

Infliximab for the Treatment of Extensive Plaque Psoriasis – Regulation, Cost and Reimbursement

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The case reported by Amital et al. in this issue of *IMAJ* [1], in addition to its impressive results, raises one of the most difficult dilemmas of modern medicine – the economic possibilities of modern society lagging behind the technological potential, an issue aggravated by the Regulator and Courts.

Funding new health technologies in Israel

The National Health Insurance Law, enacted in 1995, determined a basic mandatory National List of Health Services to be provided by public funding to all Israeli residents. From year to year the social and professional demands to add new and expensive technologies (drugs, medical devices, treatments, procedures) are increasing, notwithstanding the limited resources (<10%) allocated by the Ministry of Finance to cover the addition of new health technologies to the NLHS. This year, only 20 million shekels (approximately \$4,400,000) were allocated for this purpose, covering about 1% of the cost of new requested and important technologies. Each year, a committee – appointed by the Minister of Health and comprising representatives of government departments, the healthcare organizations and the public – decides which technologies are to be added to the NLHS within the limits of the allocated budget. These recommendations are based on a thorough assessment and prioritization of each technology, taking into consideration clinical, economic, social, ethical and legal aspects according to predefined criteria [2]. Although the Israeli NLHS is one of the most comprehensive and progressive “health baskets” in the world, each year too many important new technologies are not included, hence the HCOs are not obliged to supply them to patients.

According to the National Health Insurance Law all Israeli citizens are entitled to the same health services as defined in the NLHS. The provision of a medical technology not included in the NLHS in special conditions is complicated by the courts. According to the National Health Insurance Law (1994, sec. 21a) and the Patient Rights Law (1996, sec. 4), any discrimination among patients in services provided by a healthcare organization is prohibited. Therefore, if an HCO approves the funding of a health technology not included in the NLHS for one patient, even as an act of compassion, it must provide funding for the same technology to all its members suffering from a similar condition.

The claim of discrimination is the basis of many lawsuits by patients against their HCOs, with patients claiming that either they suffer from a unique condition of their ailment that merits special consideration and funding of a technology not included in the NLHS, or that they deserve the provision of the technology because other patients with a similar condition have received funding for same technology from the HCO. For example, in the case of *Brume vs. MHCS (Maccabi Healthcare Services) & The State of Israel* (2001), the claimants asked the court to rule that MHCS would fund paclitaxel (Taxol[®], Bristol-Myers Squibb), an antitumor drug that was neither registered in Israel nor included in the NLHS for the required indication. Their claim was based on the fact that another patient with the same ailment had received the drug from MHCS, therefore refusal to fund the same drug for the claimants would be an act of discrimination. MHCS admitted that it had funded the drug for another patient with the same condition, however it was by mistake, and the policy of MHCS is not to fund the drug in any case for this indication. Moreover, other patients who had asked for this drug had also been refused. The court upheld MHCS's view and ruled that since MHCS had admitted that there was a mistake in funding the drug for one patient and since the declared policy of MHCS is not to fund the drug for this indication, it would not have to fund it for the claimants.

In order not to face the consequence of providing a new and expensive health technology that is not included in the NLHS (or for indications not included in the NLHS) to a large number of patients and thus spending considerable funds for which the HCO is not reimbursed by the government, it has to act by either a policy that states: “no health technology which is not included in the NLHS will be funded by the HCO, without any exceptions,” or alternatively funding these technologies to unique patients in whom an exception to the rules of approved therapy can be made due to their specific condition, without any act of discrimination. In MHCS, a special committee – comprising an expert physician, a clinical pharmacologist and the chief pharmacist – has the authority to approve the provision of a drug (or one of its indications) not included in the NLHS for clinically unique patients. A clear distinction can usually be made between these unique patients and other individuals suffering from the same disease.

NLHS = National List of Health Services

HCO = healthcare organization

MHCS = Maccabi Healthcare Services

In addition to these ways of tackling the issue, an HCO may adopt a policy of funding an essential technology not included in the NLHS to all the patients who need it. This policy has been adopted by MHCS to offer patients state-of-the-art new lifesaving technologies before they are included in the NLHS. Prior to the introduction of such a new technology, a thorough Health Technology Assessment is performed, in which safety, effectiveness, costs and cost-effectiveness data are presented to MHCS management, enabling it to prioritize one technology over another and often limiting it to patients who are not only candidates for benefiting from the technology but whose quality of life merits such an incremental expenditure. To this end a special "Technology Forum" carries out the assessment based on expertise of the scientific and medical leaders in the field.

Infliximab for the treatment of extensive plaque psoriasis

The case of infliximab for extensive plaque psoriasis highlights the presented procedure and dilemma. The desire to provide all patients with most advanced health technologies having the potential to improve their quality of life is hindered by the limited resources of the national healthcare system. Hence the need to prioritize technologies and introduce only the most essential ones, leaving many effective technologies out of reach.

