobulins would minimise the risk of adding SCIg to the NPPL resulting in an increase in the overall volume of immunoglobulin (although this risk of an increase in the overall volume of immunoglobulin would be further minimised by being limited to the smaller list of circumstances identified on page 4 of the NBA Cycle 1 Assessment)
- MCA 5b, financial implications for government health budgets: should be rated as “uncertain” in preference to “no impact”, because the basis of accepting any cost offsets relies on separately accepting that adding SCIg to the NPPL would trigger the delivery of immunoglobulins in the home rather than the hospital setting, whereas this consequential step is likely to be delayed, and its effect on costs is likely to be diminished by any introduction of cost-shifting, particularly to patients
- MCA 10, clinical need: should be rated “moderately positive” because, if the theoretical gains in health and safety and a suitable home delivery arrangement without inappropriate cost-shifting do eventuate, they would address an identified clinical need by improving the overall management of a subgroup of patients requiring immunoglobulin therapy.