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Long-Term Safety of JAK Inhibitors in Dermatology: A Literature Review of 2020-2025

Marcela Słomianny
ORCID: https://orcid.org/0009-0004-8029-1422
slomiannymarcela@gmail.com
Górnośląskie Centrum Medyczne im. prof. Leszka Gieca Śląskiego Uniwersytetu Medycznego w Katowicach
ul. Ziołowa 45-47, 40-635 Katowice

Michał Czechowski
ORCID: https://orcid.org/0009-0009-7038-6731
michat.czechowski@gmail.com
Medical University of Silesia
Poniatowskiego 15, 40-055 Katowice, Poland

Gabriela Sikora
ORCID: https://orcid.org/0009-0002-4627-7403
gabriela.sikora1029@gmail.com
Medical University of Lublin
Aleje Racławickie 1, 20-059 Lublin, Poland

Karolina Kutnik
ORCID: https://orcid.org/0009-0008-2250-1232
karolinakutnik98@gmail.com
Medical University of Lublin
Aleje Racławickie 1, 20-059 Lublin, Poland

Karolina Kolada
ORCID: https://orcid.org/0009-0005-4960-9604
karolinakolada2001@gmail.com
Medical University of Lublin
Aleje Racławickie 1, 20-059 Lublin, Poland

Katarzyna Gunia
ORCID: https://orcid.org/0009-0003-0111-5758
katarzyna.gunia2000@gmail.com
Samodzielny Publiczny Zakład Opieki Zdrowotnej MSWiA im. Sierżanta Grzegorza Załogi w Katowicach
Wita Stwosza 39/41, 40-042 Katowice

Filip Dudek
ORCID: https://orcid.org/0009-0004-1810-7452
fdudek11@outlook.com
Medical University of Lublin
Aleje Racławickie 1, 20-059 Lublin, Poland

Dominik Lese
ORCID: https://orcid.org/0009-0009-8944-1059
dominiklese@gmail.com
University of Silesia in Katowice
Bankowa 12, 40-007 Katowice

Corresponging Author

Marcela Słomianny, e-mail slomiannymarcela@gmail.com

ABSTRACT

Background. In recent years, Janus kinase (JAK) inhibitors have become an important therapeutic option in dermatology. Agents such as abrocitinib, upadacitinib, baricitinib, deucravacitinib, and ruxolitinib have significantly changed the management of chronic inflammatory skin diseases, including atopic dermatitis, alopecia areata, psoriasis, and vitiligo. By targeting specific signalling pathways within the JAK–STAT axis, these drugs provide rapid and targeted immunomodulation, offering an alternative to traditional systemic therapies and biologics. However, their long-term safety remains a concern, particularly regarding infections, laboratory abnormalities, dermatologic adverse effects, malignancies, and thromboembolic events.

Aim. To summarize the current evidence on the safety profile of JAK inhibitors used in dermatology focusing on data published after 2020.

Material and methods. A literature search was conducted in PubMed, Scopus, Frontiers and Cochrane Library databases for studies published between January 2020 and December 2025.

Results. JAK inhibitors are effective and generally well tolerated when prescribed with appropriate patient selection and monitoring. The most frequently reported adverse events included infections, laboratory abnormalities, and mild dermatologic reactions, while serious complications such as malignancies or thromboembolic events were uncommon.

Conclusion. Evidence from 2020–2025 indicates that JAK inhibitors are effective and generally safe in dermatology. Continued patient monitoring, individualized risk assessment, and further long term studies are necessary to fully characterize their safety profile.

Keywords: JAK inhibitors, dermatology, adverse events, safety profile, laboratory abnormalities, targeted therapy, long-term

1. Introduction

Janus kinase (JAK) inhibitors are a biologically distinct class of small-molecule therapies that modulate intracellular signaling pathways involved in immune-mediated diseases. These agents inhibit JAK family enzymes (JAK1, JAK2, JAK3, and TYK2), thereby blocking phosphorylation of signal transducers and activators of transcription (STATs) and downstream signaling of pro inflammatory cytokines such as interferon-γ, interleukins (IL-4, IL-13, IL-22),

and other mediators implicated in chronic cutaneous inflammation (Samuel et al., 2023). This mechanism enables broad suppression of pathologic immune responses central to several dermatologic conditions.

