COMMISSION ON HUMAN MEDICINES
ISOTRETINOIN IMPLEMENTATION ADVISORY EXPERT WORKING GROUP
Minutes of the meeting held on 12th May 2023 at 14:00 via videoconference.

Members Present

[redacted]

MHRA Presenters

[redacted]
Ms C Blake

MHRA Staff

[redacted]
Dr A Cave
Ms L Henderson

Invited Expert

[redacted]

Committee Services

[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.
1.3	The Chair introduced the aims of the meeting and the topics for discussion.
2.	**Minutes from the 31st March Meeting**
2.1	Approved
3.	**Finalisation of isotretinoin prescriber recommendations and process for implementation**
3.1	The paper was summarised for the group. The group agreed: (i) that the lead prescriber could include a consultant paediatrician with specialist accreditation in dermatology (or equivalent experience for those trained prior to these modules) and working within a consultant dermatologist agreed pathway, (ii) that specialist accreditation in adolescent health was not appropriate as a lead prescriber but could be a second prescriber, (iii) that lead prescribers should be Band 8 or above to ensure no confusion, (iv) that GPs should be given the option to opt-in as additional prescribers, (v) that when the additional prescriber is the MDT, there should be someone present who is eligible to be the lead prescriber (it is not required for the named lead prescriber to be present).
3.2	The function of the additional prescriber was discussed and noted to be required to reduce variation in practice in a vulnerable population, and support the decision that isotretinoin is the correct treatment. The term “lead prescriber” was agreed as a descriptor for prescribers. Alternative wording for additional prescriber was discussed to avoid confusion that 2 signatures were needed on the prescription. There was also concern about the word independent as the second person may be in the same team or Trust. Wording such as additional approver and supporting opinion was suggested. The chair suggested use of “second named healthcare professional” to be used in documents and further consideration of the terminology considered through drafting of the final report.
3.3	It was noted that in the prescriber document, section 13 – it should read **dispensing**, not **prescribing**. And in section 12, the reference should be to section **7**(iii)
4	**Mental health and sexual dysfunction assessment and monitoring framework including referral pathways when problems occur**
4.1	Mental Health

4.1.1	The paper was summarised for the group. The group advised that (i) a mental health PROM eg.PHQ-9 and GAD-2 or 7 should be completed by the patient prior to the first appointment (while waiting, (ii) that a measure of impact of acne should also be completed. This may be a quality of life PROM such as Dermatology Quality of life index (DLQI) or an acne impact PROM such as Cardiff Acne Disability Index (CADI) or Assessment of psychological and social effects of acne (APSEA). The British Society for Paediatric and Adolescent Dermatology (BSPAD) questionnaire "You and Your Skin" might be useful for younger patients and (iii) that these assessments should be repeated at follow-up within 3 months for starting isotretinoin. These answers would contribute to the risk assessment that the prescriber undertakes on whether to prescribe isotretinoin and are only part of a global assessment of the patient. The Group advised that the prescriber should take all factors into account to decide whether a referral for mental health was required. It was noted that these recommendations were based on the BSPAD recommendations that had already been approved by the Royal College of Psychiatrists. It was noted that PHQ-9 and GAD-2 and 7 are available in many languages and those could be used if required.
4.1.2	The group advised that there should be follow-up questions at all appointments, regardless of whether a mental health PROM is completed. It would be useful for these to be an aide memoire and include questions on changes, new concerns, and screening questions eg.PH2/GAD2 questions.
4.1.3	The group advised that if problems are identified during treatment, it was felt that the dermatology team and pharmacists should know the local pathway and system such as self-help, crisis teams, Child and Adolescent Mental Health Services (CAMHS). If problems occur after treatment has stopped it was felt that the patient should see the GP who should liaise with the dermatology and mental health teams.
4.2	Sexual Function
4.2.1	The Group advised that patients should be informed of the risks and that the clinicians should ask questions and that there should be guidance on the topics to be covered but that a formal questionnaire was not required. The Group noted the discussion should be appropriate for the development of the patient and patients should be given the opportunity to discuss this confidentially without parents present. At follow-up questions should determine whether any change in sexual function has been experienced. The group advised the term sexual function should be used rather than sexual dysfunction which was deemed to be difficult to understand.
4.2.2	The Group advised in the event of identified issues, the patient should be referred back to the GP, the psychosexual service or the local sexual health clinic. However, any guidance should not be explicit as pathways are changing. It was suggested that there should be locally agreed services and systems and that prescribers should be made aware of referral processes.

