

# Health Technology Briefing

## January 2025

### Ruxolitinib cream for treating prurigo nodularis

Company/Developer Incyte Corporation

☐ New Active Substance

☒ Significant Licence Extension (SLE)

NIHRIO ID: 37174

NICE TSID: Not available

UKPS ID: Not available

### Licensing and Market Availability Plans

Currently in phase III clinical trials

### Summary

Ruxolitinib cream is in clinical development for the treatment of prurigo nodularis (PN). PN is a chronic skin disorder in which people have firm, raised bumps on the skin known as nodules. These nodules are very itchy and scratching the affected skin can cause the condition to worsen. The exact cause of PN is currently unknown but it is believed that altered function of the immune system and nerves in the skin are associated with itching, which results in the formation of nodules. PN is associated with psychological distress, impaired sleep, and poor quality of life. Current treatments for PN have varied effectiveness and can cause side effects with both short and long-term use. Due to this, there is a need to develop additional treatment options for these patients.

Ruxolitinib works by blocking two enzymes in the body which are called Janus kinases (JAK). Two of these specific enzymes (JAK1 and JAK2) are known to be involved in pathways that contribute to impairment of skin barrier function, inflammation, and itching within conditions such as PN. Therefore, inhibiting these enzymes can reduce symptoms associated with the disorder. Ruxolitinib cream is administered directly to the skin to the affected area twice daily. If licensed, ruxolitinib cream would offer an additional treatment for adult patients with PN.

## Proposed Indication

Treatment of adults with prurigo nodularis (PN).<sup>1</sup>

## Technology

### Description

Ruxolitinib cream (opzelura) is a topical therapy that works by specifically blocking Janus Kinase (JAK)1 and JAK2, two enzymes that are involved in several cytokine pathways that contribute to inflammation in the skin, itch, and disruption of skin barrier function.<sup>2</sup> JAK inhibitors (JAKis) are a family of tyrosine kinase inhibitors that block downstream signalling and production of signal transducer and activator of transcription (STAT) proteins, leading to a reduction in interleukin (IL)-1b, IL-6, IL-17, IL-23, interferons, and tumour necrosis factor- $\alpha$ . JAKis also inhibit the type 2 cytokines, including IL-4, IL-13, and IL-31. Reduced signalling in this pathway leads to a reduction of inflammation and itch associated with PN.<sup>3</sup>

Ruxolitinib cream is currently in phase III clinical development for the treatment of adults with PN. In the phase III clinical trials (TRuE-PN1, NCT05755438; TRuE-PN2, NCT05764161), participants applied ruxolitinib 1.5% cream twice daily to the affected areas as a thin film for 12 weeks, followed by a 40-week open label extension period where participants applied ruxolitinib 1.5% cream twice daily.<sup>1,4</sup>

### Key Innovation

PN remains a difficult condition to treat because there are currently no targeted treatments approved. The overall goal in treating PN is to break the itch-scratch cycle and reduce pruritus to heal nodules.<sup>5</sup> Because the pathogenesis of PN is not fully understood, the therapies available for PN have had limited success in reducing itch and nodule formation.<sup>6</sup> People with PN consider the presence of itch as the most burdensome aspect of the disease.<sup>7</sup> Multiple topical agents are employed but often are ineffective, leading to trial of systemic or immunosuppressive therapies that also have variable effectiveness but come with potentially severe, toxic side effects.<sup>8</sup>

JAKis such as ruxolitinib have strengths that include rapid therapeutic effects, convenient administration, and dosage flexibility. In particular, JAKis seem to provide considerable itch reduction in various dermatological diseases in a relatively short time (generally, a few days) compared with conventional pruritus treatments.<sup>9</sup> If licensed, ruxolitinib cream would offer an alternative topical treatment option for patients with PN.

