**No.31015/28/2023-Pricing (E-23315)**
GOVERNMENT OF INDIA
MINISTRY OF CHEMICALS & FERTILIZERS
DEPARTMENT OF PHARMACEUTICALS
.....

Room No. 340-B, A Wing, Shastri Bhawan,
New Delhi-110 001.

## Order

M/s Macleods Pharmaceuticals Limited (hereinafter called the "Applicant") filed a Review Application dated 02.02.2023 under Para 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) against price fixation order issued vide S.O. No. 87(E) and 89(E) dated 06.01.2023 by the National Pharmaceutical Pricing Authority (NPPA). Vide its aforesaid Order, NPPA, inter alia, fixed the ceiling price of the formulations as following:

| Notification number and date | Brand Name | Composition |
|---|---|---|
| S.O. 5938(E) dated 19/12/2022 (corrigendum S.O. 89(E) 06.01.2023) | Mefomin 500MG Tablet SR 10's | Metformin 500MG (Sustained release) |
| S.O. 87(E) dated 06/01/2023 | XMBETA 25MG Tablet 10's | Metoprolol 25MG (Extended release) |
| S.O. 87(E) dated 06/01/2023 | METOMAC 25 Tablet 10's | Metoprolol 25MG (Extended release) |
| S.O. 87(E) dated 06/01/2023 | XMBETA 50MG Tablet 10's | Metoprolol 50MG (Extended release) |
| S.O. 87(E) dated 06/01/2023 | METOMAC 50 Tablet 10's | Metoprolol 50MG (Extended release) |

2. On the aforesaid plaint, reference was invited by the Department of Pharmaceuticals from NPPA. Both the parties entered appearance on 01.06.2023 and presented their respective logics.

### 3. Major contentions raised by the Applicant:

It was contended, on behalf of the Applicant, that NPPA has erred in determining the ceiling price of the above drug and hence may be directed to revise the same on the following grounds:

3.1 The formulation "Mefomin 500mg tablet SR 10's", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" are not included in Schedule-I listed out in the final list of scheduled formulations with effect from 11th November, 2022, and hence, the formulations "Mefomin 500mg tablet SR 10's", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" and "Xmbeta 50mg tablet 10's" and "Metomac 50 Tablet 10's" must not be included in the calculation of ceiling price for any other scheduled formulation. Therefore, NPPA has erred by including modified release formulations "Mefomin 500mg tablet SR", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" in its calculation of ceiling price for conventional "Metformin 500mg", "Metoprolol 25mg" and "Metoprolol 50mg" tablets respectively.

3.2 Sr. No. 18.3.1.6 of Schedule-I of DPCO, 2013 includes "Metformin" and specifically the strengths of 500mg, 1000mg conventional release tablets and 1000mg modified release tablets. It is pertinent to note that modified release 500mg tablets are not explicitly included in the Schedule-I of DPCO, 2013 and hence, any formulation containing Metformin 500mg in a modified release must be construed as a non-scheduled formulation. Sr. No. 10.1.4 of Schedule-I of DPCO, 2013 includes "Metoprolol" and specifically the strengths of 25mg, 50mg, 100mg conventional release tablets and 100mg modified release tablets. It is pertinent to note that modified release 25mg and 50mg tablets are not explicitly included in the Schedule-I of DPCO, 2013 and hence, any formulation containing Metoprolol 25mg or 50mg in a modified release must be construed as a non- scheduled formulation.

3.3 Explanation Note 6 to the Schedule-I of DPCO, 2013 as amended on 11th November, 2022 clearly states as under:

> *"Innovation in medicine must be encouraged. The formulations developed through incremental innovation or novel drug delivery systems like lipid/liposomal formulations etc. should be considered as included only if specified in the list against any medicine. Such different formulations should be considered differently for purposes such as procurement policy, pricing, etc"*

Thus, even if the formulations, "Mefomin 500mg tablet SR 10's" containing "Metformin 500mg Sustained Release", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" containing "Metoprolol 25mg Extended Release" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" containing "Metoprolol 50mg Extended Release" were deemed to be included in the Schedule-I of DPCO, 2013, it must have been given a separate ceiling price.