5.	**Defining treatment indications including how to define acne severity and other treatments (4.1 of SmPC wording)**
5.1	The wording of the SmPC was discussed and whether the proposed additional wording *"In patients under 18 years of age two independent prescribers must agree that there is no other effective treatment before initiation of isotretinoin therapy"* was implementable in clinical practice.
5.2	The wording of the indication was discussed extensively. Some of the group felt the wording was appropriate in terms of the balance of risks and benefits and that 'most appropriate treatment' may not be as strong the terms 'no other effective treatment'. Concerns were conversely raised that 'no other effective' was too absolute. It was suggested that there was reference to no other effective treatments and also that national guidelines should be followed. There was a divergence of opinion within the group about the proposed wording change, with no clear consensus for finalised wording.
6.	**Acknowledgment of risk form including pregnancy concerns**
6.1	Comments on the acknowledgment of risk form were provided by the group
6.1.1	• Discussion about the frequencies of side effects and the CHM report findings that there is no accurate data. Although some of the group did feel that there was adequate evidence to suggest that the risk was not high for example for mental health (numbers are unconfirmed but the psychiatric risks are rare). The group suggested that the wording "low incidence but unknown" be put on the acknowledgment form in relation to the frequency of mental health effects. • Sadness should be replaced as this reflects an emotional state rather than mood. • More information on mental health should be included in the patient guide. • There is a lot of information for a patient to absorb and the language reading level was too high in the risk acknowledgment form. • Update prescriber terminology.
7.	**Patient information - what/how/when/where (including possible pre-clinic information), patient reminder card, decision aid**
7.1	*Comments on the patient reminder card.* The group suggested the possible addition of Non-NHS providers e.g. Samaritans and SHOUT text service for out of hours in the patient reminder card if possible. Also, an addition of advice to contact the local mental health crisis service was suggested with aligned wording on the acknowledgement of risk form.

7.2	*Comments on the patient guide.* The group advised that one patient guide was preferable. The Group advised in the absence of accurate figures for many side effects no frequency figures should be included. The Group advised the current section on allergies is not consistent with the SmPC and there should be a separate statement from the BAD.
7.3	*Comments on the patient risk prioritisation guide.* Some members of the group disagreed with the paper's statement that ' as there are unknown frequencies of occurrence of the mental health and sexual function side effects it would not be possible for a decision aid to be developed.' Rather the patient decision aid should explain the limited data, as this is important for decision making. For example, serious side effects have been reported, data is not available, expert opinion is that…
7.4	*Next steps* The Group advised that the MHRA revise materials and liaise with MAHs and patients and re-circulate materials to the group prior to submission to the CHM.
8.	**Prescriber Materials**
	The need for a template referral guideline for GPs, a template GP Proformas and a clinic follow up proforma was advised. These materials should be developed as best practice guides rather than mandated for GP's and made available on a central platform rather than sent to GPs. They should be further developed by BAD and engagement with local medical committees would facilitate introduction of materials and measures.
9.	**Monitoring compliance with and impact of recommendations and future research**
9.1	The paper on future research was presented. The Group noted the need to examine the effect of the risk minimisation in the UK rather than use data from registry data in Scandinavia.
9.2	A Post Authorisation Safety Study (PASS) to determine the effectiveness of the recommendations, and BADBIR registry data on acitretin and Model Hospital were all supported as future research proposals.
10.	**Discussion on acne severity**
10.1	The definition of severe acne was discussed. The group advised that as there no common consensus on what severe acne is (i.e. it is subjective), appropriate research and evidence was needed for a grading system. It was noted that mild acne can also cause scarring e.g. acne excoriée.

10.2	It was also discussed that grading of acne severity does not consider mental health. Mental health (and particularly, the impact of the acne on mental health) is important to assess but should be done separately. The group advised that further research was needed to aid understanding on what constitutes severe acne and associated impact. In addition, there should be further research on how to measure the effect of acne on quality of life and its improvement due to isotretinoin treatment.
11.	**Next steps and how to seek agreement from IIG on final recommendations to CHM regarding all of the above**
11.1	The group agreed external SharePoint should be used to seek agreement from IIG on final recommendations to CHM.
11.2	The chair explained to group that they can comment on the documents/materials where they have expertise.
11.3	It was agreed that patient input on materials via groups from the Royal College of Paediatrics and Child Health (young people and their carers) should be sought.
12.	**Any Other Business**
	None raised.

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