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4 July 2013

IMMEDIATE – DICLOFENAC NEW CONTRAINDICATIONS AND WARNINGS AFTER A EUROPE-WIDE REVIEW OF CARDIOVASCULAR SAFETY

Please see the attached letters regarding advice from Dr Sarah Branch, Deputy Director, MHRA which provides important new information about the non-selective non-steroidal anti-inflammatory drug diclofenac.

1. Please could Medical Directors in NHS Boards forward the message to :-

- All general practitioners – please ensure this message is seen by all practice nurses and non-principals working in your practice and retain a copy in your locum information pack.
- Deputising Services
- Accident & Emergency Departments
- All relevant hospital doctors
- Directors of Nursing
- Relevant healthcare professionals

2. Please could Directors of Public Health forward the message to :-

- Chief Executives NHS Boards

3. Please could Directors of Pharmacy forward the message to :-

- Community Pharmacists
- Hospital Pharmacists
- Medicines Information Pharmacists

Thank you for your co-operation.

Yours sincerely

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July 4, 2013

Diclofenac: new contraindications and warnings after a Europe-wide review of cardiovascular safety

Dear healthcare professional

I am writing to inform you about important new information for the non-selective non-steroidal anti-inflammatory drug (NSAID) diclofenac.

Summary

Available data indicate that the cardiovascular risk with diclofenac is similar to that of the selective COX-2 inhibitors. Consistent with COX-2 inhibitors, diclofenac is now contraindicated in those with: ischaemic heart disease; peripheral arterial disease; cerebrovascular disease; or established congestive heart failure (New York Heart Association [NYHA] classification II–IV).

Background

An increased risk of heart attack and stroke with some non-selective non-steroidal anti-inflammatory drugs (NSAIDs)—such as diclofenac—is well recognised, particularly with long-term use of high doses and in patients who are already at high risk. Warnings for healthcare professionals and patients have been included in the product information and in the British National Formulary for some years.

The European Medicines Agency's Pharmacovigilance Risk Assessment Committee (PRAC) has recently recommended updates to the treatment advice for diclofenac in light of the findings of a Europe-wide review of the cardiovascular safety of NSAIDs (see http://www.ema.europa.eu/ema/index.jsp?curl=pages/news_and_events/news/2013/06/news_detail_001816.jsp&mid=WC0b01ac058004d5c1). The review found further evidence that the arterial thrombotic risk with diclofenac is similar to that for the selective COX-2 inhibitors.

A recently published meta-analysis[1] of clinical trial data provides further evidence that the arterial thrombotic risk with diclofenac is similar to that of COX-2 inhibitors. This analysis found that of 1000 patients allocated to diclofenac for a year, three more had major vascular events, compared with placebo.

The new treatment advice applies to systemic formulations (ie, tablets, capsules, suppositories, and injection available both on prescription and via a pharmacy, P); it does not apply to topical (ie, gel or cream) formulations of diclofenac.

1. Coxib and traditional NSAID Trialists' (CNT) Collaboration. *Lancet* published online May 20, 2013: http://dx.doi.org/10.1016/S0140-6736(13)60900-9

Advice for healthcare professionals:
New advice for diclofenac

- Diclofenac is now contraindicated in patients with established:
  - ischaemic heart disease
  - peripheral arterial disease
  - cerebrovascular disease
  - congestive heart failure (New York Heart Association [NYHA] classification II–IV)

  Patients with these conditions should be switched to an alternative treatment at their next routine appointment

- Diclofenac treatment should only be initiated after careful consideration for patients with significant risk factors for cardiovascular events (eg, hypertension, hyperlipidaemia, diabetes mellitus, smoking)

Reminder of existing advice for all NSAIDs

- The decision to prescribe an NSAID should be based on an assessment of a patient's individual risk factors, including any history of cardiovascular and gastrointestinal illness (see http://cks.nice.org.uk/nsaids-prescribing-issues#!scenariorecommendation)

- Naproxen and low-dose ibuprofen are considered to have the most favourable thrombotic cardiovascular safety profiles of all non-selective NSAIDs

- The lowest effective dose should be used for the shortest duration necessary to control symptoms. A patient's need for symptomatic relief and response to treatment should be re-evaluated periodically

Additional advice for pharmacists:
Non-prescription availability of diclofenac

Diclofenac is available to buy in a pharmacy without a prescription at low doses (up to 75 mg/day) for short-term use (3 days). Pharmacists are asked to take the following steps when supplying diclofenac without prescription:

- Ask questions to exclude supply for use by people with established cardiovascular disease and people with significant risk factors for cardiovascular events

- Advise patients to take diclofenac only for 3 days before seeking medical advice

- Advise patients to take only one NSAID at a time

This letter is accompanied by an information sheet for patients who may be affected by this new information, which you may like to use to help in your consultation with them.

