Response to the Royal College of General Practitioners Inclisiran Position Statement

V.2 10.07.23

Overview

The Royal College of General Practitioners (RCGP) published an inclisiran position statement on 02.09.2021 and updated the document on 16.08.22. The statement includes considerations if inclisiran is initiated, detailed below.

Since inclisiran is a black triangle drug, if you do decide to prescribe it before the long-term outcome and safety data is realised, please ensure you:

- *Undertake shared decision-making with your patients, ensuring a full and detailed informed consent is taken, documenting the lack of long-term evidence and unknown long term safety profile of this new and novel medication,*
- *Encourage your patients to report all side effects to you, however minor, ensuring you fill in a MHRA "yellow card" when they are reported to you and*
- *Report any potential drug interactions or concerns of your own at the earliest opportunity*

Request: To detail how Health Innovation Manchester and the Greater Manchester (GM) ICB have implemented the RCGP inclisiran recommendations for inclisiran delivery across primary care

Response:

The delivery approach for the NHS Lipid Management Programme, including inclisiran delivery, has very much been in partnership with the ICB. GM colleagues have been involved and instrumental in the development of the Greater Manchester Lipid Management Pathway for Secondary Prevention Cardiovascular Disease (CVD), GMMMG inclisiran prescribing guidance and Greater Manchester Case Finding tool. All these resources were produced through a series of task and finish groups made up of clinicals from across GM and in consultation with governance groups, such as GMMMG, the GM CVD Prevention Oversight Group and the GM Clinical Effectiveness Group. All GM lipid management resources are available on the HInM website here.

To meet the requirements of the RCGP position statement we did the following:

1. ***RCGP Statement: Undertake shared decision-making with your patients, ensuring a full and detailed informed consent is taken, documenting the lack of long-term evidence and unknown long term safety profile of this new and novel medication***

Response

a. We have produced a GM inclisiran patient leaflet which was co-produced with patients and approved by GMMMG. One of the requests was to ensure that the long-term evidence was clearly highlighted in the leaflet, and we included a check list for patients to complete to ensure their clinician has talked through this.
b. The GMMMG inclisiran prescribing, ordering and cost information includes considerations before prescribing which mirror the ask by the RCGP, including about the long-term evidence. This went through GMMMG consultation.
c. Inclisiran template on practice clinical systems. This template was developed with the GM CVD Lead and GM Shared Services to ensure the consent process is easily documented on patient notes before inclisiran is initiated. This includes a consent check list for clinicians to tick once the shared decision making has occurred, including long-term evidence. This was also developed as a key concern was that writing this information would increase the burden on primary care, so the aim was to reduce this burden and simplify the consent process, without losing the required detail. ***See Appendix 1***
d. An additional recommendation was included in the GM Lipid Management Pathway for Secondary Prevention CVD (yellow highlight box) for *'NB: Recommendation for a LFT and lipid profile initially at 3 months and LFT, AST and FBC at yearly review ***' - *** To be reviewed after long-term study outcome data published'*
e. *Update to the* GMMMG inclisiran prescribing, ordering and cost information June 2023 following publication of inclisiran safety paper. *'No safety signals have been seen during clinical trials for inclisiran which have been published so far. However, the longest duration of any clinical trial to date is 18 months. Slightly more than 200 patients have now been followed up over 4 years where inclisiran displayed sustained reductions in LDL cholesterol and was well tolerated with injection site reactions the only'*[1]
f. Undertaking shared decision making with patients and documenting informed consent is common with new drugs and GPs routinely consent for new drugs as best practice.[2]

[1] Long-term efficacy and safety of inclisiran in patients with high cardiovascular risk and elevated LDL cholesterol (ORION-3): results from the 4-year open-label extension of the ORION-1 trial (Lancet Diabetes Endocrinol 2023 published online. https://doi.org/10.1016/S2213-8587(22)00353-9 (Accessed 07/07/2023)
[2] Decision making and consent, General Medical Council, 09.11.2022. Decision making and consent - professional standards - GMC (gmc-uk.org) (Accessed 10/07/2023)

