To: All interested organisations

5 August 2013

Our reference: **MLX 382**

CONSULTATION ON AVAILABILITY OF DICLOFENAC AS A PHARMACY MEDICINE

Introduction

1. We are writing to consult you on the continued availability of diclofenac as a Pharmacy (P) medicine and in particular on risk minimisation measures advised by the Commission on Human Medicines.

Application to England, Wales, Scotland and Northern Ireland

2. This consultation is being made available in England, Wales, Scotland and Northern Ireland. The proposed changes would apply throughout the United Kingdom.

Background

3. As a result of an EU-wide review of the cardiovascular (CV) risks of the non-steroidal analgesic diclofenac, the European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recently recommended new contraindications, warnings and precautions to all marketing authorisation for diclofenac.

http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/06/news_detail_001816.jsp&mid=WC0b01ac058004d5c1

http://www.mhra.gov.uk/NewsCentre/Pressreleases/CON286868

4. Diclofenac is a non-selective non-steroidal anti-inflammatory (NSAID) available in a variety of indications, forms, dosages and pack size quantities for relieving pain and inflammation. It is available as injections; tablets and capsules for oral use; and as gels and creams for topical use. A summary of UK products containing diclofenac appears in **Appendix 1.**

5. Studies have consistently shown that when given systemically (by means such as capsules, tablets or injections) there is an increased risk with diclofenac of cardiovascular side effects, such as heart attack or stroke compared to other similar painkillers, such as ibuprofen and naproxen. The risks are similar to those of selective COX -2 inhibitors, another group of painkillers.

6. The evidence of additional risk is clear when diclofenac is used at a high dose (150mg) daily and for long term treatment. The findings could not rule out the possibility that this

increased risk could be associated with the low doses and short lengths of treatment of non-prescription products.

7. The new advice is that people who have serious underlying heart or circulatory conditions, such as heart failure, heart disease, circulatory problems or a previous heart attack or stroke, should not use diclofenac. Patients with certain cardiovascular risk factors (such as high blood pressure, raised blood cholesterol, diabetes or smoking) should only use diclofenac after careful risk assessment. Healthcare professionals have also been advised to periodically re-assess the need for patients to continue taking the medicine. The product information recommends that NSAIDs be used at the lowest effective dose for the shortest period of time necessary to control pain symptoms.

8. The new advice does not apply to topical (ie, gel or cream) formulations of diclofenac.

Availability of diclofenac without prescription

9. Diclofenac is available in the UK without prescription in tablet form as a P medicine, supplied from pharmacies by or under the supervision of a pharmacist, under the following circumstances:

Indication: For the short term relief of headache, dental pain, period pain, rheumatic and muscular pain, backache and the symptoms of colds and flu, including fever, in adults and children aged 14 years and over.
Maximum strength: 25mg
Maximum dose: 25mg
Maximum daily dose: 75mg
Maximum duration of treatment: 3 days
Maximum pack size: 225mg of product (9 x 25mg tablets)

Recommendations of the Commission on Human Medicines (CHM)

11. In June 2013 the CHM considered the implications of the PRAC recommendations for the current circumstances for non-prescription classification in the UK of medicinal products containing diclofenac in oral dosage forms.

12. The CHM noted that it was difficult to identify people with high cardiovascular risk although the risk would be higher with age. The CHM also considered that the wide availability of other NSAIDs without prescription – as P and GSL medicines – presented a risk that the products could be used together and that indications for OTC diclofenac were wide ranging, and included colds, flu and fever.

13. The CHM advised that a number of measures should be taken to strengthen the risk minimisation of oral diclofenac as a P medicine, including:

- Removing from the indications, ‘the symptoms of colds and flu, including fever’,
- Strengthening the warnings on the pack about use by those with cardiovascular disease or with significant risk factors for cardiovascular events

- Strengthening warnings on the pack and about not taking diclofenac with other NSAIDs.
- Engaging with the pharmacy profession to support the implementation of further measures to minimise the risk of OTC diclofenac
- Requesting that the Marketing Authorisation Holders prepare a Risk Management Plan to strengthen the risk minimisation of oral diclofenac as a P medicine.

Options for risk minimisation

14. The MHRA wishes to take into account all stakeholders views when reaching a final position on regulatory action, and therefore seeks views on the following options for risk minimisation.

