



Dear Vet,

During your career you most likely have had to diagnose cats with the 100% deadly virus FIP at some point. You probably have felt the undeniable feeling of frustration because you had to tell the owners that there was no cure for this disease, that it was only a death sentence to their beloved cats. That the only thing you could offer your patients was a respectful euthanizing, *maybe* with a short period of palliative care to make their last day('s) as comfortable as possible.

### **HOWEVER**

FIP no longer has to be a death sentence! "FIP Warriors" has successfully treated in excess of a hundred thousand of cats worldwide with the virus inhibitor GS-441524 already.

### **FIP WARRIORS**

"FIP Warriors" is a *global support group* for cat owners and cat rescuers (including veterinarians) who (have) decided to start with the treatment of GS-441524 on a diagnosed cat with FIP. The support in this group is completely done by volunteers who have (had) a FIP cat themselves and who would like to give other FIP cats a chance to survive.

"FIP Warriors" has studied years of trustworthy researches, examining autopsies on deceased FIP cats, comparing and studying symptoms, blood results, ultrasounds, X-rays, abnormalities, etcetera. Because of all that, a lot of knowledge and expertise has been gathered and built up to recognize FIP (and which form of FIP) and also how to treat FIP in cats. Luckily, more and more veterinarians are aware of the treatment.

## **GS-441524**

“FIP Warriors” only works with GS brands that provide consistent quality medication. Samples of all brands are regularly tested and brands of insufficient or dubious quality (e.g. in terms of concentration, acidity and purity) are banned worldwide within the “FIP Warriors” network. This has happened with the brands **Aino** and **SAK** for example.

A good number of good brands are almost always immediately available worldwide, including a ‘house brand’ but also various brands and variants with an adjusted acidity that are milder when injected due to a higher PH.

Unfortunately, Gilead Sciences, the patent holder of GS-441542, has not released the medicine GS-441542 for veterinary use yet. Therefore, the treatment can't be prescribed by veterinarians. Owners/rescuers of FIP cats are free to treat their cat with GS-441524. With the exception of UK and Australia where BOVA supplies Remdesivir and GS tablets (at a high price)

This is best done with a support group that has proved to be successful. With a high percentage of FIP survivors “FIP Warriors” is proud to be a successful support group that can offer the owner/rescuer a complete personalized guidance and reliable medication throughout the entire period of treatment, including the observation period and a possible relapse.

Some of these brands also offer a guarantee scheme, provided that treatment instructions are strictly followed and regular blood tests are done on time to monitor the cat's progress.

Some offer a 50% discount on the price of the medication if the treatment is needed for more than 12 weeks, or in the case of a relapse within 12 weeks after the end of treatment (i.e. during the observation period), some even 100% but usually at a higher price level.

Although it is always recommended to at least start with 2 to 4 weeks on injections to get the cat stable as soon as possible, oral medication is also available this is at double the mg of the injectables due to the bioavailability.

Fortunately, we see more and more veterinarians who bring this treatment to the attention of their clients and offer the legally permitted possible support themselves from the sidelines. For these veterinarians, and especially for those who are not yet familiar with this way of treating FIP, we have listed a number of practical matters.

### **LINKS TO “FIP WARRIORS”**

Due to the International character of the organization, "FIP Warriors" mainly uses Facebook for communication and information provision:

“FIP Warriors 5.0” group for owners with FIP cats:

<https://www.facebook.com/groups/804374446995270>

### **OTHER INFORMATIVE LINKS**

<https://pubmed.ncbi.nlm.nih.gov/30755068/> Efficacy and safety of the nucleoside analog GS-441524 for treatment of cats with naturally occurring feline infectious peritonitis (Niels C Pedersen et al)

<https://pubmed.ncbi.nlm.nih.gov/32441826/> Antiviral treatment using the adenosine nucleoside analogue GS-441524 in cats with clinically diagnosed neurological feline infectious peritonitis (Peter J Dickinson et al)

<https://sockfip.org/> (including overview of FIP research)

<https://icatcare.org/advice/feline-infectious-peritonitis-fip/>

<https://sockfip.org/is-there-a-definitive-test-for-fip/>

<https://www.dvm360.com/view/feline-infectious-peritonitis-strategies-diagnosing-and-treating-deadly-disease-young-cats/>

## **WHAT IS FIP**

FIP (Feline Infectious Peritonitis) is a mutation of FeCV (Feline Enteric Coronavirus) that allows the virus to move in other tissues instead of just staying in the intestines via macrophages.

