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# Anakinra

**Anakinra**, sold under the brand name **Kineret**, is a biopharmaceutical medication used to treat rheumatoid arthritis, cryopyrin-associated periodic syndromes, familial Mediterranean fever, and Still's disease.<sup>[3]</sup> It is a recombinant and slightly modified version of the human interleukin 1 receptor antagonist protein.<sup>[3]</sup> It is marketed by Swedish Orphan Biovitrum.<sup>[1]</sup> Anakinra is administered by subcutaneous injection.<sup>[2]</sup>

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## Medical uses

It is used as a second line treatment to manage symptoms of rheumatoid arthritis after treatment with a disease-modifying antirheumatic drug (DMARD) has failed.<sup>[1][2]</sup> It can be used in combination with some DMARDs.<sup>[1][2][4]</sup>

It is used to people with a cryopyrin-associated periodic syndrome, including neonatal-onset multisystem inflammatory disease.<sup>[1][2]</sup>

It is used to treat Schnitzler's syndrome (off label in the US).<sup>[5]</sup> Its response rate is such that it has been suggested that "Treatment failures should lead to reconsider the diagnosis."<sup>[6]</sup>

## Anakinra



### Clinical data

<b><u>Trade names</u></b>	Kineret
<b><u>AHFS/Drugs.com</u></b>	<u>Monograph</u> ( <a href="https://www.drugs.com/monograph/anakinra.html">https://www.drugs.com/monograph/anakinra.html</a> )
<b><u>MedlinePlus</u></b>	a602001 ( <a href="https://medlineplus.gov/druginfo/meds/a602001.html">https://medlineplus.gov/druginfo/meds/a602001.html</a> )
<b><u>License data</u></b>	<span><span><span></span></span><span> </span></span> EU <span><span><span></span></span><span> </span></span> EMA: by INN ( <a href="http://www.ema.europa.eu/ema/index.jsp?curl=%2Fpages%2Fmedicines%2Flanding%2Fepar_search.jsp&amp;mid=&amp;searchTab=searchByKey&amp;alreadyLoaded=true&amp;isNewQuery=true&amp;status=Authorised&amp;status=Withdrawn&amp;status=Suspended&amp;status=Refused&amp;keywordSearch=Submit&amp;searchType=inn&amp;taxonomyPath=&amp;treeNumber=&amp;searchGenericType=generics&amp;keyword=Anakinra">http://www.ema.europa.eu/ema/index.jsp?curl=%2Fpages%2Fmedicines%2Flanding%2Fepar_search.jsp&amp;mid=&amp;searchTab=searchByKey&amp;alreadyLoaded=true&amp;isNewQuery=true&amp;status=Authorised&amp;status=Withdrawn&amp;status=Suspended&amp;status=Refused&amp;keywordSearch=Submit&amp;searchType=inn&amp;taxonomyPath=&amp;treeNumber=&amp;searchGenericType=generics&amp;keyword=Anakinra</a> )

Off label, it is used to treat systemic juvenile idiopathic arthritis (SJIA), gout, calcium pyrophosphate deposition (CPPD), Behçet's disease, ankylosing spondylitis, uveitis, and other auto-inflammatory syndromes.<sup>[7]</sup>

In December 2021, the European Medicines Agency authorized the use of anakinra "to treat COVID-19 in adults with pneumonia requiring supplemental oxygen (low or high flow oxygen) and who are at risk of developing severe respiratory failure, as determined by blood levels of a protein called suPAR (soluble urokinase plasminogen activator receptor) of at least 6 ng per ml."<sup>[3][8][9]</sup>

## Safety

It was not tested in pregnant women, but appeared to be safe in animal studies.<sup>[2]</sup>

It should not be used in people who have active infections or latent tuberculosis, who have low white blood cells counts, or who are taking TNF inhibitors.<sup>[2]</sup>

## Adverse effects

More than ten percent of people taking Anakinra have injection site reactions, headaches, and have increased cholesterol levels.<sup>[1]</sup> Between one and ten percent of recipients have severe infections, decreased white blood cells, or decreased platelets.<sup>[1]</sup> It is unclear if taking Anakinra increases cancer risk; studies are complicated by the fact that people with rheumatoid arthritis already face higher cancer risk.<sup>[1][4]</sup>

