

To Secretariat PBAC

I wish to respond to your Draft terms of References with respect to market surveillance of the drug Ezetimibe.

I am a non-interventionist cardiologist with many years of practice mainly in diagnosis and secondary prevention with expertise in lipid metabolism and therapy. I have provided advice to Heart Foundation policy in these matters, written the appropriate chapters in Abnormal Lipid Results and Australian and international medical journals. I have served on relevant national and international committees.

### **Term of Reference 1.**

I am fully sympathetic with the rising costs of PBS listed drugs and fully support listing based on firm evidence. I recognise that the changing approach to optimal lipid lowering therapy which is based on the best evidence has led to LDL targets such as are difficult to achieve in the highest risk individuals.

I have prescribed Ezetrol for many years but only in high risk patients whose LDL-C posed further risk if not lowered adequately. The 2 obvious groups were/are: a. Patients truly intolerant to statins, or tolerant to very low but suboptimal dosage and b. patients at the highest risk such as those with familial hypercholesterolaemia. The addition of Ezetrol to a statin has been gratifyingly successful in the majority of patients. In those totally intolerant to statins the use of Ezetrol has at least ameliorated the risk.

Although for many years there have been no conclusive outcome data on ezetimibe alone, the IMPROVE –IT trial has clearly indicated that the drug by lowering LDL-C to levels not previously achieved did also lead to fewer future CHD events.

In this regard I have found the recent availability of co-packs containing either atorvastatin or rosuvastatin with ezetimibe particularly helpful in ensuring greater compliance by patients due in my opinion to the cost saving to the patient.

Undoubtedly IMPROVE-IT will increase utilisation but that is inevitable with best practice that leads to reduced direct and indirect costs.

### **Term of Reference 2**

I would find it disturbing if the current criteria and guidelines for preventing adverse cardiovascular outcomes through lipid lowering therapy were compromised by linking pre-IMPROVE-IT usage of ezetimibe with post-IMPROVE-IT usage. It is inevitable that usage will increase since doctors generally do comply with guidelines that are based on robust evidence. Most current guidelines recommend “intensive” lipid lowering for very high risk patients.

There have been 2 additional trials which depend in part on surrogate endpoints, although these surrogates have been strongly associated with adverse outcomes. The first showed that elevated CRP levels were lowered significantly together with LDL-C in IMPROVE-IT which further explained the benefit of ezetimibe/simvastatin intervention (EA Bohula et al Circulation 2015;132:1224). Elevated CRP has been shown in other trials such as JUPITER to increase adverse CHD outcomes.

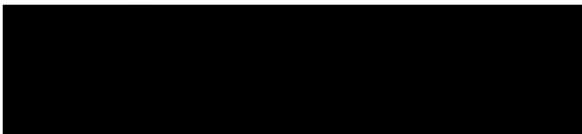
The second study has demonstrated greater coronary plaque regression (an elusive achievement with statins alone) when ezetimibe was co prescribed with atorvastatin (see Editorial in Journal American College of Cardiology 2015;68:508-510).

### **Term of Reference 3**

It would be unfortunate to consider changes to PBS that would compromise best practice guidelines that include intensive or maximal LDL-C lowering with statin or when required with statin/ezetimibe. Full assessment would be advisable of current opinion held by highly experienced cardiologists and lipid specialists. Current utilisation of Ezetrol is almost certainly biased to the pre-IMPROVE-IT era and should not be used to prejudice any valid increased usage based on the most recent information. The co-pack and more recent single tablet availability of statin cum ezetimibe should be viewed favourably in that compliance by patients and costs to patients are simultaneously greatly improved. My patients are accordingly delighted with its availability. The effect on LDL-C lowering is truly synergistic.

I submit my response fully aware of the need for PBS listing to reflect best medical practice and to take into account cost-benefit considerations. On the latter point I am not a health economist but the literature is replete with the high benefit:cost ratio of adequate LDL-C lowering in high risk patients.

Yours sincerely



Professor Paul Nestel AO MD FRACP FCANZ FTSE  
Professor of Medicine  
Consultant Physician, Heart Centre, Alfred Hospital, Melbourne  
Senior Scientist, Baker IDI Heart & Diabetes Institute, Melbourne.

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