FIPV strains from FCoV (Feline Corona Virus) differ from FeCV in that they no longer multiply well in the intestines, but preferably infiltrate in the macrophages; the important cells of the immune system. The virus then spreads itself throughout the body, when the spreading is not stopped by a good immune system, a cat will develop clinical signs of FIP.

If the virus affects the blood vessels in the abdomen, they will leak and the cat will develop wet FIP, this can also happen around the lungs (pleural FIP) or cause an edema in the brain.

If the virus is (partially) controlled by the cat's immune system, it can enter the blood vessels of other tissues, such as lymph nodes, liver, kidneys, lungs, skin, eyes and/or brain and cause inflammation there. The cat then gets dry FIP and possibly also Ocular and/or Neurological FIP. Dry FIP can switch to wet FIP and vice versa. Combinations of different types are frequent we will then name the disease according to the worst case that needs the highest dose.

Research in the US shows that 0,3-1% of cats die due to the effects of FIP. This percentage can be much higher in catteries, shelters and other places where more than 5 cats are kept.

FIP itself, as far as research shows, is not contagious and therefore mutates every time in a new host (cat). Unlike FeCV, the mutated form is usually not found in feces in large enough amounts and is therefore not contagious from cat to cat.

Cats are most sensitive until the age of 2 years and at old ages. In healthy adult cats it is less common, but still possible. Stress, physical and mental condition (illness, surgery, relocation, adoption, etc.), can be a trigger for not being able to control the virus, especially just after infection. Vaccinations in FeCV infected cats, for example FeLV vaccination and Rabies vaccination can also be a trigger.

Certain purebred cats may have a higher risk due to genetics, for example British cats, Scottish Folds, Maine Coons, Sacred Birmans, Devon and Cornish Rexes, Sphinxes and Oriental Shorthairs because these breeds are terribly overbred. This seems to be more common in certain gene lines than in the breed itself, unless the breed has already been bred extensively and all lines already have the mutations. More research needs to be done on this.

Breeders are advised to sterilize cats where FIP has been detected in the gene line and no longer breed with that gene line, in the hope of breeding more cats with a natural resistance to FCoV in order to reduce the genetic factor in the future.

### **DIAGNOSIS FIP**

<https://www.merckvetmanual.com/generalized-conditions/feline-infectious-peritonitis/overview-of-feline-infectious-peritonitis/>

Diagnosis can be difficult because there are no definitive tests yet. An immuno-histochemistry on infected tissue is possible, but sometimes this cannot be done pre-mortem because the cat is already very weak. Thus, it is often a diagnosis of exclusion, especially with the dry form.

When it comes to wet FIP, the fluid that is present in the abdominal cavity and/or chest cavity can be checked for FCoV. If there are no leaks in the intestines, there should normally be no FCoV in the fluid. For neuro FIP a CFS can be checked by a specialist although this has more risks for complications like paralysis.

A Rivalta test is a simple in-house test that you can run on fluid from the chest or abdominal cavity to help diagnose FIP as the cause of the effusion. However, it is not specific enough since each protein-rich liquid is likely to produce a positive result. If negative FIP is less likely also is the test more accurate on young cats where lymphoma is a lot less likely. False negatives are possible so it is not sufficient as the only test to rule out FIP.

Mix a drop 98% acetic acid of 5ml distilled water in a test tube. Put a drop of the effusion on top of this solution and observe its movement. If the effusion disappears, it is transudate and there is no question of FIP. If the effusion is still clearly visible, it is an exudate, but it is not diagnostic of FIP.

PCR test: Positive results are almost 100% certain, but keep in mind that a negative PCR result only gives 70% certainty.

If all other indicators indicate FIP or no other diagnosis can be made, a diagnostic start of treatment with GS-441524 (preferred) is advised.

In most cases, the FIP patient improves within 12 to 72 hours after starting treatment with GS-441524.

## **FIP TYPES AND SYMPTOMS**

The symptoms are difficult to diagnosis because they can also appear in other diseases.