## Chemistry

Anakinra differs from the sequence of Interleukin 1 receptor antagonist by one methionine amino acid added to its N-terminus; it also differs from the human protein in that it is not glycosylated, as it is manufactured in *Escherichia coli*.<sup>[2]</sup>

## History

It was approved for medical use in the US in 2001,<sup>[2]</sup> and in the European Union in 2002.<sup>[1][3]</sup>

	<span>US</span> <span>DailyMed</span> : <span>Anakinra</span> (https://dailymed.nlm.nih.gov/dailymed/search.cfm?labeltype=all&query=Anakinra)
<b>Pregnancy category</b>	<span>AU</span> : B1
<b>Routes of administration</b>	<u>Subcutaneous</u>
<b>ATC code</b>	L04AC03 (WHO (https://www.whooc.no/atcddd_index/?code=L04AC03))
<b>Legal status</b>	
<b>Legal status</b>	<span>AU</span> : S4 (Prescription only) <span>CA</span> : R-only <span>UK</span> : POM (Prescription only) <sup>[1]</sup> <span>US</span> : R-only <sup>[2]</sup> <span>EU</span> : Rx-only <sup>[3]</sup>
<b>Pharmacokinetic data</b>	
<b>Bioavailability</b>	95%
<b>Metabolism</b>	predominantly kidney
<b>Elimination half-life</b>	4-6 hrs
<b>Identifiers</b>	
<b>IUPAC name</b>	Recombinant human Interleukin-1 receptor antagonist protein; syn. N2-I-methionyl-interleukin 1 receptor antagonist (human isoform x reduced)
<b>CAS Number</b>	143090-92-0 (https://commonchemistry.cas.org/detail?cas_rn=143090-92-0) ✓
<b>DrugBank</b>	DB00026 (https://www.drugbank.ca/drugs/DB00026) ✓
<b>ChemSpider</b>	none
<b>UNII</b>	9013DUQ28K (https://

In 2018, NHS England published a *Clinical Commissioning Policy: Anakinra to treat periodic fevers and autoinflammatory disorders (all ages)* allowing Anakinra to be commissioned as a first-line treatment for Schnitzler's syndrome and in cases where the first-line treatment is not effective for Familial Mediterranean fever, Hyper-IgD syndrome also known as Mevalonate kinase deficiency, and TNF receptor associated periodic syndrome (TRAPS),<sup>[10]</sup> and a *Clinical Commissioning Policy: Anakinra/tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults)*, allowing Anakinra to be commissioned for adult-onset Still's disease "as a third line treatment where patients are refractory to steroid-sparing effect DMARDs".<sup>[11]</sup>

In December 2020, Anakinra was approved by the US Food and Drug Administration for the treatment of deficiency of the interleukin-1–receptor antagonist (DIRA), a rare autoinflammatory disease of infancy.<sup>[12]</sup> In 2021, it was announced that the Ministry of Health of the Russian Federation had approved the use of Anakinra for the treatment of CAPS.<sup>[13]</sup>

In October 2021, NHS England published *Clinical Commissioning Policy: Anakinra for Haemophagocytic Lymphohistiocytosis (HLH) for adults and children in all ages*, allowing Anakinra to be used in the treatment of HLH.<sup>[14]</sup>

## Society and culture

### Legal status

Approvals

Country	Condition								
	RA	CAPS	FMF	AOSD	Schnitzler's	MKD	TRAPS	DIRA	HLH
US	2001							2020	
UK				2018	2018	2018	2018		2021
EU	2002	2002	2002						
Russia		2021							

## Research

Anakinra effectively treated meningitis caused by a rare genetic mutation in the gene NALP3 in a 67-year-old man enrolled in the Undiagnosed Diseases Network.<sup>[15]</sup> Researchers at Johns Hopkins University announced in 2019 that anakinra given to pregnant mice with Zika virus had reduced fetal deaths and birth defects.<sup>[16]</sup> In November 2019, researchers at the University of Manchester reported that Anakinra might have a use in preventing breast cancer from spreading to the bones.<sup>[17][18]</sup>

