COMMISSION ON HUMAN MEDICINES

ISOTRETINOIN IMPLEMENTATION ADVISORY EXPERT WORKING GROUP

Minutes of the meeting held on 31st March 2023 at 14:00 via videoconference.

Members Present

[redacted]

MHRA Presenters

[redacted]

MHRA Staff

Dr A Cave
Ms L Henderson
[redacted]

Invited Expert

[redacted]

Governance

[redacted]

Apologies

[redacted]

1.	**Introductions and announcements**
1.1	The Chair welcomed members and outlined the confidential nature of the proceedings and that the meeting was to be recorded for the purposes of minute taking.
1.2	The Chair reminded members to provide their relevant declarations of interest if they have not already done so and outlined the companies involved.
2.	**Minutes from the 1st March Meeting**
2.1	Approved
3.	**Follow up on action points from the 1st March Meeting**
3.1	**Definition of two Prescribers:**
3.1.1	The Group agreed that the person making the decision to initiate isotretinoin in adults could be the following: • a consultant dermatologist • an associate specialist dermatologist • a nationally accredited GPwER or GPwSI with historical local accrediatation • a junior medical doctor with evidence of competency in isotretinoin initiation working under the supervision of these physicians • a Band 8 Nurse consultant or CNS or Band 8 pharmacist working independently, but within a framework of a dermatological service In addition to the above, in children, the Group agreed a consultant paediatrician within a dermatologist pathway and with an additional interest qualification could also be the person making the decision to initiate isotretinoin. The agreed prescribers must be able to make an independent decision.
3.1.2	The Group agreed that the initial assessment should be face to face and subsequent meetings could sometimes be remote as long as there are no concerns (video preferably). The group discussed that considerations were required for those with a disability, and for remote/rural prescribing.
3.1.3	The Group discussed how the independence of the two prescribers of isotretinoin could be assured. It was discussed how the second prescriber must be able to ensure the therapeutic indication is properly followed. The Group discussed how it would be helpful to have a statement for the second prescriber to sign to confirm that they have operated independently. Guidance around this should not be prescriptive to allow for local variability and solutions. In the event prescribers cannot come to a shared and mutual decision, a further opinion may be considered.
3.1.4	The Group agreed that the second prescriber may conduct a remote review of history and images +/- telephone/video consultation if needed, however in most cases, images would not be essential.
3.1.5	The Group agreed that a GP could serve as a one of the prescribers if the GP was comfortable with the workload and the responsibility.

3.1.6	The Group agreed that an MDT opinion could serve as a one of the prescribers, as long as the appropriate expertise was represented on the MDT in addition to the person who had referred the patient to the MDT.
3.1.7	The Group discussed how the definition of the term supervision for initiation and ongoing monitoring of isotretinoin should be left broad for interpretation by the prescribers. Where the supervision of patients who are stable after initiation of treatment would not require the initiator to physically see the patient, the initiating prescriber should be easily contactable or if this is not possible, another prescriber able to initiate isotretinoin should be contactable.
3.1.8	The Group agreed that each community service would not need a nominated pharmacy, as long as the pharmacies had the information and education materials regarding the safe dispensing and supply of isotretinoin.
3.2	**Proposed Acknowledgement of Risk Forms**
3.2.1	The Group was asked to provide written comments on the proposed Acknowledgement of Risk Forms that had been circulated prior to the meeting.
3.2.2	The Group advised that the terms female and women required standardisation throughout the forms.
3.2.3	The Group also discussed that prescribers initiating isotretinoin should ensure that the patient understood the information provided, and that patients should sign to confirm that this has been done, as an understanding of the benefits and risks is hard to confirm.