### Regulatory & Development Status

Ruxolitinib cream currently has Marketing Authorisation in the UK/EU for the treatment of non-segmental vitiligo with facial involvement in adults and adolescents from 12 years of age.<sup>10</sup>

Ruxolitinib cream is also in phase II and/or III clinical development for:<sup>11</sup>

- Atopic dermatitis
- Non-segmental vitiligo with genital involvement
- Cutaneous lichen planus
- Lichen sclerosis
- Hidradenitis suppurativa
- Chronic hand eczema

## Patient Group

### Disease Area and Clinical Need

Prurigo nodularis (PN) is an inflammatory skin condition characterised by intensely pruritic (itchy) nodules on the skin. Patients with PN suffer from an intractable itch-scratch cycle leading to impaired sleep, psychosocial distress and a significant disruption in quality of life.<sup>6</sup> PN can appear on its own or be associated with other skin diseases or underlying medical conditions that affect multiple body systems, such as cancer, diabetes, chronic kidney disease or AIDS. The exact cause of PN is unknown, but altered function of the immune system and nerves in the skin is believed to be associated with heightened sensations of itchiness (pruritus) that leads to frequent scratching.<sup>12</sup> PN can be difficult to treat, taking months or even years to clear and may not resolve completely, often rendering it a chronic condition.<sup>13</sup>

In England, the estimated prevalence of PN is 3.27 per 10,000 population and the estimated incidence is 2.88 per 100,000 patient-years.<sup>14</sup> In England (2023-2024) there were 296 finished consultant episodes (FCE) for PN (ICD-10 code L28.1) leading to 275 finished admission episodes, 236 day cases and 242 FCE bed days.<sup>15</sup>

### Recommended Treatment Options

There is no treatment option recommended by the National Institute for Health and Care Excellence for PN.

Treatment options for PN are aimed at stopping skin itching and include:<sup>16</sup>

- Topical corticosteroids
- Antihistamines
- Emollients
- Immunosuppressants such as oral corticosteroids, ciclosporin, methotrexate, azathioprine

## Clinical Trial Information

|                        |                                                                                                                                                                                                                                                                                                                                                                      |
|------------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <b>Trial</b>           | <b>TRuE-PN1; <a href="#">NCT05755438</a></b> ; A Phase 3, Double-Blind, Randomised, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream in Participants With Prurigo Nodularis<br><b>Phase III</b> – Active, not recruiting<br><b>Location(s)</b> : 7 EU countries, USA, Argentina, Canada and Chile<br><b>Primary completion date</b> : October 2024 |
| <b>Trial Design</b>    | Randomised, parallel assignment, quadruple-blind                                                                                                                                                                                                                                                                                                                     |
| <b>Population</b>      | N=204 (actual); adults with clinical diagnosis of prurigo nodularis for 3 months or longer; aged 18 years to 99 years.                                                                                                                                                                                                                                               |
| <b>Intervention(s)</b> | Ruxolitinib cream 1.5% (topical) twice daily for 12 weeks, followed by a 40-week open label extension period where participants will apply ruxolitinib 1.5% cream twice daily                                                                                                                                                                                        |
| <b>Comparator(s)</b>   | Matched placebo cream                                                                                                                                                                                                                                                                                                                                                |
| <b>Outcome(s)</b>      | Primary outcome measure:                                                                                                                                                                                                                                                                                                                                             |

|                    |                                                                                                                    |
|--------------------|--------------------------------------------------------------------------------------------------------------------|
|                    | Worst-Itch Numeric Rating Scale (WI-NRS) $\geq$ 4-point improvement in WI-NRS score response [Time frame: week 12] |
| Results (efficacy) | -                                                                                                                  |
| Results (safety)   | -                                                                                                                  |

|                    |                                                                                                                                                                                                                                                                                                                                                                                          |
|--------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Trial              | <b>TRuE-PN2</b> ; <a href="#">NCT05764161</a> ; A Phase 3, Double-Blind, Randomised, Vehicle-Controlled, Efficacy and Safety Study of Ruxolitinib Cream in Participants With Prurigo Nodularis<br><b>Phase III</b> – recruiting<br><b>Location(s)</b> : Eight EU countries, USA, Australia, Switzerland, Canada, and Republic of Korea<br><b>Primary completion date</b> : November 2024 |
| Trial Design       | Randomised, parallel assignment, quadruple-blind                                                                                                                                                                                                                                                                                                                                         |
| Population         | N=180 (estimated); adults with clinical diagnosis of prurigo nodularis for 3 months or longer; aged 18 years to 99 years.                                                                                                                                                                                                                                                                |
| Intervention(s)    | Ruxolitinib cream 1.5% (topical) twice daily for 12 weeks, followed by a 40-week open label extension period where participants will apply ruxolitinib 1.5% cream twice daily                                                                                                                                                                                                            |
| Comparator(s)      | Matched placebo cream                                                                                                                                                                                                                                                                                                                                                                    |
| Outcome(s)         | Primary outcome measure:<br>Worst-Itch Numeric Rating Scale (WI-NRS) $\geq$ 4-point improvement in WI-NRS score response [Time frame: week 12]                                                                                                                                                                                                                                           |
| Results (efficacy) | -                                                                                                                                                                                                                                                                                                                                                                                        |
| Results (safety)   | -                                                                                                                                                                                                                                                                                                                                                                                        |