	<u>precision.fda.gov/uniiisearch/srs/unii/9013DUQ28K)</u>
<b>KEGG</b>	D02934 ( <a href="https://www.kegg.jp/entry/D02934">https://www.kegg.jp/entry/D02934</a> ) ✓
<b>ChEMBL</b>	ChEMBL1201570 ( <a href="https://www.ebi.ac.uk/chembl/index.php/compound/inspect/ChEMBL1201570">https://www.ebi.ac.uk/chembl/index.php/compound/inspect/ChEMBL1201570</a> ) ✗
<b>Chemical and physical data</b>	
<b>Formula</b>	C <sub>759</sub> H <sub>1186</sub> N <sub>208</sub> O <sub>232</sub> S <sub>10</sub>
<b>Molar mass</b>	17 257.66 g·mol <sup>−1</sup>
	✗✓ (what is this?) (verify)

In 2021, it was reported that Anakinra appeared to reduce the neuropathic pain experienced by patients undergoing chemotherapy with vincristine, saying that "repurposing anakinra may be an effective co-treatment strategy to prevent vincristine-induced peripheral neuropathy".<sup>[19][20]</sup>

A review published in 2022 found that "Anakinra appears to show efficacy for numerous dermatologic conditions, with the strongest evidence for hidradenitis suppurativa, Behçet's disease, Muckle–Wells syndrome, and SAPHO syndrome." and concluded that "Overall, anakinra appears to be a promising option in the treatment of numerous dermatologic inflammatory conditions refractory to first line therapies, but further and higher-quality data is needed to clarify its therapeutic role."<sup>[21]</sup>

## COVID-19

Anakinra is undergoing multiple clinical trials to treat COVID-19 patients, by targeting mechanisms in patients with hyperinflammation.<sup>[22]</sup> In 2021 a review and meta-analysis of 9 studies involving 1,119 cases concluded that "Available evidence shows that treatment with anakinra reduces both the need for invasive mechanical ventilation and mortality risk of hospitalized non-intubated patients with COVID-19 without increasing the risk of adverse events."<sup>[23]</sup>

As of July 2021, the European Medicines Agency (EMA) is evaluating an application to extend the use of anakinra to include treatment of COVID-19 in adults with pneumonia who are at risk of developing severe respiratory failure (inability of the lungs to work properly).<sup>[24]</sup> According to study results published in September 2021 in *Nature Medicine*, hospitalized COVID-19 patients at increased risk for respiratory failure showed significant improvement after treatment with Anakinra.<sup>[25][26]</sup>

## References

1. "Kineret 100 mg solution for injection in a pre-filled syringe - Summary of Product Characteristics (SmPC)" (<https://www.medicines.org.uk/emc/product/559>). UK Electronic Medicines Compendium. Retrieved 2 March 2022.
2. "Kineret- anakinra injection, solution" (<https://dailymed.nlm.nih.gov/dailymed/drugInfo.cfm?setid=d9d74915-6606-4570-9c52-c4001d3177de>). *DailyMed*. 30 December 2020. Retrieved 2 March 2022.
3. "Kineret EPAR" (<https://www.ema.europa.eu/en/medicines/human/EPAR/kineret>). *European Medicines Agency*. Retrieved 20 July 2021. Text was copied from this source which is copyright European Medicines Agency. Reproduction is authorized provided the source is acknowledged.
4. Singh JA, Hossain A, Tanjong Ghogomu E, Kotb A, Christensen R, Mudano AS, et al. (May 2016). "Biologics or tofacitinib for rheumatoid arthritis in incomplete responders to methotrexate or other traditional disease-modifying anti-rheumatic drugs: a systematic review and network meta-analysis" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068903>). *The Cochrane Database of Systematic Reviews*. **2016** (5): CD012183. doi:10.1002/14651858.CD012183 (<https://doi.org/10.1002%2F14651858.CD012183>). PMC 7068903 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7068903>). PMID 27175934 (<https://pubmed.ncbi.nlm.nih.gov/27175934>).
5. Gusdorf L, Lipsker D (August 2017). "Schnitzler Syndrome: a Review". *Current Rheumatology Reports*. **19** (8): 46. doi:10.1007/s11926-017-0673-5 (<https://doi.org/10.1007%2Fs11926-017-0673-5>). PMID 28718061 (<https://pubmed.ncbi.nlm.nih.gov/28718061>). S2CID 13780498 (<https://api.semanticscholar.org/CorpusID:13780498>).

