

No. 31015/25/2016-PI.I
GOVERNMENT OF INDIA
MINISTRY OF CHEMICALS & FERTILIZERS
DEPARTMENT OF PHARMACEUTICALS

B Wing, Janpath Bhavan,
New Delhi 110 001

Subject: Review application of M/s FDC Limited against price fixation of “Carboxymethylcellulose - 0.5%” vide NPPA order No. S.O. 1561(E) dated 27.04.2016 issued under Drugs (Prices Control) Order, 2013 (DPCO 2013).

Ref: 1) Review application dated 06.05.2016
2) NPPA notification under review S.O. No.1561(E) dated 27.04.2016
3) Record Note of discussions held in the personal hearing held in the matter on 30.6.2016.

1. This is a petition under paragraph 31 of the Drugs (Prices Control) Order, 2013 (hereinafter called the DPCO) filed by M/s FDC Limited (hereinafter called the petitioner) against notification S.O. No.1561(E) dated 27.04.2016 issued by the National Pharmaceutical Pricing Authority (hereinafter called the NPPA) fixing the ceiling price of Carboxymethylcellulose – 0.5%.

2. The petitioner has contended as under:

- i. **PIXELUB UNIMS** presentation is a unit dose **preservative free** 0.4 ml Carboxymethylcellulose - 0.5%. **PIXELUB UNIMS** is not same as Carboxymethylcellulose - 0.5% listed under 25.7.1 of the DPCO Schedule 1/ NLEM 2015 because it is a unit dose of 0.4 ml and preservative free (unlike multi dose eye drops containing preservatives).
- ii. **Preservatives in Multi Dose cause adverse effect:** Dry eye disease is a chronic condition for which drug has to be administered in eyes for very long duration. The available multi dose preparations contain various preservatives which are known to cause cytotoxicity / corneal toxicity. Preservatives can disrupt the lipid layer of the tear film, and lead to worsening of dry eye disease. The inflammation induced by chronic use of preservatives can alter the function of conjunctival goblet cells and reduce the amount of mucin present of the ocular surface, which leads to changes in the composition of the tear film that can exacerbate chronic dry eye disease. These findings are published are well documented in numerous scientific journals.
- iii. **US Study-** side effects of preservatives: they attach from a scientific journal published in the US titled “Effects of Common Ophthalmic Preservatives on Ocular Health” by a leading medical Professional Dr. Robert Noecker duly highlighting his findings on adverse effects caused by preservatives used in dry eye medicine preparations.

- iv. **Indian Study** – side effects of preservatives: They also attach from another Indian scientific journal titled “Ocular Preservatives: associated risks and newer options” by five medical professionals from Punjab University duly highlighting their findings on adverse effect caused due to preservatives used in medicines used for dry eye.
- v. **Other Scientific Studies of side effects of Preservatives:** These and other scientific evidences establish beyond doubt that the preservatives cause corneal toxicity. Therefore, a dosage form such as PIXELUB UNIMS, which does not contain any preservative, has significantly higher safety/efficacy over multi dose eye drops.
- vi. **Recommendations of Core Committee on NLEM 2015:** The Core Committee of experts was constituted by the Ministry of Health & Family Welfare (MOHFW), Government of India under the chairmanship of Dr. VM Katoch, the then Secretary, Department of Health Research (DHR) to review the old NLEM 2011 and finalize the new NLEM 2015. This expert committee has recognized in its report that any dosage form of a medicine shall not be covered under DPCO price control.
- vii. **Ceiling Price for UNIMS fixed based on 37 Multi Dose preparations:** it is observed from the NPPA published worksheet used for computation of Carboxymethylcellulose-0.5% ceiling price that there are 37 medicinal preparations which are multi dose and each one of these contain any of the above preservatives. There is a lone unit dose preparation free of any preservative. It establishes that UNIMS or unit dose preservative free preparation is not common as its production is technologically intensive, requires huge capital investment, results in lower yield and higher production costs.
- viii. **DOP to advise NPPA to clarify non applicability to UNIMS:** In view of the Core committee recommendation to exclude medicines from price control, which has “**significant difference in terms of efficacy-safety profile over the dosage form mentioned in the NLEM list**”.

