**Isotretinoin: Regulator adds prescribing safeguards after review of side effects**

*BMJ* 2023; 383 p2545 doi: <https://doi.org/10.1136/bmj.p2545>

Dear Editor,

I am extremely disappointed at the new MHRA legislation around the prescription of oral isotretinoin and I suspect all UK dermatologists feel the same way. Indeed, there are a list of words that I could use to try and express my feeling including angry, let down, incredulous, undermined and dejected. It is a sad day when evidence is not used to influence clinical practice and instead disproportionate weight is given to the overvalued views of a minority of individuals with significant personal agendas and emotional bias attending a stakeholder event. The silent vast majority of patients have not been heard. Hearsay has trumped science. The opinion of dermatologists working at the coal face, who have been the only prescribers of isotretinoin for 40 years has not been heard. We know that isotretinoin is a safe and highly effective medication. The only side effect tends to be dose-dependent mucocutaneous dryness. A so-called “expert group” with no experience with isotretinoin have bowed down to pressure from stakeholders’ views that isotretinoin causes depression and sexual dysfunction despite overwhelming evidence to the contrary accrued over many years and continuing to be produced.1,2 Certain individuals who have taken isotretinoin and at the same time or months or years later (which does not fit a scientific modal of causality) developed physical or psychological symptoms and had a vendetta against isotretinoin trying to get it banned completely. The persistent symptoms are often non-specific and could be consistent with somatic symptom disorder which is common in the population.3 It can be human nature to try and blame an external factor and in modern life, forums on social media develop which can perpetuate overvalued beliefs in keeping with an internet meme. The MHRA yellow card reporting system is inherently flawed as one apparent adverse event can be reported multiple times.

Many side effects even those listed as “common” on isotretinoin package inserts are spurious and merely found incidentally in the normal population with levels fluctuating up and down eg anaemia, neutropenia, thrombocytopenia and thrombocytosis. Despite these abnormalities of FBC being listed as occurring in up to 1 in 10 people FBC monitoring is not recommended which causes confusion and worry for patients.4 This shows the lack of credibility in the MHRA. Surely clinical studies of hundreds of thousands of patients is superior.

To enforce asking about sexual health at baseline and at every consultation could cause significant harm via the nocebo effect in often young sexually immature individuals.
The vast majority of patients with acne do not have a mental illness before starting isotretinoin and their emotional health is not compromised when taking it. Most patients will be a bit demoralised, frustrated and have some minor affective symptoms which may reach the threshold of social anxiety disorder with reduced self-confidence and avoidance behaviour quite common. These patients will be helped by improving and likely clearing their acne but with the new legislation they may well be harmed by dermatologists being more reluctant to prescribe. Many studies have shown that isotretinoin can improve mental health and indeed may be protective against suicide with consistent finding of reduced rates of self-harm compared to the background population and in those taking antibiotics for acne.5 Also, to enforce regular use of 2 screening questionnaires (PHQ-9 and GAD) at baseline and for every consultation as part of the drug licence is unhelpful and a step too far. Of course, prescribers should be vigilant for signs of distress or a new or evolving mental illness in all dermatology patients but an impersonal tick box questionnaire is not a substitute for skilled talking and listening and asking the appropriate questions. The proforma can then be used if clinically indicated when it can indeed be a useful adjunct to check for any trend. There will always be a tiny minority of patients who have an undiagnosed mental illness when isotretinoin is initiated eg body dysmorphic disorder, emotionally labile personality disorder or an eating disorder or develop such a disorder incidentally during or after a course of isotretinoin. These illnesses are associated with an increased life time suicide risk.

The final unprecedented new legislation which will likely cause harm is the need to have 2 doctors approve the initiation of isotretinoin in under 18s. This goes against the autonomy of a doctor and shows a lack of respect and trust in dermatologists. If a dermatologist sees a patient under age 18 with acne then we should continue to let them do their job which they are trained to do and often have many years of experience prescribing isotretinoin. Why would a colleague ever wish to disagree? Thus will become a pointless tick-box exercise with no benefit to anyone and merely worry patients and their families unnecessarily as to why a second opinion is needed. They would be quite right in thinking, “gosh this must be a very dangerous drug if a second opinion is needed!”. To add to the nocebo effect we are creating for our vulnerable patients, a recent Patient Information Leaflet on mental health and isotretinoin6 has a link to a resource for children and young people , “When bad things happen”.7 You couldn’t make it up. If that wouldn’t put you off, what would?

It does not have to be this way. The Australasian College of Dermatologists have recently published an excellent position statement with sensible evidence-based recommendations which puts the UK to shame.8 I commend Tan and his colleague in New Zealand for calling out the critical flaws in the MHRA recommendations – they are quite right.9 We have let down our patients and the British Association of Dermatologists have not done enough to prevent this authoritarian legislation based on misinformation and the demonising of isotretinoin. I do hope we can reverse it and let common sense and evidence-based medicine return.

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**Competing interests:**No competing interests

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