No.31015/10/2023-Pricing (E-23267)
GOVERNMENT OF INDIA
MINISTRY OF CHEMICALS & FERTILIZERS
DEPARTMENT OF PHARMACEUTICALS
.....

Room No. 207, D Wing, Shastri Bhawan,
New Delhi-110 001.

Order

M/s Abbott Healthcare Private Limited (hereinafter called the "Applicant") filed a Review Application dated 11.01.2023 under Para 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) against the price fixation order issued vide S.O. No. 5938 (E) dated 19.12.2022 by the National Pharmaceutical Pricing Authority (NPPA). Vide its aforesaid Order, NPPA, inter alia, fixed the retail price of Clarithromycin Extended Release / Modified Release 500 mg Tablet under para 31 of DPCO, 2013

2. On the aforesaid plaint, a reference was invited by the Department of Pharmaceuticals from NPPA. Both parties entered appearance on 05.04.2023 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 retail price of the above drug and hence may be directed to revise the retail price of their formulation on the following grounds:

3.1 Abbott Healthcare Pvt. Ltd. (AHPL) is engaged in the manufacturing and marketing of Celex OD 500 mg, 5's Tablets, which is a formulation of Clarithromycin 500 mg in Extended Release/Modified Release. The "Celex" trademark was earlier owned by GlaxoSmithKline Pharmaceuticals Limited, Dr. Annie Besant Road, Worli, Mumbai and was assigned to Abbott Laboratories, 100 Abbott Park, IL 60064 - 6400, USA on 24th April 2002. AHPL is an affiliate of Abbott Laboratories, USA. The Applicant contended that NPPA Issued a notification S.O. 5938 (E) dated 19th December 2022, fixing the ceiling price of conventional Clarithromycin 500 mg formulation. However, while fixing the ceiling price of conventional Clarithromycin 500 mg formulation NPPA has erroneously extended the same to include the price of the non-scheduled formulation "Celex OD 500 mg, 5's", which is a modified release formulation of Clarithromycin 500 mg.

3.2 The Applicant submitted that Clarithromycin 500 mg in Extended Release/Modified Release dosage form is not a part of the revised Schedule-I notified with effect from 11th November, 2022. Hence, the formulation "Celex OD 500 mg 5's" must not be included in the calculation of the ceiling price for any other scheduled formulation. Sr. No. 6.2.2.4 and 6.4.3 of the new Schedule I of DPCO 2013 includes "Clarithromycin" specifically in the strengths of 250mg, 500mg, and 750mg only in the dosage form of conventional tablets. It is pertinent to note that Modified Release 500 mg tablets have not been explicitly included in Schedule-I of DPCO 2013. Hence, any formulation containing Clarithromycin 500 mg tablets in a modified release dosage form must not be construed as a scheduled formulation. Therefore,

NPPA has patently erred by including the modified release formulation "Celex OD 500mg 5's" in its calculation of the ceiling price for conventional Clarithromycin 500 mg tablets.

3.3 Explanation Note 6 to 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, the formulation, "Celex OD 500mg 5's" containing "Clarithromycin 500 mg Extended Release/Modified Release" cannot be considered as part of the revised Schedule I of DPCO 2013. Therefore, the price of the same should not be included in the calculation of the ceiling price of the conventional Clarithromycin 500 mg formulation. Further. the ceiling price notified for conventional Clarithromycin 500 mg formulation cannot be extended to our formulation, "Celex OD 500mg 5's".

3.4 The Company referred to the Report of NLEM 2022, wherein the Standing National Committee of Medicines (SNCM) has clearly 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 offer advantages over conventional formulations including improved patient compliance- by reducing the frequency of drug administration, reducing the total cost of therapy by reducing the number of pills required etc. 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.

3.5 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..."

Thus, it is clear that the SNCM has also categorically recognized that there is a significant difference between conventional tablets and modified release tablets.

3.6 The incremental innovation of modified release tablets has also been specifically discussed and acknowledged in the SNCM Report and hence, inclusion of conventional tablets in NLEM 2022 / Schedule I of DPCO 2013 does not imply inclusion of a modified release tablet. The SNCM has specifically recommended under the heading of "NLEM and the need to encourage innovations" that:

The committee deliberated in detail, about the issue of inclusion of improved formulations of a medicine developed through radical/ incremental innovation involving technology. The committee considered that such formulations including novel drug delivery systems like lipid/liposomal formulations, modified release formulations of a medicine, which are developed to overcome certain disadvantages associated with the use of conventional formulations, will be considered included only if specified in the list against the medicine.

Therefore, it is amply clear that as per the Expert Committee, modified release formulations of a medicine will have to be considered as included only if it is specified in the list against the medicines, which is not the case here.

3.7 Additionally, there are several judicial precedents whereby the Delhi High Court has specifically held that modified release formulations are to be considered as being distinct from conventional formulations for the purpose of ceiling price fixation under DPCO 2013.

3.7.1 The Single Bench of the Delhi High Court in judgment dated July 17, 2018 in W.P. {C) 11802/2016 titled Modi-Mundi Pharma Pvt. Ltd. vs Union of India & Ors. held that a notification fixing ceiling price of conventional Tramadol Tablet cannot be extended to the formulation - TRD Cantin 100 mg. tablet CR 10 which is a controlled release/modified release formulation. The Court held that:

.....Thus, given the narrow definition of the term 'scheduled formulation', the only question to be examined is whether the medicine is specified in the Schedule-I to the DPCO 2013. And, as discussed above, the Explanation (2) to the Schedule-I to the DPCO-2013 expressly provides that formulation developed through incremental innovation or novel drug delivery system such as sustain release/control release would be considered included only if specified in the list against any medicine. Since it is not disputed that CR-Technology is an innovative drug delivery system, the Formulation cannot be considered as included as it is not specifically mentioned.

While an appeal filed against the aforesaid judgment is still pending, no stay has been granted in favour of UoI/NPPA in the matter and the judgment of the Single Bench dated July 17, 2018 is still operative.

3.7.2 Similarly, the Single Bench of the Delhi High Court in judgment dated September 17, 2018 in W.P. (C) 1257/2018 titled Intas Pharmaceuticals Limited & Anr. vs Union of India & Anr. set aside an overcharging order issued against Intas with regard to Ceftas 400 Tablets which is a modified release formulation of Cefixime for which ceiling price was fixed by NPPA. The Court held that NPPA's contention that all versions of the formulations irrespective of the drug delivery system or innovation are included in Schedule-I of the DPCO 2013 is erroneous.

While an appeal filed against the aforesaid judgment is still pending, no stay has been granted in favour of UoI/NPPA in the matter and the judgment of the Single Bench dated September 17, 2018 is still operative.

3.7.3 Further, the Delhi High Court vide its judgment dated March 20, 2019 in W.P. (C) 7589/2018 titled Sanofi India Ltd. & Anr. vs Union of India & Ors. distinguished conventional Metformin vis-a-vis Metformin sustained release formulations in the context of considering a particular formulation as a 'new drug' under DPCO 2013.

3.8 By virtue of notification 5.0. 5249 (E) dated 11th November 2022, formulation "Celex OD 500mg S's" containing "Clarithromycin 500 mg Extended Release" is not a scheduled formulation as "Clarithromycin 500 mg" in modified release format has not been included under the revised Schedule-I of DPCO 2013. The ceiling price calculation of Clarithromycin 500 mg tablets must only include conventional tablets and not modified release formulations in the same strength.

3.9 The subject formulation "Celex OD 500mg S's" containing "Clarithromycin 500 mg Extended Release" cannot be characterized or qualified as being a scheduled formulation in terms of the revised Schedule-I of DPCO 2013 notified on 11th November 2022. Therefore, by no stretch of imagination, the price calculation of a conventional tablet should include the prices of modified release formulations as the same is not in consonance with the explanation note 6 to Schedule-I of DPCO 2013.

3.10 The Applicant was aggrieved that despite the fact that the captioned formulation "Celex OD 500mg S's" is not a part of the revised Schedule-I of DPCO 2013, NPPA by error has included the same to calculate the ceiling price of conventional Clarithromycin 500 mg formulation and an attempt has been made to erroneously treat the same as scheduled formulation in contravention of contents of S.O. 5249(E) dated 11th November, 2022 as well as the SNCM Report on NLEM 2022.

3.11 The formulation "Celex OD 500mg, 5's", which is a modified release formulation of Clarithromycin 500 mg, is a non-scheduled formulation and not covered by the ceiling price so fixed for conventional Clarithromycin 500 mg tablet. Therefore, the calculation of conventional tablets of Clarithromycin 500 mg is incorrect and must be rectified by removing Celex OD 500 mg, 5's tablet and other Extended Release/Modified Release forms, from the draft working sheet.

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 on 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, 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 the same as was followed for the 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 the same as followed for the 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 variants. If the petitioner's suggestion is considered, the prices of Modified releases will not be covered under Schedule-I in cases where only Conventional variants are mentioned and will make the MR variants of the formulation de-regulated.

5. Examination:

5.1. The National List of Essential Medicines (NLEM) prepared by the Standing National Committee on Medicines (SNCM) under the Ministry of Health and Family Welfare (MoH&FW) forms the very basis of Schedule-I of the Drugs Prices Control Order (DPCO) 2013, which is amended, whenever the NLEM is revised. The latest NLEM (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, under the facts cited under the above paras of 5.1 and 5.2, the arguments and logics given by NPPA are acceptable.

6. Decision:

The action of NPPA fixing the ceiling prices of Clarithromycin Extended Release / Modified Release 500 mg vide S.O. No. 5938 (E) dated 19.12.2022 is upheld and the Review Application under consideration is accordingly rejected.

Issued on this, the 8th day of February, 2024.

(**Awadhesh Kumar Choudhary**)
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[For and on behalf of the President of India]

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Copy to:

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