Option 1
14.1 No new risk minimisation measures

Option 2
14.2 Implement all the measures identified by CHM:

- Remove from the indications, 'the symptoms of colds and flu, including fever',
- Strengthen the warnings on the pack about use by those with cardiovascular disease or with significant risk factors for cardiovascular events
- Strengthen warnings on the pack and about not taking diclofenac with other NSAIDs.
- Engage with the pharmacy profession to support the implementation of further measures to minimise the risk of OTC diclofenac
- Request that the Marketing Authorisation holders prepare a Risk Management Plan to strengthen the risk minimisation of oral diclofenac as a P medicine.

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 would continue to be available without prescription.

Summary of comments sought

15. We would welcome views on the merits of the proposals and options outlined in the paragraphs above and to receive any further views that responders would wish to make. We particularly wish to receive the views of:

- Marketing Authorisation holders for medicinal products containing diclofenac
- Medicines users and patient organisations, particularly those with experience of self management of pain
- Health professionals and professional organisations

Impact assessment

16. We think that the proposals contained in this consultation document will have little substantive adverse impact on industry or on patients. Overall, we consider that the proposal has no new significant effect on the sector and will not impose any additional costs or have any effect on issues of equality.

17. Similarly, the proposal does not impose any additional regulatory or financial burdens on the public sector but we would welcome views on whether an impact assessment would be useful and if so, any data to support the preparation of one.

18. We do not believe that the proposal in this consultation will have any adverse effect on any equality issue. We would welcome information on any instances where you believe that there will - or could be - any adverse affect on equality issues under any of the following:

Competition Assessment
Small Firms Impact Test
Legal Aid
Sustainable Development
Carbon Assessment
Other Environment
Health Impact Assessment
Race Equality
Disability Equality
Gender Equality
Human Rights
Rural Proofing

How to respond

19. We would be grateful if any comments in response to this letter could be emailed to: reclassification@mhra.gsi.gov.uk alternatively they may be addressed to: Colette McCreedy, Self Medication Specialist and Unit Manager, Medicines and Healthcare products Regulatory Agency, 3rd Floor, 151 Buckingham Palace Road, London SW1W 9SZ. Comments must arrive no later than **28 October 2013.** Comments received after this date will not be taken into account.

Circulation of proposals

20. This consultation letter is being brought to the attention of those organisations listed at Annex A. Copies of the consultation are also available from our website - www.mhra.gov.uk and replies are welcome from all interested parties.

21. This consultation abides by consultation criteria set out in the revised Code of Practice on Consultation published by the Department for Business Innovation & Skills and viewable in full via

http://www.berr.gov.uk/whatwedo/bre/consultation-guidance/page44420.html

Responses: Confidentiality and Disclaimer

22. The information you send us may be passed to colleagues within the Government or related agencies. Furthermore, information provided in response to this consultation, including personal information, may be published or disclosed in accordance with the access to information regimes. These are primarily the Freedom of Information Act 2000 (FOIA), the Data Protection Act 1998 (DPA) and the Environmental Information Regulations 2004.

23. If you want the information that you provide to be treated as confidential, please be aware that, under the FOIA, there is a statutory Code of Practice with which public authorities must comply and which deals, amongst other things, with obligations of confidence. In view of this it would be helpful if you could explain why you regard the information you have provided as confidential. If we receive a request for disclosure of the information we will take full account of your explanation, but we cannot give an assurance that confidentiality can be maintained in all circumstances. An automatic confidentiality disclaimer generated by your IT system will not, of itself, be regarded as binding on us.

24. Please ensure that your response is marked clearly, if you wish your response (whole or in part) and name to be kept confidential. Confidential responses will be included in any statistical summary of numbers of comments received and summary of views expressed.

25. The Agency's Information Centre at 151 Buckingham Palace Road will supply copies on request. An administrative charge, to cover the cost of photocopying and postage, may be applied. Alternatively, personal callers can inspect replies at the Information Centre by prior appointment (telephone 0203080 6351).

Colette McCreedy
MHRA VRMM

APPENDIX 1

Diclofenac Products authorised as Pharmacy only (P) in the UK

Boots Joint Pain Relief 12.5mg Film-Coated Tablets
Double Action Pain Relief 12.5mg Tablets (Actavis)
Voltarol Pain-eze Tablets
Voltarol Joint Pain 12.5mg Tablets
Voltarol Pain-eze extra strength 25mg tablets

To: Colette McCreedy
Self Medication Specialist and Unit Lead,
Medicines and Healthcare products Regulatory Agency,
3rd Floor,
151 Buckingham Palace Road, London SW1W 9SZ.

From: _____

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* 1. I support Option 1

* 2. I support Option 2

* 3. I support Option 3

* 4. I have no comment to make on the proposals in the MLX

*5. My comments on the proposals in the MLX are below/attached.