Infliximab (Remicade[®], Schering Plough) – a chimeric monoclonal antibody with high specificity, affinity and avidity for tumor necrosis factor-alpha (the pro-inflammatory signaling molecule) – is currently approved in the United States, Europe and Israel as third-line therapy for rheumatoid arthritis and Crohn's disease. The drug is also included in the Israeli NLHS for these conditions and, therefore, its cost is reimbursed by the government for these indications.

Recently, infliximab was proven effective in additional conditions such as ankylosing spondylitis, psoriatic arthritis and severe refractory psoriasis [2–6]. As these indications have not yet been registered in Israel they cannot be considered for inclusion in the NLHS and, by implication, funding by the government. Consequently, should an HCO consider the introduction of infliximab for these unregistered indications, it will have to find a special budget to cover its cost.

MHCS has made a seminal decision to provide such funding as third-line treatment for ankylosing spondylitis and psoriatic arthritis. The projected annual number of these patients in Israel who might benefit from this treatment is 90 and 130, respectively. The annual cost of treating these patients with infliximab is estimated as 14.5–29 million shekels. A similar cost analysis conducted by the Department of Health Technology Policy at MHCS estimated the net annual cost of treating one psoriasis patient with infliximab to be between 66,000 (3 mg/kg, 65 kg, 8.5 doses per year on average) and 132,000 shekels (5 mg/kg, 65 kg, 8.5 doses per year on average). Dermatologists predict the annual number of patients in Israel who may benefit the most from such a treatment to be around 20, limiting the eligibility to patients with plaque psoriasis that is refractory to all other treatments and who have been hospitalized at least twice during the last year. However, since the disease is prevalent, it would be

very difficult to limit its use to these 20 particular patients only, hence a more realistic estimate is 100–500 patients per year, whose cost of treatment would rise to 13.2–66 million shekels annually. This treatment may lead to short and long-term indirect savings such as reduction in hospital admissions for severe exacerbations of disease, fewer physician visits, less use of other technologies (e.g., psoralen plus ultraviolet) and drugs. Another indirect saving to society is less absenteeism. On the other hand, there are additional indirect costs associated with this treatment, such as carrying out a purified protein derivative test and chest X-rays for every candidate patient before treatment (since treatment with infliximab may exacerbate tuberculosis), as well as the treatment of adverse effects. No studies have been reported to date of the cost-effectiveness of treating severe refractory psoriasis with infliximab.

In summary, although treatment with infliximab for severe refractory psoriasis may be very effective in improving the quality of life, our estimate of 100–500 patients who will need it every year will create a direct additional annual cost of 13.2–66 million shekels to the Israeli public healthcare system. Although it would be prudent to approve the funding of infliximab for a few very severe cases of plaque psoriasis, an attempt to typify these patients may be considered illegal discrimination as defined by law. The limited resources and the availability of other innovative technologies that may be more cost-effective lead us to conclude that currently it is impossible to fund infliximab for plaque psoriasis without undermining the budgetary balance.

The complex issue detailed here will become even more acute as new and effective, albeit very expensive technologies continue to emerge, posing more challenges to healthcare policymakers.

References

1. Amital A., Ingber A, Rubinow A. Infliximab-induced remission of extensive plaque psoriasis. *IMAJ* 2003;5:827–8.
2. Shani S, Siebzehner MI, Luxenburg O, et al. Setting priorities for the adoption of health technologies on a national level – the Israeli experience. *Health Policy* 2000;54:169–85.
3. Sieper J, Braun J. New treatment options in ankylosing spondylitis: a role for anti TNF alpha therapy. *Ann Rheum Dis* 2001;60:58–61.
4. Brandt J, Haibel H, Cornely D, et al. Successful treatment of active AS with the anti tumor necrosis factor alpha monoclonal antibody Infliximab. *Arthritis Rheum* 2000;43:1346–52.
5. Van Der Bosch F, Kruijthof E, Baeten D, et al. Effect of a loading dose regimen of 3 infusions of chimeric monoclonal antibody to tumor necrosis factor alpha (Infliximab) in spondyloarthritis: an open pilot study. *Ann Rheum Dis* 2000;59:428–33.
6. Antoni C, Dechant C, Hanns-Martin Lorenz PD, et al. Open-label study of Infliximab treatment for psoriatic arthritis: clinical and magnetic resonance imaging measurements of reduction of inflammation. *Arthritis Rheum* 2002;47:506–12.
7. Chaudhari U., Romano P., Mulcahy LD, et al. Efficacy and safety of Infliximab monotherapy for plaque-type psoriasis: a randomized trial. *Lancet* 2001;357:1842–7.

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