Eprodisate disodium (Kiacta) for AA amyloidosis

LAY SUMMARY

AA amyloidosis is a rare and serious condition that can happen as a complication of other chronic diseases such as rheumatoid arthritis. It leads to abnormal proteins being deposited throughout the body, but particularly affects the kidneys. Many patients eventually have kidney failure and need to start dialysis. At the moment, there is no treatment for AA amyloidosis itself, only the chronic disease that is causing it.

Eprodisate disodium (Kiacta) is a new drug being developed for AA amyloidosis. It is taken as a tablet twice a day. A study is currently running to see how well it works and whether it is safe to use.

If it is licensed in the UK, eprodisate disodium will be the first treatment specifically available for people with AA amyloidosis.

NIHR HSRIC ID: 5094
TARGET GROUP

- AA amyloidosis.

TECHNOLOGY

DESCRIPTION

Eprodisate disodium (Kiacta; Fibrillex; eprodisate sodium; NC 503; NC-503) is a small-molecule orally bioavailable inhibitor of AA amyloid deposition. It is a negatively charged, sulphonated molecule of low-molecular weight that has structural similarities to heparin sulphate¹. Eprodisate disodium is thought to inhibit the formation of AA amyloid fibrils by inhibiting their interactions with glycosaminoglycans, which are a universal constituent of amyloid deposits, and inhibiting the interaction between glucosaminoglycans and amyloid fibrils remains a promising therapeutic approach².

Eprodisate disodium is not currently licensed for any indication. In phase III clinical trials, eprodisate disodium was administered orally at 400mg twice daily and adjusted as per the creatinine clearance (CrCL) level.

INNOVATION and/or ADVANTAGES

If licenced, eprodisate disodium will provide the first treatment option specifically targeted at AA amyloidosis.

DEVELOPER

Auven Therapeutics.

AVAILABILITY, LAUNCH OR MARKETING

In phase III clinical trials.

PATIENT GROUP

BACKGROUND

Amyloidosis is a group of rare but serious conditions caused by deposits of abnormal protein, called amyloid, in tissues and organs throughout the body³. AA amyloidosis is a multisystem disorder complicating chronic infections or inflammatory diseases⁴. It is characterised by extracellular deposits of fibrils composed of fragments of serum amyloid A (SAA), an acute phase reactant protein. Symptoms include a range of non-specific diffuse problems, however the kidney is the most frequent organ involved, manifesting as progressive proteinuria and renal impairment³. Although the spleen, adrenal glands, liver and gut are also frequent sites of amyloid deposition, the clinical picture is typically dominated by renal involvement⁵.
NHS or GOVERNMENT PRIORITY AREA

This topic is relevant to:

CLINICAL NEED and BURDEN OF DISEASE

Overall, an estimated 125 to 600 new cases of amyloidosis are diagnosed in the UK each year and most occur in older people. Around 70% of AA amyloidosis is associated with rheumatic diseases such as rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, and juvenile idiopathic arthritis. The prevalence of the asymptomatic phase of AA amyloidosis in rheumatoid arthritis can range between 0.5% and 14%. Renal AA amyloidosis is a serious complication of these conditions, with a median survival time after onset of dialysis of 2.37 years and a 5 year survival rate of only 30%.

In 2013-2014, there were 2,068 admissions for AA amyloidosis (ICD10 E85) in England, resulting in 6,664 bed days and 2,391 finished consultant episodes. 638 deaths from AA amyloidosis were registered in England and Wales during 2013 (ICD-10 E85).

PATIENT PATHWAY

RELEVANT GUIDANCE

NICE Guidance
• None identified.

Other Guidance
• None identified.

CURRENT TREATMENT OPTIONS

In the absence of a specific treatment for AA amyloidosis, clinical management relies on the treatment of the underlying inflammatory disease or infection. The aim of treatment of AA amyloidosis is to control the underlying inflammatory disease and thereby reduce the amount of serum amyloid A protein in the blood. There is some evidence that the early control of underlying inflammatory condition may effectively slow or even halt the progression of AA amyloidosis. A growing understanding of genetic factors which predispose to the formation of amyloid may also help in the future to identify those particularly at risk.

EFFICACY and SAFETY

<table>
<thead>
<tr>
<th>Trial</th>
<th>NCT01215747, CL-503012; eprodisate disodium vs placebo; phase III.</th>
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<tbody>
<tr>
<td>Sponsor</td>
<td>C.T. Development America Inc.</td>
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<tr>
<td>Status</td>
<td>Ongoing.</td>
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<tr>
<td>Source of information</td>
<td>Trial registry.</td>
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Horizon Scanning Research & Intelligence Centre

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<thead>
<tr>
<th>Location</th>
<th>EU (incl UK), USA and other countries.</th>
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<tr>
<td>Design</td>
<td>Randomised, placebo-controlled.</td>
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<td>Participants</td>
<td>n=261; aged 18-80 years; confirmed AA amyloidosis; persistent proteinuria &gt;1g/24 hours at 2 distinct 24 hour urine collections; CrCL &gt;25ml/min/1.73m² at 2 distinct 24 hour urine collections.</td>
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<tr>
<td>Schedule</td>
<td>Randomised to 400mg eprodisate disodium oral twice daily; or placebo, oral twice daily.</td>
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<td>Follow-up</td>
<td>Not reported.</td>
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<tr>
<td>Primary outcome/s</td>
<td>Time to decrease of 40% or more in CrCL; increase of 80% or more in serum creatinine (SCr) or progression to end-stage renal disease (ESRD).</td>
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<tr>
<td>Secondary outcome/s</td>
<td>Rate of change in CrCL over time; estimated glomerular filtration rate (eGFR); serum cystatin C, urinary protein/creatinine ratio; serum amyloid A; a persistent increase in serum creatinine of 80% or more; all-cause mortality.</td>
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<td>Expected reporting date</td>
<td>Estimated completion date reported as June 2016.</td>
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ESTIMATED COST and IMPACT

COST

The cost of eprodisate disodium is not yet known.

IMPACT - SPECULATIVE

Impact on Patients and Carers

☑ Reduced mortality/increased length of survival
☐ Other:
☑ Reduced symptoms or disability
☐ No impact identified

Impact on Health and Social Care Services

☐ Increased use of existing services
☐ Re-organisation of existing services
☐ Other:
☑ Decreased use of existing services
☑ Need for new services
☑ None identified

Impact on Costs and Other Resource Use

☑ Increased drug treatment costs: new treatment option.
☑ Other increase in costs: more patients eligible for treatment.
☐ Other:
☑ Reduced drug treatment costs
☐ Other reduction in costs:
☑ None identified

Other Issues

☐ Clinical uncertainty or other research question identified:
☑ None identified
REFERENCES