

MEDICAL IMAGING SERVICES

AbbVie Protocol M16-011

A Phase 3, Randomized, Double-Blind, Study Comparing Risankizumab to Placebo in Subjects with Active Psoriatic Arthritis (PsA) Who Have a History of Inadequate Response to or Intolerance to at Least One Disease Modifying Anti-Rheumatic Drug (DMARD) Therapy

Image Acquisition Guideline

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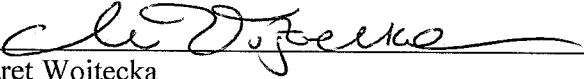
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15 Nov 2018
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Document Revision History

Version	Date	Author	Description
1.0	10-Oct-2018	Farhan Syed	Initial release of the document
2.0	15-Nov-2018	Sherri Ievers	Imaging Schedule and footnotes on page 4 updated to from "Week 54" to "Week 52"

Introduction

PAREXEL Informatics has developed the following acquisition guidelines for standardization of the study imaging components across radiology centers participating in the AbbVie M16-011 clinical trial. Provided here are image acquisition guidelines for the following imaging modalities:

- Bilateral Hands and Feet X-ray

Important Notes

- Regularly scheduled imaging for this study should be acquired in strict adherence to these guidelines.
- Images sent to PAREXEL shall be clear of any marks, writings, measurements or annotations.
- Keep imaging data (including raw/original data) digitally archived until PAREXEL has provided feedback on the quality of the images.
- All confidential site and patient information must be de-identified prior to sending the data to PAREXEL.
- Image data is sent to PAREXEL within 48 hours of acquisition

IMPORTANT: Imaging modality, anatomical coverage and acquisition parameters should remain consistent across all imaging visits for any given study subject.

IMAGING SCHEDULE

IMAGING ANATOMY	IMAGED ANATOMY	IMAGING SCHEDULE*
X-RAY*	Bilateral Hands (PA view) Bilateral Feet (AP View)	Screening/Baseline Week 16** Week 24 Week 52 Week 100 Premature discontinuation***

*X-rays of hands and feet will be performed for all subjects at Screening, Week 24, Week 52, and Week 100.

**All subjects who fail to attain at least a 20% improvement in either or both tender joint count (TJC) and swollen joint count (SJC) at Week 12 and Week 16 will have an additional radiographic examination at Week 16.

*** All subjects will receive radiographs of hands and feet if they discontinue from the study or from study drug at or after Week 12 and if it has been at least 12 weeks from when radiographs were last obtained during Period 1 or at least 24 weeks during Period 2. In such subjects, radiographs should be obtained as close as possible to the date of study drug discontinuation.

- X-rays of hands and feet must be performed during the screening process in compliance with the imaging acquisition guidelines (IAG) and image quality acceptability must be confirmed via central QC by PAREXEL.
- Screening x-rays of hands and feet will serve as baseline x-rays for central Van der Heijde's modified Sharp scoring for PsA.

**** Patient safety in relation to image acquisition is the responsibility of the Investigator sites. ****

**For inquiries regarding these guidelines, please contact:
TEAM 236765
Fax: +1 978 222-8466 Email: 236765-Imaging@PAREXEL.com**

ADDITIONAL NOTES

SENDING IMAGING TO PAREXEL

Electronic Transfer preferred

- For X-rays acquired using digital X-ray instruments only (DR, DX, CR, etc.), not conventional.
- Images shall be raw and uncompressed DICOM
- eTransfer will automatically blind the image header information

Shipment via Courier

- For original hard copy films from conventional radiography instruments OR digitally acquired X-ray when not using eTransfer (preferred)
- Blank Digital Media and all shipping supplies can be provided by PAREXEL
- If using optical disc, submission shall be limited to 2 studies per disc at a maximum (1 patient / study on each disc side)

Hardcopy Film: only for conventional instruments

- Original hard copy films must be sent to PAREXEL. To ensure a back-up copy is available on site, a duplicate original (laser-printed) hard copies films should be obtained.
- All X-rays should be appropriately labelled for the right (R) and left side (L) for all both hands and feet.

Guidelines

- **Keep all parameters constant for subsequent imaging performed during the study.**
- **Keep imaging data (including raw/original data if possible) digitally archived until PAREXEL has provided feedback regarding the quality of the images.**
- **Send ALL images acquired for the study to PAREXEL until instructed otherwise.**
- **Images sent to PAREXEL shall be clear of any marks, writings, measurements or annotations.**
- **All confidential patient information must be de-identified prior to sending the data to PAREXEL.**

Thank you for your participation and cooperation in this clinical study.

