

## Rheumatoid Arthritis (RA)

Rheumatoid Arthritis is another autoimmune condition, this time characterised by joint inflammation causing joint pain and swelling. There is no specific diagnostic blood test, yet test results showing inflammation combined with x-rays showing abnormal joints are usually diagnostic.

Initial treatment is with anti-inflammatories (these must be used with caution in PBC) but, in some cases, stronger medication to suppress the inflammatory response may also be used.

## Medications and PBC

### Disease Modification Therapies

#### Ursodeoxycholic Acid

Ursodeoxycholic acid (or Urso or UDCA) is a naturally occurring bile acid. The Chinese have known for over 5000 years that the bile from bears (brown not polar) can help with jaundice but the role of UDCA in PBC was identified more recently! The benefit was discovered when it was used for the treatment of gall stones.

UDCA is a naturally occurring bile acid and helps reduce progression of PBC. We know that those who show a biochemical response have a better outcome. The drug is safe and has few side effects (such as tummy upset). UDCA is given at a dose of 13-15mg/kg/day and is a lifelong therapy. It can be taken several times a day but seems effective when taken as a single daily dose. UDCA rarely helps the itching or fatigue.

#### Obeticholic Acid

Not everyone responds to or can tolerate UDCA. A newly licensed drug is Obeticholic Acid (OCA). This is another bile acid and has been shown to be effective in people with PBC but has some side-effects such as itching. As the first new licensed therapy in PBC, it has been approved for use in countries such as USA, Canada, Germany and all of the UK (as of June 2017). We would expect many more countries to license and make OCA available in time.

### Symptom Modification Therapies

#### For itching

#### Cholestyramine

Cholestyramine is used for the treatment of itching. The medication is sometimes also used for the treatment of hyperlipidemia. Cholestyramine comes as a powder

which can be taken dissolved in water or other liquid or sprinkled on food. The chemicals that cause itching (such as autotaxin) are excreted in the bile and then into the bowel but are reabsorbed further down in the bowel. Cholestyramine binds these chemicals and so prevents reabsorption: this means Cholestyramine should be given when there is most bile in the bowel (i.e. just before and after breakfast). It takes time to reach full efficacy (several weeks usually) so do be patient when starting it. Cholestyramine may also bind other drugs and vitamins so you should seek advice when you are taking other medications, as it will be important to take your other meds separately from your cholestyramine. It may occasionally cause tummy upsets.

## Other drugs

When cholestyramine does not control the itch adequately or if side-effects are troublesome, doctors will try other second-line medications. These are not licensed for use in the treatment of itch. Medications that may be tried include rifampicin, sertraline and naltrexone.

Rifampicin is an anti-microbial agent that is used for the treatment of TB but does help some people with itching. The drug can damage the liver so liver tests to have to be closely monitored. It also turns urine, tears and other secretions yellow so this may affect contact lens wearers. Rifampicin also affects the metabolism of some drugs so you must be careful of any interaction before you start the drug.

Sertraline is most commonly used as an anti-depressive agent but it also has some effect in treating the itch of PBC. It may cause drowsiness.

Naltrexone is a drug that is given amongst other indications to help withdrawal from opiates. It may be effective in some people with itching. The drug may cause severe side-effects, such as paranoia and delusions, and a sensation of 'cold turkey' so it has to be started with great care and sometimes under supervision. These side-effects are seen on starting the drug and people rapidly become tolerant.

Plasmaphoresis (or plasma exchange) or MARS dialysis are treatments which are occasionally used for severe itch. These are invasive treatments where blood is 'cleaned' like kidney dialysis.

## Lethargy/fatigue

There are, as yet, no specific treatments for lethargy associated with PBC. Some people have used modafinil.