3.4 It need to be appreciated by virtue of notification S.O. 5249 (E) dated 11th November 2022, formulations "Mefomin 500mg tablet SR" containing "Metformin 500mg Sustained Release", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" containing "Metoprolol 25mg Extended Release" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" containing "Metoprolol 50mg Extended Release" are classified as a non- scheduled formulation. The ceiling price calculation of Metformin

500mg, Metoprolol 25mg and Metoprolol 50mg tablets must only include conventional tablets and not modified release formulations containing the same strength.

3.5 The subject formulations "Mefomin 500mg tablet SR" containing "Metformin 500mg Sustained Release", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" containing "Metoprolol 25mg Extended Release" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" containing "Metoprolol 50mg Extended Release" were not characterised or qualified as being a scheduled formulation on 11th November 2022. By no stretch of imagination, the price calculation of a conventional tablet should include the prices of modified release formulations in direct violation of Explanation Note 6 to Schedule-I of DPCO, 2013.

3.6 The Applicant referred to the Report on amendment of NLEM 2022 wherein the SNCM committee has stated under the heading "Use of the term 'Modified Release' with respect to tablets/capsules" that

> *"Modified release dosage forms are drug delivery systems (DDS) that, by virtue of their formulation and product design, provide drug release in a modified form which is different from that of the conventional/ immediate release dosage forms. The oral modified release (MR) dosage forms are developed by altering the rate/kinetics and site of drug release and absorption to confer advantages like improved patient compliance, optimized efficacy and/or reduced adverse events. This may be achieved through specialized formulation design or innovative manufacturing methods. The various types of delivery technologies could be as extended, delayed, controlled, prolonged, multiphasic release system, etc.*
>
> The modified release dosage forms may sometimes offer advantages over conventional formulations such as improved patient compliance - by reducing the frequency of drug administration, reduction in the total cost of therapy as lesser number of pills may be required. The MR forms may also offer better bioavailability. Another advantage that modified release dosage forms may offer is to minimize the fluctuations in drug plasma concentrations and facilitating continuous levels above minimum effective concentrations. This may also avoid certain adverse drug reactions.
>
> In NLEM 2015, various modified release solid oral dosage forms were listed as sustained release, controlled release, delayed release, extended release, prolonged release, etc. However, the drug delivery systems are evolving rapidly, and the pharmaceutical industry is increasingly focusing on novel drug delivery systems. Many of these are often introduced with incremental innovation. To broadly reflect all such modified release dosage forms, in NLEM 2022, the term Modified Release has been used to represent controlled release, sustained release, prolonged release, extended release etc. with respect to tablets and capsules as the case may be..."

3.7 Thus, it is clear that the SNCM has also clarified that there is a significant difference between conventional tablets and modified release tablets. The incremental innovation of modified release tablets has also been specifically discussed and

acknowledged and hence, inclusion of conventional tablets in NLEM 2022 / Schedule-I of DPCO, 2013 does not imply inclusion of a modified release tablet.

3.8 The formulations "Mefomin 500mg tablet SR", "Xmbeta 25mg tablet 10's" & "Metomac 25 Tablet 10's" and "Xmbeta 50mg tablet 10's" & "Metomac 50 Tablet 10's" are a modified release formulation which are to be classified as non-scheduled formulation. Therefore, the calculation of conventional tablets of Metformin 500mg, Metoprolol 25mg and Metoprolol 50mg are incorrect and must be rectified.

## 4. Gist of clarifications made by NPPA:

NPPA on the other side argued that the instant review is not tenable on the following grounds:

4.1 The methodology approved and followed for the pricing of MR Variant/Conventional Variant by the Authority is as below:

> *"Wherever, MR variant is specifically mentioned in any formulation the data of only MR variants (CR, SR, XL, ER delayed release etc.) may be considered for fixation of ceiling price. However, where MR variant is not specifically mentioned, data of conventional as well as MR variants may be considered for ceiling price fixation. This is in line with methodology of NLEM 2015 also. Similarly, where DT/effervescent/soluble/MD, etc. is specifically mentioned in any formulation in any formulation the data of only such variants may be considered. However, in absence of any variant being specifically mentioned, the DT/ effervescent /soluble/MD may be considered along with conventional form"*

Further, the above methodology is same as was followed for fixation of ceiling prices under NLEM 2015. (Reference 105th Authority meeting).

