Efficacy and Safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis

Protocol No : **PPP/TCT/01** Version no :01 Date: 25/06/2025

Title: An open-label, balanced, randomized parallel group study to evaluate the efficacy and safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis

Protocol No.	**:**	**PPP/TCT/01**
Version	**:**	**01**
Clinical Study site	**:**	**Department of Dermatology and Clinical Pharmacology & Therapeutics, Nizam's institute of medical sciences, Hyderabad**

Investigator's Declaration

I, the undersigned, have read and understood this protocol and hereby agree to conduct the study in accordance with this protocol and to comply with all the requirements regarding the obligations of investigators and all other pertinent requirements of Ethical guidelines for biomedical research on human participants, ICMR (2017), ICH GCP guidelines, NDCT rules by Central Drugs Standard Control Organization (CDSCO) (2019), 'Good Laboratory Practice (GLP)', WHO guidelines and applicable other regulatory requirements.

I agree to comply with all relevant SOPs required for the conduct of this study. I further agree to ensure that all associates assisting in the conduct of this study are informed regarding their obligations.

_____ _____

Signature **Date**

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_____ _____

Signature **Date**

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Efficacy and Safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis

Protocol No : **PPP/TCT/01** Version no :01 Date: 25/06/2025

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Efficacy and Safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis

Protocol No : **PPP/TCT/01** Version no :01 Date: 25/06/2025

Synopsis

Title	**An open-label, balanced, randomized parallel group study to evaluate the efficacy and safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis**
Objectives	**Primary Objective** • To compare the efficacy of Tofacitinib versus Methotrexate in achieving a ≥75% reduction in Palmoplantar Psoriasis Area and Severity Index (ppPASI-75) at 24 weeks. **Secondary Objectives** • To evaluate the safety profile of Tofacitinib versus Methotrexate (incidence of adverse events). • To compare efficacy of Tofacitinib versus Methotrexate in achieveing Palmoplantar Investigator's Global Assessment (ppIGA) score of 0/1 at the end of 24 weeks • To assess time to initial response (≥50% reduction in ppPASI) between the two groups . • To assess time to achieving ppIGAscore of 0/1 in the two groups • To compare quality of life improvements using the Dermatology Life Quality Index (DLQI) at 12 and 24 weeks between the two groups.
Study Methodology	**Study Design: Interventional, randomized, active-controlled, balanced, parallel group, single centre study.** **Study Duration:** Total duration is 24 months. Treatment duration for each patients is 24 weeks. **No. of Patients:** 50 patients in each arm Patients diagnosed with palmoplantar psoriasis based on clinical picture fulfilling the eligibility criteria will be randomized to either of the treatment arms At baseline: ppPASI, ppIGA, and DLQI score will be assessed along with all other biochemical and pathological investigations and treatment initiated • **Follow-Up Visits**: Weeks 4,8, 12, 24 (assess ppPASI, DLQI, adverse events, labs). • **End of Study (Week 24)**: Final assessment, including ppPASI, DLQI, and safety data. • Treatment will be discontinued if any treatment emergent

	SAEs occur
Study Drugs	• **Group A : Tofacitinib Arm**: Oral Tofacitinib 5 mg twice daily • **Group B : Methotrexate Arm**: Oral Methotrexate 15 mg weekly (with folic acid 5mg once weekly , 24 hours after Methotrexate). • Treatment allocation will be randomly assigned based on block randomization generated using MS Excel.
Efficacy assessments	• Palmoplantar Psoriasis Area and Severity Index (ppPASI) ppPASI is a measure of psoriatic disease severity taking into account qualitative lesion characteristics (erythema, thickness and scaling) and degree of skin surface area involvement on defined anatomical regions. ppPASI scores range from 0 to 72, with higher scores reflecting greater disease severity. Erythema, thickness, and scaling are scored on a scale of 0 (none) to 4 (very severe) in both Palms and Soles. Degree of involvement on each of the Palm and Sole is scored on a scale of 0 (no involvement) to 6 (90% to 100% involvement). The total qualitative score (sum of erythema, thickness, and scaling scores) is multiplied by the degree of involvement for each anatomic region and then multiplied by a constant. These values are summed to yield the PASI score. • Palmoplantar Investigator's Global Assessment (ppIGA) score at 8, 16 and 24 weeks • Dermatology Life Quality Index- Consists of 10 Self administered questions grouped in 6 domains with each question scored on a 4 point Likert scale. The total score ranges from **0 to 30**, with higher scores indicating greater impairment of quality of life. o Symptoms and feelings (Questions 1 and 2) o Daily activities (Questions 3 and 4) o Leisure (Questions 5 and 6) o Work and school (Question 7) o Personal relationships (Questions 8 and 9) o Treatment (Question 10)
Clinical Safety measures	• Safety will be determined by no clinically significant deviation from normal in findings of medical history, physical examination and laboratory tests at 4, 12 and 24 weeks

