Suspension of marketing authorization for ingenol mebutate

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DEAR EDITOR, The authors of the British Association of Dermatologists' (BAD) clinical guidelines for managing actinic keratosis¹ and the BAD's Therapy & Guidelines subcommittee wish to notify readers of the 2017 guideline publication that the marketing authorization for ingenol mebutate has been suspended by the UK's Medicines and Healthcare products Regulatory Agency (MHRA), as of 27 January 2020.² This is due to emerging evidence^{3,4} suggesting possible links between use of the product and an increased risk of developing skin cancers. The manufacturers are recalling all stocks of this medication.⁵ Further advice is available at the MHRA website.⁶

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- 4 US National Library of Medicine. Efficacy and safety of ingenol mebutate gel 0.06% when applied once daily for 2, 3 or 4 consecutive days to a treatment area of approximately 250 cm² on trunk and extremities in subjects with actinic keratosis. Available at: https://clinicaltrials.gov/ct2/show/NCT01998984 (last accessed 1 July 2020).
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6 Medicines and Healthcare products Regulatory Agency. Picato. Available at: https://www.gov.uk/search/all?keywords=picato&order= relevance (last accessed 1 July 2020).

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Reduction in skin cancer diagnosis, and overall cancer referrals, during the COVID-19 pandemic

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DEAR EDITOR, The COVID-19 pandemic has led to a marked reduction in the number of patients accessing the UK's National Health Service for emergency reasons.¹ The cause for this decline is as yet unknown, and it is likely to be multifactorial. We investigated whether there had been a similar reduction in urgent cancer referrals – known in England as the two-week wait (TWW) pathway – and subsequent diagnosis of skin cancer in our dermatology service.

Malignant melanoma (MM) is the fifth most common cancer in the UK.² Cutaneous squamous cell carcinoma (SCC) also has a significant risk of mortality.³ The early diagnosis of MM and SCC is critical to improving patient survival,⁴ a principle that applies to all cancers.

The number of TWW referrals our department has received over the past 5 years has increased (Figure 1a). Using our cancer tracking database, we identified a dramatic 34.3%reduction in referrals in February to April 2020 compared with the same period in 2019 (Figure 1b). The largest decrease was in April 2020, with 335 TWW referrals received, which was 56.4% lower than in April 2019 (768).

More concerning is that the number of skin cancers diagnosed in patients referred on the TWW pathway in March 2020 was lower than in previous years (28 in March 2020, 52 in March 2019; Figure 1c). Using our average conversion rate (percentage of TWW referrals with a histological diagnosis of skin cancer) over the last 5 years (6.95%), and based on the average increase in referrals, we expected to diagnose 125 MMs and SCCs in March and April 2020. Assuming the conversion rate remains stable, this number will drop to 59, a 53% reduction. The reduction in referrals and subsequent skin cancer diagnoses in our patient population is a major concern. Ultimately, many of these cases may present with more advanced disease and poorer outcomes as a consequence.

We investigated whether this trend was observed across a range of other TWW cancer referral pathways in our hospital. We report here the same concerning pattern of decreased referrals across a wide variety of cancer types (Figure 1d).

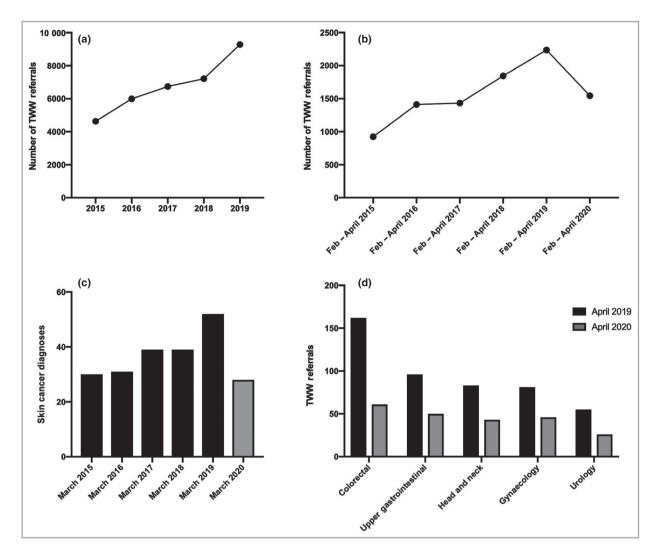


Figure 1 Skin cancer referrals and diagnoses dropped in the period of February to April 2020. (a) Increasing trend of two-week wait (TWW) referrals over the last 5 years. (b) The number of referrals made from February to April 2020 compared with the same period in previous years. (c) The number of skin cancer diagnoses among referred patients in March 2020 compared with previous years. (d) The number of TWW referrals across a range of specialties in our hospital in April 2020 compared with April 2019.

During the post-COVID pandemic recovery phase there may be a significant rebound wave of TWW skin cancer referrals to dermatology departments across the country. This may further test already stretched resources. Predicting this peak will enable advance planning of the provision of appropriate clinic capacity and associated levels of staffing.

The detrimental consequences of the COVID-19 pandemic to clinical practice will not be understood for some time to come. These findings are a wake-up call to prepare for an upswing in skin cancer referrals later this year. The findings also suggest this trend in referrals may lead to delayed diagnosis, with poorer prognosis, of a wide range of cancers.

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News and Notices

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New BJD Associate Editor



I graduated from Oxford University and Guy's Hospital Medical School in 1971. My training in Dermatology and Infectious Disease was in Guy's Hospital, the St John's Institute of Dermatology, the London School of Hygiene and Tropical Medicine (LSHTM) and the Centre for Disease Control, Atlanta, USA. My first appointment as a consultant

dermatologist was at St Johns in 1979 and as a Senior Lecturer at LSHTM and honorary consultant microbiologist at University College Hospital. I moved to the Mary Dunhill Chair of Funding sources: C.H.E. is supported by a National Institute for Health Research (NIHR) Academic Clinical Fellowship. C.E.M.G. and R.B.W. are supported by the Manchester NIHR Biomedical Research Centre.

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Cutaneous Medicine, Kings College London (KCL) in 1989, becoming Dean of the St John's Institute in 1996. I moved to Queen's University Belfast as Dean of the Faculty of Medicine and Health Sciences in 2001 and returned to KCL as Professor of Cutaneous Infection in 2009 where I am currently emeritus.

My clinical and scientific interests are skin infections and global health dermatology and have worked or carried out research in different parts of Africa, Latin America and the West Pacific. I was Chairman of the International, Foundation for Dermatology between 2001 and 2015 and am a technical adviser to WHO on Neglected Tropical Disease of the Skin.

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