|                 |                                                                                                                                                                                                                                                                           |
|-----------------|---------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Trial           | <b>PRUX</b> ; <a href="#">EudraCT 2019-004739-22</a> ; Efficacy of ruxolitinib cream in Prurigo nodularis patients: A randomised, placebo-controlled pilot study<br><b>Phase II</b> – Completed<br><b>Location</b> : Germany<br><b>Study completion date</b> : March 2021 |
| Trial Design    | Placebo-controlled, randomised, double-blind                                                                                                                                                                                                                              |
| Population      | N=20 (actual); adults and elderly patients with symptomatic prurigo nodularis with active skin manifestations; aged 18 years and older                                                                                                                                    |
| Intervention(s) | Ruxolitinib cream 1.5% (topical)                                                                                                                                                                                                                                          |
| Comparator(s)   | Matched placebo cream                                                                                                                                                                                                                                                     |
| Outcome(s)      | Primary outcome measure:                                                                                                                                                                                                                                                  |

|                    |                                                                                                                                            |
|--------------------|--------------------------------------------------------------------------------------------------------------------------------------------|
|                    | Change in numeric rating scale for itch from baseline to evaluation of secondary end point in placebo versus ruxolitinib-treated patients. |
| Results (efficacy) | -                                                                                                                                          |
| Results (safety)   | -                                                                                                                                          |

### Estimated Cost

The cost of ruxolitinib cream is not yet known.

### Relevant Guidance

#### NICE Guidance

- NICE technology appraisal in development. Nemolizumab for treating prurigo nodularis. TA11566. Expected date of issue to be confirmed.
- NICE technology appraisal guidance. Dupilumab for treating moderate to severe prurigo nodularis. TA955. March 2024.

#### NHS England (Policy/Commissioning) Guidance

- NHS England. 2024 NHS Standard Contract for Specialised Dermatology Services (Adults and Children). A12/S/a
- NHS England. 2013/14 NHS Standard Contract for Specialised Allergy Services (All ages). B09/S/b.

#### Other Guidance

- British Association of Dermatologists. Patient Information Leaflets (PILs): Nodular Prurigo. 2023.<sup>16</sup>
- International Forum for the Study of Itch (IFSI). IFSI guideline on chronic prurigo including prurigo nodularis. December 2020.<sup>17</sup>

### Additional Information

Incyte Corp did not enter information about this technology onto the UK PharmaScan database; the primary source of information for UK horizon scanning organisations on new medicines in development. As a result, the NIHR Innovation Observatory has had to obtain data from other sources. UK PharmaScan is an essential tool to support effective NHS forward planning; allowing more effective decision making and faster uptake of innovative new medicines for patients who could benefit. We urge pharmaceutical companies to use UK PharmaScan so that we can be assured of up-to-date, accurate and comprehensive information on new medicines.

### References

- 1 Clinicaltrials.gov. *A Study to Evaluate the Efficacy and Safety of Ruxolitinib Cream in Participants With Prurigo Nodularis (PN) (TRuE-PN2)*. Trial ID: NCT05764161. 2024. Status: Active, recruiting. Available from: <https://clinicaltrials.gov/study/NCT05764161> [Accessed 19 Nov 2024].

- 2 National Eczema Association. *FAQ - Opzelura (Ruxolitinib) Cream*. 2024. Available from: <https://nationaleczema.org/ruxolitinib-faq/> [Accessed 11 Nov 2024].
- 3 Dagenet CB, Saadi C, Phillips MA, Park S, Tran KA, Kincannon JM, et al. Landscape of prurigo nodularis clinical trials. *JAAD Reviews*. 2024;2:127-36. Available from: <https://doi.org/10.1016/j.jdrv.2024.09.006>.
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