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OFFICIAL POSITION STATEMENT **September 2021**

Tocilizumab shortage and IL-6 inhibitor treatment of pregnant hospitalised patients with severe COVID-19; sarilumab a possible treatment option

Summary

- Clinical trials have shown tocilizumab to be an effective treatment for hospitalised patients with severe COVID-19
- Due to high demand there is currently a global shortage of tocilizumab
- The Department of Health and Social Care have recommended that equal consideration be given to tocilizumab or sarilumab for all adult patients hospitalised due to COVID-19 who meet the required criteria for interleukin-6 receptor inhibitor treatment
- There have not yet been any official recommendations provided around which treatment option would be the most appropriate for pregnant women
- There are currently no published data regarding the safety of sarilumab use in human pregnancy; as such, it may be preferable to reserve stores of tocilizumab for use in pregnant women
- The available evidence relating to the safety of tocilizumab use in pregnancy, although somewhat limited, does not suggest that tocilizumab is teratogenic or fetotoxic
- Given that monoclonal antibodies have highly selective pharmacological effects, it is anticipated that sarilumab will have a pregnancy safety profile similar to that of tocilizumab. In instances where tocilizumab is unavailable, the benefits of sarilumab treatment in hospitalised pregnant patients with severe COVID-19 who meet the requirements for IL-6 receptor inhibitor treatment will likely outweigh the risks
- To aid the timely collection of pregnancy outcome data, healthcare professionals are encouraged to report cases of sarilumab exposure in pregnancy to UKTIS

Detailed position statement

Tocilizumab is a humanised monoclonal IgG1 antibody that binds and inhibits both soluble and membrane-bound interleukin-6 (IL-6) receptors, thereby inhibiting the pro-inflammatory activity of IL-6.[1] Randomised clinical trials have demonstrated that tocilizumab given to hospitalised patients with severe COVID-19 reduces the risk of death, lessens the need for mechanical ventilation, and decreases time spent in hospital.[2] Due to high demand, there is currently a global shortage of tocilizumab.[3] Sarilumab is also a human monoclonal antibody selective for the IL-6 receptor[4] which is not currently associated with supply chain problems.

The Department of Health and Social Care have published recommendations that equal consideration should be given to tocilizumab or sarilumab for all adult patients hospitalised due to COVID-19 who meet the required criteria for IL-6 inhibitor treatment.[3] However, there have not been any official recommendations provided around which treatment would be most appropriate for pregnant women.

There are currently no published data regarding the safety of sarilumab use in human pregnancy. Preclinical reproductive toxicity studies (using animal models) undertaken by the manufacturer have not been published in the peer-reviewed literature. Product literature states that pregnant Cynomolgus monkeys given intravenous sarilumab once-weekly from early gestation to birth experienced AUC plasma concentrations 83 times those seen in human therapy.[4] No adverse effects on the mother, embryo, fetus or neonate (up to 1 month after birth) were described.[4]

Given the limited evidence-base available regarding the safety of sarilumab use in pregnancy, it may be preferable for stores of tocilizumab to be reserved for pregnant women. A narrative review published in August 2021 has summarised the published data on tocilizumab use in pregnancy.[5] This literature review identified more than 600 pregnancies exposed to tocilizumab. Although adverse pregnancy outcomes have been described following maternal tocilizumab use in pregnancy, including cases of congenital anomaly, miscarriage, low birth weight and preterm delivery, the crude rates of these events do not appear notably increased above the respective background rates. Therefore, there is currently no compelling evidence that tocilizumab is teratogenic or fetotoxic. There is little data on tocilizumab exposure in the second and third trimesters when placental transport is highest, and the effects of tocilizumab on the developing immune system are unclear. Guidance from Public Health England (issued 2017) specifies that live vaccines should not be used until the infant is 6 months old following in utero biologic immunosuppressant exposure[6, 7] and it is reasonable to apply this recommendation to tocilizumab and sarilumab.

Given that monoclonal antibodies have highly selective pharmacological effects, it is anticipated that sarilumab will have a pregnancy safety profile similar to that of tocilizumab. In instances where tocilizumab is unavailable, the benefits of sarilumab treatment in hospitalised pregnant patients with severe COVID-19 who meet the requirements for IL-6 receptor inhibitor treatment will likely outweigh the risks.

As no human pregnancy data are currently available for sarilumab, careful collation of pregnancy outcome data is advised. To aid this data collection, healthcare professionals are encouraged to report cases of sarilumab exposure in pregnancy to UKTIS.

References

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