In dermatology, JAK inhibitors have been approved for the treatment of multiple chronic inflammatory diseases, including atopic dermatitis (AD), alopecia areata (AA), psoriasis, vitiligo,and cutaneous lupus erythematosus. Agents such as abrocitinib and upadacitinib (selective JAK1 inhibitors), baricitinib (JAK1/2), deucravacitinib (TYK2), and topical ruxolitinib have demonstrated high efficacy in both randomized clinical trials and real-world studies, leading to their widespread adoption in clinical practice (Samuel et al., 2023; Corbella-Bagot et al., 2023).

The rapid onset of action and mechanistic versatility of JAK inhibitors allows for targeting Th1,Th2, and Th17/Th22 pathways concurrently, offering advantages in complex inflammatory networks observed in dermatologic diseases (Samuel et al., 2023). Despite these clinical benefits, the immunomodulatory nature of JAK inhibitors has raised concerns regarding long-term safety, particularly with respect to infectious complications, laboratory abnormalities, and other systemic and cutaneous adverse events. Systematic reviews and meta-analyses have identified an elevated risk of infections, including viral reactivation (e.g., herpes simplex virus and varicella-zoster virus), compared with placebo in randomized trials, while serious and opportunistic infections remain infrequent (Isufi et al., 2024; Mansilla-Polo & Morgado-Carrasco, 2024).

Real-world registry data further suggest that rates of overall and herpesvirus infections are higher in patients with AD treated with JAK inhibitors than in those receiving biologics such as dupilumab, emphasizing the importance of patient-specific risk assessment (Corbella-Bagot et al., 2023).

Consequently, recent guidelines highlight the importance of careful monitoring and risk mitigation strategies, including vaccination against herpes zoster prior to therapy initiation in immunocompromised dermatologic patients (Samuel et al., 2023).

Accordingly, this review summarizes recent evidence (2020–2025) on adverse events observed in clinical trials and real-world studies involving patients treated with JAK inhibitors for dermatologic indications. It emphasizes both common and uncommon safety outcomes, including cutaneous, laboratory, and infectious adverse events, to inform clinical monitoring and optimize treatment outcomes in dermatologic populations.

2.Methodology

A literature search was conducted in PubMed, Scopus, and Cochrane Library databases for studies published between January 2020 and December 2025. Search terms included: “JAK inhibitors”,“dermatology”, “safety”, “adverse events”, and “long-term”. Eligible publications included randomized controlled trials (RCTs), long-term extension studies, systematic reviews, meta analyses, and real-world data analyses. Studies related to non-dermatologic indications (e.g.,rheumatoid arthritis, ulcerative colitis) or published before 2020 were excluded. Data were synthesized narratively, focusing on dermatologic populations.

3. Literature review

3.1. Infections

The most common adverse events associated with JAK inhibitors in dermatology are upper respiratory tract infections (URIs) and Varicella zoster virus (VZV) reactivation. URIs, nasopharyngitis, and mild viral infections have been reported in 6–15% of patients receiving abrocitinib or upadacitinib (Samuel et al., 2023; Isufi et al., 2024).

Herpesvirus reactivation, particularly VZV, is a notable concern. Systematic reviews and meta-analyses demonstrate that oral JAK inhibitors are associated with a significantly increased risk of herpes zoster compared with placebo, while serious infections and opportunistic infections do not appear to be significantly elevated in placebo-controlled randomized trials (Ireland et al., 2024; Isufi et al., 2024; Yoon et al., 2023). Real-world registry data further indicate that rates of overall and herpesvirus infections are higher in patients with atopic dermatitis treated with JAK inhibitors than those receiving biologics such as dupilumab (van der Gang et al., 2025) The risk appears to be dose dependent and increases with longer treatment duration, particularly for upadacitinib (Samuel et al., 2023; Isufi et al., 2024). Patient-specific factors, including older age, comorbidities, and prior viral exposure, also influence infection risk.

