Tuberculin syringes can also be used, but are not generally recommended because the potential for confusion is substantial. If using 100U/mL or TB syringes to measure 40U/mL insulin doses:

- Determine the required dose in units.
- If using U-100 insulin syringes (orange top), multiply the required Units of U-40 insulin by 2.5 (*e.g.* If required dose is 10 units, 10 x 2.5=25 units).
- If using TB syringes, multiply the required Units of U-40 insulin x 0.025 (*e.g.*, If the required dose is 10 Units, 10 x 0.025= 0.25 mL).

Reuse of Insulin Syringes: Reuse of disposable insulin syringes has been suggested to reduce client costs. However, disposable insulin syringes are usually siliconized, and reuse can result in contamination of vials of insulin with silicone oil, causing a white precipitate and impairment of biological effects.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS:

Porcine insulin zinc suspension 40 U/mL in 10 mL vials, intermediate-acting; *Vetsulin®* (Intervet) in U.S.; *Caninsulin®* (Intervet) in Canada & Europe; (Rx). FDA approved for use in dogs.

Protamine zinc insulin (beef 90%/pork 10%) 40 U/mL in 10 mL vials; long-acting; *PZI VET®* (IDEXX); (Rx). Not fully FDA approved, but distribution is allowed under the Medically Necessary Veterinary Products Policy for use in cats.

HUMAN-LABELED PRODUCTS:

Note: partial listing; includes only those products generally used in veterinary medicine.

Insulin Injection, ***Regular*** *— (short-acting):*

Human (rDNA): 100 U/mL in 10 mL vials; *Humulin® R* (Eli Lilly); *Novolin®R & Novolin R® Prefilled* (Novo Nordisk); (OTC)

Isophane (Neutral Protamine Hagedorn; ***NPH****) — (intermediate-acting):*

Human (rDNA) 100 U/mL in 10 mL vials, 5 x 1.5 mL prefilled syringes & 5 x 3 mL pen insulin delivery devices; *Humulin®N* (Lilly); *Novolin®N & Prefilled* (Novo Nordisk); (OTC)

Human (rDNA) Cartridges (suspension) 100 U/mL in 5 x1.5 mL & 5 x 3 mL; *Novolin N® PenFill* (Novo Nordisk); (OTC)

Combination: Insulin Isophane & Regular Injection (suspension):

Human (rDNA) 100 U/mL 70% isophane insulin (NPH) & 30 % insulin injection (regular) in 5 x 3 mL disposable pen insulin delivery devices, 10 mL vials & 5 x 1.5 mL prefilled syringes; *Humulin® 70/30* (Lilly); *Novolin® 70/30 & Prefilled* (Novo Nordisk); (OTC)

Human (rDNA) Cartridges (suspension): 100 U/mL; 70% isophane insulin (NPH) & 30% insulin injection (regular) in 5 x 1.5 & 5 x 3 mL; *Novolin® 70/30 PenFill* (Novo Nordisk); (OTC)

Human (rDNA) Injection (suspension): 100 U/mL; 50% isophane insulin (NPH) & 50% insulin injection (regular) in 10 mL vials; *Humulin® 50/50* (Lilly); (OTC)

Insulin Glargine Injection—(long-acting):

Human (rDNA) 100 U/mL in 10 mL vials & 3 mL cartridge system for use with *OptiClik*; *Lantus®* (Aventis); (Rx)

INTERFERON ALFA, HUMAN RECOMBINANT

(in-ter-***feer***-on) Roferon-A®, Intron-A®

IMMUNOMODULATOR

Prescriber Highlights

- Cytokine used to alleviate clinical effects of certain viral diseases; little scientific info available to document safety/efficacy in small animals
- Cautions: Preexisting autoimmune disease, severe cardiac disease, pulmonary disease, "brittle" diabetes, Herpes infections, hypersensitivity to the drug, or CNS disorders
- Adverse Effects: In cats, adverse effects are apparently uncommon with PO; higher dosages given parenterally may cause malaise; fever, allergic reactions, myelotoxicity & myalgia are possible

Uses/Indications

Interferon alfa use in veterinary medicine in the past has primarily been centered on its oral/buccal administration in cats to treat non-neoplastic FeLV disease. Oral interferon may also be of benefit in the treatment of ocular herpes infection.

Feline interferon-omega has recently become available in several countries and it may be found significantly useful in treating viral diseases in both cats and dogs. A separate monograph for this agent, follows this one.

