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Review Article

Taxane-Related Hypersensitivity Reactions and Their Management: A Narrative Review

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ABSTRACT
The major chemotherapeutic agent used in cancer, especially in breast, ovarian, lung and other solid tumours, is taxanes, i.e., Paclitaxel and Docetaxel. Even though they are widely used in our clinical settings, they are not free of side effects. One of the major side effects is hypersensitivity reactions, which may vary from minor rash and flushing to potentially fatal anaphylaxis. This is a narrative review that provides a comprehensive overview of taxane-induced hypersensitivity reactions, including their epidemiology, mechanisms, and clinical presentation, with greater emphasis on their management. Hypersensitivity reactions can occur during the initial cycles of therapy, within minutes of infusion, or eventually in subsequent cycles. The underlying mechanisms are complex, which involve not only immunological but also non- immunological pathways, including mast cell activation triggered by taxanes. In order to make taxane therapy more effective, proper preventive strategies are essential. Standard premedication regimens, including corticosteroids, antihistamines, ondansetron and H2 receptor antagonists, are routinely employed to reduce the risk of immediate hypersensitivity. Desensitisation protocols have emerged as an effective approach for patients who develop hypersensitivity reactions but require continued taxane therapy. The implementation of these strategies, along with the proper monitoring by a clinical pharmacist, results in the gradual reintroduction of the drug under controlled conditions. A multidisciplinary approach involving a pharmacist is essential for the effective management of taxane-induced hypersensitivity reactions and to ensure its safety and efficacy.

1. INTRODUCTION

Taxanes such as paclitaxel and docetaxel are chemotherapeutic agents used in the treatment of the majority of solid tumours. Still, they are not free of side effects. The hypersensitivity reactions (HSRs) with taxanes result in minor rash and flushing to potentially fatal anaphylaxis. Even with regular corticosteroid and antihistamine premedication, large evaluations and guidelines show that 5–10% of individuals experience rapid HSRs, and 1-3% experience severe reactions (Begum et al., 2023 & Boulanger et al., 2014).

Taxane HSRs are currently one of the most prevalent chemotherapeutic drug allergies seen in contemporary oncology treatment, according to recent editorial and narrative work (Park, 2024). Rapid identification and standardized emergency care are

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crucial because these responses usually happen after the first or second infusion and can manifest as bronchospasm, hypotension, chest discomfort, urticaria, or isolated cardiovascular collapse (Begum et al., 2023 & Villarreal-González et al., 2023). The mechanism of immediate reactions is believed to involve several overlapping pathways: complement activation with the production of anaphylatoxins, non-IgE-mediated direct degranulation of mast cells and basophils, and IgE- or IgG-mediated mast-cell activation to the taxane or its solvent (Cremophor EL or polysorbate 80) (Eviq, 2017).

The major management strategies to reduce the severity of HSR include premedication protocol and rapid drug desensitisation (RDD). Although premedication lowers overall incidence and severity, it does not totally avoid reactions, and in order to properly re-expose high-risk individuals, specialised desensitisation procedures are frequently needed (Boulanger et al., 2014 & Eviq, 2017).

Pharmacovigilance data from an adverse-drug-reaction monitoring centre in India have shown clinically significant taxane-induced HSRs, highlighting the necessity of regular reporting mechanisms, consistent grading using CTCAE and active surveillance (Begum et al., 2023).

Despite these developments, reported incidence, risk factors and therapeutic strategies for taxane HSRs vary significantly between centres and nations. (Villarreal-González et al.,2023 & Feldweg et al., 2005) So, it is necessary to synthesize current evidence from a clinical-pharmacy perspective, with an emphasis on identifying high-risk patients, optimizing premedication regimens, and implementing desensitization protocols that are feasible in busy oncology units. Therefore, the purpose of this narrative review is to critically evaluate current approaches for the prevention and management of taxane-induced hypersensitivity reactions in cancer patients, with a focus on the roles of premedication and desensitization protocols.