<b>Type FIP</b>	<b>Symptoms</b>
General	<ul style="list-style-type: none"> <li>✓ Lethargy</li> <li>✓ Fever</li> <li>✓ Reduced appetite</li> </ul>
Wet FIP	<ul style="list-style-type: none"> <li>✓ Fluid in abdominal or chest cavity (bright yellow, protein rich fluid that is thread pulling) *only when the cat is terribly uncomfortable, remove up to 30% of fluid to ease breathing.</li> </ul>
Pleural FIP	<ul style="list-style-type: none"> <li>✓ Fluid round the lungs * remove up to 30% of fluid to ease breathing.</li> <li>✓ Fluid in the lungs * remove completely ASAP!!</li> </ul>
Dry FIP	<ul style="list-style-type: none"> <li>✓ Mainly chronic inflammations of blood vessels in several organs ('pyogranulomatous' inflammation)</li> <li>✓ Lymph nodes swollen</li> <li>✓ Damage to the liver, kidneys, lungs or skin. (depending on the mutation, everything may be normal or only some are infected)</li> <li>✓ Granulomas</li> </ul>
Ocular FIP	<ul style="list-style-type: none"> <li>✓ Visible damage to eye, bleeding or scar tissue on eye</li> <li>✓ Uveitis may appear as turbidity in the eye (eyes) with keratin precipitates</li> </ul>
Neuro FIP	<ul style="list-style-type: none"> <li>✓ Spasms/tremors</li> <li>✓ Muscle weakness</li> <li>✓ Wobbly walking (from uncontrollably -ataxia- to paralysis)</li> <li>✓ Fluid in brain *Immediately apply an IV to drift the fluid and reduce the pressure on the brains.</li> <li>✓ Acute Cerebral Edema *IV with Mannitol + Furosemide or Hypertonic Saline at 7,5%. Also administer Cortisone. And in any case (if available) also administer 15mg/kg GS ASAP (preferably before admission) every 12 hours, until the cat is stable. Regular medication can be given at a standard dosage.</li> <li>✓ Epilepsy *Phenobarbital or Levetiracetam + optionally prednisone 1mg/kg. DURING an attack Valium is often inserted rectally</li> </ul>

## **POSSIBLE INDICATIONS IN BLOOD TESTS**

- Lymphopenia (low number of lymphocytes, a type of white blood cells)
- Neutrophilia (increased number of neutrophils, a type of white blood cells)
- Anemia (in severe cases Erythropoietin (Epogen®, Procrit®) or Darbepoetin can be prescribed, blood transfusion is possible and sometimes needed but invasive and general heavy for cats if one already has the right blood-type.
- Increased globulin concentrations (one of the most important groups of proteins in the blood), alb/glob ratio <0.8 FIP possible, >0.8 FIP less likely. Gamma-glob high, ALB often low/low normal.
- Increased liver enzymes (e.g. ALT, ALP)
- Increased bilirubin (and jaundice or yellowing of the gums and eyes)

### **❖ FIP Medications/Antivirals:**

At this moment there are only 4 ways to cure FIP:

GS- 441524	Metabolite of Remdesivir.
GS-5734 / Remdesivir	In Australia on this moment in research good Results through IV, possible kidney failure as a side effect and also some liver issues, hence GS-441524 has the preference.
GC-376	Needs a much higher dose and seems to have reduced access through eye/blood and brain/blood barriers.

EIDD2801 and EIDD 1931 (Molnupiravir and metabolite can be used but is more toxic and should ONLY be used in case of resistance. Possible mutagenic although no cases have been seen yet and it will suppress the bone marrow causing low white cell counts. This HAS been observed especially on higher doses or longer treatments. Most common signs are floppy ears and hair loss around the mouth.



All virus inhibitors work by reducing the viral load by blocking the reproduction of the virus if it uses the antiviral as a building block so that the cat can remove the virus itself through its own immune system.

The therapy can, for GS-441524, be done by Injections, capsules, or pills.

In a weakened cat the oral uptake can be problematic so it is advised to use injections for the first 2 to 4 weeks till the cat is stable enough to absorb the oral medication.

Oral medication must contain about 2x the dose in mg as only a 40-60% bioavailability has been observed.

Despite the fact that a very low dose was used in the initial study (initially 2mg/kg and later 4mg/kg for wet FIP), over the years we have now set the dosages per type of FIP at much higher doses to prevent relapse and death.

As far as is known from the over hundred thousand cases, there are no mentionable additional side effects at higher doses. Doses of up to 40 mg/kg have been given without any problems.