Pharmacology/Actions

The pharmacologic effects of the interferons are widespread and complex. Suffice it to say, that interferon alfa has antiviral, antiproliferative, and immunomodulating effects. Its antiproliferative and antiviral activities are thought to be due to its effects on the synthesis of RNA, DNA, and cellular proteins (oncogenes included). The mechanisms for its antineoplastic activities are not well understood, but are probably related these effects as well.

Pharmacokinetics

Interferon alfa is poorly absorbed after oral administration due to its degradation by proteolytic enzymes and studies have not detected measurable levels in the systemic circulation, however, there may be some absorption via upper GI mucosa.

Interferon alfa is widely distributed throughout the body, although it does not penetrate into the CNS well. It is unknown if it crosses the placenta. Interferon alfa is freely filtered by the glomeruli, but is absorbed by the renal tubules where it is metabolized by brush border or lysosomes. Hepatic metabolism is of minor importance. The plasma half-life in cats has been reported as 2.9 hours.

Contraindications/Precautions/Warnings

When used parenterally, consider the risks versus benefits in patients with preexisting autoimmune disease, severe cardiac disease, pulmonary disease, "brittle" diabetes, Herpes infections, hypersensitivity to the drug, or CNS disorders.

Adverse Effects

When used orally in cats, adverse effects are apparently uncommon. Higher dosages given parenterally to cats may cause malaise; fever, allergic reactions, myelotoxicity, and myalgia are possible. Cats given human interferon-alfa parenterally may develop significant antibodies to it after 7–8 weeks of treatment. When used systemi-

cally in humans, adverse effects have included anemia, leukopenias, thrombocytopenia, hepatotoxicity, neurotoxicity, taste sensation changes, anorexia, nausea, vomiting, diarrhea, dizziness, "flu-like" syndrome, transient hypotension, skin rashes, and dry mouth. Except for the "flu-like "syndrome, most adverse effects are dose-related and may vary depending on the condition treated.

Reproductive/Nursing Safety

Safety during pregnancy has not been established; high parenteral doses in monkeys did not cause teratogenic effects, but did increase abortifacient activity. In humans, the FDA categorizes this drug as category ***C*** for use during pregnancy (*Animal studies have shown an adverse effect on the fetus, but there are no adequate studies in humans; or there are no animal reproduction studies and no adequate studies in humans.*)

It is not known whether this drug is excreted in milk.

Overdosage/Acute Toxicity

No information was located. Determine dosages carefully.

Drug Interactions

The following drug interactions have either been reported or are theoretical in humans or animals receiving interferon and may be of significance in veterinary patients:

- **ACYCLOVIR, ZIDOVUDINE, VIDARABINE:** Additive or synergistic antiviral effects may occur when interferon alfa is used in conjunction with zidovudine (AZT) or acyclovir. This effect does not appear to occur with vidarabine, although increased toxicities may occur. The veterinary significance of these potential interactions is unclear.

Doses

- **DOGS:**

For cutaneus T-cell lymphoma and severe cases of oral/cutaneus papillomas:

a) 1.5–2 million units/m2 SC 3 times weekly (White 2000)

For immunosuppression:

a) 1 Unit/5 kg PO once daily for 7 days. Treat alternate weeks or continuously. (Greene and Watson 1998)

- **CATS:**

For indolent lip ulcers:

a) 60–120 Units PO or SC daily (White 2000)

For treatment of FeLV-infected cats:

a) Low dose: 30 U cat PO daily; 7 days on, 7 days off); Hi dose: 10,000–1,000,000 U/kg SC once daily. Little in the way of large, controlled trials to determine which, if any, immunomodulating therapies (interferon or other agents) are likely to benefit FeLV-infected cats. (Levy 2004)

For treatment of FIV-infected cats:

a) 30 U cat PO daily; 7 days on, 7 days off (Barr and Phillips 2000)

For adjunctive treatment of FHV-1-infected cats:

a) For chronic infections: 30 U cat PO daily; 7 days on, 7 days off; repeat cycle. May also use topical ophthalmic therapy: one drop of 25–50 IU/mL of saline in affected eye(s) q4–6 hours. (Powell 2002)

b) For acute life-threatening infections in kittens: 10,000 IU/kg SC daily for up to 3 weeks (Lappin 2003b)

For treatment of FIP-infected cats:

a) For exudative form (wet): 20,000 U/cat IM once daily for 14–21 days. For nonexudative form (dry): 30 U/cat PO once daily for 7 days. Treat alternate weeks. (Greene and Watson 1998)

