PAN MERSEY APC

PAN MERSEY AREA PRESCRIBING COMMITTEE
PRESCRIBING POLICY STATEMENT
REF: PS14 FINAL
APC BOARD DATE: 11 SEP 2013

NHS
Pan Mersey
Area Prescribing Committee

HYALURONAN intra-articular injection
(for example Orthovisc®, Ostenil®, Synvisc®, Synvisc-One®)

BLACK

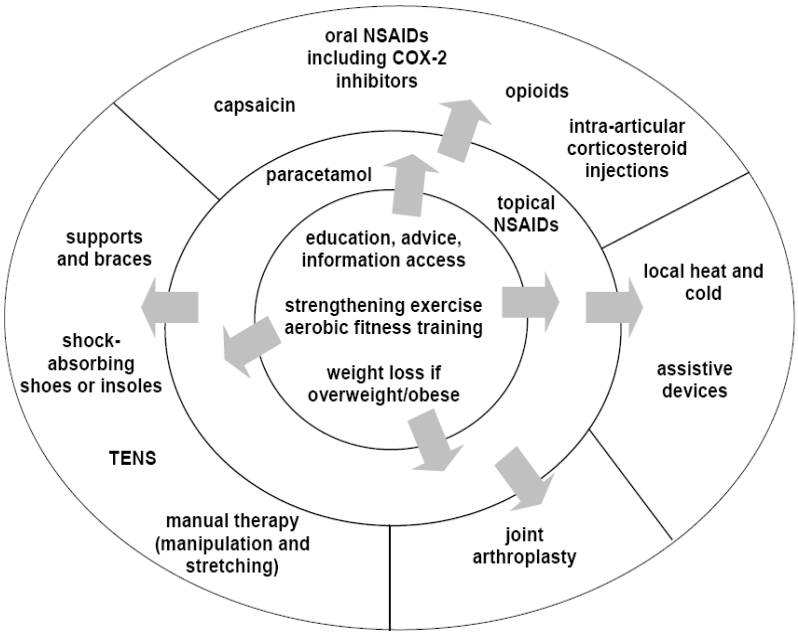
The Pan Mersey Area Prescribing Committee does not recommend the routine use of HYALURONAN intra-articular injections in the treatment of osteoarthritis.

The NHS National Institute for Health and Care Excellence (NICE) clinical guideline on osteoarthritis (CG59 2008[1]) does not recommend the use of intra-articular hyaluronan injections for the treatment of osteoarthritis (OA).

NICE concluded from their cost-consequence analysis that the estimate of cost-effectiveness for these preparations was outside the realms of affordability to the NHS, and in one case was dominated by placebo. Sensitivity analyses on the individua that the efficacy would need to be three to five times higher which the cost-consequence analysis was based, before re effectiveness to the NHS.

Patients with OA should be managed in accordance with N

Figure 1 – NICE CG59 summary of treatment recommendatic



Start at the centre and work outward. Treatments are arranged in the order in which they should be considered for people with OA. The centre circle comprises the core treatments which should be considered for every person with OA. Where further treatment is necessary, consideration should be given to the second ring, which contains the 'safer' pharmaceutical treatment options. The outer circle gives adjunctive treatments, which all meet at least one of the following criteria; less well-proven efficacy, less symptom relief or increased risk to the patient.

NICE CG59 is currently being reviewed. Hyaluronan injections have been included in the scope for this review. The expected publication date is February 2014. This statement will be reviewed following publication of the updated NICE OA CG.

Note: Patients who are not eligible for treatment under this policy may be considered on an individual basis where their GP or consultant believes exceptional circumstances exist that warrant deviation from the rule of this policy. If appropriate an exceptional funding request will be required following the usual locally defined process.

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EFFECTIVENESS

Hyaluronic acid (HA) is a naturally occurring polysaccharide in the synovial fluid, which acts as a lubricant and shock absorber. In patients with OA, synovial hyaluronic acid is depolymerized and cleared at higher rates than normal. In an attempt t o improve mechanical function HA preparations were devised for intra-articular injection.

The NICE OA CG highlighted that the research evidence on the efficacy of intra-articular HA in knee OA was difficult to interpret due to confounders of different molecular weights of the hyaluronic acid preparations, different injection schedules (ranging from once weekly to a series of five injections), poor trial design despite large numbers of studies, e.g. lack of intention-to-treat analyses, limitations in blinding; and on a balance of the chance of benefit, risk of harm and cost NICE have recommended they should not be routinely used for the treatment of OA.

Since publication of the NICE OA CG, a further systematic review and meta-analysis in 2012 of viscosupplementation in knee OA has been published (n=12,667). Primary outcomes were pain intensity and flare-ups. Secondary outcomes included function and adverse effects. Overall 71 trials (n=9617) showed HA moderately reduced pain but there was significant between-trial heterogeneity, non-blinded assessment and publication bias making interpretation difficult. 18 of the larger trials with blinded outcome assessment (n=5094) showed a clinically irrelevant effect size for pain reduction (-0.11, [CI -0.18 to -0.04]). The minimal clinically important difference in effect size was taken to be -0.37 (corresponding to a 0.9cm difference on a 10 cm visual analogue scale)

SAFETY

In the 2012 systematic review and meta-analysis the primary safety outcome was a flare-up in the injected knee. 6 trials (n=811) showed an increase in risk of flare-ups (RR, 1.51 [95% CI, 0.84 to 2.72]). For the secondary safety outcomes, 14 trials (n=3667) showed that intra-articular HA increased the risk for serious adverse events (RR, 1.41 [CI, 1.02 to 1.97]), dropouts due to adverse events (RR 1.33 [95% CI, 1.01 to 1.74]) and local adverse events (RR 1.34 [95% CI, 1.13 to 1.60]) all of which were statistically significant. Serious adverse events were defined as events resulting in inpatient hospitalization, prolongation of hospitalization, persistent or significant disability, congenital abnormality of offspring, life-threatening events, or death.

COST

Costs taken from Drug Tariff August 2013 and are per treatment due to variability in course length

Orthovisc 1xprefilled syringe 2ml	£65
Ostenil 1xprefilled syringe 20mg/2ml	£34
Synvisc 3xprefilled syringes 2ml (1 treatment)	£205
Synvisc -One	£205

PATIENT FACTORS

The current published research evidence for HA does not suggest there are any subgroups of people with OA who may be expected to gain significant more benefit than others.

IMPLEMENTATION

In summary the balance of efficacy, safety and cost does not support the routine use of HA preparations in the treatment of OA. A major limitation of the present research evidence is the poor methodological quality and reporting quality of many of the trials, Some trials showed unrealistically large effect sizes of 2 to 3 times that what would be expected for total joint replacement. Reasons for these unrealistic effect sizes include methodological deficiencies or chance. Many reports did not provide adequate data on adverse events, which is concerning in light of the observed safety signals and the low quality of reporting of safety data means it is difficult to interpret the probable causes of serious adverse events.

REFERENCES

1. NICE CG59 February 2008. Osteoarthritis http://guidance.nice.org.uk/CG59/ (accessed 10/06/13).
2. Rutjes A, Juni P, da Costs BR, et al. Viscosupplementation of arthritis of the knee. A Systematic Review and Meta-analysis. Ann of Intern Med 2012; 157: 180-91.