Antibiotic Pathway for Severe Uncontrolled Hidradenitis Suppurativa – Clinical Guideline

Ref no: CG-Anti/2021/075

This pathway is intended for use in patients with severe hidradenitis suppurativa (HS) where other conventional treatments have failed. Typically the regime is used to stabilise severe disease affecting several sites e.g. axillae, sub-mammary area, groin, perineum, buttocks. Patients will usually have multiple inflammatory nodules, abscesses, draining sinuses and significant scarring. Their **Physician Global Assessment (PGA)** should be **severe**, with a **Hurley stage of 2 or more** (see appendix 2 and 3).

The regime is used to stabilise a severe disease before surgery, or to allow maintenance therapy with Co-trimoxazole, Dapsone, or other agents.

To be considered for this regime, patients should have shown an inadequate response to single agent antibiotics (e.g. Doxycycline) and combination antibiotics (e.g. Rifampicin and Clindamycin) in the past.

These guidelines were made in agreement with ambulatory care and the OPAT (Outpatient Parenteral Antimicrobial Therapy) team. The OPAT service allows medically stable patients to have intravenous antibiotics in the outpatient setting. Please note the OPAT service is only for patients who are not acutely unwell or require hospital admission for IV antibiotics. The **contact details** for the **OPAT team** can be found in **appendix 4**.

Antibiotics regime summary:

The antibiotic regime consists of an **initiation phase** followed by a **consolidation phase**:

Initiation Phase	IV Ertapenem 1g given via Midline in the community for 6 weeks. This treatment is organised through the OPAT service
Consolidation Phase	1) Oral Rifampicin 450 mg od (patients less than 50 kg) or 600mg od (patients weighing more than 50kg), Moxifloxacin 400 mg od (see appendix 4) and Metronidazole 400mg tds for 6 weeks 2) Oral Rifampicin 450 mg od (patients less than 50 kg) or 600mg od (patients weighing more than 50kg), Moxifloxacin 400 mg od (see appendix 4) for a further 6 weeks

These guidelines set out a summary of the **'Initiation Phase'** pathway, accompanied by a flow chart, and then a detailed explanation of how to enter a patient into the pathway. Lastly there is a summary of the **'consolidation phase'**.

Summary of Initiation Phase Pathway

Patient reviewed by consultant dermatologist and determined to have severe HS requiring treatment on this pathway.

Complete patient assessment tool (Appendix 1)

1. For first time exposure to Ertapenem, patient admitted to ambulatory care for first dose. This is administered via a cannula under clinical supervision. If patient has had Ertapenem before then the regime can be administered as an outpatient via the OPAT service.

2. OPAT receives referral via telephone or extra med referral and then contacts patient to attend OPAT clinic (LRCH, Room 16 specialist rehabilitation centre ground floor) at specified date and time.

3. Patient arrives at OPAT clinic (LRCH) as previously confirmed
    a. Admitted under referring consultant
    b. Routine baseline observations done by OPAT staff

4. Midline inserted (if no vascular access)
    a. Routine baseline bloods taken through line (by OPAT team)

5. Assessment of patient/social needs to decide how Ertapenem will be administered:
    a. Self/carer administered, *or*
    b. Daily attendance at OPAT clinic, LRCH, *or*
    c. Home visit by OPAT nurse

6. Patient education of requirements during OPAT treatment
    a. OPAT antibiotic passport given to patient

7. Weekly OPAT review during therapy
    a. Bloods weekly
    b. OPAT MDT and video telemedicine for patient queries
    c. Patient who self/carer administered will be required to attend OPAT clinic (LRCH) at least once a week.
    d. If clinical concerns (escalation pathway):
        i. Discussion with OPAT pharmacist/consultant
        ii. If concerns about effectiveness of treatment/rising inflammatory markers/failure of vascular access/unable to place replacement line/social status etc., the referring clinician will be contacted.
        iii. Non-compliant patients and those who are not socially suitable for OPAT therapy will be discharged from the OPAT service and the referring clinician will be contacted.
        iv. Unwell patients:
            a) Out-of-hours: patient should contact 111
            b) During working hours: the referring clinician will be contacted for advice/admission

8. OPAT will inform referring consultant/team on completion of therapy and midline removed. If the referring clinician does not want the vascular access line to be removed at the end of OPAT therapy, they will be expected to arrange district nurse follow up, to ensure appropriate line care in the community.