To prepare a *3 U/mL solution for oral administration*: Using the 3 million IU vial (see below), dilute the entire contents into 100 mL of sterile water; mix well. Resulting solution contains approximately 30,000 IU/mL. Take 0.1 mL of this solution and add to one liter of sterile saline that has 4 mL of 25% albumin added to it. Albumin is optional but adds stability. Solution is now 3 U/mL. Divide into aliquots of 15 mL and freeze, preferably at –70°C. Thaw as needed and keep refrigerated. Discard unused portion after 60 days. Discard unused 30,000 U/mL solution within 2–3 hours of making initial dilutions.

Preparation of solution for *30 U/mL oral administration*: Using the 3 million IU vial (see below), dilute the entire contents into a 1 L bag of sterile normal saline; mix well. Resulting solution contains approximately 3,000 IU/mL. Divide into aliquots of either 1 or 10 mL and freeze. By diluting further 100 fold (1 mL of 3000 IU/mL solution with 100 mL of sterile saline, or 10 mL with 1000 mL of sterile saline) a 30 IU/mL solution will result. Some have advised aliquoting the diluted solution into 1 mL volumes for freezing up to a year; defrost as necessary. Once defrosted, the drug can be refrigerated up to one week. Freezing the most dilute solutions is associated with loss in activity unless protein such as albumin (see above) is added during dilution. (Greene, Hartmannn et al. 2006)

Client Information

- Owners should be made aware of the "investigational" nature of this compound and understand that efficacy and safety have not necessarily been established.

Chemistry/Synonyms

Prepared from genetically engineered cultures of E. coli with genes from human leukocytes, interferon alfa-2a is commercially available as a sterile solution or sterile powder. Human interferon alfa is a complex protein that contains 165 or 166 amino acids.

Interferon may also be known as: IFN-alpha, interferon-alpha, Ro-22-8181 (interferon alfa-2a), Sch-30500 (interferon alfa-2b); there are many internationally registered trade names available.

Storage/Stability/Compatibility

Commercially available products should be stored in the refrigerator; do not freeze the accompanying diluent. Do not expose solutions to room temperature for longer than 24 hours. Do not vigorously shake solutions.

An article proposing using this product in cats for the treatment of FeLV states that after dilution of 3 million IU in one liter of sterile saline the resultant solution remains active for years if frozen or for months if refrigerated. However, data corroborating this is apparently not available.

Dosage Forms/Regulatory Status

VETERINARY-LABELED PRODUCTS: None

HUMAN-LABELED PRODUCTS:

Interferon Alfa-2a (recombinant rIFN-A; IFLrA) Injection: Prefilled syringes: 3 million I.U./syringe (0.5 mL single-use syringes); 6 million I.U./syringe (0.5 mL single-use syringes); 9 million I.U./syringe (0.5 mL single-use syringes); *Roferon-A*® (Hoffman La-Roche); (Rx)

Interferon Alfa-2b (recombinant (IFN-alpha2; rIFN-a2; a-2-interferon) Powder for Injection: 5 million IU/vial; 10 million IU/vial; 18 million IU/vial; 25 million IU/vial & 50 million IU/vial in vials with a mL, 2 mL or 5 mL diluent/vial; *Intron A*® (Schering); (Rx)

Interferon Alfa-2b (recombinant (IFN-alpha2; rIFN-a2; a-2-interferon) Injection: 3 million IU/dose; 5 million IU/dose, & 10 million IU/dose in multidose pens; *Intron A*® (Schering); (Rx)

Interferon Alfa-2b (recombinant (IFN-alpha2; rIFN-a2; a-2-interferon) Solution for Injection: 3 million IU/vial, 5 million IU/vial; 10 million IU/vial; 18 million IU/vial & 25 million IU/vial in vials, Pak-3, -5, -10 (vials & syringes); & in multidose vials (22.8 million IU/3.8 mL/vial or 32 million IU/3.2 mL/vial); *Intron A*® (Schering); (Rx)

Interferon Alfa-N3 (human leukocyte derived) Injection: 5 million IU/mL (8 mg NaCl, 1.74 mg Na phosphate dibasic, 0.2 mg K phosphate monobasic, 0.2 mg KCl) in 1 mL vials; *Alferon N* ® (Interferon Sciences Inc.); (Rx)

INTERFERON-Ω (OMEGA)

