Drug & Poison Information Center Bulletin
Faculty of Pharmacy - Tanta University

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Fatal Drug Mix-Ups Prompt EMA Safety Warning on Tranexamic Acid Use

Tranexamic acid (TXA) is a synthetic antifibrinolytic agent that prevents and controls bleeding in various conditions such as trauma, surgery, postpartum hemorrhage, and menorrhagia in adults and children (≥1 year). It works by inhibiting plasminogen conversion to plasmin, thereby stabilizing blood clots and reducing fibrinolysis. TXA is considered safe and effective when administered intravenously in accordance with guidelines.

Neurotoxicity Risk from Wrong Route of Administration

Recent European reports have revealed fatal medication errors where TXA was mistakenly given intrathecally, epidurally, or intracerebrally instead of intravenously. When TXA enters the cerebrospinal fluid, it acts as a potent neurotoxin by blocking gamma-aminobutyric acid (GABA) and glycine receptors, causing severe neuronal hyperexcitability. This leads to seizures, muscle rigidity, and sometimes cardiac arrhythmias. Even very small intrathecal doses (10–20 mg) can cause convulsions, paralysis, or death. Since no specific antidote or standardized treatment exists for TXA-induced neurotoxicity, outcomes are often fatal.

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When introduced into the cerebrospinal fluid, TXA becomes a neurotoxin, causing severe neuronal hyperexcitability by antagonizing GABA and glycine receptors. This can lead to serious outcomes such as seizures, muscle rigidity, cardiac arrhythmias, convulsions, and death, with no specific antidote available for TXA-induced neurotoxicity, resulting in devastating consequences.

European Medicines Agency (EMA) Pharmacovigilance Findings

Following reviews by the EMA's Pharmacovigilance Risk Assessment Committee (PRAC), it was found that labeling confusion with TXA ampoules, often mistaken for local anesthetics during spinal or epidural anesthesia, led to serious adverse effects, including acute back pain, myoclonus, seizures, arrhythmias, and cardiorespiratory arrest post-injection.

EMA Safety Recommendations

The EMA issued a safety communication to healthcare institutions, urging them to:

- Label TXA syringes and ampoules as "For Intravenous Use Only."
- Physically separate TXA storage from local anesthetic agents in operating theaters and anesthesia carts.
- Implement staff education and double-check protocols before spinal or epidural procedures.
- Update electronic prescribing systems and barcode verification to prevent administration route errors.

The EMA announced updates to product labeling and packaging for injectable TXA formulations, emphasizing intravenous use only, with changes to appear in national registries and on the EMA's official website.

Clinical Implications:

Spinal anesthesia usage in obstetrics, orthopedics, and trauma surgery presents a significant risk of ampoule mix-up, particularly with intravenous TXA. Hospitals are recommended to audit their storage and labeling practices, strengthen team communication protocols, and regularly review incident reports to enhance medication safety.

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Four Emerging Anti-Obesity Therapies to Watch in 2026

Obesity continues to be a major global health issue linked to metabolic diseases and cardiovascular complications. By 2026, four emerging drugs Retatrutide, CagriSema, Orforglipron, and Oral Semaglutide are anticipated to significantly advance obesity treatment. The following summary outlines each agent based on its mechanism of action, clinical efficacy, dosing regimen, and potential side effects.

1. Retatrutide (Eli Lilly)

- **Mechanism of Action:** Retatrutide is a once-weekly injectable triple agonist gastric inhibitory polypeptide (GIP), glucagon-like peptide-1 (GLP-1), and glucagon receptors, that reduces appetite, increases energy expenditure, and improves glucose control.
- **Efficacy:** Phase 2 studies showed up to 24.2% mean weight loss at 48 weeks, highlighting its strong potential as an obesity treatment.
- **Dosing:** Given as a once-weekly subcutaneous injection with dose titration for better tolerance.
- **Side Effects:** Mainly gastrointestinal symptoms such as nausea, vomiting, and diarrhea, more frequent at higher doses.
- **Current Status:** In Phase 3 trials; not yet approved for clinical use.

2. CagriSema (Novo Nordisk)

- **Mechanism of Action:** Combines **cagrilintide** (an amylin analogue that promotes satiety and slows gastric emptying) with **semaglutide** (a GLP-1 receptor agonist) to achieve synergistic appetite suppression and weight reduction.
- **Efficacy:** The **REDEFINE** Phase 3 studies showed **~20.4% weight loss at 68 weeks** in non-diabetic patients and clinically meaningful loss in those with type 2 diabetes.
- **Dosing:** Once-weekly subcutaneous injection. Combination dosing and titration schedules remain under regulatory evaluation.
- **Side Effects:** Typical incretin-related gastrointestinal effects, including nausea and vomiting; transient in most patients.
- **Current Status:** Undergoing regulatory review; expected to launch in 2026 pending approval.