Flow Chart of 'Initiation Phase' pathway

Patient with HS
For IV Ertapenem 1g OD for 6 weeks

If this is first exposure to antibiotic **refer to ambulatory care (see step 1 in dermatology clinic assessment, page 2)** to allow monitoring during first dose. If patient has had antibiotic before then make OPAT referral.

Referral to OPAT
- Ensure eligibility (green box) and exclusion criteria (red box) are checked
- Referral to OPAT via ExtraMed (see next page)*
  - Please specify:
    - Indication (Diagnosis)
    - Antibiotic required and Duration
    - Comorbidities
    - Social circumstances
    - Midline insertion organised by OPAT
    - Patient contact number
- If patient needs to start antibiotics within 2 working days, please also contact OPAT by telephone (see next page)§

ELIGIBILITY CRITERIA FOR OPAT
- Patient willing to have IV therapy at home and able to give consent
- Satisfactory social and domestic conditions (e.g. mobility, access)
- Residing within Derbyshire area

EXCLUSION CRITERIA
- Patients requiring inpatient offloading and/or inpatient physiotherapy
- History of drug/substance abuse

Assessment by OPAT
- Occurs at OPAT clinic (LRCH) within 1 week of referral
- 3 options depending on OPAT assessment:
  - Self/carer administration of antibiotics
  - Daily attendance at OPAT clinic (LRCH)
  - Home visits by OPAT nurse
- Social assessment
- Insertion of vascular access line
- Baseline bloods taken

During OPAT IV treatment
- Patient reviewed at the weekly virtual OPAT MDT
  - Video telemedicine for problem-shooting
  - Patients who self/carer administered would be required to attend the OPAT clinic (LRCH) at least once a week
- Weekly blood tests (unless otherwise advised)
- OPAT will inform referring team of any issues

Escalation Pathway
- **Non-compliant patients & those not socially suitable for OPAT**– to be discharged from OPAT and the referring clinical to be contacted
- **Unwell patients -**
  - OOH: patient should contact 111
  - During working hours: the referring team will be contacted for advice/ admission
- OPAT will inform referring team of any other issues

- OPAT will inform referring consultant/team on completion of therapy
- Vascular access will be removed (unless otherwise advised)
- If the referring clinician does not want the vascular access line to be removed at the end of OPAT therapy, they will be expected to arrange district nurse follow up, to ensure appropriate line care in the community.

How to make a referral to ambulatory care:

a. Dermatology doctor may call the nurse in charge on 07384457839 or extension 85477.
b. The nurse in charge will:
    i. Take patients details
    ii. Let reception staff know and book them on the system
    iii. Enter patient details onto EDIS so nursing staff can keep track of the patient in the department
    iv. First dose will be administered with a cannula in ambulatory care

How to make a referral to OPAT – through Whiteboard (ExtraMed) or telephone or email

ExtraMed referral:

a. Admit patient to virtual ward 'ZOPAT'
    i. Log into ExtraMed
    ii. Find patient with hospital number
    iii. Add visit
    iv. Admit to 'ward'. Chose ward ZOPAT.
    v. You are now on the virtual ZOPAT ward; Find your patient in the Left hand column and drag your patient into an ED bed. Save.
b. OPAT referral
    i. Select patient → Plans → Services → OPATv6
c. Fill out OPAT referral form on Whiteboard
    i. Mandatory fields are Medical Assessment:
        1. **Antibiotic and duration of treatment**
        2. **Patient's contact number**
        3. **Clinician's contact number**