Yours sincerely

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Diclofenac: information for patients

Summary and key messages

- Diclofenac is one of a group of important medicines (anti-inflammatory medicines) used to treat arthritis, and other conditions that cause pain and inflammation.
- As with any medicine, diclofenac may cause side effects in some people. Most side effects are mild, but very rarely they can be serious.
- Research has shown that the risk of some heart and blood vessel problems may be higher with diclofenac (when taken by mouth) than with some alternative anti-inflammatories
- You should speak to your GP or pharmacist at your next routine appointment or visit if you are taking diclofenac (tables, capsules, or suppositories) and you have a condition such as heart failure, other heart disease (eg, angina), circulatory problems causing leg pain, or if you have had a heart attack or stroke. Your doctor or pharmacist will recommend an alternative treatment. Tell your doctor or pharmacist if you are taking any heart medicines, or have had any heart or circulatory problems in the past.
- You should always use the lowest dose of anti-inflammatory medicine that controls your symptoms, and stop taking the medicine if it is no longer needed. Do not take more than one type of anti-inflammatory medicine at the same time (for example, do not take ibuprofen and diclofenac at the same time). The risks are much lower with anti-inflammatory creams or gels.

Further information

What is diclofenac?

Diclofenac is a type of non-steroidal anti-inflammatory drug (or 'NSAID'). Anti-inflammatory drugs are widely used important medicines in the treatment of arthritis and other conditions that cause pain and inflammation. Diclofenac, along with ibuprofen and naproxen, is among the most widely used anti-inflammatory medicines in the UK. There are various other anti-inflammatory medicines available—among them, newer, types called 'coxibs' (there are two: celecoxib and etoricoxib).

The main brand of diclofenac is Voltarol but it is also available as generic medicines or medicines for joint pain relief.

What is the known safety profile of anti-inflammatory drugs?

As with all medicines, anti-inflammatory drugs such as diclofenac may cause side effects (adverse reactions) in some people. A full list of known side effects can be found in the patient information leaflet accompanying your medicine. Minor stomach or intestinal symptoms (such as pain, nausea, vomiting or diarrhoea) are among the most common problems; rarely (in less 1/1000 people) these effects can be more serious.

In recent years, research has shown that anti-inflammatory medicines may cause rare but potentially serious side effects on the heart and circulatory system. In particular, they may slightly increase the risk of heart attack or stroke. Your doctor or pharmacist will take these risks into account when advising on the right treatment for you. The newer coxib anti-inflammatories generally have a lower risk of stomach and intestinal side effects, but a higher risk of heart and circulatory side effects compared to the older NSAID anti-inflammatories.

What is the new information and advice on using diclofenac?

The latest evidence continues to show that the benefits of diclofenac outweigh the risks; however, its heart and blood vessel risk appears to be similar to those for coxibs. As a result, your doctor and pharmacist will no longer recommend diclofenac for you, if you are at particular risk of some of these problems.

What should I do if I'm taking diclofenac?

- You should speak to your GP or pharmacist at your next routine appointment or visit if you have a condition such as heart failure, other heart disease (eg, angina), circulatory problems causing leg pain, or if you have had a heart attack or stroke. Your doctor or pharmacist will recommend an alternative treatment. Diclofenac may no longer be suitable for you if you have significant risk factors for cardiovascular disease (such as high blood pressure, diabetes, or smoking) and so your doctor or pharmacist may consider an alternative treatment

- For many patients, diclofenac will continue to provide safe and effective pain relief and so your treatment may not need to change. However, the lowest effective dose of diclofenac should be used for the shortest duration necessary to control any symptoms. Therefore, your healthcare provider may periodically assess your pain relief and response to treatment and so it is important that you attend any scheduled routine appointments

- Speak to your healthcare provider (doctor, nurse or pharmacist) if you have any concerns about the new information about diclofenac

- You can continue to take diclofenac cream or gel as before, as the risks are much lower for diclofenac when it rubbed into the skin