4.	**Assessment of mental health and sexual dysfunction during treatment -Age-appropriate monitoring tools, frequency and mode of administration**
4.1	The Group discussed the domains of mental health that required screening, whether mood symptomatology should be evaluated, including anxiety as well as the depression, and that the inclusion of suicidality was very important. The group noted that although the PHQ 9 is widely used, it is not necessarily better or worse than other screening questionnaires and in the adult form, does not emphasise suicidality (which in this population would be an important modification) and does not record any anxiety symptoms. The group advised a validated questionnaire would be preferable, but that the MHRA should seek advice and recommendations on suitable assessment tools from relevant professional bodies and the Child and Adolescent Mental Health Services (CAMHS). The Group also noted research undertaken by the British Society for Paediatric and Adolescent Dermatology regarding young persons, where more than one tool and conversations were used to identify young patients with skin conditions requiring additional support. In addition, the group noted for young patients, time may be needed with them on their own as well as with their parents to answer difficult questions. The Group agreed that a framework for mental health to help inform dermatology care is needed, that different approaches may be needed for young people and adults, and that the assessment tools may only be one aspect of that framework.
4.2	The Group agreed that mental health status should be reviewed at each appointment for isotretinoin, but that completion of a questionnaire was not required at every appointment unless there were any concerns. However, a questionnaire should be used at some point after initiation. The group discussed the tool should be used as a conversation starter rather than relying on the score and should be filled out during the appointment rather than at home on their own. The group also recommended continuity of care was important. The Group advised that prescribers could have a specific psychiatric link - i.e., to a named individual in adult and/or CAMHS with whom concerns could be discussed and referred to if necessary. This could be impractical and there should be defined pathways for onward referral when concerns arise
4.3	The Group advised that the framework approach described for mental health could also apply for discussing sexual dysfunction history in adolescents. The 6 Ps of sexual health history would be one recommended framework (CDC). The group noted that the use of unvalidated PROMS in this age group must be avoided and that the safeguarding aspects of asking young people about sexual function including confidentiality, handling disclosures, and chaperones versus independent consultation must be considered. Any proposal should be discussed with the Child Protection Group of RCPCH.

4.4	The Group did not discuss if both mental health and sexual health should be assessed prior to prescription of isotretinoin and then monitored monthly while on isotretinoin
4. 5	The Group agreed that the initiation of isotretinoin should be face to face but subsequent evaluations can be remote as long as there are no concerns (video preferably). See also 3.1.2.
4. 6	The Group did not discuss if issues were identified, if patients should be referred to a specialist in mental health or sexual function as appropriate following local clinical guidance. The group discussed that pathways are needed.
5.	**Educational materials for prescribers**
5.1	The Group discussed the option of asking MAHs to produce educational materials for healthcare professionals, for example a healthcare professional guide or brochure. It was also suggested a multidisciplinary approach was required for training, which should include any primary care health professionals that have interactions with the patients prescribed isotretinoin. Furthermore, asking for patient feedback (either locally or through BAD) for their experiences when they are prescribed isotretinoin was also suggested to help shape the training.
6.	**Monitoring compliance and impact of recommendations**
7.1	It was discussed how, an audit would be useful to monitor compliance, as well as monitoring the number of prescriptions, the number of pregnancies and number of Yellow Card reports received regarding isotretinoin. Furthermore, community services that are already initiating isotretinoin should be a part of this audit. The group suggested the Prescribing Observatory for Mental Health (POMH) could be approached given their role in audits of trusts in England and Wales, as they may be able to audit adherence to guidelines.
8.	**Future research and feasibility of registry**
8.1	The Group noted new studies such as Acne ID, to explore low dose vs high doses of isotretinoin and specific side effects, but that the size of studies may limit conclusions on safety. The group advised more research was required to investigate other known and suspected rare side effects of isotretinoin. Ongoing monitoring of side effects of isotretinoin is crucial. The group discussed the difficulties in capturing side effects such as mental health and sexual dysfunction in patients taking isotretinoin (as well any pregnancies during/after treatment) given that treatment is generally short term and is normally prescribed in secondary care with linkage problems to primary care for long term follow up. The group advised more research is needed to explore the persistence of any side after stopping the isotretinoin treatment. A proactive, long-term registry would be the more effective approach to capture the true incidence of side effects and understand the persistence of any adverse events. However, the group noted if enrolment were compulsory it may become a barrier to treatment for some patients. Finally, the Group suggested that BAD's data on acitretin (which is also a retinoid), where there is data on the longer-term use in patients, could be reassuring.

9.	**Next Steps**
9.1	The Group was informed that communication of the recommendations of the CHM and publication of the report would be in April. The group was informed that following the final Isotretinoin Implementation Advisory Expert Working Group meeting, the advice of the group would be summarised and provided to CHM for their opinion, comments, and final recommendations.
10.	**Any Other Business**
10.1	The Groups were advised that the CHM Report had been updated following discussions held at the last Isotretinoin Implementation Advisory Expert Working Group meeting to incorporate changes for clarity or any contradictory areas of the report. These minor changes were approved by Professor Sir Munir Pirmohamed.
	Date and Time of Next Meeting Friday 12 May 14:00

Agreed by the committee and the chair at its 12/05/2023 meeting as a true and accurate record of proceedings.