British Pharmacological Society response to MHRA consultation of availability of diclofenac as a pharmacy medicine

BPS (British Pharmacological Society) supports option 3 –

(14.3) ***amend the current conditions for supply of diclofenac as a P medicine so that preparations for oral use can no longer be supplied without prescription.*** *This would result in diclofenac tablets currently authorised as P medicines being required to be reclassified from P to POM (Prescription Only). Topical formulations could continue to be available without prescription.*

On the basis that:

- Diclofenac is associated with an increased cardiovascular risk in comparison to other commonly used NSAIDS [1]. There are safer therapeutic options (e.g. ibuprofen) within NSAIDs and diclofenac does not offer a unique benefit compared to these treatments
- Evidence indicates that the cardiovascular risk with diclofenac is similar to that of COX-2 inhibitors, as a result of which the MHRA has issued warnings that diclofenac is contraindicated in patients with ischaemic heart disease [2]
- Diclofenac has been shown to have a cardiovascular effect within the first week of use in patients with prior myocardial infarction and was associated with a hazard ratio of 3.26 [3]. This also points to the possibility of early risk of cardiovascular toxicity in individuals with an as-yet unknown cardiovascular risk.
- The new advice from EMA recommends diclofenac is only used after a careful risk assessment. It is unlikely that all pharmacists will be able to conduct a cardiovascular risk assessment in all individuals in all circumstances before they dispense diclofenac as a P medicine. The evidence of this risk is clearest with high doses but the risk cannot be excluded in relation to lower doses of diclofenac. Thus there may be a potential for harm, even if steps are taken to minimise the risks associated with over-the-counter (OTC) diclofenac.
- There may be a subset of patients who find diclofenac useful and are willing to consent to any potential increased cardiovascular risk. However this decision should be reached after consultation with, and prescribing by, healthcare professionals.
- There is drive to reduce the amount of prescribed oral diclofenac for reasons of safety, as outlined above. The continued availability of diclofenac as a P medicine sends a mixed message about its safety and therefore could impact negatively upon the success of this drive for more appropriate use.

In summary:

- A drug can be reclassified from POM to P if Ministers are satisfied that it would be 'safe to allow it to be supplied without a prescription' so it is a medicine which **no longer** meets a range of criteria including that it 'is likely to present a direct or

indirect danger to human health, even when used correctly, if used without the supervision of a doctor'

- BPS considers that it is likely to present a danger to human health because:
    - Even if concerns are raised via the implementation of Option 2 this may only take patients with established cardiovascular disease into account. Patients with undiagnosed but increased cardiovascular risk would likely be identified by using a risk-assessment tool that all GPs now routinely use which includes serum cholesterol levels, age, Body Mass Index, gender and smoking. The patient and pharmacist may not be aware of this risk and therefore the patient could inadvertently be put at risk. This would present a direct danger to human health.
    - It should not always been assumed that the medicine is being taken as intended (either in dosage or duration of treatment). Either taking higher doses or taking diclofenac for longer periods than advised could further increase the cardiovascular risk.

About BPS

BPS is the primary UK learned society concerned with research into drugs and the way they work. Our members work in academia, industry, and the health services, and many are medically qualified. The Society covers the whole spectrum of pharmacology, including laboratory, clinical, toxicological and regulatory aspects.

Clinical pharmacology is the medical speciality dedicated to promoting safe and effective use of medicines for patient benefit. Clinical pharmacologists work as consultants in the NHS and many hold prominent positions in UK Universities.

References

[1] McGettigan P, Henry D. Cardiovascular risk with non-steroidal anti-inflammatory drugs: systematic review of population-based controlled observational studies. PLoS Med 2011;8(9): e1001098. doi:10.1371/journal.pmed.1001098

[2] Drug Safety Update 2013;6(11)
http://www.mhra.gov.uk/Safetyinformation/DrugSafetyUpdate/CON286975

[3] Schjerning Olsen A et al. Time-dependent Cox proportional hazard analysis of risk of death according to duration of nonsteroidal antiinflammatory drug (NSAID) treatment in patients with prior myocardial infarction. Circulation 2011;123:2226-2235.