

## **GMMM Psoriasis Biologics Pathway**

### **Background:**

Psoriasis is a common inflammatory skin condition which is frequently (30%) associated with an inflammatory arthropathy known as psoriatic arthritis (PsA) and if left untreated is often life ruining. Compelling data demonstrate that the impact on quality of life for patients living with psoriasis is comparable or worse than diabetes, heart disease and cancer<sup>1</sup>. Thus, it is imperative that for those with the most severe disease effective treatment strategies are utilised.

The National Institute for Health and Care Excellence (NICE) have published individual HTAs for each of the 5 licensed systemic biological therapies for psoriasis; namely adalimumab, etanercept, infliximab (Anti-tumour necrosis factor alpha inhibitors -TNFi), ustekinumab (Interleukin 12/23 inhibitor) and most recently (anticipated July 22<sup>nd</sup>) secukinumab (Interleukin 17A inhibitor). Each of these individual biologics has approval for use following failure or unsuitability to methotrexate, ciclosporin and phototherapy when patients also have disease severity scores of psoriasis area and severity index (PASI) and Dermatology Life quality Index (DLQI) of  $\geq 10$  and  $>10$  respectively (Infliximab parameters are higher).

Currently the psoriasis pathway in Greater Manchester allows 3 lines of biologic use before submitting an individual funding request (IFR). This allows sensible access to biologics without inundating the CSU / CCGs with IFRs.

Given the publication of a new HTA for secukinumab it is necessary to update the GMMM psoriasis biologic pathway and we would propose that 3 lines of biologic use is still acceptable as opposed to adding secukinumab as a 4<sup>th</sup> choice in the pathway.

**In line with NICE we propose that all 5 drugs can be used 1<sup>st</sup> line with rarer scenarios being applicable to:**

- **Infliximab (\*or biosimilar for new patients) when patients have unstable disease and rapid control is required**

**Or**

- **Etanercept - when infection risk is a significant concern.**

**Thus, the 3 core agents in the algorithm are *adalimumab, ustekinumab and secukinumab*.**

### **Logic for the 3 core drugs:**

Each of the 3 core drugs targets a different cytokine: adalimumab (TNF); ustekinumab (IL-23) and; secukinumab (IL17A). It is likely that the key driver of any individual's disease is one of these 3 cytokines so if one agent fails a 2<sup>nd</sup> or 3<sup>rd</sup> is likely to work.

Each of the 3 drugs has clinical trial data demonstrating a 75% reduction in PASI, known as PASI 75, of at least 70% <sup>2,3,4</sup>.

Ustekinumab and secukinumab have demonstrated superiority to etanercept in large well designed clinical trials. <sup>2,4</sup>

Secukinumab has demonstrated superiority to ustekinumab in a large well-designed clinical trial<sup>5</sup>.

All 3 drugs have efficacy for psoriatic arthritis<sup>6,7,8</sup> although the TNFi drugs (adalimumab from core set) are the gold standard drugs in this scenario<sup>7</sup>

Although all 3 drugs are highly efficacious in the short term, biologic drugs do have an attrition rate year on year of approximately 15% such that if switches are not allowed longer term disease control, for what is a life-long condition, will be lost. Ustekinumab has a lower attrition rate versus adalimumab<sup>9</sup>, no such "real world" data are available for secukinumab as yet.

We have audited our use of ustekinumab and adalimumab locally and led on a national ustekinumab study showing that both these drugs work following failure of other biologics – all studies have been published in the British Journal of Dermatology <sup>10,11,12</sup>.

As secukinumab has come to the market later many patients in the clinical trial programme had failed prior biologics and secukinumab was show to be efficacious in such scenarios <sup>4</sup>.

### **The Choice of Drug.**

#### **1<sup>st</sup> Line**

There are numerous factors which would influence the choice of which drug should be used at which point in the pathway.

In those with psoriasis (minus PsA) **ustekinumab is 1<sup>st</sup> line** on the basis of better drug survival and a now well established safety record<sup>9</sup>.

In those with both psoriasis and PsA (or signs of early PsA / risk of PsA) **adalimumab is the 1<sup>st</sup> line** choice drug.

Whilst safety data are being accrued in the real world **secukinumab would be 1<sup>st</sup> choice in settings where there are concerns or possible problems with the other 2 drugs** e.g. demyelination risk / tuberculosis risk / rapid efficacy required. Given the access costs to secukinumab are slightly cheaper than existing drugs and the high clinical efficacy, including superiority to ustekinumab, this agent may in a short period of time (1-2 years) be considered 1<sup>st</sup> line in an increasing range of scenarios as experience is gained in the real world setting.

## **2<sup>nd</sup> Line**

After failing either adalimumab or ustekinumab, secukinumab would be used based on the high efficacy levels in psoriasis, the clinical trial data showing that the agent will work in patients who have failed other biologics and the FUTURE studies showing promising efficacy in the setting of PsA. If secukinumab has been used 1<sup>st</sup> line we would recommend either **ustekinumab or adalimumab depending on the presence of PsA (adalimumab) or not (ustekinumab)**.

In the rare scenarios when etanercept or infliximab (or biosimilar) have been used 1<sup>st</sup> line we would recommend secukinumab based on the same logic given above.

## **3<sup>rd</sup> Line**

Acknowledging that PsA often develops after the development of psoriasis those patients who have failed ustekinumab or secukinumab, or who go on to develop PsA whilst on these agents, would be best treated with adalimumab based on its efficacy for both psoriasis and PsA.

In those patients who have failed adalimumab and secukinumab we would suggest ustekinumab based on the completely differing mechanism of action for this agent vs the 1<sup>st</sup> two agents and the excellent tolerability and persistence data that support the use of ustekinumab in people who develop adverse events on other biologic drugs.

**There are other clinical factors which will also inform into the decision around choice of drug which may have current or future relevance and also add significant support to the need for 3 therapeutic options:**

- Risk of candida infection with secukinumab that may make this a poor choice in those prone to such infections.
- Presence of inflammatory bowel disease would be a contraindication for the use of secukinumab
- Body weight – ustekinumab has 2 dosing regimens with those > 100KG getting access to the higher dose of drug, for heavier patients this may be of relevance.

- Immunogenicity risk –emerging data show that certain drugs such as adalimumab may be neutralised by anti-drug antibodies. It is not immediately clear which populations are at risk of this but work that our unit is leading on nationally will help inform this.
- Genetic factors - Certain HLA subtypes may make patients more or less likely to respond to ustekinumab.

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