Image Acquisition Guidelines for X-Ray Assessments M16-011

PAREXEL has developed the following **Image Acquisition Guidelines (IAGs)** for standardization of the study imaging components across radiology centers participating in the M16-011 clinical trial. This IAG will provide high level requirements for the imaging required in this study. Provided here are IAGs for 1) X-Ray of hands including wrists and 2) X-Ray of feet.

IMAGE RESOLUTION REQUIREMENTS

Digital Images: Images **MUST** be acquired with high resolution. A digital resolution of 100 microns (digital pixel spacing 0.10 x 0.10 mm) is preferred. If your instrument is not capable of 100 micron resolution, then PAREXEL may still be able to qualify your instrument at a different resolution (85 to 175 microns). This will be determined as part of site qualification. Instruments with resolution outside of the 85 to 175 range will be evaluated on a case by case basis with approval from Abbvie. *Please use this optimal digital resolution for which your instrument was qualified for all study imaging during this trial.*

Hardcopy Films: Sites with conventional scanners **MUST** acquire images using **high resolution, single emulsion or mammography grade film** and compatible cassette. Hardcopy films should be 11"x14". In order to ensure compliance for this study, PAREXEL will provide these films and cassettes to all conventional sites. Please be sure to use these specific supplies for all study imaging.

IMAGE TRANSFER METHOD

Digital Images: If images are digitally acquired PAREXEL expects a digital transfer method (i.e. eTransfer is preferred or CD-ROM, DVD) to be used. Digital images cannot be printed on film for submission to PAREXEL. Digital images must be in uncompressed DICOM format or proprietary scanner format.

Hardcopy Films: Original high resolution X-Rays should be provided to PAREXEL on **single emulsion or mammography grade film**. PAREXEL will provide these films and cassettes to all conventional sites. Please be sure to use these specific supplies for all study imaging. Please complete and apply subject labels provided by PAREXEL. Use PAREXEL provided shipping supplies for courier shipment to PAREXEL. Original X-rays should be clearly marked as such and will be returned to the site, per the site's request, as soon as possible following acceptance at PAREXEL.

POSITIONING TEMPLATES

For all M16-011 subject imaging (irrespective of instrument type), please remember to use the PAREXEL positioning templates. Place the correct template (Left or Right accordingly) on the cassette/receptor then position each hand/foot on top of the positioning template aligned with the hand/foot outline. If unable to align the hand to the positioning template as requested please use positioning descriptions to best orient anatomy as described.

HAND X-RAYS (Posterior-Anterior view)

Goal: Consistent, high quality images with good bone detail for assessment of joint space narrowing & erosions

Important Reminders:

- Parameters and positioning used during Baseline imaging for the patient should be kept consistent for all follow up imaging.
- Always use the PAREXEL positioning template.
- Each hand must be imaged one at a time using one film/capture for each extremity.
- Remove jewelry where possible (if not, shift so does not obscure any joint). Please adhere to institutional policies and procedures for shielding.

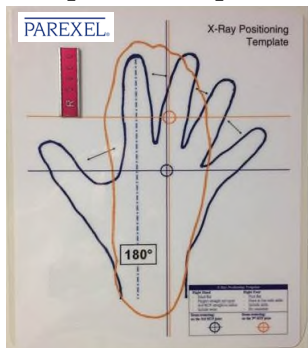


Fig.1. Positioning Template (Right)

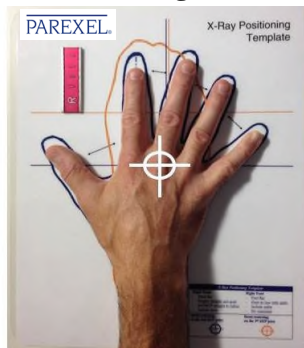


Fig. 2 Good Alignment



Fig. 3 Good Image Quality



Patient Positioning: Patient must be seated next to the imaging table with the **elbow flexed 90 degrees**. The **elbow should be at the same level as the shoulder**.

1. With the correct positioning template (Left or Right accordingly) on the cassette/receptor, position the hand/wrist (palm down) on the template according to the hand outline (Fig. 1).
2. Fingers straightened, if possible, and only slightly separated. Fingers should not be strained far apart.
3. Hand and wrist flat on the template (and cassette/receptor) to avoid joint magnification.
4. **Align 2nd metacarpal in a straight line with the radius (180 degrees, Fig. 2).** Use a sandbag placed across the forearm just above the wrist to avoid motion.