2. METHODOLOGY

2.1 Data Sources and Search Strategy

A narrative literature search was conducted to identify relevant publications on taxane – induced hypersensitivity reactions and their management. Electronic databases including PubMed, Google Scholar, ResearchGate, and ScienceDirect were searched. Search terms included 'taxane-related hypersensitivity reactions', 'paclitaxel hypersensitivity', 'docetaxel hypersensitivity', 'premedications', 'drug desensitisation', 'anaphylaxis', 'CTCAE guidelines' and 'clinical pharmacist'. The search included articles published between 2005 and 2026.

Inclusion criteria:

- Original research article
- Case reports
- Systematic and narrative reviews

Exclusion criteria:

- Non – English publications
- Conference abstracts without full text
- Duplicate publications

3. EPIDEMIOLOGY OF TAXANE- INDUCED HYPERSENSITIVITY REACTIONS

Among the cytotoxic drugs with the highest risk of infusion-related hypersensitivity reactions (HSRs) are taxanes, primarily paclitaxel and docetaxel. The overall prevalence of taxane-induced HSRs varied from approximately 3 to 33% across 18 observational studies with 8,333 patients, reflecting variations in demographics, regimens and classifications (Park et al., 2025). An HSR to paclitaxel or docetaxel can occur in 30–50% of individuals without premedication, typically during the first or second infusion. Although the prevalence of mild-to-moderate reactions is reduced to about 5–10% by routine premedication with corticosteroids and H1/H2 antihistamines, severe, potentially fatal events still happen (Feldweg et al., 2005& Bayrak Durmaz et al.,2024).

About 10% of premedicated individuals experience HSRs of any grade with paclitaxel, and 2–5% experience severe events in spite of conventional prophylaxis. When premedication was not optimized, even greater rates were found in early experiments (Pellegrino et al., 2017).

Pharmacovigilance centre data demonstrated the prevalence of HSRs in standard oncology therapy. 30 of the 258 (~12%) recorded chemotherapy-related ADRs in one Indian tertiary-care adverse-drug-reaction monitoring centre were taxanes, all of which were HSRs (22 paclitaxel, 8 docetaxel). About 77% of HSRs were classified as not preventable, highlighting the difficulties of anticipating these responses even with guideline-based premedication. The majority of HSRs manifested with shortness of breath (~70%), urticaria, or flushing, and were graded as moderate to severe (Begum et al., 2023) (Table 1).

Table 1: Hypersensitivity Reaction Monitoring – CTCAE v5.0 Grading (Grade 1–5) (National Cancer Institute, 2017)

Hypersensitivity Reaction Monitoring – CTCAE v5.0 Grading (Grade 1–5) CTCAE Grade	**Clinical correlation**
1	Transient flushing, mild itching, mild rash; no breathing difficulty; vitals stable.
2	Urticaria/pruritus needing antihistamine; mild bronchospasm responding quickly; brief stop/slow infusion.
3	Persistent bronchospasm, hypotension, or angioedema needing repeated IV meds; recurrence after restart; admission/extended observation.
4	Severe bronchospasm/airway compromise or shock; requires adrenaline and ICU-level urgent care.
5	Death related to an adverse event.

4. MECHANISM OF ACTION OF TAXANE-INDUCED HYPERSENSITIVITY REACTIONS

Both immune and non-immune mechanisms are involved in taxane-induced hypersensitivity reactions (HSRs), which are immunologically diverse. Immediate reactions, which can range from flushing and urticaria to complete anaphylaxis, usually happen in the first few minutes of infusion (Weiszhár et al., 2012). Taxane HSRs frequently reflect a combination of solvent-related pseudo-allergy, direct mast-cell activation and in a subset of patients, real IgE- or IgG-mediated responses to the taxane or its excipients, in contrast to traditional IgE-mediated drug allergy, where a single mechanism predominates. (Park, 2024 & Straughn & Kaur, 2021)

The solvent systems utilized to create traditional taxanes have been identified as playing a key function. While docetaxel and cabazitaxel are made with polysorbate 80, paclitaxel is dissolved in ethanol and polyoxyethylated castor oil (Cremophor EL) (Weiszhár et al., 2012 & Straughn& Kaur, 2021).