6. Néel, Antoine; et al. (October 2014). "Long-term effectiveness and safety of interleukin-1 receptor antagonist (anakinra) in Schnitzler's syndrome: A french multicenter study". *Autoimmunity Reviews*. **13** (10): 1035–1041. doi:10.1016/j.autrev.2014.08.031 (https://doi.org/10.1016%2Fj.autrev.2014.08.031).
7. "Anakinra (Kineret)" (https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Treatments/Anakinra-Kineret). *American College of Rheumatology*. Retrieved 2021-11-22.
8. "EMA recommends approval for use of Kineret in adults with COVID-19" (https://www.ema.europa.eu/en/news/ema-recommends-approval-use-kineret-adults-covid-19). *European Medicines Agency*. 16 December 2021. Retrieved 2 March 2022. Text was copied from this source which is copyright European Medicines Agency. Reproduction is authorized provided the source is acknowledged.
9. Aripaka, Pushkala; Karimi, Amna (16 December 2021). "EU regulator builds Omicron defences with approvals of GSK-Vir, Sobi drugs" (https://www.reuters.com/business/healthcare-pharmaceuticals/eu-regulator-okays-covid-19-treatments-gsk-vir-sobi-2021-12-16/). *Reuters*. Retrieved 17 December 2021.
10. NHS England (29 June 2018). *Clinical Commissioning Policy: Anakinra to treat periodic fevers and autoinflammatory disorders (all ages)* (https://www.england.nhs.uk/wp-content/uploads/2018/07/1713-anakinra-for-periodic-fever.pdf) (PDF). Retrieved 9 July 2018.
11. NHS England (29 June 2018). *Clinical Commissioning Policy: Anakinra/tocilizumab for the treatment of Adult-Onset Still's Disease refractory to second-line therapy (adults)* (https://www.england.nhs.uk/wp-content/uploads/2018/07/1609-anakinra-and-tocilizumab-for-aosd.pdf) (PDF). Retrieved 13 July 2018.
12. Kaufman, Michelle B. (2 February 2021). "FDA Approves New Rituximab Biosimilar & Anakinra to Treat a Rare Disease" (https://www.the-rheumatologist.org/article/fda-approves-new-rituximab-biosimilar-anakinra-to-treat-a-rare-disease/). *The Rheumatologist*. Retrieved 4 February 2021.
13. "Kineret approved in Russia for the treatment of CAPS" (https://www.thepharmaletter.com/article/kineret-approved-in-russia-for-the-treatment-of-caps). *The Pharma Letter*. 17 February 2021. Retrieved 18 February 2021.
14. NHS England (October 2021). *Clinical Commissioning Policy: Anakinra for Haemophagocytic Lymphohistiocytosis (HLH) for adults and children in all ages* (https://www.england.nhs.uk/wp-content/uploads/2021/10/1924-Clinical-commissioning-policy-anakinra-for-haemophagocytic-lymphohistiocytosis-1.pdf) (PDF). Retrieved 14 October 2021.
15. Kolata G (2019-01-07). "When the Illness Is a Mystery, Patients Turn to These Detectives" (https://www.nytimes.com/2019/01/07/health/patients-medical-mysteries.html). *The New York Times*. Retrieved 2019-01-09.
16. "Rheumatoid Arthritis Drug Diminishes Zika Birth Defects in Mice" (https://www.hopkinsmedicine.org/news/newsroom/news-releases/rheumatoid-arthritis-drug-diminishes-zika-birth-defects-in-mice). *Newsroom*. Johns Hopkins Medicine. 6 May 2019. Retrieved 5 September 2019.
17. "Arthritis drugs could be repurposed to help prevent breast cancer spreading to the bone, study suggests" (https://www.manchester.ac.uk/discover/news/arthritis-drugs-could-be-repurposed-to-help-prevent-breast-cancer-spreading-to-the-bone-study-suggests/). *Press release*. University of Manchester. 20 November 2019. Retrieved 21 November 2019.
18. Eyre R, Alférez DG, Santiago-Gómez A, Spence K, McConnell JC, Hart C, et al. (November 2019). "Microenvironmental IL1β promotes breast cancer metastatic colonisation in the bone via activation of Wnt signalling" (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6825219). *Nature Communications*. **10** (1): 5016. Bibcode:2019NatCo..10.5016E (https://ui.adsabs.harvard.edu/abs/2019NatCo..10.5016E). doi:10.1038/s41467-019-12807-0 (https://doi.org/10.1038%2Fs41467-019-12807-0). PMC 6825219 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6825219). PMID 31676788 (https://pubmed.ncbi.nlm.nih.gov/31676788).