3. Orforglipron (Eli Lilly)

- **Mechanism of Action:** A **small-molecule oral GLP-1 receptor agonist**, designed to mimic the incretin effect without peptide injection. Its oral bioavailability offers a patient-friendly alternative to injectables.
- **Efficacy:** Early clinical trials indicate meaningful weight loss compared with placebo, with ongoing studies expected to define its full potential.

Dosing: Administered orally once daily. Being a small molecule, it may not require fasting conditions like peptide-based oral agents.

- **Side Effects:** Gastrointestinal discomfort, nausea, and possible drug-drug or food interactions due to oral metabolism.
- **Current Status:** In late-stage clinical trials; expected regulatory submission in 2026.

4. Oral Semaglutide (Novo Nordisk)

- **Mechanism of Action:** An **oral GLP-1 receptor agonist** that enhances insulin secretion, delays gastric emptying, and reduces appetite. It serves as a reference standard for oral incretin therapies.
- **Efficacy:** Demonstrates glycemic control and moderate weight loss in patients with type 2 diabetes. Injectable forms yield greater efficacy, but oral formulation provides convenience.
- **Dosing:** Taken orally once daily in a fasting state with water; patients must wait at least 30 minutes before food intake.
- **Side Effects:** Nausea, abdominal discomfort, and diarrhea are most common; these typically decrease with continued use.
- **Current Status:** Approved for type 2 diabetes; potential expansion for obesity treatment under investigation.

New anti-obesity drugs like Retatrutide, CagriSema, Orforglipron, and Oral Semaglutide offer improved efficacy, personalized care, and convenient options, with trials ongoing to confirm long-term safety and effectiveness.

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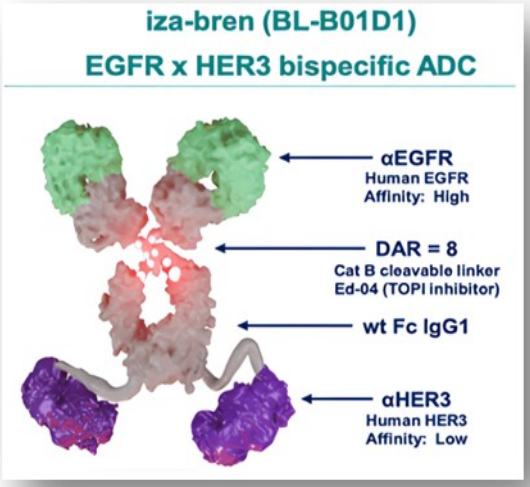
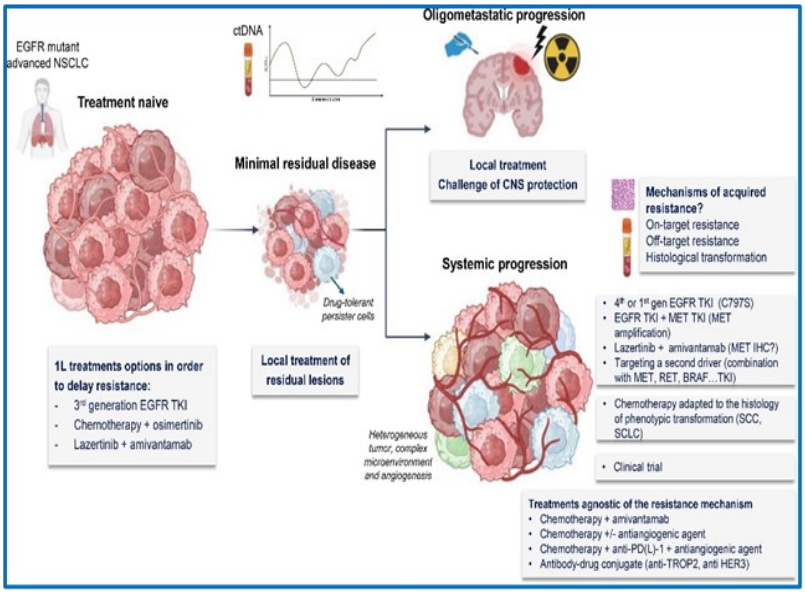
Bispecific Innovation in Motion: Iza-Bren Gains FDA Breakthrough Status in NSCLC

Iza-Bren (izalontamab brengitecan), an EGFR×HER3 bispecific antibody-drug conjugate (ADC) carrying a topoisomerase -I (TPO1) inhibitor payload, has demonstrated robust response rates in patients with previously treated solid tumors. It recently received **U.S. Food and Drug Administration (FDA)** ***Break-through Therapy Designation*** for EGFR-mutant non-small cell lung cancer (NSCLC), marking a major milestone and accelerating pivotal clinical studies.