Outcome Measures	Primary Outcome • Proportion of patients achieving ppPASI-75 at 24 weeks between the two groups. Secondary Outcome • Incidence and severity of adverse events (e.g., hepatotoxicity, infections) between the two groups • Time to ≥50% ppPASI reduction between the two groups • Change in DLQI scores from baseline to weeks 12, and 24 weeks between the two groups. • Proportion of patients with Palmoplantar Investigator's Global Assessment (ppIGA) score of 0/1 in the two groups. • Treatment discontinuation rates due to adverse events between the two groups.
Statistical analysis	• Summary statistics, depending upon the normality of data , within group comparison at different time-points by repeated measures ANOVA or Friedman test, between group comparison by Independent t test or Mann-Whitney U test. Categorical variables will be compared using Chi-square test. Multivariable regression will be used to identify predictors of treatment response

List of Abbreviations and symbols:

%	**Percentage**
ADR	**Adverse Drug Reaction**
AE	**Adverse Event**
ALT	**Alanine Amino Transferase**
ANOVA	**Analysis of Variance**
AST	**Aspartate Amino Transferase**
ADP	**Adenosine Diphosphate**
DLQI	**Dermatology Life Quality Index**
JAK-STAT	**Janus Kinase - Signal Transducer and Activator of Transcription**
PPP	**Palmoplantar Psoriasis**
PsA	**Psoriatic arthritis**
ppPASI	**Palmoplantar Psoriasis Area and Severity Index**
ppIGA	**Palmoplantar Investigator's Global Assessment**
SGOT	**Serum Glutamic Oxaloacetic Transaminase**
SGPT	**Serum Glutamic Pyruvic Transaminase**
TH 17	**T helper 17 cells**
TNF-α	**Tumour Necrosis Factor alpha**
SAE	**Serious Adverse Event**

Efficacy and Safety of Tofacitinib versus Methotrexate for Recalcitrant Palmoplantar Psoriasis

Protocol No : **PPP/TCT/01** Version no :01 Date: 25/06/2025

AIM: To determine Efficacy and safety of Tofacitinib versus Methotrexate for the treatment of patients with Recalcitrant Palmoplantar Psoriasis

1. Background:

Palmoplantar psoriasis (PPP) is a chronic, debilitating form of psoriasis affecting the palms and soles with an incidence of 2% to 40% among individuals with psoriasis and psoriatic arthritis (PsA) [1]. This condition often proves resistant to standard treatments and can persist for many years, leading to notable limitations in movement and dexterity [2]. Research indicates that only 27.4% of PP patients respond favourably to topical treatments, while the majority necessitate systemic interventions [3].

Various factors including smoking, stress and trauma can trigger PP in genetically susceptible individuals leading to excessive cytokine production and keratinocyte proliferation. Inducible IL-23 expression can trigger a TH17 response with local production of TNF-α, IL-17, and IL-22. JAK enzymes transduce signals from these cytokine receptors via the JAK-STAT (Signal Transducer and Activator of Transcription) pathway, promoting inflammation and keratinocyte hyperproliferation[4,5]. Symmetrically distributed erythematous, hyperkeratotic, scaly and at times fissured plaques are the hallmark of PPP. Lesions of psoriasis may be present at other sites in some patients[5]

Patients with PPP often suffer from severe itching, pain and functional impairment resulting in poor self-image and the quality of life is affected. The recalcitrant nature of the disease indicates the need for systemic therapy, however there are no standardized guidelines for treatment due to lack of robust data.[6]

Palmoplantar psoriasis is more challenging to treat compared with Psoriasis of other skin areas. The use of topical therapies, ultraviolet phototherapy, oral retinoids, methotrexate, and anthralin , often results in inadequate treatment results[7]. Newer small molecules and biologics have increased the possibilities of effective treatment. Biologics like Adalimumab, Alafacept, Bimekizumab, Etanercept, Guselkumab, Infliximab, Ixekizumab, Secukinumab, and Ustekinumab are currently approved for the treatment of Palmoplantar psoriasis[8]. However, the high cost of these therapies and need for parenteral administration further exacerbates the burden of an already debilitating condition. In a developing country like India, the use of biologics is often limited by financial constraints.

