

* **IN THE HIGH COURT OF DELHI AT NEW DELHI**

Reserved on: 10.10.2019

Date of Decision : 05.11.2019

+ **W.P.(C) 10111/2018 & CM APPL. 39483/2018 & 39411/2019**
ALKEM LABORATORIES LTD. Petitioner
Through: Ms.Ishani Chandra & Ms.Shubhie
Wahi, Advs.

versus

UNION OF INDIA AND ANR. Respondents
Through: Mr.Kirtiman Singh, CGSC &
Mr.Ripu Daman Bhardwaj, CGSC
with Mr.Waize Ali Noor,
Mr.Rohan Anand, Mr.Prateek
Dhanda & Mr.T.P. Singh, Advs.

+ **W.P.(C) 10751/2018 & CM APPL. 41873/2018, 41874/2018 &
41875/2018**

M/S LEEFORD HEALTHCARE LTD. Petitioner
Through: Mr.Aditya P.Arora and Mr. Udit
Chauhan, Adv.

versus

UNION OF INDIA AND ANR. Respondents
Through: Mr.Kirtiman Singh, CGSC &
Mr.Ripu Daman Bhardwaj, CGSC
with Mr.Waize Ali Noor,
Mr.Rohan Anand, Mr.Prateek
Dhanda & Mr.T.P. Singh, Advs.

+ **W.P.(C) 11285/2018 & CM APPL. 43810/2018 & 43811/2018**
HORIZON BIOCEUTICALS PVT LTD Petitioner

Through: Mr.Prabhat Kr. Chaurasia, Adv.

versus

DRUGS CONTROLLER GENERAL OF INDIA & ANR

..... Respondents

Through: Mr.Kirtiman Singh, CGSC &
Mr.Ripu Daman Bhardwaj, CGSC

with Mr.Waize Ali Noor,
Mr.Rohan Anand, Mr.Prateek
Dhanda & Mr.T.P. Singh, Advs.

+ **W.P.(C) 11399/2018 & CM APPL. 44090/2018 & 44091/2018**
ZEE LABORATORIES LTD. Petitioner
Through: Mr.Siddhant Bambha, Adv.

versus

UNION OF INDIA AND ANR. Respondents
Through: Mr.Kirtiman Singh, CGSC &
Mr.Ripu Daman Bhardwaj, CGSC
with Mr.Waize Ali Noor,
Mr.Rohan Anand, Mr.Prateek
Dhanda & Mr.T.P. Singh, Advs.

CORAM:
HON'BLE MR. JUSTICE NAVIN CHAWLA

1. These petitions have been filed challenging the Notification bearing SO No. 4380 (E) dated 07.09.2018, issued by the respondent no.1, prohibiting the manufacture, sale and distribution for human use of drug Fixed Dose Combination (FDC) of Nimesulide + Diclofenac with immediate effect. The above Notification has been passed by the respondent no.1 exercising its power under Section 26A of the Drugs and Cosmetics Act, 1940 (hereinafter referred to as the 'Act').

2. Section 26A of the Act is reproduced hereinunder:-

“26A. Powers of Central Government to prohibit manufacture, etc., of drug and cosmetic in public interest.—
Without prejudice to any other provision contained in this Chapter, if the Central Government is satisfied, that the use of any drug or cosmetic is likely to involve any risk to human beings or animals or that any drug does not have the therapeutic value claimed or purported to be claimed for it or

contains ingredients and in such quantity for which there is no therapeutic justification and that in the public interest it is necessary or expedient so to do, then, that Government may, by Notification in the Official Gazette, [regulate, restrict or prohibit] the manufacture, sale or distribution of such drug or cosmetic.”