(in-ter-*feer*-on oh-*may*-ga) Virbagen Omega®, Recombinant Omega Interferon of Feline Origin, rFelFN-ωOmega

IMMUNOMODULATOR

Prescriber Highlights

- Immunomodulating cytokine labeled for treating FeLV & FIV in cats & Parvo in dogs; not commercially available in USA
- Appears to be well tolerated; adverse effects include: hyperthermia, vomiting, diarrhea (cats), fatigue (cats)
- Increases in ALT & decreases in RBC, WBC, & platelet counts have been seen
- Treatment may be very expensive

Uses/Indications

Omega interferon (feline) is labeled (in the EU) for dogs 1 month of age or older for the reduction in mortality and clinical signs of parvovirus (enteric form). In cats 9 weeks of age or older, it is labeled for treating FeLV and/or FIV, in non-terminal clinical stages. It may be of benefit in treating canine distemper, acute feline calicivirus infections, FIP, or topically for feline herpetic keratitis, but data is still being gathered to document efficacy.

Pharmacology/Actions

Omega interferon is a type 1 interferon related to alpha interferon. Its principle action is not as a direct anti-viral, but by acting on virus-infected cells inhibiting mRNA and translation proteins thereby inhibiting viral replication. It may also nonspecifically enhance immune defense mechanisms.

Pharmacokinetics

It has been stated that omega interferon pharmacokinetics in dogs and cats is similar to that of human interferons. After intravenous injection, omega interferon is rapidly bound to specific receptor sites on a variety of cells. Highest tissue levels are found in the liver and kidneys. Interferon is filtered in the renal glomeruli and catabolized in the kidneys. In dogs, volume of distribution at steady state is about 0.1L/kg. Biphasic elimination occurs with an alpha half-life of 3.14 hours and a beta half-life of 0.24 hours. Total body clearance is 6.9 mL/min/kg.

Contraindications/Precautions/Warnings

The manufacturer cautions against vaccinating dogs currently being treated with omega interferon and not to vaccinate until the patient appears to have recovered. As both FeLV and FIV infections are known to be immunosuppressive, the manufacturer states that cat vaccinations are contraindicated during and after omega interferon treatment.

There are several different interferons available for use in humans (several sub-types of alpha, beta, or gamma interferon); one cannot be substituted for another.

Adverse Effects

In cats and dogs, hyperthermia (3–6 hours post-dose) and vomiting have been reported. Slight decreases in RBCs, platelets and WBCs, and increased ALT have been observed but, reportedly, these indices return to normal within a week of the last injection.

Additionally, soft feces/mild diarrhea and transient fatigue may be noted in cats. Intravenous administration to cats may cause increased incidence and severity of adverse effects.

Dogs may develop antibodies to interferon omega if treatment is prolonged (beyond labeled dosage period) or repeated.

Reproductive/Nursing Safety

Safety during pregnancy or lactation has not been established.

Overdosage/Acute Toxicity

10X overdoses in dogs and cats caused mild lethargy/somnolence, slight hyperthermia, slight increases in respiratory and heart rates. In animals tested, signs resolved within 7 days and no treatment was required.

Drug Interactions

No reported drug interactions at the time of writing, but use caution when using other drugs that can be hepatotoxic or myelosuppressive.

Laboratory Considerations

No specific concerns were noted

Doses

- **DOGS:**
  a) For treatment of parvovirus as labeled: 2.5 million Units/kg IV once daily for 3 days. The earlier the dog is treated, the more likely of success. (Label information; *Virbagen Omega*®—Virbac UK)
- **CATS:**
  a) For treatment of FeLV or FV as labeled: 1 million Units/kg SC once daily for 5 days. Three separate 5-day treatments performed at day 0, day 14, and day 60. (Label information; *Virbagen Omega*®—Virbac UK)

Monitoring

- Monitor for efficacy for infection treated
- CBC and hepatic function tests suggested

Client Information

- This drug is best administered on an inpatient basis where the patient may be observed and supported

Chemistry/Synonyms

Interferon omega of feline origin is a type 1 recombinant interferon obtained from silkworms after inoculation with a recombinant baculovirus. It is provided commercially as a lyophilisate powder with a separate solvent.

Recombinant omega interferon of feline origin may also be known as: Interferon omega, omega interferon, interferon-ω, IFN-ω, IFN-ω (feline recombinant), rFelFN-ω, and *Virbagen Omega*®.