❖ **Dosage per type of FIP:**

<b>TYPE FIP</b>	<b>DOSAGE (per 24 hrs)</b>	<b>Treatment at least 84 days of daily medication. Then, if free of FIP symptoms and with good blood counts, 84 days of observation for relapses.</b>
Wet FIP (preferably a short duration of infection)	6 mg/kg, if not eating well or little or no activity 8 mg/kg	
Pleural FIP	8 mg/kg, if not eating well or little or no activity 10 mg/kg	Pleural FIP is more problematic due to respiratory problems therefore a higher dose is advised than with normal wet FIP.
Dry FIP (without neurological or eye problems)	6 mg/kg, if not eating well or little or no activity 8 mg/kg	Assuming there are no neurological or ocular issues.
Ocular FIP	Minimum 10 mg/kg to cross the blood-eye barrier	Only ocular, in initial stage and without neuro.
Neuro FIP	12 mg/kg to cross the blood-brain barrier	In case of very critical cases a higher dosage or 2 x daily. In acute cerebral edema: after initial dose of 15mg/kg 10mg/kg every 12 hours till the cat is stable (generally a couple of weeks) [supplemented with IV of Mannitol + furosemide or Hypertonic saline at 7.5% or 9%. In addition, administer cortisone 1-2mg/kg (See neuro document point 6)

## Other points of attention:

- Adjust the dose to weight at LEAST once per week, with kittens or cats that lost a lot of weight preferably more or daily to avoid underdosing.
- In severe neuro FIP or with cats that stopped eating one can support the cat with a low oral dose of prednisone (max 1-2 mg/kg) and Cerenia/Maropitant. or Mirtazapine. Mirtazapine is given at a dose of 0.44 mg/kg. If the dose is higher (Pills of 15mg can be hard to cut in small enough pieces) a dose upto 3x this can be given every 72hrs. Mirataz a cream for the ears can also be used but can be irritating for the cat.
- Please be VERY careful to not overdose with Mirtazapine.
- Metacam can be given in case of discomfort or low fever, but not in combination of prednisolone/cortisones!
- **Acute cerebral edema:** Some cats can get an acute cerebral edema due to FIP. The cat must then be rushed to the vet / emergency clinic for the head trauma protocol
  - An immediate dose of 15mg/kg of GS-441524 followed by 10mg/kg every 12 hrs until the cat is stable (usually a few weeks)
  - IV of furosemide followed by a bolus of mannitol or Hypertonic saline of 7.5% - 9%.
  - In addition administer 1-2mg/kg prednisolone. Potassium supplement if necessary since this can be lowered due to the furosumide.
  - READ NEURO DOCUMENT!

### ❖ **KNOWN PERSON SIDE EFFECTS:**

- Possible diarrhea. This is generally in the initial stages and generally does not last long, most likely with oral medication. Probiotics advised if it lasts more than 1-3 days.
- Itching: Rare but possible is that the cat gets an itch, generally is this not serious but can be annoying. Prednisone at 0.5mg/kg can sometimes provide some relief, or ribes nigrum solution (1 pipette) or an antihistamine.
- Inflammation at injection sites. This is a more common 'side effect' due to the acidity of the GS-441524 solution. The sores usually do not require any additional treatment other than avoiding that area for injections till healed eventually one can add a crème to sooth the area a honey based cream (eg Vetramil) is often used.

❖ **Additional info:**

Kidney support:

Virbac Pronefra

Semintra

Liver support:

Zentoni/denamarin , SamE or Samylin

probio

saccharomyces boulardii

Mefloquine:

NOT a cure but it can help in severe cases to reduce the effects of the virus dose is 10-12mg/kg every 3 days

Fever:

Metacam (upto 40C)

Tolfedine 2mg/kg ONLY OVER 40-40.5C ! can be repeated if still over 40C after 12hrs

Filgrastrim

In case of VERY low white cell counts:

Granulocytes Colony stimulating factor

6mcg/kg 0.1ml/kg of the 5ml solution (0,5 + 4,5 glucose)

To dissolve in glucose 5%

you can dilute 0,5ml filgrastim in 4.5ml glucose

❖ **Last but not least , some of the sources of inspiration for doing this volunteer work:**

The FIP Warrior survivors (own cats and rescued cats) of FIP Warriors® Netherlands- Belgium:

