**ENCLOSURE 5 APPENDIX 1**

**Paper presented to AWMSG in June 2006**
**AWPAG considered comments recorded in AWMSG minutes in July 2006**
**Paper subsequently updated and brought back to AWMSG for endorsement**

This paper sets out proposed national prescribing indicators to monitor Local Health Board prescribing patterns across Wales for 2007/8 The methods and principles used to determine the indicators and targets are also set out.

**Summary:**

The All Wales Medicine Strategy Group (AWMSG) is asked to support implementation of the following prescribing indicators.

| **Indicator** | **Unit** | **Target** |
|---|---|---|
| Generic prescribing | Percentage | 78% |
| Inappropriate generic prescribing | Percentage | Maintain performance levels within the lower quartile or show a reduction towards the quartile below |
| Hypnotics and Anxiolytics | DDD per 1,000 patients | Maintain performance levels within the lower quartile or show a reduction towards the quartile below |
| Statins | Simvastatin as a percentage of all statin prescribing | Maintain performance levels within the upper quartile or show an increase towards the quartile above |
| NSAIDs | DDD per 1,000PUs | Maintain performance levels within the lower quartile or show a reduction towards the quartile below |

**Background:**

At the October 2003 meeting of AWMSG it was agreed that prescribing indicators were useful tools to promote rational prescribing. It was also noted there was unease with indicators that had an over-emphasis on cost rather than quality.

Prior to the establishment of AWMSG, prescribing advisers produced the basket of indicators that were used to monitor prescribing patterns across Local Health Groups. AWMSG tasked the All Wales Prescribing Advisory Group (AWPAG) with developing national indicators for 2007/08. A sub-group was set up to develop this issue consisting of the following AWPAG members:

Mrs Nicola John
(National Public Health Service Wales & AWPAG Chair)
Mrs Delyth Simons (lead)
(Head of Pharmacy & Medicines Management Pembrokeshire LHB)
Dr Mark Daniels
(General Practitioner Neath Port Talbot)
Mrs Judith Vincent
(Head of Pharmacy & Medicines Management Swansea LHB) (unable to attend working group meeting on 13/04/06)
Mr Rob Davies
(Pharmacist (North Wales))
Mr William Duffield (unable to attend working group meeting on 13/04/06)

**Method**

The Working Group was informed of the prescribing indicators set for 2006/07 and used these as a starting point to develop indicators and targets for 2007/8. Additional factors taken into account also included consideration of the evidence base and current prescribing patterns across Wales.

A number of principles were agreed to clarify the aims in developing an indicator:

- Indicators should be evidence based
- Indicators should be clear, easily understood and applicable at practice level
- Targets should be challenging but achievable, and based on the principle of encouraging all LHBs to achieve the prescribing rates of the best quartile
- Targets should be set based on prescribing data for the quarter ending March 2008

The following indicators are proposed as the next step in developing indicators, which are clear, easily understood and have achievable targets. In addition, the indicators should, wherever possible, continue to be an integral part of an educational programme that targets the relevant professionals to reinforce the likelihood of achieving a favourable outcome.

To bring about the necessary change several of the proposed indicators will require sustained input over a number of years. This should not deter endeavours to deliver change and achieve measurable progress year on year.

AWPAG have agreed the indicators, and have expanded the paper to include:

- further evidence for the new statin indicator
- undertaking further work to update the basket of drugs included in the inappropriate generics category

Work is ongoing to explore methods of including only those drugs which should be prescribed generically in the generic basket, with a view to possibly setting a different target for 2008/2009. This work will be progressed over the coming months, but does not affect the decision making and the recommendations to Welsh Assembly Government for the set of 2007/2008 indicators.

**Generic prescribing**

*Purpose*: appropriate generic prescribing can make considerable savings with no difference in therapeutic outcome.

*Unit of measure:* Percent items generic medicines prescribed

*Target for 2007/2008:* Percent items generic medicines prescribed moving towards 78% or achieving 78 %.

**Inappropriate generic prescribing**

There are certain drugs where generic prescribing is not appropriate, and the following drugs should be prescribed by brand name:

| | |
|---|---|
| ***Aminophylline*** | ***Modified release preparations only*** |
| ***Ciclosporin*** | |
| ***Diltiazem*** | ***Modified release preparations only*** |
| ***Lithium*** | |
| ***Mesalazine*** | |
| ***Nifedipine*** | ***Modified release preparations only*** |
| ***Theophylline*** | ***Modified release preparations only*** |

*Unit of measure:* Percent items prescribed by generic name

*Target for 2007/08:*

- Maintain performance levels within the lower quartile or
- Reduction towards the quartile below

**Hypnotics and anxiolytics**

*Purpose*: There are disproportionately more hypnotics and anxiolytics prescribed in Wales compared to England than in any other drug category.

*Unit of measure:* Defined daily dose of hypnotics (4.1.1.) and anxiolytics (4.1.2) prescribed per 1000 patients.

*Target for 2007/08:*

- Maintain performance levels within the lower quartile or
- Reduction towards the quartile below

It is recognised that prescribing of hypnotics and anxiolytics is appropriate in some circumstances, and that for some geographical areas this is a more challenging agenda than others. Good practice needs to be promoted and a reduction in the prescribing of hypnotics and anxiolytics targeted.

**Statins**

The National Institute for Healthcare and Clinical Excellence (NICE) technology appraisal -Statins for the Prevention of Cardiovascular Disease states[1]:

- Statin therapy is recommended for adults with clinical evidence of cardiovascular disease (CVD).

- Statin therapy is recommended as part of the management strategy for the primary prevention of CVD for adults who have a 20% or greater 10-year risk of developing CVD. This level of CVD risk should be estimated using an appropriate risk calculator, or by clinical assessment for people for whom an appropriate risk calculator is not available (for example, older people, people with diabetes or people in high-risk ethnic groups).

NICE state that statin therapy should usually be initiated with a drug with a low acquisition cost (taking into account required daily dose and product price per dose).

The NICE meta-analysis of all placebo-controlled trials (primary and secondary prevention studies) that published data in a usable form indicated that therapy with a statin was associated with a statistically significant reduction in risk of all-cause mortality, cardiovascular mortality, coronary heart disease (CHD) mortality and fatal myocardial infarction (MI).

Similarly a recent meta-analysis by Zhou and colleagues looking at the evidence for pravastatin, simvastatin and atorvastatin showed there was no difference among the statins in reducing fatal CHD, non-fatal MI, fatal and non-fatal strokes, all CVD, or mortality due to any cause.[2] All the studies showed a similar reduction in lipid levels.

Simvastatin 20–40mg daily has been shown in large, well conduction clinical trials (4S and HPS) [3, 4] to reduce clinically relevant events such as heart attacks and strokes.

Atorvastatin 10mg daily also has clinical outcome data showing evidence of benefit (ASCOT-LLA and CARDS).[5,10] However, it is over four times the cost of generic simvastatin 40mg daily.

Pravastatin has also recently become available as a generic product. Pravastatin does have clinical outcome data from the PROSPER study.[6] However, in the ALLHAT–LLT study, no significant benefits of pravastatin were seen.[7] It is pragmatic to use pravastatin 40mg daily in simvastatin or atorvastatin intolerant patients where benefits and risks have been assessed.

At this time no studies of rosuvastatin that reported clinical events (patient orientated outcomes) as outcomes have been published. Only evidence for rosuvastatin is with surrogate markers (disease orientated outcomes).

**NICE plan to review and produce a guideline on lipid modification (December 2007). At NICE have not looked at the issue of whether a set dose of statin (e.g simvastatin 40mg at night, atorvastatin 10mg daily or pravastatin 40mg at night) should be used, as has been used in the trials, or whether to titrate up statin doses according to response in order to meet target cholesterol levels, which guidelines tend to support.**

The following table shows the absolute and percentage reductions in LDL-cholesterol concentration according to the statin and the daily dose used.[8]

| | 5mg | 10mg | 20mg | 40mg | 80mg |
|---|---|---|---|---|---|
| **Atorvastatin** | | **1.79 (1.62 to 1.97) 37%** | 2.07 (1.90 to 2.25) 43% | 2.36 (2.12 to 2.59) 49% | 2.64 (2.31 to 2.96) 55% |
| **Fluvastatin** | | | 1.02 (0.90 to 1.13) 21% | 1.30 (1.19 to 1.41) 27% | 1.58 (1.40 to 1.76) 33% |
| **Pravastatin** | | 0.95 (0.83 to 1.07) 20% | 1.17 (1.10 to 1.23) 24% | 1.38 (1.31 to 1.46) 29% | |
| **Rosuvastatin** | 1.84 (1.74 to 1.94) 38% | 2.08 (1.98 to 2.18) 43% | 2.32 (2.20 to 2.44) 48% | 2.56 (2.42 to 2.70) 53% | |
| **Simvastatin** | | 1.31 (1.22 to 1.40) 27% | 1.54 (1.46 to 1.63) 32% | **1.78 (1.66 to 1.90) 37%** | 2.01 (1.83 to 2.19) 42% |

From this table it can be seen simvastatin 40mg at night reduces LDL-cholesterol to the same extent as atorvastatin 10mg daily.