Research has demonstrated that polysorbate 80 and Cremophor EL are strong complement system activators in human serum, producing the anaphylatoxins C3a and C5a and causing complement activation-related pseudo-allergy (CARPA) (Weiszhár et al., 2012). These anaphylatoxins can then cause mast cells and basophils to degranulate through their surface receptors, which release histamine, tryptase, leukotrienes and other mediators that cause bronchospasm, increased vascular permeability and vasodilation. Paclitaxel has also been shown to cause direct, non-IgE-mediated histamine release from basophils, which may be a factor in rapid-onset reactions (Weiszhár et al., 2012).

The important involvement of solvents is further supported by the different behaviour of albumin-bound paclitaxel (nab-paclitaxel). In pharmacovigilance databases and comparative clinical investigations, nab-paclitaxel—which is produced without Cremophor EL—has continuously demonstrated a significantly lower reporting rate of anaphylactic events as compared to solvent-based paclitaxel (de Leon et al., 2013 & Pellegrino et al., 2017).

True adaptive immune responses can also take place in certain patients with acute taxane HSRs, case reports and small series have shown positive skin tests and drug-specific IgE, indicating an IgE-mediated mechanism that targets either the taxane core or its excipients. Furthermore, it is thought that T-cell-mediated processes are responsible for delayed hypersensitivity reactions (DHRs) to taxanes, which include interstitial pneumonitis, severe cutaneous adverse reactions, and maculopapular eruptions that develop more than six hours after exposure and frequently after several treatment cycles (Villarreal-González et al., 2026).

When considered collectively, the available data suggest that taxane HSRs result from a combination of direct mast-cell stimulation and vehicle-driven complement activation, which is superimposed on classical IgE- or T-cell-mediated allergy in some patients. This explains the variation in clinical patterns and the requirement for customized management approaches (Pellegrino et al., 2017 & Weiszhár et al., 2012).

5. CLINICAL PRESENTATION AND GRADING OF TAXANE-INDUCED HYPERSENSITIVITY REACTIONS

The clinical presentation of taxane-induced hypersensitivity reactions (HSRs) is wide, ranging from minor skin complaints to potentially fatal anaphylaxis. The majority of acute HSRs are similar to type I responses, exhibiting flushing, erythema, urticaria, pruritus, dyspnea, wheeze/bronchospasm, chest tightness, back pain, abdominal discomfort, hypotension, tachycardia, angioedema and in rare cases, cardiovascular collapse (Febina et al., 2025 & Tsao et al., 2022). The most common infusion-related responses to taxanes, typically of mild to moderate intensity, were flushing, chest tightness and dyspnea, according to a prospective observational analysis study of premedicated patients (Febina et al., 2025). An Indian pharmacovigilance study from a tertiary center discovered that taxane HSRs frequently manifested as rashes, urticaria, face redness and shortness of breath, with one fatal event and sporadic severe allergy (Begum et al., 2023)

The instantaneous taxane HSRs always happen early in the infusion and during the initial treatment cycles. Reactions typically occur within the first five to ten minutes of infusion and primarily during the first or second injection (Febina et al., 2025). On the other hand, T-cell-mediated delayed hypersensitivity reactions (DHRs) to taxanes, such as maculopapular exanthema, severe cutaneous adverse reactions, or interstitial pneumonitis, happen more than six hours after exposure, frequently after several cycles. Such delayed reactions can put chemotherapy at risk, and cannot proceed further without post-medication or quick drug desensitisation procedures (Villarreal-González., et al., 2026).

The Common Terminology Criteria for Adverse Events (CTCAE, currently version 5.0) is used by the majority of oncology centres to grade taxane HSRs based on their severity. Grade 1 events usually involve limited cutaneous symptoms only; grade 2 includes more pronounced symptoms like generalized urticaria, mild bronchospasm, or transient hypotension without the need for aggressive intervention; grade 3–4 reactions have marked respiratory or cardiovascular compromise and satisfy anaphylaxis criteria (Boulanger et al., 2014). Incorporating CTCAE-based grading into their clinical recommendations, Boulanger et al. linked grades to management pathways that ranged from immediate adrenaline administration and consideration of desensitization or alternative therapy after grade 3–4 events to infusion interruption and symptomatic treatment for grade 1-2 reactions. In line with these frameworks, Febina et al. discovered that the majority of infusion-related reactions in premedicated patients were ≤ grade 2 (Febina et al., 2025), while Begum et al.'s pharmacovigilance data revealed a higher percentage of moderate to severe events in routine practice, underscoring population variation and the significance of methodical grading and documentation (Begum et al., 2023).