Parameters:

- **Film/Resolution:** Conventional X-ray: **high resolution, single emulsion** film. Digital: optimal and consistent digital resolution (100 micron pixel size preferred). Be consistent with the resolution accepted for your instrument during site qualification.
- **Film Focus Distance (FFD): 40 inches** (102 cm)
- **Beam centering:** on the **3rd MCP joint**, perpendicular to the plane of the film (Fig. 1).
- **Exposure settings:** Suggest 60kVp and 3 mAs. Optimize for sharp bone detail.
- **Collimate** to film.

Anatomical Coverage and Image Quality Control Checks:

- **Ensure inclusion of the entire hand and wrist, including at least 1 inch of forearm.**
- **Ensure optimal visualization of the wrist, MCP, PIP & DIP joints (Fig. 3).**
- **PA view with left/right markers visible and accurate to anatomy.** *Oblique views are not required.*
- **Ensure that follow up visits are consistent with baseline: X-ray instrument, patient positioning, acquisition parameters (mAs, kV, FFD, focal spot, film and cassette type or digital resolution).**
- **Please inform PAREXEL if your methods or results deviate from these guidelines or from those used at Baseline for each patient.**

FOOT X-RAYS (Antero-Posterior view)

Goal: Consistent, high quality images with good bone detail for assessment of joint space narrowing & erosions

Important Reminders:

- **Parameters and positioning used during Baseline imaging for the patient should be kept consistent for all follow up imaging.**
- Always use the PAREXEL positioning template.
- Each foot must be imaged one at a time using one film/capture for each extremity.
- Please adhere to institutional policies and procedures for shielding.
- Remove jewelry where possible (if not, shift the jewelry so it does not obscure any joint).

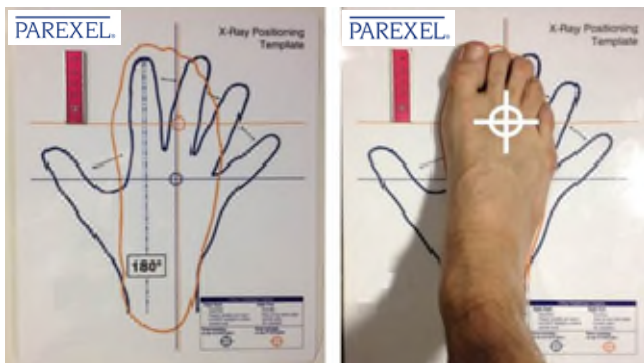


Fig. 4 Positioning Template (Right)



Fig. 5 Good Image Quality

Patient Positioning: The patient should be **lying supine on the imaging table** with the **knee flexed** and the plantar surface of the foot centered flat on the cassette/panel with the long axis of the foot parallel to the midline of the film/receptor.

1. Align the **knee with the ankle** (no internal or external rotation).
2. Ensure that the **foot is placed flat on the template and cassette/receptor** to avoid magnification of joints (Fig.4).
3. If possible, toes should be flat and not compressed by tight socks.

Parameters: Film/Resolution: Conventional X-ray: **high resolution, single emulsion** film. Digital: optimal and consistent digital resolution (100 micron pixel size preferred). Be consistent with the resolution accepted for your instrument during site qualification.

- **Film Focus Distance (FFD): 40 inches** (102 cm)
- **Beam centering: between the 2nd and 3rd MTP joints**, angled 10 degrees towards the head (Fig. 4).
- **Exposure settings:** Suggest 60kVp and 3 mAs. Optimize for sharp bone detail.
- **Collimate** to film.

Anatomical Coverage and Image Quality Control Checks:

- **Ensure inclusion of the entire foot and ankle** including at least 2 inches of distal tibia (Fig.4).
- Ensure **optimal visualization** of the **forefoot** (Fig. 5).
- **AP view with left/right markers visible and accurate to anatomy.**

Be Consistent: For follow-up timepoints use the same x-ray instrument, patient positioning, acquisition parameters (mAs, kV, FFD, focal spot, film and cassette type or digital resolution) as that used for Baseline.

Please contact PAREXEL immediately if your methods or results deviate from these guidelines or from those used at Baseline for each patient.

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