2. ***RCGP statement: Encourage your patients to report all side effects to you, however minor, ensuring you fill in a MHRA "yellow card" when they are reported to you and***
3. ***Report any potential drug interactions or concerns of your own at the earliest opportunity***

Response

a. The GM inclisiran patient leaflet highlights the need for reporting of side effects and that inclisiran is a black triangle drug and has the link for where to report these concerns or interactions. This is also included in the patient check list at the end of the leaflet.
b. We have developed Inclisiran education webinars on our lipids resources page. A secondary care clinician talks through the safety data and that inclisiran is a black triangle drug and how to report any side effects.
c. Black triangle symbols are included with inclisiran in the GM Lipid Management Pathway for Secondary Prevention CVD to highlight this.
d. An additional recommendation was included in the GM pathway (yellow highlight box) for *'NB: Recommendation for a LFT and lipid profile initially at 3 months and LFT, AST and FBC at yearly review ***' - *** To be reviewed after long-term study outcome data published*
e. Safety considerations are included in the GMMMG inclisiran prescribing, ordering and cost information. *'Safety considerations: Inclisiran is a "Black Triangle" drug and all suspected side effects should be reported via the Yellow Card system.'*

Appendix 1- inclisiran template

Cohort 4a - Eligible for Injectables

ACTION FOR PRACTICE:

Review eligibility for:

- Ezetimibe (LDL-C value equal or greater to 1.8 mmol/L)
- Inclisiran (LDL-C value equal or greater to 2.6 mmol/L)
- Referral for PCSK9-i as GM Lipid Flowchart (LDL-C >3.5/4*) *4 = High Risk CVD (single previous event) *3.5 = Very High Risk CVD (recurrent events / multiple vascular beds)

If patient confirmed statin intolerance, see:

NHS Statin Intolerance Pathway

☐ Patient on maximal tolerated lipid lowering therapy	Text		No previous entry
☐ Statin not tolerated	Text		No previous entry
☐ Statins contraindicated	Text		No previous entry
☐ Statin not indicated	Text		No previous entry
Allergies / Adverse Reactions to Statins			No previous entry

Inclisiran Scheduling

Inclisiran is administered as a subcutaneous injection: initially, again at 3 months, followed by every 6 months.

Missed Doses:

If a planned dose is missed by less than 3 months, Inclisiran should be administered and dosing continued according to the patients' original schedule, i.e. month 0, 3, 9, 15, 21 etc. with scheduling **NOT** adjusted for doses delayed by less than 3 months.

If a planned dose is missed by more than 3 months, a new dosing schedule should be started.

Consider doses administered elsewhere.

Consent:

If patient is eligible for Inclisiran ensure fully informed patient consent and document the following:

- Inclisiran has demonstrated considerable effectiveness in lowering LDL-C.
- However, no patient-orientated outcome evidence such as a reduction in heart attacks or strokes is available. This will not become available until 2026 or 2027.
- No safety signals have been seen during clinical trials for Inclisiran which have been published so far. However, the longest duration of any clinical trial to date is 18 months.

There is limited other medical experience with treatments using the same mechanism of action - small interfering RNA molecules.

Does patient consent to Inclisiran?			No previous entry
	Text	Inclisiran has demonstrated considerable effectiveness in l	

Patient Leaflet

If patient requires 1st Dose, record correctly in medication screen when administering.

Diary entries:

2nd Dose:

☐ Add a diary entry reminder to book a follow up appointment in 3 months	Follow Up	14-Feb-2023	No previous entry
	Text		

3rd and Ongoing Doses:

☐ Add a diary entry reminder to book a follow up appointment in 6 months	Follow Up	14-Feb-2023	No previous entry
	Text		