6. MANAGEMENT OF HYPERSENSITIVITY REACTIONS

6.1 Premedication Strategies

Premedication has become the standard of therapy for traditional paclitaxel, docetaxel and cabazitaxel regimens because the majority of acute taxane HSRs happen during early infusions and can be severe. Combinations of corticosteroids, H1-antihistamines, ondansetron and H2-antagonists should be given prior to each taxane dose, according to the Committee for the Evaluation of Practices in Oncology (CEPO) guidelines and the Australian eviQ resource. While docetaxel regimens often employ oral dexamethasone 8 mg twice daily for three days beginning the day before therapy, paclitaxel regimens typically comprise dexamethasone 20 mg orally 12 and 6 hours before infusion along with intravenous H1/H2 blockers 30–60 minutes before treatment (Eviq, 2017).

Among the premedications, corticosteroids are essential to the majority of regimens. But in older and diabetic patients, high-dose dexamethasone is associated with hyperglycaemia, sleeplessness, mood swings, and an increased risk of infection. Therefore, some observational studies have implemented same-day low-dose dexamethasone for weekly paclitaxel or docetaxel. There are a few reliable randomised studies comparing high- versus low-dose steroid premedication, and any steroid-sparing strategy should be used with close observation for breakthrough HSRs (Foreman et al., 2022; eviq, 2017, & BOPA, 2020).

There is a growing doubt about the function of H2-antagonists as a premedication drug, as there was no recognised difference in HSR rates between patients receiving standard triple premedication (dexamethasone, chlorphenamine, and H2-antagonist) and those receiving only dexamethasone and chlorphenamine, according to Foreman et al.'s prospective, multicentre cohort study of paclitaxel premedication, which included 680 patients (Foreman et al., 2022). Professional organizations like British Oncology Pharmacy Association (BOPA) have released position statements endorsing the removal of H2-antagonists from conventional paclitaxel premedication due to similar findings. Although several recent studies have questioned the role of H2 receptor antagonist in taxane premedication regimens, its use continues to vary across institutions. Some centres have adopted simplified premedication protocols that exclude H2 blockers based on emerging evidence, but some other centres continue to include them in the regimen due to local institutional policies, clinician preferences and existing treatment protocols.

Premedication lowers but does not eliminate the risk of taxane HSRs. Therefore, premedication must always be used in conjunction with the proper infusion-unit preparation (emergency drugs, trained staff, and observation protocols).

6.2 Rapid Drug Desensitisation

Rapid drug desensitization (RDD) provides a safe way to reintroduce the offending medication for patients who have moderate or severe HSRs but still need taxane therapy. In 17 patients who had previously experienced severe responses, the traditional Brigham and Women's Hospital 12-step, 3-bag protocol—first detailed by Feldweg et al.—successfully administered 77 cycles of paclitaxel or docetaxel; the majority of desensitizations were finished without notable breakthrough reactions (Feldweg et al., 2005).

The effectiveness and safety of this strategy have also been validated by other studies. According to Caiado et al., the 12-step protocol enabled the completion of therapy in the great majority of cases in a Portuguese cohort of 189 patients undergoing 1,471 desensitization procedures to antineoplastic drugs (124 of them were taxanes); breakthrough reactions happened in roughly 20% of procedures but were typically mild and managed within the protocol (Caiado et al., 2020). In a more recent multicentre trial (Bayrak Durmaz et al., 2024), the trial exclusively looked at taxane RDD and discovered that, during 255 desensitisation cycles, 93.7% of infusions were finished and there were no fatalities or life-threatening incidents.

RDD methods usually entail premedication with steroids and antihistamines, followed by the injection of escalating taxane concentrations in 12 or more steps over a period of many hours (Bayrak Durmaz et al., 2024 & Feldweg et al., 2005). Although new "one-bag" or same-day desensitization protocols have been created to streamline logistics, the 3-bag, 12-step strategy is still the best-validated method according to the majority of evidence (Caiado et al., 2020). Patients with grade 2–4 acute HSRs in whom the taxane is deemed necessary and in whom other treatments (such as nab-paclitaxel) are not suitable or accessible are typically the only ones eligible for desensitisation.