Methotrexate is one of the oldest and most widely used systemic agents in the treatment of psoriasis. However, palmoplantar psoriasis is often inherently resistant to therapy and tends to respond sub optimally to methotrexate. Methotrexate efficacy in palmoplantar psoriasis ranges from 24-40% in prospective studies conducted in Indian settings[9,10].

This underscores the limited efficacy of methotrexate in treating this challenging variant of psoriasis.

Tofacitinib is a small-molecule Janus kinase (JAK) inhibitor, specifically targeting JAK1 and JAK3 with moderate activity against JAK2 and TYK2 which are involved in the signalling of a variety of cytokines present in psoriasis (IL-23, IL-22 and IFN-gamma). Tofacitinib's systemic action targets this underlying immune dysregulation, potentially offering relief in recalcitrant cases where topical or localized therapies fail. Tofacitinib inhibits expression of interleukin (IL)-17A, IL-17F, IL-22 and IL-23R, all of which have been implicated in the pathogenesis of psoriasis.[11,12] Tofacitinib is FDA approved for Rheumatoid arthritis, Psoriatic arthritis, ulcerative colitis, Ankylosing spondylitis and Polyarticular Course Juvenile Idiopathic Arthritis [13]

A case-series by Mazumdar et al,[14] showed that tofacitinib significantly improved palmoplantar psoriasis in all 7 patients and complete resolution in 4 patients at a dose of 11 mg once daily with a median time of 3 months and no adverse events were reported.

Tofacitinib's efficacy in plaque psoriasis provides indirect support for its use in PPPs, given shared inflammatory pathways (e.g., IL-23/Th17 axis). Two large multicenter phase 3 randomized-controlled trials[15] and a meta-analysis[16] of more than 3,700 patients demonstrated tofacitinib's efficacy for the treatment of moderate to severe plaque type psoriasis. A recent meta-analysis by wang et al[17] reported PASI75 achievement in 39.9–72.7% of plaque psoriasis patients at doses of 5–15 mg twice daily (RR=4.38, 95% CI 2.51–7.64 at 12 weeks). While not specific to PPPs, these findings suggest potential efficacy due to mechanistic overlap.

Tofacitinib can cause upper respiratory tract infection, nasopharyngitis, diarrhea, and headache infection, thrombosis, malignancy and gastrointestinal perforation[13] and as per FDA label, screening for latent tuberculosis, complete blood count, lipid and liver function tests have to be done prior to initiation of Tofacitinib.

This study aims to provide real-world evidence for the role of Tofacitinib in the management of recalcitrant Palmoplantar psoriasis

2. Study Objectives:

Primary Objective

- To compare the efficacy of Tofacitinib versus Methotrexate in achieving a ≥75% reduction in Palmoplantar Psoriasis Area and Severity Index (ppPASI-75) at 24 weeks.

Secondary Objectives

- To evaluate the safety profile of Tofacitinib versus Methotrexate (incidence of adverse events) between the two groups
- To compare efficacy of Tofacitinib versus Methotrexate in achieving Palmoplantar Investigator's Global Assessment (ppIGA) score of 0/1 at the end of 24 weeks.
- To assess time to initial response (≥50% reduction in ppPASI) between the two groups
- To assess time to achieving ppIGA score of 0/1 in the two groups
- To compare quality of life improvements using the Dermatology Life Quality Index (DLQI) at 12 and 24 weeks between the two groups.

3. Methodology:

Study site: Department of Dermatology and Clinical Pharmacology & Therapeutics at Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India.

Study design: Interventional, randomized, active-controlled, balanced, parallel group, single centre study.

Study duration: Total duration is 24 months. Treatment duration for each patients is 24 weeks.