Most infections are mild to moderate, although rare serious infections have been reported.

Observational studies suggest that the risk of herpes zoster may be higher with JAK inhibitors than with biologics such as dupilumab (Isufi et al., 2024).

Given the increased risk of herpes zoster reactivation in dermatology patients receiving systemic immunomodulatory therapy, prophylactic vaccination with the recombinant zoster vaccine (RZV,e.g., Shingrix®) is recommended for adults at increased risk, ideally

administered before the initiation of JAK inhibitor therapy to optimize protection (Guenther, 2023). Live vaccines should generally be avoided during JAK inhibitor therapy, and the use of inactivated vaccines is preferred.

Vaccination and other preventive strategies, such as monitoring for early signs of infection and patient education, are key to minimizing infectious complications and enabling safe long-term use of JAK inhibitors in dermatologic practice (Guenther, 2023; Samuel et al., 2023; Isufi et al., 2024).

3.2. Malignancies

Concerns about malignancy risk with Janus kinase (JAK) inhibitors initially arose from rheumatology data, particularly with tofacitinib, which reported slightly increased incidences of lymphoma and lung cancer (Ytterberg et al., 2022). However, the overall clinical picture in dermatologic populations appears more nuanced. Meta-analyses incorporating randomized clinical trials and long-term extensions have shown no statistically significant increase in overall malignancy incidence for patients treated with JAK inhibitors compared with placebo or methotrexate, although comparisons with TNF inhibitors suggested a relative increase that requires further investigation (Russell et al.,2023).

Additionally, long-term literature reviews indicate that the incidence rates of malignancy (excluding non-melanoma skin cancer) with oral JAK inhibitors are comparable to those observed with other broader immunomodulators, supporting a generally favorable long-term safety profile in dermatologic practice (Lamberg et al., 2024).

Rare cases of non-melanoma skin cancers (NMSC) and other solid tumors have been reported during treatment with Janus kinase (JAK) inhibitors in long-term clinical trials and real-world observational studies. However, current dermatology-specific evidence does not demonstrate a consistent increase in overall malignancy risk compared with other systemic therapies used for inflammatory skin diseases.

Available data suggest that reported malignancies are more likely related to patient-specific factors, including advanced age, prior history of cancer, cumulative immunosuppressive exposure, and coexisting comorbidities. Continuous post-marketing surveillance is therefore recommended, particularly in patients with pre-existing cancer risk. Clinicians should balance therapeutic benefits with potential oncologic risks and adhere to standard cancer screening protocols. (Samuel et al., 2023; Yoon et al., 2023).

3.3. Cardiovascular and Thromboembolic Events

Although concerns about major adverse cardiovascular events (MACE) and venous thromboembolism (VTE) associated with Janus kinase (JAK) inhibitors initially arose from rheumatology studies, current dermatology-focused evidence does not demonstrate a consistent increase in these events (Ingrassia et al., 2023; Samuel et al., 2023). Meta-analyses of randomized clinical trials involving patients with inflammatory skin diseases indicate no significant increase in MACE, VTE, or all-cause mortality compared with placebo or active comparators (Ingrassia et al., 2023; Yoon et al., 2023).

Short- and medium-term studies in atopic dermatitis, alopecia areata, psoriasis, and vitiligo populations report low absolute incidence rates of cardiovascular and thromboembolic events, comparable to control groups (Ingrassia et al., 2023; Samuel et al., 2023). Patients with pre-existing cardiovascular risk factors — including advanced age, smoking, dyslipidemia, obesity, diabetes, or prior thromboembolic events — may be at higher risk and therefore require closer clinical monitoring.

Mechanistic and pharmacologic studies suggest that JAK inhibitors may influence platelet activity,lipid metabolism, and inflammatory pathways involved in cardiovascular homeostasis; however, these effects have not translated into a clinically significant increase in cardiovascular risk in dermatology populations to date (Zhang et al., 2023). The lower incidence of cardiovascular events observed in dermatologic cohorts, which are generally younger and have fewer comorbidities than rheumatology populations, may partly explain these differences (Ingrassia et al., 2023).