4.2 The MR variants form an integral part of essential and lifesaving drugs and taking them out of price control is not the objective of SNCM. NLEM as well as Revised Schedule-I of DPCO, specifically mentions as below:

**"All modified release formulations of same strength such as sustained release, controlled release, extended release, prolonged release etc. are included."**

4.3 Further, this methodology followed in relation to conventional / modified releases is same as followed for fixation of ceiling prices under NLEM 2015. Examples are:

**Case 1: Formulation appearing in Schedule-I: Metformin 500mg**

Since, the variant i.e. Conventional / modified is not stated in Schedule-I, all variants were considered included in Schedule-I and the ceiling price was fixed considering all the variants. Further, the ceiling price was applicable to all variants.

**Case 2: Formulation appearing in Schedule-I: Metformin 1000mg and Metformin 1000mg MR**

Since, both variants i.e. conventional and MR are specifically stated in the schedule, separate prices were fixed for both i.e. conventional and non-conventional variant. If the petitioner's suggestion is considered, the prices of Modified releases will not be covered under Schedule-I in case where only conventional variants are mentioned and will make the MR variants of the formulation de-regulated.

4.4 Further, the market shares of Plain/conventional and MR for the subject formulation is as follows:

MAT (Rs. in Crore) July, 2022

| Formulation | Plain / Conventional | MR | Total |
|---|---|---|---|
| Metformin Tablet 500 mg | 96.48 | 153.41 | 249.89 |
| Metoprolol Tablet 25mg | 35.24 | 197.53 | 232.77 |
| Metoprolol Tablet 50mg | 39.76 | 234.77 | 274.53 |

It is seen from the table above that modified release tablets has substantial market share i.e. 61%, 85% and 86% approx. in case of Metformin 500mg, Metoprolol Tablet 25mg and Metoprolol Tablet 50mg, respectively (July 2022 database). If the same are not considered to be scheduled as contended by the company, majority of the market will become deregulated, which is not the intent of NLEM, 2022.

**5. Examination:**

5.1 The National List of Essential Medicines (NLEM) prepared by Standing National Committee on Medicines (SNCM) under Ministry of Health and Family Welfare (MoH&FW) forms the very basis of Schedule-I of the DPCO, 2013 which is amended, whenever the NLEM is revised. The latest NLEM (2022) was notified on 13.09.2022 and accordingly, Schedule-I to DPCO, 2013 was revised on 11.11.2022 vide Gazette Notification SO No. 5249 (E).

5.2 The NLEM is prepared with the objective of satisfying the priority health care needs of the population. The list is made based on disease prevalence, efficacy, safety and comparative cost-effectiveness of the medicines. The aim behind formulating NLEM is to ensure that these medicines are available in adequate quantity, in appropriate dosage forms and strengths with assured quality. NLEM does recognize such innovations in drugs where substantial improvements, effectiveness and efficacy have been introduced either in terms of quality or in the delivery system or both. Accordingly, NLEM mentions such innovative drugs separately under different categories commonly named as Modified Release (MR) versions in the same list where such criteria are fulfilled. When the same is not mentioned separately, then all such varieties of such drugs for the specified dosages are considered to be part of variants appearing in the list. The objective of NLEM, inter alia, is to ensure availability of the essential drugs as well. This objective may be adversely affected by the exclusion of different variants from the NLEM based on criteria such as MR etc., as such exclusion

may encourage essential drugs simply moving out of NLEM. This may not be in line with the spirit and purpose of including these drugs in the list of essential medicines in the first instance.

5.3 Therefore, in view of the facts as at paras 5.1 and 5.2 above, arguments and logics given by NPPA are accepted.

**6. Decision:**

The action of NPPA fixing the ceiling price of subject formulations is upheld and the Review Application under consideration is accordingly rejected.

Issued on this, the 10th day of October, 2024.

10/10/2024

**(Awadhesh Kumar Choudhary)**
Sr. Economic Adviser to the Government of India
[For and on behalf of the President of India]

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**Copy to:**

1. Chairperson, NPPA, New Delhi
2. PSO to Secretary (Pharma), Shastri Bhawan, New Delhi
3. Technical Director, NIC for uploading the order on DoP's Website.
4. Guard File