** My reply may be made freely available.*
** My reply is confidential.*
** My reply is partially confidential (indicate clearly in the text any confidential elements)*

Signed: _____

** Delete as appropriate*

APPENDIX 2

MLX 382

N:B THE ATTENTION OF AT LEAST THE FOLLOWING HAS BEEN DRAWN TO THIS CONSULTATION. HOWEVER, THIS LISTIS NOT EXHAUSTIVE AND REPLIES ARE WELCOME FROM ALL INTERESTED PARTIES

ABPI
ACTAVIS
ARTHRITIS CARE
ASSOC OF ANAESTHETISTS OF GB AND IRELAND
ASTHMA & ALLERGY RESEARCH
ASSOC OF INDEPENDENT MULTIPLE PHARMACIES
BOOTS
BRIT ASSOC OF PHARMACEUTICAL WHOLESALERS
BRITISH DIABETIC ASSOCIATION
BRITISH HEART FOUNDATION
BRITISH PAIN SOCIETY
BRITISH RETAIL CONSORTIUM
BRITISH SOCIETY OF GASTROENTEROLOGY
CHEMIST AND DRUGGIST
COMMUNITY PHARMACY MAGAZINE
COMPANY CHEMIST ASSOCIATION LTD
CONSUMERS ASSOCIATION
DEPARTMENT OF AGRICULTURE
DISPENSING DOCTORS ASSOCIATION
DOCTOR MAGAZINE
GENERAL MEDICAL COUNCIL
GENERAL PRACTITIONERS COMMITTEE
HEALTH SERVICE COMMISSIONER
IMPERIAL CANCER RESEARCH FUND
MEDICAL PROTECTION SOCIETY LTD
MEDICAL WOMENS FEDERATION
NATIONAL AIDS TRUST
NATIONAL ASSOCIATION OF GP CO-OPERATIVES
NATIONAL FARMERS UNION ENGLAND & WALES
NATIONAL FEDERATION OF RETAIL NEWSAGENTS
NATIONAL PHARMACY ASSOCIATION
NEUROLOGICAL ALLIANCE
NOVARTIS CONSUMER HEALTH
OPTHALMIC GROUP COMMITTEE
OTC BULLETIN
PHARMACEUTICAL SERVICES NEGOTIATING COMMITTEE
BRITISH INTERNATIONAL DOCTORS ASSOC
PATIENTS ASSOCIATION
ROYAL COLLEGE OF GENERAL PRACTITIONERS
ROYAL COLLEGE OF NURSING

ROYAL COLLEGE OF NURSING (N IRELAND)
ROYAL COLLEGE OF PATHOLOGISTS
ROYAL COLLEGE OF PHYSICIANS & SURGEONS
ROYAL COLLEGE OF PHYSICIANS (LONDON)
ROYAL COLLEGE OF PSYCHIATRISTS
ROYAL COLLEGE OF RADIOLOGISTS
ROYAL COLLEGE OF SURGEONS (EDINBURGH)
SCOTTISH GENERAL PRACTITIONERS COMMITTEE
SCOTTISH WHOLESALE DRUGGISTS ASSOCIATION
TERRANCE HIGGINS TRUST
VETERINARY MEDICINES DIRECTORATE (VMD)
ROYAL COLLEGE OF SURGEONS
CENTRAL MEDICAL ADVISORY COMMITTEE
COMMITTEE FOR PRACTITIONERS &
GENERAL PRACTITIONERS ASSOCIATION (NI)
BRIT ASSOC OF EUROPEAN PHARM DISTRIBUTOR
BRITISH GENERIC MANUFACTURERS ASSOC
NURSING & MIDWIFERY COUNCIL
BRIT CARDIAC PATIENTS ASSOCIATION
BRITISH MEDICAL ASSOCIATION
ASSOCIATION OF PHARMACEUTICAL IMPORTERS
DRUG INFORMATION PHARMACISTS GROUP
NORTHERN IRELAND CONSUMER COUNCIL
DHSSPS
BMA (WALES)
THE BRITISH SOCIETY FOR ALLERGY
BRITISH ASSOCIATION OF EUROPEAN PHARMACEUTICAL DISTRIBUTORS
BRITISH GERIATRIC SOCIETY
UK INTERPROFESSIONAL GROUP
ASSOCIATION OF BRITISH CARDIAC NURSES
HEALTH WHICH
UK HOMOEOPATHIC MEDICAL ASSOCIATION
SURGICAL DRESSINGS MANUFACTURERS ASSN
INTERNATIONAL RESEARCH CONSULTANTS
NATIONAL BACK PAIN ASSOCIATION