Clinical recommendations emphasize baseline cardiovascular risk assessment, patient education regarding symptom recognition, and periodic monitoring of blood pressure and lipid profiles during treatment (Samuel et al., 2023). Overall, available evidence suggests that JAK inhibitors used in dermatology are associated with a low short- to medium-term cardiovascular and thromboembolic risk, although long-term safety data remain limited and continued surveillance is warranted.

3.4. Laboratory Abnormalities

Laboratory abnormalities are a well-documented but generally mild and reversible adverse effect of Janus kinase (JAK) inhibitors in dermatology. Common findings include elevated lipid levels (total cholesterol, LDL, HDL), transient lymphopenia, mild increases in hepatic transaminases, and occasional elevations in creatine phosphokinase (CPK) observed across

phase 2 and 3 trials (Samuel et al., 2023; Kirchhof., 2024). These changes are usually asymptomatic and rarely require treatment discontinuation.

Oral JAK inhibitors such as abrocitinib, upadacitinib, and baricitinib have consistently shown increases in lipid profiles early after therapy initiation, with these changes stabilizing over time but warranting careful surveillance, especially in patients with underlying cardiovascular risk factors (Paolino et al., 2025; Isufi et al., 2025). A systematic review and meta-analysis of randomized clinical trials demonstrated that oral JAK inhibitors are associated with increases in high-density and low-density lipoprotein cholesterol across multiple indications, including atopic dermatitis and psoriasis, highlighting the need for routine lipid monitoring (Paolino et al., 2025; Isufi et al., 2025).

Dermatology-specific consensus recommendations advise baseline laboratory assessments followed by repeat evaluations approximately 4–12 weeks after treatment initiation, including complete blood count (CBC), lipid panel, liver enzymes, and CPK measurements, and periodic monitoring thereafter to detect clinically meaningful abnormalities (Kirchhof et al, 2024). Follow-up lipid and liver enzyme assessments are crucial for identifying metabolic changes that may benefit from lifestyle modifications or pharmacologic interventions, such as statin therapy (Kirchhof et al, 2024).

Transient lymphopenia, neutropenia, mild transaminase elevations, and occasional CPK increases have been observed but are usually reversible and rarely necessitate therapy modification (Samuel et al., 2023). Phase 3 trials in atopic dermatitis populations have reported dose-dependent decreases in platelet counts with abrocitinib and variable lymphocyte/neutrophil changes with other JAK inhibitors, often normalizing with continued therapy (Samuel et al., 2023). Mild CPK elevations were also noted in a minority of patients, often without clinical sequelae (Samuel et al., 2023).

Ongoing laboratory surveillance every 3–6 months remains a practical approach to detect clinically significant abnormalities early and guide management decisions, particularly in patients with baseline metabolic or hematologic risk factors (Kirchhof et al., 2024; Samuel et al., 2023).

In summary, laboratory abnormalities associated with JAK inhibitors in dermatologic practice are typically mild and manageable, but regular monitoring is essential to optimize safety and inform personalized treatment strategies (Samuel et al., 2023).

Table 1. Recommended Laboratory Monitoring for Patients on JAK Inhibitors in Dermatology

Laboratory parameter	Baseline	4–12 weeks after initiation	Ongoing monitoring	Rationale / clinical considerations
Complete blood count (CBC) with differential	✓	✓	Every 3–6 months	Detection of transient lymphopenia, neutropenia, anemia, and platelet count changes; abnormalities are usually mild and reversible
Platelet count	✓	✓	Every 3–6 months	Dose-dependent platelet decreases reported, particularly with abrocitinib; typically normalize with continued therapy
Lipid profile (total cholesterol, LDL, HDL)	✓	✓	Every 3–6 months	Early increases commonly observed after treatment initiation; levels generally stabilize but warrant monitoring, especially in patients with cardiovascular risk factors
Liver enzymes (ALT, AST)	✓	✓	Every 3–6 months	Mild and transient transaminase elevations reported; persistent abnormalities may require further evaluation
Creatine phosphokinase (CPK)	✓	✓	Periodically or if clinically indicated	Occasional asymptomatic elevations reported; rarely associated with clinical consequences

*Laboratory abnormalities associated with JAK inhibitors are typically mild, asymptomatic, and reversible; routine monitoring allows early identification of clinically relevant changes and supports safe long-term therapy.