1. Disease Background : Why EGFR-mutant NSCLC Needs New Options



EGFR-mutant NSCLC accounts for a substantial subset of lung cancers, and while EGFR tyrosine kinase inhibitors (TKIs) (including third generation agents such as osimertinib) produce high initial response rates, most patients eventually develop acquired resistance, leaving limited treatment options after TKI and platinum-based therapy. Emerging modalities like ADCs and bispecific antibodies offer novel mechanisms by targeting multiple pathways or delivering cytotoxics directly to tumor cells. Iza-Bren is the leading agent in this class and is being tested alone and with EGFR TKIs.

2. What is Iza-Bren? (Mechanism & Design)

Iza-Bren (also called BL-B01D1/BMS-986507 in some trials) is a bispecific ADC that binds EGFR with high affinity and HER3 with lower affinity, connected via a cleavable linker to a TOP1 inhibitor payload (Ed-04 or related TOP1 inhibitor). The dual targeting is intended to block EGFR/HER3 signaling (reducing proliferation/survival signals) and selectively deliver a potent cytotoxic payload into tumor cells. This design aims to address tumors that rely on EGFR/HER3 signaling and to retain activity in heterogeneous or resistant disease.

3. Regulatory Status & Major News (Late-2025)

The FDA granted ***Breakthrough Therapy Designation*** to izalontamab brengitecan for patients with locally advanced or metastatic **EGFR-mutant NSCLC** who have progressed after EGFR TKIs and platinum-based chemotherapy recognizing preliminary evidence of substantial improvement over available therapies and supporting expedited development.

4. Key Clinical Data Highlights

- In early clinical evaluations, **Iza-Bren** demonstrated substantial antitumor activity in patients with advanced NSCLC. Findings from dose-escalation and expansion cohorts indicated meaningful objective responses and durable disease control, particularly among individuals harboring **EGFR mutations**. These outcomes provided the rationale for advancing the agent into subsequent Phase 2 and 3 investigations.
- Preliminary studies of **Iza-Bren with osimertinib** have shown highly encouraging efficacy signals, suggesting potential synergistic activity between the bispecific ADC and EGFR-targeted therapy. These early observations are being further examined in randomized clinical trials to confirm the consistency and magnitude of benefit.
- Beyond NSCLC, early-phase research has revealed promising activity across a range of **solid tumors**, including **HER2-low or negative breast cancer** and **nasopharyngeal carcinoma**. Ongoing multicenter studies are expected to clarify the breadth of Iza-Bren's clinical utility and to define its place in future treatment algorithms for epithelial malignancies

5. Safety and Tolerability (Summary)

Reported adverse events in early trials have included ADC-class toxicities (e.g., cytopenias, gastrointestinal effects, and off-tumor toxicities consistent with payload exposure) and other treatment-related events. Several reports emphasize a manageable safety profile but also highlights the importance of dose selection and monitoring in combination regimens (some media/analysis pieces note toxicity signals as the program advances into larger trials). Close pharmacovigilance in Phase 2/3 trials will be key.

6. Ongoing Pivotal Trials and Next Steps

Bristol Myers Squibb (licensed global rights from SystImmune for many regions) and collaborators have initiated multiple pivotal programs, including randomized Phase 2/3 studies in EGFR-mutant NSCLC, bladder/urothelial carcinoma, and breast cancer settings; trials compare Iza-Bren with standard chemotherapy or add it to EGFR TKIs.

7. Practical Considerations for Pharmacists & Clinicians

- Anticipate ADC-specific handling/administration protocols and monitoring for cytopenias and non-hematologic toxicities.
- For EGFR-mutant NSCLC, expect evolving sequencing questions regarding whether Iza-Bren will be paired with frontline TKIs or reserved after TKI failure which depends on ongoing Phase 3 results.
- Biomarker testing (EGFR mutational analysis; HER3 expression/contextual markers) will be important to define the populations most likely to benefit.

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Vision

The vision of Tanta University DPIC is to improve national healthcare service through provision of evidence-based, unbiased, patient oriented drug information services & adverse drug reporting system.

Mission

* Responding to drug inquiries related to the use of the drug and providing the health care professionals and patients with drug information related to the patient's care to achieve the optimal use of the drug in addition to the provision of other toxicological managing information.
* Educational activities to support the rational optimal use of drugs as well, supporting research activities.
* Continuous medical education and training courses in various fields of pharmacy for students, undergraduates, postgraduate students, and researchers.
* Issuing a Drug Information Bulletin periodically to take a look at medical & pharmaceutical news.
* Supporting the National Pharmaceutical Vigilance Program by following up and monitoring side effects and problems related to use of pharmaceutical preparations within regional hospitals.
* Contributing to the establishment of various treatment protocols and prescription booklet services in regional hospitals.

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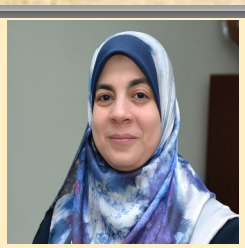

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