3. As the present petition has a history attached to it, it would be useful to first briefly indicate the same.

4. By the Notification No. 706 E dated 10.03.2016, the respondent no.1 had prohibited the manufacture and sale of the above drug in exercise of its power under Section 26A of the Act. The said order was passed based on a report of an Expert Committee known as Kokate Committee Report. The recommendation of the said Committee insofar as the above drug is concerned, is reproduced hereinbelow:-

<i>Final Recommendations of the Experts Committee during the meetings held w.e.f 4th to 9th January, 2016 with respect to applications of FDCs received by the O/O DCG (T) for proving safety and efficacy categorized under category “a”</i>					
<i>S.No of main list</i>	<i>Name of FDC</i>	<i>Strengt h</i>	<i>Dosage Form</i>	<i>Categorization of the FDC by the Experts Committee as per Terms of references</i>	<i>Final Recommendations by Committee</i>
Xxxx					
12	Nimesulide BP + Diclofenac Sodum IP	100mg +50 mg	Soft Gelatin Capsules	a, 1. Nimesulide in combination has potential of misuse and have documented safety concern. 2. No addition advantage but hepatotxi potential of nimesulide and adverse effects add up. 3. Pharmacodynamically irrational FDC as both have same mechanism of action	The replies/clarification wherever available from firms and earlier data submitted by them were thoroughly examined. The Committee observed that data submitted and available peer reviewed scientific evidences do not

				(both drugs acting on the same enzyme). Thus, combining two NSAIDs does not and cannot improve the efficacy of treatment. It only adds to the cost of therapy and more importantly, to the adverse effect. Chandler S. Gautam, Lekha Saha, Fixed dose drug combination (FDCs); rational or irrational; a view point Br J Clin Pharmacol/65:5/795-796 Kasarla Raju, A, XXX IRRATIONAL DRUG COMBINATIONS Vol. 3 (Issue 2 [2013] 52-56	support the rationality of this FDC. Hence, the Committee considered this FDC as irrational.
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5. Aggrieved of the above Notification, the petitioner filed a Writ Petition before this Court, being WP (C) no. 2667/2016. The same alongwith various other petitions were allowed by this Court by a judgment and order dated 01.12.2016.

6. The respondent challenged the above order before the Supreme Court and the Supreme Court by a detailed judgment dated 15.12.2017, titled ***Union of India and Anr. vs. Pfizer Limited and Others***, (2018) 2 SCC 39, *inter alia* directed as under:-

“31. On the facts of these cases, a suggested course of action was stated by the learned counsel appearing on behalf of the appellant-petitioners. This course is that instead of now remitting the matter back to the Delhi High Court for an

adjudication on the other points raised in the writ petitions, the case of 344 FDCs that have been banned, plus another 5 FDCs that have been banned, which comes to 349 FDCs [barring 15 FDCs that are pre-1988 and 17 FDCs which have DCG(I) approval] pursuant to the Kokate Committee Report, by Notifications of the Central Government under Section 26-A of the Drugs Act, should be sent to the DTAB, constituted under Section 5 of the Drugs Act, so that it can examine each of these cases and ultimately send a report to the Central Government. We reiterate that only on the peculiar facts of these cases, we think that such a course commends itself to us, which would obviate further litigation and finally set at rest all other contentions raised by the petitioners. We say so because we find that the Kokate Committee did deliberate on the 344 FDCs plus 5 FDCs and did come to a conclusion that the aforesaid FDCs be banned, but we are not clear as to what exactly the reasons for such conclusions are, and whether it was necessary in the public interest to take the extreme step of prohibiting such FDCs, instead of restricting or regulating their manufacture and supply. In order that an analysis be made in greater depth, we, therefore, feel that these cases should go to the DTAB and/or a sub-committee formed by the DTAB for the purpose of having a relook into these cases. It is important, however, that the DTAB/sub-committee appointed for this purpose will not only hear the petitioner-appellants before us, but that they also hear submissions from the All-India Drugs Action Network. The DTAB/sub-committee set up for this purpose will deliberate on the parameters set out in Section 26-A of the Drugs Act, as follows.

32. First and foremost in each case, the DTAB/sub-committee appointed by it must satisfy itself that the use of the Fixed Dose Combinations (FDC) in question is likely to involve any one of the aforesaid three things:

(a) that they are likely to involve any risk to human beings or animals; or

(b) that the said FDCs do not have the therapeutic value claimed or purported to be claimed for them; or

(c) that such FDCs contain ingredients and in such quantity for which there is no therapeutic justification.

