SAFETY ALERT

DRAP SAFTEY ALERT NO. 17

SUSPENSION OF DRUG REGISTRATIONS OF DICLOFENAC POTASSIUM 75MG AND 100MG

UPDATE FROM REGISTRATION BOARD, PAKISTAN.

Date: 15th of June 2022.

Target Audience:

- Provincial Drugs Control Units and Provincial Pharmacovigilance Centres.
- Manufacturers and Importers of Diclofenac Potassium 75mg and 100mg;
- Healthcare Professionals; and
- Patients, consumers or caregivers.

Problem or Issue:

The Registration Board of Drug Regulatory Authority of Pakistan (DRAP) in its 317th meeting held on 16-17th of May 2022 in light of discussions, risk-benefit analysis and public health impact, suspend all drug registrations of Diclofenac Potassium 75mg and 100mg under Section 7 (11) (d) read with Section 42 of the Drugs Act, 1976 due to the reason that these formulations are neither approved by any Reference Regulatory Authority nor any safety and efficacy data regarding these products is available with any registration holder. These formulations will stay suspended for a period of one (01) year; or if safety and efficacy is well established through indigenous clinical trials in accordance with the Bio Study Rules, 2017; or if it is approved by the Reference Regulatory Authorities, whichever is earlier. Likewise, Registration holders were directed to suspend the manufacturing and import of these drug products immediately and to withdraw available stocks from the market in the larger public interest. The decision applies to all registration holders of Diclofenac Potassium 75mg and 100mg except those who have obtained interim relief from the Hon'ble Lahore High Court, Lahore.

Background:

The Registration Board in its 258th meeting held on 25th and 26th April, 2016 had decided that Diclofenac Potassium is not registered in any reference country in doses more than 50mg, thus decided to issue show-cause notices to manufacturers of Diclofenac Potassium (75 and 100mg) for de-registration of these products. Subsequently, the registration board in its 288th meeting, dated 14-15th Feb 2019, decided that all registration holders of Diclofenac Potassium 75mg & 100mg shall be called for personal hearings. However, DRAP's Authority in its 70th meeting held

on 05th Sep 2019 decided that **"***For formulations containing "drugs" which were previously registered by the Registration Board and have proof of availability and prescription of last 10 years but are not available in the Reference Regulatory Authorities shall continue to be considered/ registered as drugs until and unless withdrawn on Safety, Efficacy and Quality reasons*".

Accordingly, Registration Board in its 296th meeting held on 8-10th Sep, 2020 decided that *"Since, all such formulations which are not approved by the Reference Regulatory Authorities; the safety and efficacy profile cannot be established in the absence of a well-established system for reporting of adverse events, so a reference shall be forwarded to DRAP's Authority with the request to review the decision taken in its 70th meeting held on 05-09-2019. In this regard, PE&R Division shall prepare a comprehensive document/agenda for consideration of Authority, keeping in view the practices adopted by RRA for all such formulations."*

Meanwhile, the policy of reliance on reference regulatory authorities was approved by the Authority in its 73rd meeting held on 06-11-2019. Subsequently, the registration board in its 313th meetings, dated 16-18th Nov, 2021 decided to issue show causes to registration holders/ manufacturers under Section 7 (11)(d) of the Drug Act, 1976 and opportunity of personal hearings. The decision of the Registration Board was endorsed by Authority in its 128th meeting of Authority held on 14th Dec 2021 and decided that "*Drug formulations/strengths which were previously registered by the Registration Board but are not available in any Reference Regulatory Authorities, shall be reviewed and disposed-off keeping in view of safety and efficacy evidence/data in the Reference Regulatory Authorities*."

Many of registration holders of Diclofenac Potassium 75mg and 100mg challenged the Show Cause Notices issued for cancellation of their drugs stating violation of the decision taken in 70th Meeting of the DRAP Authority held on the 05-09-2019. However, the decision taken in the 70th Meeting of the DRAP Authority has been reviewed in the 128th Meeting held on 14-12-2021, whereby the Registration Board was allowed to review and dispose of the registration of drugs keeping in view their safety and efficacy. The Registration Board in its 315th meeting held on 1st Feb 2022 noted the information and advised to provide the opportunity of a personal hearing in the next meeting of the Registration Board.

Meanwhile, the Pharmaceutical Evaluation and Registration Division of the DRAP reviewed all the available facts and finding along with the product monograph of diclofenac potassium in stringent regulatory authorities which depicts that the daily dose of diclofenac potassium is from 75- to 200mg in divided doses, whereas the maximum strength of available diclofenac potassium tablet is 50mg. The Division also prepared two questions that were communicated for guidance to various RRA's including USFDA, Health Canada, MHRA UK, Sweden, TGA Australia and BNF.

Lastly, the registration board in its meeting 317th meeting dated 16th to 17th May, 2022 after giving personal hearings to registration holders of diclofenac potassium 75-100mg, discussion during the meeting, risk-benefit analysis and public health impact of the Diclofenac Potassium 75mg and 100mg, decided to suspend drug registrations of Diclofenac Potassium 75mg and 100mg under Section 7 (11) (d) read with Section 42 of the Drugs Act, 1976 in the larger public interest for 1 year or earlier subject to some conditions.

Therapeutic Goods Affected.

Name: **Diclofenac Potassium 75MG and 100MG (Not 50mg or below)**

Diclofenac potassium is used in divided doses for treatment of pain or primary dysmenorrhea; relief of osteoarthritis, relief of rheumatoid arthritis etc. It is approved by various reference regulatory authorities in 12.5mg, 25mg and 50mg tablet strengths. A daily dose of diclofenac potassium is from 75-200mg in divided doses, whereas the maximum strength of available diclofenac potassium tablet is 50mg. However, in Pakistan, as per the PER Division, it was also approved in the strength of 75 and 100mg.

Advice for patients.

Patients and consumers are informed that the Registration Board of Drug Regulatory Authority of Pakistan (DRAP) in its 317th meeting held on 16-17th of May 2022 in light of discussions, risk-benefit analysis and public health impact suspended all drug registrations of Diclofenac Potassium 75mg and 100mg, therefore, those patients who are using diclofenac potassium in the aforementioned strengths may consult/ speak with their healthcare professionals to shift/change their treatment to standard strength of 50mg of diclofenac potassium or other treatment options available in the market.

Advice for healthcare professionals.

Healthcare professionals are informed that the Registration Board of Drug Regulatory Authority of Pakistan (DRAP) in its 317th meeting held on 16-17th of May 2022 in light of discussions, risk-benefit analysis and public health impact suspended all drug registrations of Diclofenac Potassium 75mg and 100mg under Section 7 (11) (d) read with Section 42 of the Drugs Act, 1976 due to the reason that these formulations are neither approved by any Reference Regulatory Authority nor any safety and efficacy data regarding these products is available. Healthcare professionals may stop prescribing diclofenac potassium having a strength of 75mg and 100mg to patients. Diclofenac Potassium in the strength of 50mg may be prescribed to the patient instead of Diclofenac Potassium of 75mg and 100mg.

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Guidelines for reporting Adverse Drug Reactions (ADRs):

Both healthcare professionals and patients are requested to report any adverse events they have experienced with Diclofenac Potassium (75mg, 100mg or even 50mg & below) to **the National Pharmacovigilance Centre,** Drug Regulatory Authority of Pakistan through **DRAP Med Vigilance E-reporting system** or at npc@dra.gov.pk

Similarly, adverse events can also be reported through **Med Safety Mobile Application** that is available for download from the App store (For iOS devices) and Google Play (For Android devices).

References:

1. Partial Minutes of 317th Meeting of Registration Board.