**HSE COVID-19: Interim Clinical Guidance – Immunosuppressant Therapy (6th April 2020) v2**

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**Purpose**: This guidance is to aid healthcare professionals to identify patients who may be at increased risk of infection due to ongoing regular immunosuppressant therapy.

Risk is stratified into Normal Risk, Increased Risk and Higher Risk.

This information may also be used to inform any future updates about the advice for patients on immunosuppressive therapy to cocoon or otherwise.

**Target Audience**: Healthcare professionals, including those working in occupational health settings and GPs.

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**Immunosuppressant therapy sufficient to significantly increase the risk of infection**

The following is a list of immunosuppression therapies which classifies those sufficient to significantly increase risk of infection. This list is not exhaustive; for a full list and individual product Summaries of Product Characteristics (SPC) see [www.hpra.ie](http://www.hpra.ie).

Individuals who are essential workers should contact their occupational health department or GP to discuss their options for safe working.

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**Section 1: Corticosteroids**

Daily high dose corticosteroids are immunosuppressive. The following doses of prednisolone (or equivalent dose of other glucocorticoid) are likely to be immunosuppressive:

Adults and children weighing 10kg or greater:

Prednisolone 40 mg/day or greater for more than 1 week,

or 20 mg/day or greater for 2 weeks or longer

Children weighing less than 10 kg:

2mg/kg/day for 2 weeks or longer

Equivalent doses of the following glucocorticoids are likely to be immunosuppressive:

Betamethasone

Dexamethasone

Hydrocortisone

Methylprednisolone

Triamcinolone

**The following steroid treatment is not considered immunosuppressive and is not considered** **sufficient to significantly increase risk of infection:**

i. Short term (less than 7 days) irrespective of dose

ii. Long term (2 weeks or greater) less than 20mg/day of prednisolone or equivalent (however see notes in section 3).

iii. Long-term, alternate-day treatment with short-acting preparations

iv. Maintenance physiologic doses (replacement therapy)

v. Topical (skin or eyes) or by inhalation

vi. Intra-articular, bursal, or tendon injection

vii. Fludrocortisone less than 300 micrograms/day

Use of topical Calcineurin inhibitors (TCIs, e.g., Tacrolimus and Pimecrolimus) for atopic dermatitis in otherwise healthy adults does not result in significant systemic absorption or immunosuppression.

**Section 2: Immunomodulatory treatment** causes immunosuppression which may be sufficient to significantly increase the risk of infection and includes medication such as:

|  |  |
| --- | --- |
| **Azathioprine** *(Imuran®, Imuger®)***6-Mercaptopurine** *(Puri-Nethol®, Xaluprine®)***Ciclosporin** *(Neoral®, Sandimmun®, Deximune®)***Mycophenolic acid** *(Cellcept®, Myclausen®, Mycolat®, Myfenax®***Sirolimus** *(Rapamune®)* **Tacrolimus** *(Advagraf®, Dailiport®, Envarsus® Modigraf®,Prograf®, Tacforius®***Everolimus** *(Afinitor®, Certican®, Votubia®)* | **Methotrexate** *(Methofill®, Jylamvo®, Metoject®, Nordimet®)***Cyclophosphamide** *(Endoxana®)***Leflunomide** *(Arava®, Repso®)***Tenflunomide****Dimethyl Fumarate** (*Skilarence®, Tecfidera®)* |
| **Biological agents** |  |
| **TNF alpha inhibitors****Adalimumab** *(Amgevita®, Amsparity®,Halimatoz®, Hefiya®, Hulio®, Humira®, Hyrimoz®, Idacio®, Imraldi®)***Etanercept** *(Benepali®,Enbrel®, Erelzi®, Lifmior®)***Infliximab** *(Flixabi®, Inflectra®, Remicade®, Remsima®, Zessly®)***Certolizumab** *(Cimzia®)***Golimumab** *(Simponi®)* | **Biological agents for multiple sclerosis** **Fingolimod** *(Gilenya®)***Natalizumab** *(Tysabri®)***Alemtuzumab** *(Lemtrada®)***Daclizumab****Dimethyl Fumarate** (*Skilarence®, Tecfidera®)* |
| **Interleukin inhibitors****IL1****Anakinra** *(Kineret®)***Canakinumab** *(Ilaris®)***Il-6****Tocilizumab** *(RoActemra®)* | **IL17/23****Ustekinumab** *(Stelara®)***Guselkumab** *(Termfya®)***Tildrakizumab** *(Ilumetri®)***Brodalumab** *(Kyntheum®)***Ixekizumab** *(Taltz®)***Secukinumab** *(Cosentyx®)* |
| **Other mechanisms****Abatacept** *(Orencia®)***Eculizumab** *(Soliris®)***Rituximab** *(Blitzima®, Mabthera®, Ritemvia®, Rixathon®, Riximyo®, Truxima®***Apremilast** *(Otezia®)***Vedolizumab** *(Entyvio®)* | **JAK inhibitors****Tofacitinib** *(Xeljanz®)***Baricitinib** *(Olumiant®)***Ruxolitinib** *(Jakavi®)* |