33. The DTAB/sub-committee must also apply its mind as to whether it is then necessary or expedient, in the larger public interest, to regulate, restrict or prohibit the manufacture, sale or distribution of such FDCs. In short, the DTAB/sub-committee must clearly indicate in its report:

(1) as to why, according to it, any one of the three factors indicated above is attracted;

(2) post such satisfaction, that in the larger public interest, it is necessary or expedient to (i) regulate, (ii) restrict, or (iii) prohibit the manufacture, sale or distribution of such FDCs.

34. The DTAB/sub-committee must also indicate in its report as to why, in case it prohibits a particular FDC, restriction or regulation is not sufficient to control the manufacture and use of the FDC. We request the DTAB/sub-committee to be set up for this purpose to afford the necessary hearing to all concerned, and thereafter submit a consolidated report, insofar as these FDCs are concerned, to the Central Government within a period of six months from the date on which this judgment is received by the DTAB. We may also indicate that the Central Government, thereafter, must have due regard to the report of the DTAB and to any other relevant information, and ultimately apply its mind to the parameters contained in Section 26-A of the Drugs Act and, accordingly, either maintain the Notifications already issued, or modify/substitute them or withdraw them.”

7. Pursuant to the above order and in compliance thereof, the drug in question was examined by the Drugs Technical Advisory Board (DTAB). The DTAB submitted its report to the respondent no.1 wherein for the drug in question the following recommendation was made:-

“1. Nimesulide in combination has potential of misuse and safety concern. It’s use in children below 12 years is already banned in India and it’s use is limited to 15 days in adults in Europe.

2. Pharmacodynamically inappropriate FDC as both have similar mechanism of action (both drugs acting on the same enzyme). However, adverse effects of the two drugs (such as Gastrointestinal, ulceration, nephrotoxicity and hepatotoxicity) add up. Thus, combining two NSAIDs may not improve the efficacy of treatment but may increase the risk.

3. Further, Diclofenac poses specific risk to animals (vultures).

4. This combination is not as per the standard therapeutic guidelines.

There is no convincing scientific/clinical evidence/justification for the FDC.”

8. Based on the above recommendation the respondent has issued the impugned Notification.

9. The learned counsel for the petitioner in challenge to the above Notification submits that Nimesulide and Diclofenac have both been approved by Drug Controller General of India (DCGI) for sale not only independently but also as a FDC with other drugs including the Non Steroidal-Inflammatory Drugs (NSAIDs). He submits that therefore, these drugs can be prescribed independently by the doctors and also in combination with other NSAIDs. He submits that in such scenario, there was no justification for prohibiting the manufacture and sale of the said FDC.

10. The learned counsel for the petitioner submits that in terms of the judgment of the Supreme Court in ***Pfizer Limited and Others (Supra)***, DTAB/Sub-Committee was not only to satisfy itself that the use of the

FDC in question is likely to involve any one of the following; (a) that they are likely to involve any risk to human beings or animals; or b) that the said FDCs do not have the therapeutic value claimed or purported to be claimed for them; or c) that such FDCs contain ingredients and in such quantity for which there is no therapeutic justification, but also to apply its mind as to whether it is then necessary or expedient, in the larger public interest, to regulate, restrict or prohibit the manufacture, sale or distribution of such FDCs and clearly indicate in its report as to how, according to it, one of the three factors indicated above has been attracted and that it is in the larger public interest necessary or expedient to (i) regulate; (ii) restrict or; (iii) prohibit the manufacture, sale or distribution of such FDCs. The learned counsel for the petitioner submits that the reasoning given by the DTAB as reproduced hereinabove does not satisfy the conditions laid down by the Supreme Court.

11. The learned counsel for the petitioner further places reliance on Appendix VI, Schedule Y to the Drugs and Cosmetic Rules, 1945 (hereinafter referred to as the 'Rules') and specifically Clause (d) thereof, to contend that even where the claim for such FDCs is made only for convenience, the same can be approved.

12. The learned counsel for the petitioner further places reliance on the following Articles to substantiate his submission that the FDC in question is even otherwise more efficacious and in any case, there is no evidence on record that the combination would lead to adding of any adverse effects of the two drugs, combination of which form a part of the present FDC:-

- i) Spectrophotometric method for Simultaneous Estimation of Nimesulide and Diclofenac Sodium from Combined Dosage Form (Indian Journal of Pharmaceutical Sciences, accepted on 01.02.2003);
- ii) Simultaneous Reverse Phase HPLC Estimation of Nimesulide and Diclofenac Sodium (Indian Journal of Pharmaceutical Sciences, accepted on 12.02.2003);
- iii) Spectrophotometric method for Simultaneous Estimation of Nimesulide and Diclofenac Sodium from Combined Dosage Forms (Asian Journal of Pharmaceutical Analysis, accepted on 18.10.2011);
- iv) Beneficial interaction of nimesulide with NSAIDs (Medical Chemistry Research, accepted on 20.03.2007);
- v) Fixed-Dose Combination Improve Medication Compliance: A Meta-Analysis (The American Journal of Medicine, 2007);
- vi) To compare the efficacy and side effects of Diclofenac Sodium, Ibuprofen and Nimesulide during Post Operative Period of Surgical removal of impacted lower third Molar tooth (Journal of Evolution of Medical and Dental Sciences, 05.11.2015).

13. On the other hand, the learned counsel for the respondent submits that for the FDC in question the petitioners had not applied for approval under Rule 122-B of the Rules. He submits that in absence of such approval, the initial onus of proving that the FDC in question was pharmacodynamically appropriate and did not cause any risk to human beings and animals was on the petitioners. The petitioners did not meet

this onus of proof and in fact, did not file many of the Articles, which are now sought to be relied upon before this Court, before the DTAB. As far as the Articles relied upon by the petitioners are concerned, he submits that not only are they irrelevant to the controversy in question but also, because they were not placed before the DTAB, they cannot be relied upon in the present petitions.

14. I have considered the submissions made by the learned counsels for the parties. The scope of exercise to be conducted by the DTAB in terms of the judgment of the Supreme Court in ***Pfizer Limited and Ors.***(supra) has already been quoted hereinabove.

15. Before proceeding further with the consideration of the submissions of the learned counsels for the parties, it would also be relevant to take note of a few judgments that have been passed by this Court considering the challenge to other FDCs similarly prohibited by the respondent pursuant to the DTAB report, as these judgments spell out the scope of the jurisdiction of this Court while considering such challenge.

16. This Court in ***Wockhardt Limited and Anr. V. Union of India and Anr.*** (judgment dated 07.01.2019 in WP (C) 9739/2018) held that the Notification issued in exercise of powers under Section 26A of the Act are of general application and the power exercised by the Central Government under Section 26A of the Act is legislative in nature. Such power can be exercised only where the Central Government is satisfied that it is necessary to exercise the same in larger public interest. Such satisfaction would be required to be based on relevant considerations; cogent material; and by excluding irrelevant considerations. It was further held that in view of the direction issued by the Supreme Court in

Pfizer Limited and Ors.(supra), the DTAB/Sub-Committee was required to indicate its reasons for recommending that the FDC be proscribed.

17. In **Unison Pharmaceuticals Pvt. Ltd. v. Union of India and Anr.** (judgment dated 08.01.2019 in WP(C) 10403/2018), this Court held that merely because the Sub-committee had concurred with the findings of the earlier Expert Committee cannot possibly lead to the conclusion that they had not applied their mind. This Court further held that while examining the merit of the petition, this Court cannot be called upon to re-examine and re-appreciate the view of the experts on merit. This Court is not competent to decide on merit whether the FDC in question lacks therapeutic justification or presence of element of risk to human beings. This Court further held as under:

“35. The aforesaid contentions are unpersuasive. The Sub-Committee had clearly indicated that there was insufficient evidence of efficacy of Pioglitazone 7.5 mg. Thus, the Pioglitazone 7.5 mg as a standalone drug could not be recommended for use. It is obvious that in this view, the said drug could not be permitted to be used as a part of the said FDC. Therefore, the question of permitting the manufacture and sale of FDC subject to any restriction did not arise. The question of restricting or regulating the manufacture would arise only in cases where it is found that the drug has some efficacy but presents risks in certain situations. In this case, the manufacture and sale could be restricted or regulated to ensure that the drug is not sold and used in certain patients or in certain indications. Certain safeguards relating to sale of such drug could also be put in place. However, there is no scope for regulating or restricting a drug, which does not have any therapeutic justification and its efficacy is not established.”