19. Starobova H, Monteleone M, Adolphe C, Batoon L, Sandrock CJ, Tay B, et al. (May 2021). "Vincristine-induced peripheral neuropathy is driven by canonical NLRP3 activation and IL-1 $\beta$  release" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7933984>). *The Journal of Experimental Medicine*. **218** (5): e20201452. doi:10.1084/jem.20201452 (<https://doi.org/10.1084%2Fjem.20201452>). PMC 7933984 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7933984>). PMID 33656514 (<https://pubmed.ncbi.nlm.nih.gov/33656514>).
20. "Chemotherapy with fewer side effects may be on the way" (<https://www.uq.edu.au/news/article/2021/02/chemotherapy-fewer-side-effects-may-be-way-0>). University of Queensland. 15 March 2021. Retrieved 15 March 2021.
21. Tegtmeyer, Kyle; et al. (2 January 2022). "Off-Label studies on anakinra in dermatology: a review". *Journal of Dermatological Treatment*. **33** (1): 73–86. doi:10.1080/09546634.2020.1755417 (<https://doi.org/10.1080%2F09546634.2020.1755417>).
22. "Anakinra in COVID-19: important considerations for clinical trials" (<https://www.researchgate.net/publication/341554901>). *Press release*. May 2020. Retrieved 5 January 2021.
23. Barkas, Fotios; Ntekouan, Sebastian Filippas; Kosmidou, Maria; Liberopoulos, Evangelos; Lontos, Angelos; Milionis, Haralampos (2021-05-17). "Anakinra in hospitalized non-intubated patients with coronavirus disease 2019: a systematic review and meta-analysis" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8194671>). *Rheumatology*. **60** (12): 5527–5537. doi:10.1093/rheumatology/keab447 (<https://doi.org/10.1093%2Frheumatology%2Fkeab447>). PMC 8194671 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8194671>). PMID 33999135 (<https://pubmed.ncbi.nlm.nih.gov/33999135>).
24. "EMA starts evaluating the use of Kineret in adult COVID-19 patients at increased risk severe respiratory failure" (<https://www.ema.europa.eu/en/news/ema-starts-evaluating-use-kineret-adult-covid-19-patients-increased-risk-severe-respiratory-failure>). *European Medicines Agency (EMA)* (Press release). 16 July 2021. Retrieved 20 July 2021.
25. Kyriazopoulou, Evdoxia; Poulakou, Garyfallia; Milionis, Haralampos; Metallidis, Simeon; Adamis, Georgios; Tsiakos, Konstantinos; Fragkou, Archontoula; Rapti, Aggeliki; Damoulari, Christina; Fantoni, Massimo; Kalomenidis, Ioannis (2021-09-03). "Early treatment of COVID-19 with anakinra guided by soluble urokinase plasminogen receptor plasma levels: a double-blind, randomized controlled phase 3 trial" (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8516650>). *Nature Medicine*. **27** (10): 1752–1760. doi:10.1038/s41591-021-01499-z (<https://doi.org/10.1038%2Fs41591-021-01499-z>). ISSN 1078-8956 (<https://www.worldcat.org/issn/1078-8956>). PMC 8516650 (<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8516650>). PMID 34480127 (<https://pubmed.ncbi.nlm.nih.gov/34480127>).
26. "Anakinra improved survival in hospitalized COVID-19 patients" (<https://www.mdedge.com/rheumatology/article/245801/coronavirus-updates/anakinra-improved-survival-hospitalized-covid-19>). *www.mdedge.com*. Retrieved 2021-09-09.

## External links

- "Anakinra" (<https://druginfo.nlm.nih.gov/drugportal/name/anakinra>). *Drug Information Portal*. U.S. National Library of Medicine.

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