**Approved Generic drug name given first** *(Proprietary/ Brand name(s)® in brackets)*

**Section 3 Risk Stratification**

1. **Normal risk:**

People who have an auto-immune disease, are not taking immunosuppressant therapies and have no additional risks (listed below) are at similar risk to the general population. This includes other medication for auto-immune conditions, including hydroxychloroquine, sulfasalazine, mesalazine, gold products and penicillamine.

Some type 2 monoclonal antibodies for type 2 inflammation are also in this category. This includes: Reslizumab, Benralizumab, Mepolizumab, Omalizumab, Dupilumab (although people on these medicines may be in high risk groups for Covid-19 for other reasons e.g. severe respiratory disease).

1. **Increased risk:**

People taking any single medication from section 2 (and not listed in higher risk category C below) without prednisolone 5mg daily or greater in the last 4 weeks.

1. **Higher risk:**

Prednisolone 40 mg/day or greater for more than 1 week,

or 20 mg/day or greater for 2 weeks or longer

Or

People taking two or more immunosuppressant medicines.

This includes prednisolone 5mg or greater in the last 4 weeks.

Or

Cyclophosphamide or Rituximab in the last 6 months

Or

People with poorly controlled disease or a history of recurring infections (requiring medical treatment) while on immunosuppressant medication.

Or

Some people with Multiple Sclerosis (Advice being finalised, will be available via Covid-19 HSE Clinical Guidance and Evidence repository and MS Society)

Or

People taking one immunosuppressant known to increase the risk of infection or serious infection and also in one or more of the following categories:

* over 70 years of age
* solid organ transplant recipients
* have cancer and are undergoing active chemotherapy, immunotherapy, antibody treatment or other treatment which can affect the immune system,
* severe respiratory conditions including cystic fibrosis, severe asthma & severe COPD
* have rare diseases and inborn errors of metabolism that significantly increase the risk of infections (such as SCID, homozygous sickle cell)
* are pregnant and have significant heart disease, congenital or acquired

An individual’s risk may be higher or lower than these categories depending on associated risk factors or co-morbidities e.g hypertension, angina, a history of heart attack or heart failure, diabetes, kidney disease, obesity or smoking. Their clinician may assess this risk and advise them accordingly.

**Section 4: Patient information: Immunosuppressive medicines**

This information is for people who are being cared for by a:

* rheumatologist
* dermatologist
* gastroenterologist
* respiratory specialist

Being on immunosuppressive treatments does not increase your risk of getting a COVID-19 infection (coronavirus).

There is no evidence to date that being on an immunosuppressive treatment puts you at higher risk of severe disease with COVID-19. However, as other infections can cause severe illness in people who are on immunosuppressive treatment, you should take extra care.