(Emphasis supplied)

18. In ***Lupin Limited and Anr. V. Union of India and Anr.*** (judgment dated 22.02.2019 in WP(C) 10917/2018), this Court further held as under:

“27. It is also relevant to note that the Supreme Court had given a specific direction that in cases where the DTAB/Sub-committee prohibits a particular FDC, it would also give its reasons as to why restricting or recalling the said FDC, would not be sufficient to control the manufacture and use of that FDC. In the present case, the Sub-committee had highlighted a risk of overdose, however, it did not indicate in its report as to why restricting or regulating its manufacture or use, would not suffice. Thus, the report submitted by Sub-committee also is not in conformity with the directions issued by the Supreme Court in Pfizer Limited (supra). Concededly, the Central Government has based its decision solely on the report of the Subcommittee. A decision founded on an unclear report without any deliberation is manifestly arbitrary.”

19. This Court in ***M/s Microlabs Limited v. Drugs Controller General of India and anr.*** (judgment dated 13.02.2019 in WP(C) 9978/2018), held that where the FDC has therapeutic value and the potential to address the need of patient, mere availability of alternate cannot be a ground for proscribing the FDC.

20. I shall now proceed to examine the challenge to the Notification in the present case applying the law laid down by this Court in the above referred judgments.

21. The reasons given by the DTAB for proscribing the FDC in question are re-extracted herein below:

“1. Nimesulide in combination has potential of misuse and safety concern. It’s use in children below 12 years is already banned in India and it’s use is limited to 15 days in adults in Europe.

2. Pharmacodynamically inappropriate FDC as both have similar mechanism of action (both drugs acting on the same enzyme). However, adverse effects of the two drugs (such as Gastrointestinal, ulceration, nephrotoxicity and hepatotoxicity) add up. Thus, combining two NSAIDs may not improve the efficacy of treatment but may increase the risk.

3. Further, Diclofenac poses specific risk to animals (vultures).

4. This combination is not as per the standard therapeutic guidelines.

There is no convincing scientific/clinical evidence/justification for the FDC.”

22. As far as the 1st and 3rd reasons are concerned, clearly the same could not have independently formed the basis for proscribing the FDC in question, inasmuch as it is not denied that Nimesulide and Diclofenac have been independently approved for manufacture and sale.

23. At the same time, both the Kokate Committee Report as also the DTAB have opined that the FDC in question is pharmacodynamically inappropriate as both Nimesulide and Diclofenac have similar mechanism of action and therefore, their combination, though cannot improve efficacy of treatment, but may add up to the adverse effects of the two drugs thereby increasing the risk. It was further observed that there is no convincing scientific/clinical evidence/justification for the FDC.

24. In the present case, barring relying upon certain general Articles, which I shall deal with in the latter part of this judgment, the petitioners have not been able to place any material on record to show how the

above opinion of the Expert Committee as also the DTAB can be found to be arbitrary or unreasonable.

25. Admittedly, the petitioners have not taken the approval for the FDC under Rule 122B of the Rules. Rule 122E(c), includes within definition of a “New Drug”, a Fixed Dose Combination of two or more drugs, individually approved earlier for certain claims, which are now proposed to be combined for the first time in a fixed ratio, or if the ratio of ingredients in an already marketed combination is proposed to be changed, with certain claims, which is, indications, dosage, dosage form (including sustained release dosage form) and route of administration.