No. of Patients: 50 patients in each arm

Sample size calculation: Assuming a 60% ppPASI-75 response rate with Tofacitinib and 30% with Methotrexate[9-10] , with 80% power and 5% significance level, 44 patients per arm are needed. Adjusted to 50 per arm for dropouts.

Randomization: Simple randomization using MS Excel

Study Interventions

- **Group A : Tofacitinib Arm**: Oral Tofacitinib 5 mg twice daily
- **Group B : Methotrexate Arm**: Oral Methotrexate 15 mg weekly (with folic acid 5 mg weekly, 24 hours after Methotrexate).

Selection of subjects:

All subjects will undergo a screening procedure comprising of clinical examination, and laboratory investigations of blood and urine. The subjects will be selected on the basis of the following eligibility criteria.

No Evidence of teratogenic effect of Tofacitinib following paternal exposure was found in preclinical and human studies. Hence the need for male contraception was not mandatory in the study(17-19)

ELIGIBILITY CRITERIA:

3.1 Inclusion criteria:

- Patients aged 18-70 years of either gender
- Diagnosed with recalcitrant palmoplantar psoriasis (failure of at least two prior topical/systemic therapies (systemic therapy apart from methotrexate and tofacitinib) or have contraindication or intolerant to at least one conventional systemic therapy.
- Palmoplantar Psoriasis Area and Severity Index (ppPASI)[17] score ≥12 at baseline.
- Palmoplantar Investigator's Global Assessment (ppIGA)[18] score of ≥3
- All Patients whose screening Laboratory investigations are within normal limits
- Willing to provide informed consent.
- Male subjects who agree to use barrier method of contraception throughout the study and for at least 3 months after the last dose of tofacitinib
- Women of child bearing potential who have completed their family and/or are surgically sterile (defined as having undergone bilateral oophorectomy, hysterectomy, or bilateral tubal ligation).
- Post menopausal women defined as women who report at least 12 consecutive months of amenorrhea without the use of hormone replacement therapy (HRT).
- Able to adhere to follow-up visits

3.2 Exclusion criteria:

- No Previous History of any prior use of either Tofacitinib or Methotrexate since the diagnosis of Palmoplantar psoriasis
- History of any known hypersensitivity reaction to Tofacitinib or Methotrexate
- History of active tuberculosis (TB) infection within 3 years prior to the screening visit. Infections which occurred > 3 years prior to entry must have been completely treated as per RNTCP criteria

- History of incompletely treated latent (as indicated by a positive PPD [purified protein derivative] skin results) TB infection
- Latent TB infections as indicated by a Positive PPD[purified protein derivative] skin test
- History of clinically significant (as determined by the investigator) cardiac, endocrinologic, pulmonary, neurologic, psychiatric, hepatic, renal, hematologic, immunologic, or other major disease apart from Psoriasis
- History of malignancy within the last 5 years.
- History of disseminated herpes zoster or disseminated herpes simplex, or a recurrent localized, dermatomal herpes zoster
- Pregnant or breastfeeding women.
- Any Contraindications to Tofacitinib or Methotrexate
- History of clinically significant infection within 6 months prior to first dose of study drug
- History of HIV, hepatitis B or hepatitis C infection.

3.3. Outcome measures:

Primary outcomes:

- Proportion of patients achieving ppPASI-75 at 24 weeks between the two groups.

Secondary outcomes:

- Incidence and severity of adverse events (e.g., hepatotoxicity, infections) between the two groups
- Time to ≥50% ppPASI reduction between the two groups
- Change in DLQI scores from baseline to weeks 12, and 24 weeks between the two groups.
- Proportion of patients with Palmoplantar Investigator's Global Assessment (ppIGA) score of 0/1 in the two groups.
- Treatment discontinuation rates due to adverse events between the two groups.

3.4 Study procedure

The study will be initiated after obtaining approval from institutional ethics committee and following ethical principles as laid down in declaration of Helsinki. Patients diagnosed with recalcitrant palmoplantar psoriasis visiting the dermatology outpatient department will be screened for eligibility criteria after obtaining written informed consent. All relevant investigations mentioned in laboratory evaluations as part of screening will be done.

Patients satisfying the eligibility criteria will be randomized in a 1:1 ratio into Group A or Group B. Baseline assessments for disease severity and dermatology quality of life index will be performed

Follow-Up Visits: Weeks 4, 8, 12, 24 after treatment initiation (assess ppPASI, DLQI, adverse events, labs).