RDD should only be carried out in facilities with extensive surveillance, complete resuscitation capabilities and familiarity with medication allergies. Current research shows that desensitization enables the majority of patients with taxane allergy to finish scheduled chemotherapy regimens without sacrificing oncologic results, despite the resource requirements (Bayrak Durmaz et al., 2024, Feldweg et al., 2005 & Caiado et al., 2020).

6.3 Alternative Strategies: Switching Taxane or Using Nab-Paclitaxel

An alternate tactic is to use a different taxane formulation in facilities where desensitization is not available or in patients who refuse it. Cross-reactivity is uncertain, perhaps due to solvents (Cremophor EL vs polysorbate 80) and in certain situations, the taxane core itself acting as an allergen. However, small case series have documented successful usage of docetaxel in individuals who previously reacted to paclitaxel and vice versa.

After HSRs, switching from solvent-based taxanes to albumin-bound paclitaxel (nab-paclitaxel) is supported by a stronger body of data. Pellegrino et al. reported a patient with docetaxel HSR who was treated with nab-paclitaxel without experiencing responses again and their analysis of the literature found comparable cases in breast cancer (Pellegrino et al., 2017). The first case of a patient who had severe HSRs to both paclitaxel and docetaxel but tolerated nab-paclitaxel without incident was described by De Leon et al., indicating that the lack of polysorbate 80 and Cremophor EL significantly lowers risk (de Leon et al., 2013).

The safety of nab-paclitaxel in gynaecologic cancer patients with previous paclitaxel HSRs was recently investigated in a retrospective cohort from the Mayo Clinic. The results showed no recurrence of severe responses, indicating that nab-paclitaxel is a viable substitute when available (Kochuveettil et al., 2024). These data combined show that nab-paclitaxel is a useful choice for patients with solvent-related HSRs in whom ongoing taxane therapy is required, but desensitisation is not achievable, even though cost and access may restrict wider implementation.

6.4 Management of Acute Taxane Hypersensitivity Reactions

Immediate, organised care is essential when an HSR happens during taxane infusion. A methodical approach is advised by consensus recommendations and oncology emergency resources: halt the infusion, continue intravenous access, evaluate breathing, circulation, airway and provide oxygen and supportive care as needed (Feldweg et al., 2005& eviq, 2017). Temporary stoppage, symptomatic treatment with H1-antihistamines and cautious rechallenge at a slower rate may be sufficient for moderate (grade 1) reactions, which are usually restricted to localized flushing or rash.

Standard anaphylactic care, including fast intramuscular (or intravenous) adrenaline, high-flow oxygen, intravenous fluids, bronchodilators for bronchospasm and intravenous corticosteroids, must be started for moderate to severe responses (grade ≥ 2) with respiratory or cardiovascular involvement (Bayrak Durmaz et al., 2024). Until all symptoms have been resolved, the patient should be continuously watched. EviQ emphasizes that although premedication lessens severity, anaphylaxis cannot be prevented, and infusion units must always have qualified personnel and resuscitation equipment on hand (eviq, 2017).

Clinicians must determine whether and how to continue taxane therapy after stabilization. Many recommendations permit a supervised rechallenge in the same session with increased premedication and a slower infusion rate for grade 1-2 responses, especially when taxanes are crucial for disease treatment. On the other hand, instead of conventional rechallenge, patients with grade 3–4 reactions (marked bronchospasm, hypotension, hypoxia, or shock) are typically referred for allergy testing and evaluated for rapid drug desensitization (RDD) or alternative medications. Pharmacovigilance and treatment planning both depend on thorough documenting of symptoms, timing, vital signs, interventions and results (Begum et al., 2023).

6.5 Role of Clinical Pharmacist and Patient Counselling

6.5.1 Prevention of Hypersensitivity Reactions

Clinical pharmacists contribute to the development and implementation of evidence-based premedication protocols. They verify the appropriateness of corticosteroids, antihistamines and supportive medications and ensure that administration timing is optimized to minimize the occurrence of hypersensitivity reactions.

6.5.2 Monitoring During Chemotherapy

During taxane administration, pharmacists participate in real-time monitoring of patients and collaborate with oncology nurses to identify early manifestations of hypersensitivity reactions, such as flushing, urticaria, dyspnea and hypotension. Early identification allows prompt intervention and may prevent progression to severe reactions.

6.5.3 Patient Counselling

Patient counselling is a critical responsibility of clinical pharmacists. Patients should be educated regarding the purpose of premedication, the importance of adherence, expected adverse effects and symptoms requiring immediate reporting. Effective counselling improves patient awareness, promotes adherence and reduces anxiety associated with chemotherapy administration.

6.5.4 Pharmacovigilance and ADR Reporting

Clinical pharmacists play a central role in pharmacovigilance activities through adverse drug reaction identification, causality assessment, severity grading, documentation and reporting to national pharmacovigilance programmes. Continuous monitoring contributes to improved medication safety and supports evidence-based practice.

6.5.5 Role in Desensitization Protocols

For patients requiring continued taxane therapy after hypersensitivity reactions, pharmacists assist in designing desensitization protocols, preparation of serial drug dilutions, dose calculations and monitoring during re-administration. Their involvement improves protocol accuracy and patient safety.

The role of the clinical pharmacist is vital in the identification, prevention and management of hypersensitivity reactions. Their role can be categorised in 3 phases: before, during and after the chemotherapy. Before the therapy, they ensure that the patient is safe to administer the drug through collecting the patient's medical and medication history, prior drug allergies, previous chemotherapy details and providing premedications.

During the therapy, they ensure appropriateness of premedication regimens, correct drug, correct dose, proper route and timing of administration, real-time monitoring and early detection of hypersensitivity reactions. They assist the healthcare team by recommending appropriate interventions such as infusion interruption, administration of emergency medications and supportive care. In patients who develop hypersensitivity reactions, the pharmacist's role is to design and implement desensitisation protocols, ensuring safe re-administration of taxanes without compromising therapeutic outcomes. Also monitor other side effects, causality assessment, its reporting and proper documentation. (Fornasier et al., 2018).

Patient counselling, one of the major responsibilities of a clinical pharmacist, lets the patients know about their disease, drugs and side effects. It is the duty of a clinical pharmacist to educate the patients about the importance of premedication and medication adherence, risk of hypersensitivity reactions, how premedication helps to reduce the risk and proper follow-up.

To enable the timely reporting of adverse effects, the patients should be informed about the signs and symptoms of taxane-related hypersensitivity reactions, like flushing, rash, itching, shortness of breath, reduced BP and chest discomfort, etc., which helps in prompt intervention. If desensitisation is planned, patients should be reassured about the necessity of the procedure, which would improve their understanding and cooperation. Effective communication with a patient and a pharmacist helps to open up their feelings, build patient confidence in the treatment, and reassure them about the safety of the treatment (Griffin et al., 2023). Overall, patient counselling contributes to early detection, improved adherence, reduced anxiety and better clinical outcomes in patients receiving taxane-based chemotherapy.

7. CONCLUSION

In oncology practices, taxane-induced hypersensitivity reactions remain a significant clinical challenge. Even though premedication strategies are in place, these reactions are still occurring, which could impact the taxane therapy. The management of hypersensitivity reactions mainly comprises standardised premedication administration, early detection of signs and symptoms, followed by appropriate clinical intervention and desensitisation protocols, which allow patients with prior reactions to safely readminister the taxane therapy without compromising treatment outcomes. The role of the clinical pharmacist is highly recommended in this field. From identifying patient-specific characteristics, providing appropriate premedication strategies, early detection of adverse reactions, its reporting and monitoring, to implementing the effective treatment strategies. So that a balance between patient safety and optimum therapeutic outcome can be ensured. Hence, a healthcare team, along with the clinical pharmacist, is the need of the hour.

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Conflict of Interest

None declared.

Ethical Statement

In accordance with international or university standards, written ethical approval has been obtained and retained by the author(s).

Declaration of Generative AI

No artificial intelligence (AI) tools were used in the preparation of this manuscript

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