Current HSE advice on groups who should be cocooning is available here.

If you stop your medicine you may be more likely to have a flare of your condition during this period.

Immunosuppressive medicines include:

* biologic agents
* steroids
* methotrexate
* azathioprine

**Steroids**

Keep taking steroids if you are usually on them unless your doctor tells you otherwise. Stopping steroids suddenly can make you very unwell.

If you become unwell due to coronavirus or another infection, continue to take your steroids.

Never start taking steroids unless your doctor tells you to.

Steroid tablets include prednisolone – brand name: Deltacortril.

Other steroid medicines do not usually cause immunosuppression.  This includes inhalers (inhaled corticosteroids) which are often known as preventer inhalers.  It is very important to continue to take your preventer inhaler.  This will decrease your risk of an asthma attack or COPD exacerbation and reduce your respiratory symptoms.

Other steroid medicines include nasal sprays or drops, creams and eye or ear drops.  All of these medicines should be continued and used as you normally would.

### Immunosuppressive treatments

If you attend a consultant, ask them if they recommend any changes to your treatment. But do not make changes unless your doctor tells you to.

There is no evidence to-date that being on an immunosuppressive treatment puts you at higher risk of severe disease. However, as other infections can cause severe illness in people who are on immunosuppressive treatment, you should take extra care.

If you usually have regular blood tests, these should continue. But ring your hospital first as some [hospital services are disrupted](https://www2.hse.ie/services/hospital-service-disruptions/hospital-service-disruptions-covid19.html).

If you become unwell due to coronavirus or another infection, continue to take your steroids. Contact your GP or consultant to ask if they recommend any changes to your steroids or other immunosuppressant treatment. Do this before taking the next dose of your immunosuppressant treatment.

The coronavirus pandemic may last several months. If you reduce or stop your medicine you may be more likely to have a flare during this period. This means you might need to restart your treatment and attend your GP or hospital.

The immunosuppressant effect of each medicine continues for different periods of time after you stop them. You may still be immunosuppressed for a period of time if you stop them, often for many months.

Please check [www.hse.ie](http://www.hse.ie) for current HSE advice about cocooning.

If you are an essential worker on an immunosuppressant medicine, you should notify Occupational Health or your GP to discuss your options for safe working.

Further information about the level of risk with each medicine is available. This list includes some of the medicines used for the treatment of auto-immune conditions (e.g. rheumatoid arthritis, psoriasis, inflammatory bowel disease) which may increase the risk of infection in general. The list is not exhaustive and for up to date information on all licensed medicines in Ireland visit [www.hpra.ie](http://www.hpra.ie)

**References**

Individual Summary of Product Characteristics for each drug [www.hpra.ie](http://www.hpra.ie) (accessed 1st April 2020)

Occupational health guidance issued 31st March 2020. [https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/occupationalhealthguidance/Pregnant%20HCWs,%20Vulnerable%20HCWs&%20Other%20HCWs%20with%20Pre-existing%20Disease%20V3%2030%2003%2020.pdf](https://www.hpsc.ie/a-z/respiratory/coronavirus/novelcoronavirus/guidance/occupationalhealthguidance/Pregnant%20HCWs%2C%20Vulnerable%20HCWs%26%20Other%20HCWs%20with%20Pre-existing%20Disease%20V3%2030%2003%2020.pdf)

National Immunisation Guidance. Immunisation of Immunocompromised Persons Ch 3. <https://www.hse.ie/eng/health/immunisation/hcpinfo/guidelines/chapter3.pdf> (accessed 1st April 2020)

The HSE list of immunosuppressants from sepsis programme: <https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/list-of-immunosuppressant-medication.pdf> (accessed 1st April 2020)

Current HSE.ie text on immunosuppressants [www.hse.ie/coronavirus](http://www.hse.ie/coronavirus) in the Treatment section updated 20th March 2020.