End of Study (Week 24): Final assessment, including ppPASI, DLQI, and safety data.

3.5 . Assessment for safety:

Vital signs (Blood pressure, heart rate measurement, respiratory rate and temperature) at baseline and all follow up visits. Laboratory Investigations (apart from serology and Montoux test) as listed in Table 1 will be done on 4, 12 and 24 weeks.

Tolerability will be assessed by any treatment emergent adverse events and if any clinically significant abnormal laboratory values are found at 4, 12 and 24 weeks. At investigator discretion lab values may be done at any time point for safety concern. Adverse events will be managed as per standard treatment guidelines of the Institution.

Table 1: Laboratory evaluations performed during screening are as follows:

<table>
<tr><td colspan="2">Blood tests:</td><td rowspan="2">Urine analysis:</td></tr>
<tr><td>Hematology</td><td>Biochemistry</td></tr>
<tr><td>Hemoglobin
Total RBC Count
Total WBC Count Platelet count
Differential count
Peripheral smear
PT, aPTT, INR BT, CT</td><td>Blood urea
Serum creatinine
Serum uric acid
Lipid profile
<u>Liver Function Tests:</u>
Total Bilirubin
Direct Bilirubin
SGOT (AST)
SGPT (ALT)
Alkaline Phosphatase
Total proteins
Albumin</td><td>Physical Examination
Chemical Examination
Microscopic examination Urine Toxicology
Urine Pregnancy test</td></tr>
<tr><td>Serology:</td><td></td><td>Other investigations:</td></tr>
</table>

HIV (1 & 2) antibodies HBsAg (Hepatitis B surface antigen) Anti-hepatitis C Virus (HCV) VDRL (RPR)		Montoux test

4. Withdrawal criteria:

- Subject wishes to withdraw consent on his own accord in person and the same will be considered as dropout.
- The subject is non-cooperative and non-compliant.
- The subject suffering from any other clinically significant adverse event or any significant laboratory abnormality or Serious adverse events (SAE) [SAE management will be done as per standard treatment guidelines of the institute.]

4.1 The Follow-up for Subjects Withdrawn from Investigational Product Treatment

Any subject withdrawn during the study due to any adverse event will be followed up wherever possible till resolution or until the physician believes that there will be no further change. This may involve additional visits.

Handling and reporting of Adverse Events and Serious Adverse Events:

For Any Adverse drug reaction, adverse Event or unexpected adverse drug reaction and Serious Adverse Event (SAE) the following information has to be recorded in individual Suspected adverse drug reaction reporting form:

- Type of adverse event
- Is it serious or non-serious?
- Date and time of onset
- Date and time of resolution
- Severity (mild, moderate or severe)
- Association with the study medication (remote, possibly related, probably related or definitely related)
- Action taken
- Outcome of adverse event (resolved or unresolved)
- Further details of the AE, if any.

Serious Adverse Event (SAE): A serious adverse event (experience) or reaction is any untoward medical occurrence that at any dose

- Results in death
- Is life-threatening
- Requires inpatient hospitalization or causes prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect
- Requires intervention to prevent permanent impairment or damage

Clinically significant Laboratory anomalies definition

New symptoms indicting methotrexate or tofacitinib intolerance and/or laboratory assay changes indicating intolerance to methotrexate/Tofacitinib

- WBC < 3.0 x 10^3 /uL
- Hematocrit < 32 percent
- Platelet< lower limit of normal
- AST/ALT >1.5 upper limit of normal
- Lymphocyte count less than 500 cells/mm^3
- Creatinine clearance < 40ml/min (as estimated by CKD-EPI 2021 equation)
- **5. <u>Statistical Analysis plan:</u>**
  - Data will be presented as mean ± SD or median (IQR) for continuous variables depending on distribution (assessed using the Shapiro-Wilk test). Categorical variables will be presented as Proportion**.** Within group comparison at different time-points by repeated measures ANOVA or Friedman test depending upon normality . Between group comparison for continuous variable by Independent t test or Mann-Whitney U test depending upon normality. Categorical variables will be compared using Chi-square test. Multivariable regression will be used to identify predictors of treatment response
  - A p value < 0.05 will be considered significant

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Appendix -I

The following time-and-events table illustrates the planned schedule of assessments:

	Screening (‘-28, days to day ‘-0,)	**Study Period**				
		Baseline	**Week 4**	**Week 8**	**Week 12**	**Week 24**
Informed consent	X	-	-	-	-	-
Demography	X	-	-	-	-	-
Blood sample for Hematology	X	-	X	-	X	X
Blood sample for Biochemistry	X	-	X	-	X	X
Mantoux test	X	-	-	-	-	-
Blood sample for serological examination	X	-	-	-	-	-
Urine analysis	X	-	X	-	X	X
Randomization	-	X	-	-	-	-
Palmoplantar Psoriasis Area and Severity Index (ppPASI)	X	X	X	X	X	X
Palmoplantar Investigator's Global Assessment (ppIGA) score	X	X	-	X	X	X
Dermatology Quality of Life Index	X		X	X	X	X
Vital signs measurement[#]	X	X	X	X	X	X
Adverse Events monitoring	-	X	X	X	X	X

Appendix IIa: Palmoplantar Psoriasis Area and Severity Index (ppPASI):

The **ppPASI** is a validated scoring system specifically designed to **quantify the severity of psoriasis localized to the palms and soles**. It is a modification of the Psoriasis Area and Severity Index (PASI) to address the unique challenges of assessing **palmoplantar psoriasis**, where limited body surface area involvement can be associated with significant functional impairment and reduced quality of life.

Parameter	Description	Score Range
Sites Assessed	Palms and soles (each assessed separately)	–
Clinical Signs (each site)	- Erythema (Redness) - Induration (Thickness) - Desquamation (Scaling)	0 = None 1 = Slight 2 = Moderate 3 = Severe 4 = Very severe
Area of Involvement (each site)	Percentage of the palm/sole involved	0 = 0% 1 = <10% 2 = 10–29% 3 = 30–49% 4 = 50–69% 5 = 70–89% 6 = 90–100%
Calculation (each site)	(Erythema + Induration + Scaling) × Area Score	Area score- 0.5 for each palm and sole
Total ppPASI Score	Sum of the scores from palms and soles	0 (no disease) to 72 (maximum severity)

Appendix IIb : Palmoplantar Psoriasis/Pustulosis Physician Global Assessment [PPPGA/PPPPGA] score

The PPPGA rates psoriasis severity on a scale from 0 to 4 based on erythema (redness), scaling, and the presence of pustules and fissures:

- **0 = Clear**: No signs of plaque psoriasis on hands and/or feet.
- **1 = Almost Clear**: Just perceptible erythema and scaling on the hands and/or feet.
- **2 = Mild**: Light-pink erythema with minimal scaling, with or without pustules.
- **3 = Moderate**: Dull-red erythema with diffuse scaling and skin thickening, with or without fissures and pustules.
- **4 = Severe**: Deep or dark-red erythema with pronounced scaling, thickening, and numerous fissures, with or without pustules.

Appendix II C: Dermatology Life Quality Index (DLQI)

The Dermatology Life Quality Index (DLQI) is a validated, dermatology-specific instrument designed to measure the impact of skin diseases on patients' quality of life (QoL). Developed by Finlay and Khan in 1994, it is the most widely used QoL tool in dermatology clinical trials and practice.

The DLQI consists of 10 questions, covering six domains:

Each question is scored:

- 0 = Not at all
- 1 = A little
- 2 = A lot
- 3 = Very much

Q#	Domain	Question
1	Symptoms and Feelings	Over the last week, how itchy, sore, painful or stinging has your skin been?
2	Symptoms and Feelings	Over the last week, how embarrassed or self-conscious have you been because of your skin?
3	Daily Activities	Over the last week, how much has your skin interfered with you going shopping or looking after your home or garden?
4	Daily Activities	Over the last week, how much has your skin influenced the clothes you wear?
5	Leisure	Over the last week, how much has your skin affected any social or leisure activities?
6	Leisure	Over the last week, how much has your skin made it difficult for you to do any sport?
7	Work and School	Over the last week, has your skin prevented you from working or studying?
8	Personal Relationships	Over the last week, how much has your skin created problems with your partner or any of your close friends or relatives?
9	Personal Relationships	Over the last week, how much has your skin caused any sexual difficulties?
10	Treatment	Over the last week, how much of a problem has the treatment for your skin been, for example by making your home messy, or by taking up time?