Government Bans 16 Fixed-Dose Combination Drugs Over Safety and Efficacy Concerns

Fixed-dose combination drugs banned by the government over concerns of irrational use, safety risks, and antimicrobial resistance

Combination Drugs Latest News

- The government has banned 16 fixed-dose combination (FDC) drugs, including certain antibiotic combinations and various dermatological products containing aloe vera and herbal ingredients, over concerns of irrational formulation and lack of scientific justification.

About Fixed-Dose Combination (FDC) Drugs

- A Fixed-Dose Combination drug is a formulation that contains two or more active pharmaceutical ingredients in a single dosage form, such as a tablet, capsule, or cream. FDCs are widely used across a range of conditions, including:
  - Infections (antibiotic combinations)
  - Pain management
  - Skin ailments
  - Diabetes and cardiovascular diseases
  - Cough, cold, and fever

Rational vs Irrational FDCs

- A rational FDC is one where each ingredient contributes meaningfully to the therapeutic effect, ingredients have compatible pharmacological properties, and clinical evidence shows the combination is more beneficial than using the drugs separately.
- An irrational FDC is one where the ingredients have no scientifically established rationale for being combined, or where there is little or no evidence from clinical trials to support the combination.

Regulatory Framework in India

- The Central Drugs Standard Control Organisation (CDSCO), under the Ministry of Health and Family Welfare, is the apex regulator for pharmaceuticals in India.
- The Drugs and Cosmetics Act, 1940 and its rules govern the approval, manufacture, and sale of drugs.
- The government has periodically banned irrational FDCs based on recommendations from expert committees, including a landmark ban in 2016 that affected hundreds of formulations.
- Public health experts, including scientists at the Indian Council of Medical Research (ICMR), have long warned that irrational combinations expose patients to unnecessary risks and contribute to antimicrobial resistance (AMR).

News Summary: Ban on 16 FDC Drugs

- The government has banned 16 FDC drugs, citing lack of scientific evidence, potential safety risks, and the threat of fuelling antimicrobial resistance.
- The banned products include certain antibiotic combinations and a range of dermatological products containing aloe vera and herbal ingredients.

Key Rationale for the Ban

- Public health experts explain that:
  - Irrational combinations expose patients to unnecessary drugs.
  - They increase treatment costs.

    - In the case of antibiotics, they contribute to antimicrobial resistance (AMR), a growing global health concern where bacteria, viruses, fungi, and parasites no longer respond to medicines designed to kill them.
- Combinations often lack robust clinical trial evidence showing that the ingredients work better together than when used separately.

Examples of Problematic Combinations

- **Amoxicillin + Serratiopeptidase**
    - One of the banned products combines amoxicillin (an antibiotic) with serratiopeptidase (a proteolytic enzyme).
    - Serratiopeptidase is acid-labile, meaning it can be degraded in the stomach before reaching the bloodstream.
    - No peer-reviewed randomised controlled trial has shown that adding serratiopeptidase improves bacterial clearance or reduces the amount of antibiotic required.
    - Claims of enhanced penetration are largely based on laboratory studies, not human clinical evidence.
    - No major treatment guideline recommends serratiopeptidase as an adjunct to antibiotics.
- **Norfloxacin + Tinidazole**
    - Norfloxacin treats bacterial infections, while tinidazole targets protozoal infections.
    - Patients rarely suffer from bacterial and protozoal infections simultaneously.
    - Unnecessary exposure to both drugs promotes bacterial resistance without added benefit.

Amoxicillin + Clavulanic Acid (Augmentin)

- Clavulanic acid blocks enzymes that resistant bacteria use to destroy amoxicillin.
- However, if the bacteria causing infection are not resistant, clavulanic acid is unnecessary.
- Widespread and indiscriminate use accelerates AMR.

Antimicrobial Resistance Concern

- Antimicrobial resistance is one of the most serious public health threats today. When antibiotic combinations are marketed as being more effective without sufficient evidence:
    - They encourage unnecessary or prolonged antibiotic use.
    - They increase antibiotic exposure in the community.
    - They create selective pressure on bacteria, allowing resistant organisms to survive and multiply.
- The antibiotic pipeline is running dangerously dry, making it critical to preserve the effectiveness of existing drugs.

Aloe Vera-Based Dermatological Products

- Several banned products are dermatological creams containing aloe vera along with Vitamin E, jojoba oil, olive oil, tea tree oil, and other moisturising or herbal components.
- Longevity in the market does not automatically establish scientific validity.
- Robust evidence demonstrating the superior efficacy of these combinations over individual ingredients is often lacking.
- Steroid-antifungal combinations are particularly concerning, while they provide temporary relief, steroids can suppress the skin's immune response, causing fungal infections to worsen, spread, or develop resistance.

Risks to Patients

- Using irrational FDCs exposes patients to several risks:
    - Adverse effects and drug interactions
    - Allergic reactions to unnecessary components
    - Inability to adjust individual doses, doctors cannot increase one ingredient without overdosing on the other
    - Masking underlying complications, reducing precision in treatment
    - Higher costs without added benefit

Way Forward

- **For Patients**
  - Understand that a medicine containing multiple ingredients is not necessarily more effective than a targeted treatment.
  - Consult doctors about appropriate alternatives if currently using banned products.
  - Stopping an irrational FDC does not mean stopping treatment; safer, evidence-based alternatives are available.
- **For Doctors**
  - De-escalate patients to rational therapies.
  - Prescribe medicines supported by strong clinical evidence.
  - Avoid combination products unless the combination has clear scientific support.
- **For Pharmacists**
  - Stay aware of the drug regulator's list of banned FDCs.
  - Flag irrational prescriptions where appropriate.
  - Educate patients about available alternatives.
- **For the Health System**
  - Strengthen antimicrobial stewardship programmes.
  - Enhance surveillance of AMR and irrational prescribing.
  - Promote rational use of medicines through medical education and public awareness.
  - Continue periodic review of FDCs in the market.

Broader Considerations on Vitamins and Probiotics with Antibiotics

- Experts also note that automatically combining antibiotics with vitamins or probiotics is not evidence-based:
  - Probiotics may be advised by doctors on a case-specific basis.
  - Vitamins may not be needed for short antibiotic courses, except for vulnerable groups.
  - Patients should follow their doctor's specific advice rather than relying on assumed benefits.

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