

## Plain English Summary - Prescribing Guidelines for Carbamazepine, Oxcarbazepine and Eslicarbazepine

### What is carbamazepine?

Carbamazepine is a medicine used to treat epilepsy (seizures). It is also prescribed for trigeminal neuralgia, a condition that causes sudden, severe facial pain and sometimes for bipolar disorder, which affects mood. Carbamazepine works by calming overactive electrical signals in the brain. There are similar medicines called oxcarbazepine and eslicarbazepine, which are mainly used for epilepsy.

### Why do genes matter with carbamazepine?

In some people, carbamazepine can cause serious allergic reactions, especially affecting the skin. These reactions are not dependent on the dose and are unpredictable. Research has shown that genes involved in the immune system, called *HLA* genes, can greatly increase the risk of these reactions.

People inherit different versions of these genes, which means that carbamazepine is safe for many people but can be dangerous for others. The most important versions of the *HLA* genes associated with allergic reactions to carbamazepine are:

- HLA-B\*15:02
- HLA-B\*15:11
- HLA-A\*31:01

Allergic reactions can also occur with oxcarbazepine and eslicarbazepine, albeit less frequently, often in association with the versions of the *HLA* genes reported above.

### What kinds of reactions can occur?

Most reactions happen within the first three months of treatment, as follows:

- Mild reactions may include a skin rash.
- Severe reactions are rare but can be life-threatening and include:
  - Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN), where the skin blisters and peels.
  - DRESS syndrome, which can cause rash, fever, swollen glands, facial swelling, and damage to organs such as the liver or kidneys.

It is extremely important to prevent these adverse reactions.

### Who is at higher risk?

- *HLA-B\*15:02* and *HLA-B\*15:11* are more common in people of Asian ancestry, but they can occur in anyone.
- *HLA-A\*31:01* is more common in many populations including White British and European populations.
- People may not always know or report their ancestry, so relying only on self-reported ethnicity is not the best approach.

### What do the guidelines say?

The UK guideline recommends genetic testing before starting carbamazepine, oxcarbazepine or eslicarbazepine in:

- Anyone who has never taken these medicines before
- Anyone who has taken them for less than three months

This applies to all patients, regardless of ancestry or reason for treatment.

### **How do test results affect treatment?**

- If *HLA-B\*15:02* is present, carbamazepine, oxcarbazepine, and eslicarbazepine should be avoided.
- If *HLA-A31:01* is present and *HLA-B15:02* is absent, these medicines should be avoided if an alternative is available.
- If *HLA-B\*15:11* is present, these medicines should also be avoided if an alternative is available.

If none of these genetic risk factors are found, carbamazepine (or oxcarbazepine or eslicarbazepine) can usually be prescribed with greater confidence.

### **What does this mean for patients?**

Genetic testing helps doctors choose the safest medicine before treatment begins. This reduces the risk of severe skin reactions and avoids harm that cannot be predicted by routine blood tests.

Test results should be saved in medical records so that all healthcare professionals are aware. Patients should be informed:

- why the test is done
- what the results mean
- how it affects their treatment options

### **Regulatory considerations**

Carbamazepine product information already includes warnings about genetic risk.

The current guideline emphasises that testing should be accurate, available quickly and affordable so the results can guide treatment decisions without unnecessary delay.

### **Research recommendations**

More research is still needed to understand:

- the impact of genetic variability on oxcarbazepine and eslicarbazepine safety
- the impact of genetic variability on other adverse reactions to these drugs and to other medicines with a similar chemistry
- The long-term cost-effectiveness of routine testing

### **Key message**

Carbamazepine is an effective medicine, but in some people, it can cause rare and serious immune reactions. A simple genetic test can identify those at risk before treatment starts. When risk is found, alternative drugs are available. This approach improves patient safety and supports more personalised, informed care.