Email referral:

Email all written referrals to dhft.OPAT@nhs.net

Telephone:

Call to make a referral to OPAT nurse (07471140520). A phone call to the OPAT team is recommended if OPAT assessment and initiation of IV therapy is required within 48 hours. OPAT working hours: Monday – Friday, 09:00 – 17:00

Consolidation Phase[2]

1. Review patient in clinic after 6 weeks of IV Ertapenem and complete assessment tool (Appendix 1)

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2. Ensure baseline LFT's are available (OPAT should have checked these each week the patient was on IV Ertapenem)

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3. Commence Rifampicin 450mg od (patients less than 50 kg), 600mg od (patients weighing more than 50kg), Moxifloxacin 400mg od, and Metronidazole 400mg tds orally for 6 weeks

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4. Check LFT's at 4 weeks

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5. After 6 weeks, discontinue Metronidazole and continue Rifampicin and Moxifloxacin at previous dose for further 6 weeks.

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6. Repeat LFT's at 8 weeks

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7. Review in clinic at 12 weeks. Complete HS assessment tool. Consider referral for surgery, or prophylaxis with Co-trimoxazole, Dapsone, or another agent.

Appendix 1- Patient assessment tool

	Right Axilla	Left Axilla	Right Groin	Left Groin	Perineum	Right buttock	Left buttock	Other	TOTAL
Abscesses									
Inflammatory Nodules									
TOTAL									
Draining fistula									

Abscesses = fluctuant, with or without drainage, tender or painful
Inflammatory nodules = tender, erythematous, pyogenic granuloma-type lesions

Draining fistulas = sinus tracts, with communications to skin surface, draining purulent fluid

DATE: _____

TOTAL INFLAMMATORY LESION COUNT: _____

TOTAL number of DRAINING FISTULA: _____

Physician Global Assessment- 1/2/3

Hurley Stage

DLQI

Appendix 2: Hurley stage

Stage I	Stage II	Stage III
Single/multiple abscesses	Recurrent , Single/multiple abscesses, widely separated	Diffuse or near diffuse involvement
	Sinus tracts	Multiple interconnected sinus tracts
	Cicatrization	Cicatrization

Ovadja et al 2019 [4]

Appendix 3: The PGA Score

The six-point hidradenitis suppurativa Physician Global Assessment (PGA) ranges from clear to very severe. It is used in clinical trials to measure clinical improvement in inflammatory nodules, abscesses and draining fistulae. The 6 stages are as follows;

1)Clear: No inflammatory or non-inflammatory nodules

2)Minimal: Only the presence of non-inflammatory nodules

3)Mild: Less than 5 inflammatory nodules or 1 abscess or draining fistula and no inflammatory nodules

4)Moderate: Less than 5 inflammatory nodules, or 1 abscess or draining fistula and 1 or more inflammatory nodules, or 2-5 abscesses or draining fistulas and less than 10 inflammatory nodules

5)Severe: 2-5 abscesses or draining fistulas and 10 or more inflammatory nodules

6)Very severe: More than 5 abscesses or draining fistulas [5]

Appendix 4: MOXIFLOXACIN

Fluoroquinolones can very rarely cause long-lasting, disabling, and potentially irreversible side effects. sometimes affecting multiple systems, organ classes, and senses. Patients should be advised of these risks and the actions to take. The MHRA patient information leaflet can be found here.