26. Appendix VI to Schedule Y of the Rules and specifically Clause (d) thereof, on which reliance was also placed by the learned counsel for the petitioners, is reproduced herein below:

“(d) The fourth group of FDC includes those whose individual active ingredients (or drugs from the same class) have been widely used in a particular indication(s) for years, their concomitant use is often necessary and no claim is proposed to be made other than convenience. It will have to be demonstrated that the proposed dosage form is stable and the ingredients are unlikely to have significant interaction of a pharmacodynamic or pharmacokinetic nature.”

27. A reading of the above would show that even where the claim of FDC is based on convenience, the applicant has to demonstrate that the individual active ingredients of the FDC have been widely used in a particular indication for years and their concomitant use is often necessary, but also that the proposed dosage form is stable and the ingredients are unlikely to have significant interaction of a

pharmacodynamic or pharmacokinetic nature. Therefore, the burden of proving the same has to be on the applicant, herein the petitioners. As noted hereinabove, barring making of a reference of a few general Articles, the petitioners have been unable to place before this Court any material that may have even remotely satisfied the above conditions.

28. As far as the submissions of the learned counsels for the petitioners that both Nimesulide and Diclofenac are also available in combination with acetaminophen (Paracetamol), learned counsel for the respondent submits that the same is irrelevant inasmuch as paracetamol is not considered as an NSAID.

29. As far as the submissions of the petitioners that Nimesulide and Diclofenac are also been prescribed in combination, barring making a bald statement in this regard in the petitions, there was no other material placed on record by the petitioners before the DTAB or the Kokate Expert Committee or even in this petition. During the course of the arguments, learned counsels for the petitioners handed over a chart showing that the data published by IQVIA demonstrates prescription and sale of Diclofenac and Nimesulide simultaneously and that the sale of around 30,640 units was reported in July, 2019 as compared to 46,070 units in July, 2018. In my view, the same cannot be read as evidence to show a substantial use of the two drugs in combination being prescribed by the Doctors.

30. As far as the Articles relied upon by the learned counsels for the petitioners, the Article in the American Journal of Medicine is on the

general use of a Fixed Dose Combination and not for the FDC in question.

31. The Article published in the Indian Journal of Pharmaceutical Sciences (accepted on 01.02.2003) and Asian Journal of Pharmaceuticals Analysis, 2011 are on use of Spectrophotometric method for Simultaneous Estimation of Nimesulide and Diclofenac Sodium from Combined Dosage Forms and not on the efficacy or lack of adverse effect on human beings or animals of the said FDC.

32. The other Article published in the Indian Journal of Pharmaceutical Sciences (Accepted on 12.02.2003) relates to the method for simultaneous determination of Nimesulide and Diclofenac Sodium from capsules and therefore, does not relate to the efficacy of the FDC in question.

33. As far as the Article in the Journal of Evolution of Medical and Dental Sciences, the same merely shows the efficacy of Nimesulide over Diclofenac Sodium and Ibuprofen. This Article is not related to efficacy of the FDC in question.

34. As far as the Article in the Medicinal Chemistry Research, the study was conducted on 48 male Albino Wistar rats; it certainly cannot be said to be of a nature that would show the efficacy of the FDC to an extent so as to upset the finding of the Expert Committee as also the DTAB.

35. Apart from the above, the learned counsel for the respondent rightly submits that as the above Articles were not placed by the

petitioners before the DTAB, they cannot be relied upon to challenge the findings of the DTAB.

36. As far as the submission of the learned counsel for the petitioner that the manufacture/sale of the FDC should have been restricted/regulated instead of being prohibited, as noted hereinabove, DTAB has opined that while the combination is not as per standard therapeutic guidelines, adverse affects of the two drugs add up, therefore, combining two NSAIDs may not improve the efficacy of treatment but may increase the risk. As the above opinion could not be demonstrated to be incorrect or arbitrary, no fault can be found in the decision to prohibit the manufacture/sale of the FDC in question.

37. In view of the above, this Court finds no ground to interfere with the Impugned Notification. The petitions alongwith pending applications are dismissed. There shall be no order as to cost.

NAVIN CHAWLA, J
NOVEMBER 05, 2019/rv