3.5. Dermatologic Adverse Effects

Cutaneous adverse effects are among the most frequently reported non-serious side effects of Janus kinase (JAK) inhibitors in dermatology. A systematic review and meta-analysis of phase 2 and 3 randomized clinical trials found that acne incidence is significantly increased in patients treated with JAK inhibitors compared with controls, with pooled odds ratios elevated across abrocitinib, baricitinib, upadacitinib, deucravacitinib, and deuruxolitinib; this effect was particularly notable for JAK1-selective agents (OR 4.69) and the overall dermatologic cohort (OR 4.67) (Martinez et al.,2023).

In patients with atopic dermatitis (AD), evidence from randomized clinical trials and systematic reviews indicates an increased risk of incident acne associated with JAK inhibitor therapy, particularly with higher-dose abrocitinib (200 mg) and upadacitinib at both approved doses (15 mg and 30 mg), when compared with placebo or biologic comparators such as dupilumab. In contrast, the association appears less consistent with lower doses of abrocitinib and with baricitinib, with lower and more variable acne incidence reported across studies (Martinez et al., 2023; Kim et al.,2025).

Real-world observational data and systematic reviews consistently demonstrate that acne and viral skin infections, particularly herpes simplex virus (HSV) and herpes zoster, are among the most frequently reported cutaneous adverse events in patients treated with oral JAK inhibitors. A systematic review and meta-analysis of real-world studies in atopic dermatitis identified acne as one of the most common dermatologic adverse events across abrocitinib, baricitinib, and upadacitinib, with incidence varying by agent and dose but consistently higher than in comparator therapies (Kim et al., 2025).

These cutaneous adverse events typically occur early after treatment initiation and are predominantly mild to moderate in severity, rarely resulting in permanent treatment discontinuation.

Pooled real-world evidence further confirms that acne and viral skin infections represent reproducible safety signals across observational cohorts, mirroring findings from randomize clinical trials (Kim et al., 2025; Rønnstad et al., 2025). Smaller retrospective studies support these observations, reporting manageable acneiform eruptions and occasional HSV reactivation without the need for routine dose modification or therapy interruption (Watanabe et al., 2024).

The underlying mechanisms of JAK inhibitor-associated acne and viral cutaneous reactions are thought to involve altered cytokine signaling and local immune modulation, consistent with broader evidence of immune-mediated adverse events observed across systemic JAK inhibitor use (Konzett et al., 2025; Martinez et al., 2023).

Additionally, systemic JAK inhibitor therapy has been associated with a broader spectrum of cutaneous adverse events beyond acneiform eruptions and viral infections. Review-based safety analyses relevant to daily dermatologic practice report non-infectious skin reactions and drug eruptions in patients treated with JAK inhibitors, reflecting heterogeneous cutaneous responses to immune modulation (Khokhar et al., 2025).

Inflammatory changes involving hair follicles, such as folliculitis and mild scalp irritation, have also been reported as cutaneous adverse events associated with JAK inhibitor therapy, particularly in real-world and observational settings. In patients treated with systemic or topical JAK inhibitors for alopecia areata, folliculitis and irritation of the scalp skin were noted among dermatologic adverse events and were generally mild and manageable without treatment discontinuation (Sechi et al., 2023; Papierzewska et al., 2023). Broader safety reviews of JAK inhibitors in atopic dermatitis and other dermatologic conditions additionally report nonspecific inflammatory skin reactions, including eczema herpeticum, underscoring the diversity of cutaneous responses linked to JAK inhibition (Chang, 2021; Samuel et al., 2023).