They requested this Department to advise the NPPA to clarify that Carboxymethylcellulose-0.5% in unit dose preparation of 0.4 ml is excluded from applicability of ceiling price against sr. no. 28 in the above notification S.O. 1561(E) dated 27/4/2016.

Comments of NPPA:

- (i) NPPA has fixed the ceiling price of Rs. 11.59 per ml for **Carboxymethylcellulose Eye Drop 0.5% per ml** vide S.O. 1561(E) dated 27.4.2016 under para 4, 10, 11, 14, 16, 17 & 18 of DPCO, 2013.
- (ii) Representation of company is under examination of NPPA.

3. In the personal hearing held on 30th June, 2016, the representative of the company submitted that -

- i. Dry eye disease is a chronic condition for which drug has to be administered in eyes for very long duration.
- ii. The available multi dose preparations contain various preservatives which are known to cause cytotoxicity / corneal toxicity. Preservatives can disrupt the lipid layer of the tear film, and lead to worsening of dry eye disease.
- iii. The inflammation induced by chronic use of preservatives can alter the function of conjunctival goblet cells and reduce the amount of mucin present on the ocular surface, which leads to changes in the composition of the tear film that can exacerbate chronic dry eye disease.
- iv. These findings are published and well documented in numerous scientific journals.
- v. In a scientific journal published in the US titled "Effects of Common Ophthalmic Preservatives on Ocular Health" by a leading medical professional Dr. Robert Noecker duly highlighted his findings on adverse effects caused by preservatives used in dry eye medicine preparations.
- vi. In a scientific journal published in the India titled "Ocular preservatives: associated risks and newer options" by five medical professionals from Punjab University duly highlighted their findings on adverse effect caused due to preservatives used in medicines used for dry eye.
- vii. These and other scientific evidences establish beyond doubt that the preservatives cause corneal toxicity.
- viii. Therefore, a dosage form such as PIXELUB UNIMS, which does not contain any preservative, has significantly higher safety / efficacy over multi dose eye drops.
- ix. The revised schedule I under DPCO 2013 is based on NLEM 2015 list of drugs finalized by the Core Committee of Experts under the Chairmanship of Dr. V.M. Katoch. The Core Committee has recommended that the medicines which have ***"significant difference in terms of efficacy-safety profile over the dosage form mentioned in the NLEM list"*** shall be excluded from price control under DPCO 2013. **Our preservative free product PIXELUB UNIMS is one such medicine and, therefore, should be excluded from DPCO price control.**

NPPA representative submitted that NPPA has fixed the ceiling price of Rs.11.59 per ml for **Carboxymethylcellulose Eye Drop 0.5% per ml** vide S.O. 1561(E) dated 27.4.2016 under para 4, 10, 11, 14, 16, 17 & 18 of DPCO, 2013, as per existing practice. The issue relating to price fixation of the subject formulation is under examination.

4. **Government Decision:**

In view of the above, the Government has decided that the matter may be referred by NPPA to Expert Committee constituted under para 11(4) of DPCO 2013 to examine on merit and recommend in the light of para 11(3) of DPCO, 2013, within a period of one month of the issue of this Order.

In view of the above, the present review petition stands disposed off.

Issued on this date, the 30th day of August, 2016.

(M.K. Bhardwaj)
Deputy Secretary
For and on behalf of the President of India

To

- 1. M/s. FDC Limited
142-48, S.V. Road,
Jogeshwari (W),
MUMBAI-400 102.**
- 2. The Member Secretary,
National Pharmaceutical Pricing Authority,
YMCA Cultural Centre Building, New Delhi-110001**

Copy to :

- 1. PS to Hon'ble Minister (C&F), Shastri Bhawan, New Delhi for information.**
- 2. PSO to Secretary (Pharma), Shastri Bhawan, New Delhi for information.**
- 3. T.D., NIC for uploading the order on Department's Website**