Simvastatin 20mg at night costs £2.34 for 28 days treatment, simvastatin 40mg at night costs £4.23 for 28 days treatment, atorvastatin 10mg daily costs £18.03 for 28 days treatment.[9] The NHS can treat 4 patients with simvastatin 40mg at night for less than treating 1 patient with atorvastatin 10mg daily.

Based on clinical trial evidence and cost, generic simvastatin 40mg (target dose) daily is a reasonable first-line statin choice fulfilling NICE criteria. If cholesterol target not reached using simvastatin 40mg daily then initiate atorvastatin 20mg daily.


1. National Institute for Health and Clinical Excellence. Statins for the prevention of cardiovascular events. Technology appraisal 94. January 2006
2. Zhou Z, Rahme E, Pilote L. Are statins created equal? Evidence from randomised trials of pravastatin, simvastatin and atorvastatin for cardiovascular disease prevention. Am Heart J 2006;151:273-81
3. Scandinavian Simvastatin Survival Study Group. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994;344:1383-9.
4. Heart Protection Study Collaborative Group. MRC/BHF Heart Protection Study of cholesterol lowering with simvastatin in 20,536 high risk individuals: a randomised placebo-controlled trial. Lancet 2002;360:7-22
5. Sever PS, Dahlöf B, Poulter NR, et al. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial — Lipid Lowering Arm (ASCOT-LLA): a multicentre randomized controlled trial. Lancet 2003;361:1149-58.
6. Shepherd J, Blauw GJ, Murphy MB, et al. Pravastatin in elderly individuals at risk of vascular disease (PROSPER): a randomized controlled trial. Lancet 2002;360:1623-30.
7. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major outcomes in moderately hypercholesterolemic, hypertensive patients randomized to pravastatin vs usual care. JAMA 2002;288:2998-3007.
8. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. BMJ 2003;326: 1423-9.

9. TSO Drug Tariff May 2006 accessed on 15/05/06 http://www.ppa.org.uk/ppa/edt_intro.htm
10. Colhoun HM, Betteridge DJ, Durrington PN et al Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial.Lancet.2004 364(9435):685-96

**Non-steroidal anti-inflammatory drug prescribing (NSAIDs)**

*Purpose:* There is overwhelming evidence to reduce prescribing of anti-inflammatory drugs especially in the elderly. The Committee on Safety of Medicines (CSM), now the Medicines and Healthcare products Regulatory Agency (MHRA), have issued five warnings to prescribers regarding the dangers of NSAIDs, culminating in the following warning issued in 2003:

*Reminder: Gastrointestinal toxicity of NSAIDs*

All NSAIDs, including ibuprofen and COX-2 inhibitors are associated with reports of serious gastrointestinal toxicity. The elderly and those taking concomitant aspirin are high-risk groups.

Detailed advice on the gastrointestinal safety of NSAIDs (including aspirin and selective COX-2 inhibitors) has previously been provided. The CSM continues to receive reports of serious and fatal gastrointestinal reactions associated with NSAIDs.

Prescribers are reminded:

- GI risks of NSAIDs may be minimised by selecting the lowest dose for the shortest duration.
- Risks of GI toxicity are higher in the elderly.
- Aspirin and another NSAID should only be used together when absolutely necessary - the combination substantially increases GI risk. Patients taking long-term aspirin should be reminded to avoid NSAIDs, including those bought without prescription.
- Ibuprofen is associated with the lowest GI risk of the traditional NSAIDs, but serious and fatal GI reactions have been reported in association with its use.
- Clinical trial data suggest that selective COX-2 inhibitors have GI safety advantages over standard NSAIDs, but serious and fatal GI reactions have none the less been associated with these drugs.

Ensure NSAID treatment is not contraindicated before prescribing.

(MHRA/CSM (2003) Gastrointestinal toxicity of NSAIDs. Current Problems in Pharmacogivilance. **29:** 8-9)

*Unit of measure:* Defined daily dose per 1000 PU's

*Target for 2007/08:*

- Maintain performance levels within the lower quartile or
- Reduction towards the quartile below