Overall, these observations indicate that while acne and viral infections remain the most frequently

reported cutaneous adverse events, dermatologists should also monitor for other skin changes, including eczema-like eruptions, folliculitis, and scalp irritation, which are typically mild to moderate and rarely necessitate treatment discontinuation. Careful clinical monitoring allows for early identification and management of these reactions to optimize treatment outcomes and maintain patient safety.

Table 2. Cutaneous Adverse Effects of JAK Inhibitors in Dermatology

Cutaneous Adverse Effect	Frequency / Incidence	Severity	Clinical Notes / Management	References
Acneiform eruptions	Common; up to 21% in AD patients	Mild to moderate	Usually manageable with topical therapies; rarely requires dose adjustment	Martinez et al., 2023; Kim et al., 2025; Watanabe et al., 2024
Viral skin infections (HSV, VZV)	Frequent; higher than placebo;	Mild to moderate;	Monitor for signs of reactivation; consider	Kim et al., 2025; Samuel et al., 2023; Guenther, 2023

	VZV risk dose-dependent	rare serious cases	vaccination against VZV prior to therapy	
Folliculitis / hair follicle inflammation	Occasional	Mild	Usually resolves without treatment discontinuation; maintain scalp hygiene	Sechi et al., 2023; Papierzewska et al., 2023
Mild scalp irritation	Occasional	Mild	Symptomatic care; rarely necessitates therapy modification	Sechi et al., 2023; Papierzewska et al., 2023
Eczema-like / nonspecific inflammatory eruptions	Occasional	Mild to moderate	Monitor; symptomatic management; usually does not require discontinuation	Chang, 2021; Samuel et al., 2023
Drug eruptions / non-infectious skin reactions	Rare	Mild to moderate	Evaluate for severity; discontinue therapy if severe	Khokhar et al., 2025
Eczema herpeticum	Rare	Mild to moderate	Early recognition; antiviral therapy if needed	Samuel et al., 2023

4. Discussion

The present review summarizes recent evidence on the safety profile of Janus kinase (JAK) inhibitors in dermatology, highlighting both common and less frequent adverse events observed in clinical trials and real-world studies between 2020 and 2025. Across multiple indications, including atopic dermatitis, alopecia areata, psoriasis, and vitiligo, infections remain the most frequently reported systemic adverse events. Upper respiratory tract infections and herpesvirus reactivation, particularly varicella-zoster virus (VZV), were consistently observed, with incidence rates varying by agent and dose (Samuel et al., 2023; Isufi et al., 2024; van der Gang et al., 2025). Systematic reviews and meta-analyses indicate that while JAK inhibitors increase the risk of herpes zoster compared with placebo, serious infections and opportunistic infections

remain relatively infrequent in dermatologic populations (Ireland et al., 2024; Yoon et al., 2023). Real-world registry data further highlight higher rates of viral infections in patients receiving JAK inhibitors than in those treated with biologics such as dupilumab, underscoring the importance of individualized patient assessment and preventive strategies, including vaccination against VZV prior to therapy initiation (Guenther, 2023; Samuel et al., 2023).

Laboratory abnormalities associated with JAK inhibitors are typically mild and reversible, most commonly involving transient lymphopenia, mild transaminase elevations, elevated lipid profiles, and occasional increases in creatine phosphokinase (CPK) (Samuel et al., 2023; Kirchhof, 2024; Paolino et al., 2025). These findings emphasize the importance of routine laboratory monitoring, particularly in patients with baseline metabolic or hematologic risk factors, to enable early detection and management of clinically significant changes (Isufi et al., 2025; Kirchhof et al., 2024).

Cutaneous adverse events, including acne, viral skin infections, eczema-like eruptions, folliculitis, and mild scalp irritation, are among the most frequently reported dermatologic side effects of JAK inhibitors. Acne and viral infections typically occur early in therapy and are mild to moderate, rarely necessitating treatment discontinuation (Martinez et al., 2023; Kim et al., 2025; Watanabe et al., 2024). In patients treated for alopecia areata, folliculitis and scalp irritation were reported but generally remained manageable without therapy interruption (Sechi et al., 2023; Papierzewska et al., 2023). The underlying mechanisms for cutaneous adverse events likely involve altered cytokine signaling and local immune modulation (Konzett et al., 2025; Martinez et al., 2023). Additionally, non-infectious skin reactions and drug eruptions have been reported, reflecting heterogeneous cutaneous responses to immune modulation in dermatologic populations (Khokhar et al., 2025). These findings suggest that clinicians should maintain vigilance for a spectrum of cutaneous adverse events beyond acne and viral infections, even when therapy is generally well tolerated.