CONTRAINDICATIONS & CAUTIONS (use as a checklist before prescribing)

Contraindications:

- **Hypersensitivity:** use of moxifloxacin contraindicated in quinolone hypersensitivity.
- **Tendon Damage:** contraindicated in patients with a history of tendon disorders related to fluoroquinolone use, or in patients on concomitant corticosteroids.
- **Pregnancy:** avoid - shown to cause arthropathy in animal studies.
- **Breast Feeding:** avoid - present in milk in animal studies.
- **Cardiovascular:** due to the risk of QT prolongation, avoid in patients with acute myocardial infarction, congenital or documented acquired QT prolongation, clinically relevant bradycardia, heart failure with reduced left-ventricular ejection fraction, previous history of symptomatic arrhythmias, or electrolyte disturbances, particularly in uncorrected hypokalaemia.
- **Liver disease:** avoid in patients with severe liver impairment or transaminase levels of 5 times upper limit of normal.
- **Concurrent use with other drugs that prolong the QT interval.**

Cautions:

- **Patients at risk of tendon damage** - increased risk in patients aged over 60 years, concomitant use of corticosteroids (avoid), renal failure or solid organ transplant. .
- **Patients at risk of aortic aneurysm and dissection**
- **Myasthenia Gravis:** risk of exacerbation.
- **G6PD deficiency:** risk of haemolytic reactions
- **Sunlight and UV radiation**: avoid exposure during treatment and for 48 hours after treatment.
- **Epilepsy/Seizure**: may induce convulsions in patients with or without a history of convulsions. Use with caution if history of epilepsy or conditions that predispose to seizures, and in patients on NSAIDs
- **Diabetes**: may affect blood glucose
- **Psychiatric disorder**
- **Patients at risk of heart valve disease.**

MONITORING

ECG:

- At baseline, 2 weeks then every 3 months
- After the addition of any new medications that can cause OT prolongation
- Stop moxifloxacin if QTc rises by > 20ms, or to > 500ms.

Routine Bloods:

- **U&Es, LFTs** and **FBC** should be monitored during treatment
- **Blood glucose** should be monitored regularly in patients with diabetes

Appendix 5: OPAT team contact numbers

OPAT nurse – 07471 140520
OPAT pharmacist – 07823 373820
OPAT consultant – 01332 787453

References:

1) Zouboulis CC, Bechara FG, Dickinson-Blok JL, Gulliver W, Horváth B, Hughes R, Kimball AB, Kirby B, Martorell A, Podda M, Prens EP, Ring HC, Tzellos T, van der Zee HH, van Straalen KR, Vossen ARJV, Jemec GBE. Hidradenitis suppurativa/acne inversa: a practical framework for treatment optimization - systematic review and recommendations from the HS ALLIANCE working group. J Eur Acad Dermatol Venereol. 2019 Jan;33(1):19-31.

2) Join-Lambert O, Coignard-Biehler H, Jais JP, Delage M, Guet-Revillet H, Poirée S, Duchatelet S, Jullien V, Hovnanian A, Lortholary O, Nassif X, Nassif A. Efficacy of ertapenem in severe hidradenitis suppurativa: a pilot study in a cohort of 30 consecutive patients. J Antimicrob Chemother. 2016 Feb;71(2):513-20.

3) Braunberger TL, Nartker NT, Nicholson CL, Nahhas AF, Parks-Miller A, Hanna Z, Jayaprakash R, Ramesh MS, Rambhatla PV, Hamzavi IH. Ertapenem - a potent treatment for clinical and quality of life improvement in patients with hidradenitis suppurativa. Int J Dermatol. 2018 Sep;57(9):1088-1093.

4) Ovadja ZN, Schuit MM, van der Horst CMAM, Lapid O. Inter- and intrarater reliability of Hurley staging for hidradenitis suppurativa. Br J Dermatol. 2019 Aug;181(2):344-349

5) Potter JL, Capstick T, Ricketts WM, Whitehead N, Kon OM. A UK based resource to support the monitoring and safe use of anti-tuberculosis drugs and second line treatment of multidrug-resistant tuberculosis.

6) The Hidradenitis Suppurativa Trust - https://www.hstrust.org/severities

7) BNF accessed 25/5/2021 Important safety information for all quinolones. https://bnf.nice.org.uk/drug/ciprofloxacin.html#importantSafetyInformations

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Version	1.0
Approval Date:	Medical divisional governance, 28/05/2021
Next review date	May 2024
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