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# Treatment pathway

## for newly-diagnosed, autoimmune hepatitis patients


**Budenofalk®**
**budesonide**

With as many as 29 different treatment regimens identified in a recent study, there is significant variability in the approach to care of UK AIH patients.[1]

**This pathway was developed to help inform treatment decisions using the latest recommendations published in 2020 by the American Association for the Study of Liver Disease along with outputs from round table discussions with experts in the UK.[2-4]**

# Diagnosing AIH

As there is no single diagnostic test for AIH, results from a combination of tests should be collected before confirming a diagnosis.[5]

**These features support a diagnosis of AIH and should be considered as a whole:[5,6]**

## Elevated blood tests

- Aspartate aminotransferase (AST)
- Alanine aminotransferase (ALT)
- Immunoglobulin G (IgG)

## Positive autoantibodies in the blood

- Antinuclear antibody
- Smooth muscle antibody
- Liver kidney microsomal antibody

*NB: 20% of patients with AIH do not have any autoantibodies*

## Other liver diseases ruled out

- Hepatitis B
- Hepatitis C
- Alcoholic liver disease
- Non-alcoholic fatty liver disease

## Typical findings on a liver biopsy

- Interface hepatitis with plasma cell infiltration

**AIH should not be diagnosed without a liver biopsy**

In addition to confirming an AIH diagnosis, a liver biopsy is necessary to determine the degree of liver inflammation and scarring, and presence of cirrhosis.[3] This helps inform the most suitable course of therapy for patients.[5]

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# Evidence considerations

## AASLD meta-analysis: Achieving remission[3]

Patients achieving complete biochemical remission were over twice as likely to have received budesonide + AZA than to have had predniso(lo)ne + AZA:

**OR: 2.19, 95% CI: 1.30-3.67**

*High grade of evidence*

## RCT: Time to reach biochemical remission[7]

Budenofalk + AZA:
**127 days**

Prednisolone + AZA:
**145 days**

*n=546 (91% were on prednisolone)*

## UK-AIH study: Quality of life[8]

Systemic corticosteroid use is strongly associated with detrimental effects on HRQOL, independent of remission status

- mobility issues
- problems with usual activities
- anxiety/depression
- fatigue

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## RCT: Steroid-specific side effects at 6 months[9]

Prednisolone + AZA

**53%**

n=103

Budenofalk + AZA

**28%**

n=100

Budesonide induces remission with a low rate of steroid-specific side effects (p<0.001)

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# Treating AIH[2-4]

## Start Budenofalk 9 mg/day

**If the patient has comorbidities:**

- poorly controlled diabetes
- pre-diabetes
- central adiposity/obesity
- dyslipidaemia (adverse lipid profile)
- high blood pressure
- a history of psychiatric disease
- presence of, or high risk for, osteoporosis

**If the patient has concerns about body image:**

- body weight
- facial appearance

**If the patient has mild disease:**

- ALT levels below 300–400 U/litre +
- AST levels < 300 U/litre +
- INR ≤ 1.3

## Start prednisolone 20-40 mg/day
(paediatrics: 1-2mg/kg/day)

**If the patient has:**

- cirrhosis (1 in 4 presenting patients)
- portal hypertension
- portosystemic shunts
- acute severe presentation with jaundice and coagulopathy

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# Treating AIH[2-4]

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## After 2-4 weeks

**If AST and ALT improve**
Add azathioprine, target dose:
1-2 mg/kg/day

**If AZA intolerant**
Consider mycophenolate mofetil or 6-mercaptopurine

**If no response**
Reconsider diagnosis

## Assess response at 4-8 weeks

Taper systemic steroid gradually as AST/ALT improves over the next 6 months
Continue Budenofalk 9 mg /day until AST/ALT normalise

## Assess response at 6 months

**If AST/ALT is normal**
Continue Budenofalk 6 mg/day or prednisolone 5-10 mg/day + AZA 1 mg/kg/day

**If AST/ALT has failed to normalise**
Check adherence
Re-evaluate diagnosis
Escalate therapy, consider third-line drugs

## After prolonged remission

Attempt steroid withdrawal while continuing AZA (usually 12-18 months of steroids)
Treatment with Budenofalk should be continued for at least 24 months

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# Practice Tips

Patients with severe acute liver injury with coagulopathy may reasonably be considered for a corticosteroid trial, but the risk of sepsis is genuine and management should be in conjunction with a specialist or transplant centre. Lack of response at 1 week warrants discontinuation.

Before intensifying treatment beyond dual therapy with prednisolone and azathioprine, the risks and benefits should be considered carefully.

The most common reason for apparent treatment failure or disease relapse is lack of adherence to treatment.[9]

Some data support a benign course for mild or asymptomatic AIH, but follow-up is still necessary for patients who are not treated.[9,10]

Sub-acute liver failure due to AIH can fully reverse with corticosteroids, but patients should be monitored closely.

In patients with complicated disease, consider taking advice from a specialist clinic.

Steroids are used to treat the active inflammation so it is logical to delay the introduction azathioprine for about 1 month after initiating treatment.[6]

- The failure to use azathioprine is an independent risk factor for poor outcomes in patients with AIH

Immunosuppression carries real risks and side effects – the success of the treatment relies upon patient education and involvement in the management of this chronic disease.[9,10]

Overlap with sclerosing cholangitis is much more common in children than adults, but should still be considered in adults who do not respond optimally to therapy.[11,12]

Patients differ (age, ethnicity, comorbidities, disease severity), so the risks and benefits of treatment must be tailored to the individual and their response to immunosuppression.[13]

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# Prescribing information

https://www.drfalk.co.uk/budenofalk-oral-preparations/

Further information available on request.

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**Adverse events should be reported.** Reporting forms and information can be found at www.mhra.gov.uk/yellowcard or search for MHRA Yellow Card in the Google Play Apple App Store (UK residents) or at email: medsafety@hpra.ie or at http://www.hpra.ie/homepage/about-us/report-an-issue/human-adverse-reaction-form (residents in Ireland). Adverse events should also be reported to Dr Falk Pharma UK Ltd at office@drfalkpharma.co.uk

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**Abbreviations:**
AASLD: American Association for the Study of Liver Disease
AIH: autoimmune hepatitis
ALT: alanine transaminase
AST: aspartate transaminase
AZA: azathriopine
CI: confidence interval
IgG: immunoglobulin G
HRQOL: health-related quality of life
RCT: randomised controlled trial
OR: odds ratio

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