Long-term safety concerns, such as malignancy and cardiovascular or thromboembolic events, appear less pronounced in dermatologic populations compared with rheumatology cohorts. Available evidence indicates that the incidence of malignancy is comparable to other immunomodulatory therapies, with patient-specific factors, including age and prior immunosuppressive exposure, being more influential than drug-related effects (Russell et al., 2023; Lamberg et al., 2024; Samuel et al., 2023). Similarly, major adverse cardiovascular events and venous thromboembolism are infrequent in dermatology patients receiving JAK inhibitors, although ongoing surveillance is recommended, particularly in individuals with pre-existing cardiovascular risk factors (Ingrassia et al., 2023; Zhang et al., 2023).

Overall, the reviewed literature supports the conclusion that, with careful patient selection, appropriate monitoring, and preventive measures, JAK inhibitors can be used safely in dermatologic practice. Real-world and trial-based data reinforce the reproducibility of observed safety signals and underscore the importance of proactive management strategies to mitigate adverse events.

5. Conclusion

Janus kinase inhibitors have transformed the management of chronic inflammatory skin diseases by providing rapid, targeted immunomodulation with high efficacy across multiple dermatologic indications. Evidence from 2020 to 2025 indicates that these agents are generally well tolerated, with infections, laboratory abnormalities, and mild cutaneous reactions representing the most common adverse events (Samuel et al., 2023; Martinez et al., 2023; Kim et al., 2025). Serious complications, including malignancies, cardiovascular events, and opportunistic infections, remain uncommon in dermatologic populations, although ongoing long-term surveillance is warranted, particularly for patients with predisposing risk factors (Russell et al., 2023; Ingrassia et al., 2023).

Preventive strategies, including vaccination against herpes zoster and routine laboratory monitoring, enhance patient safety and optimize outcomes (Guenther, 2023; Kirchhof et al., 2024). Clinicians should remain vigilant for a broader spectrum of cutaneous adverse events, including eczema-like eruptions, folliculitis, and scalp irritation, and provide individualized monitoring and management.

Overall, current evidence supports the safe and effective use of JAK inhibitors in dermatology when guided by careful patient assessment, clinical monitoring, and risk mitigation strategies.

Disclossure

Author Contributions:

Conceptualization: Marcela Słomianny, Michał Czechowski, Gabriela Sikora, Filip Dudek, Karolina Kutnik, Dominik Lese;

Methodology: Marcela Słomianny, Karolina Kolada, Katarzyna Gunia, , Karolina Kutnik, Gabriela Sikora;

Formal analysis: Dominik Lese, Michał Czechowski, Filip Dudek;

Investigation: Marcela Słomianny, Gabriela Sikora, Karolina Kolada, Karolina Kutnik, Katarzyna Gunia, Michał Czechowski, Filip Dudek, Dominik Lese;

Resources: Marcela Słomianny;

Data curation: Gabriela Sikora, Marcela Słomianny, Michał Czechowski, Karolina Kolada, Karolina Kutnik, Katarzyna Gunia;

Writing-rough preparation: Marcela Słomianny, Gabriela Sikora, Karolina Kolada, Karolina Kutnik, Katarzyna Gunia, Michał Czechowski, Filip Dudek, Dominik Lese;

Writing-review and editing: Karolina Kolada, Karolina Kutnik, Katarzyna Gunia;

Visualization: Michał Czechowski, Filip Dudek, Dominik Lese;

Supervision: Gabriela Sikora, Filip Dudek, Katarzyna Gunia, Karolina Kolada, Dominik Lase, Filip Dudek;

Project administration: Marcela Słomianny

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